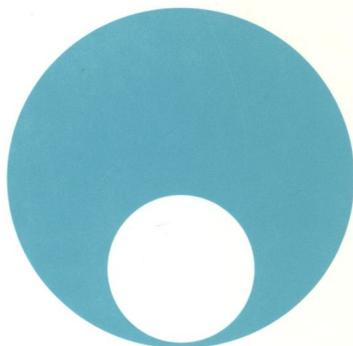


# PRIMATE REPORT

66

Aug. 2003



**Annual Report 2001/2002 of the  
German Primate Center (DPZ)**

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German Primate Center (DPZ)

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# The German Primate Center (DPZ)

## Annual Report 2001/2002

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## **The German Primate Center (DPZ) in 2001/2002**

This biennial DPZ report provides an overview of the results achieved in 2001 and 2002 and of the developments which took place during this period.

The aims of the DPZ are centred around rendering research on and with primates possible and carrying out such research ourselves. Primate research is costly and long term and necessitates an appropriate technical and personnel infrastructure. This led, in 1977, to the foundation of the DPZ, an event which was remembered in the summer of 2002 by a week of celebration with many different activities organised for the general public, a ceremony with prominent guests and a series of celebratory seminars. A detailed account of the celebrations is given in a separate article. In the opening words of the invited speaker of the ceremony, not only was the turbulent history a theme but also the particular role to be played and the duty to be fulfilled by the DPZ in the research scene.

This report clearly shows that in 2001 and 2002, the DPZ not only fulfilled its duties but also developed further in a very dynamic fashion. In the following section, some of the most important events and developments are described.

At the end of February 2001, Professor Hunsmann's term of office as scientific manager of the DPZ came to an end. He remains at the DPZ, however, as Head of the Department of Virology and Immunology. Following a transitional period under the temporary leadership of Professor Kaup, Professor Treue took up the office of scientific manager on 01.06.02 and also became head of the newly created Department Cognitive Neuroscience Laboratory.

In December 2001, the Göttingen Field Days which takes place every 2 years was organised for the third time. Arranged by Dr. Kappeler and the Department of Ethology and Ecology almost 200 participants from 18 countries met to discuss the newest research results on causes, consequences and mechanisms of sexual selection in primates.

Also in December 2001, the DPZ together with the Institute for Zoological and Wild Animal Research Berlin organised the theme of the day "Tree of Life" within the framework of the series, "Life is Variety", at the Senckenberg Museum in Frankfurt. In an exhibition and in several lectures, the development of mammals, particularly of the primates, of the ape and of the human being was explained. Together with exhibits from the museum, graphic and three-dimensional reconstructions helped to explain the evolution of prehistoric and early human beings, the developmental history of the Neanderthal man up to the present day human being. These were accompanied by lectures on evolution and biodiversity. These events, the Field Days and further smaller symposia and seminars organised by the departments help on a major scale to make the work of the DPZ known to the scientific world and also to a broader public.

An important role in the further structural development of the DPZ was played by the new C4 professorship in anthropology/sociobiology at the beginning of 2002. This position financed by the university and conceived as a bridging chair between the DPZ and the university will provide the head of the corresponding departments at the DPZ and the university. This combination of the resources of the university and the DPZ is almost unique in Germany. The development of this innovative concept together with the university in Göttingen will not only considerably strengthen the Department of Ethology and Ecology and ensure international competitiveness but will also raise cooperation with the university to a new level. This development, therefore, represents an important contribution to the efforts to strengthen the links between the DPZ and the research centres in Göttingen and to increase the scientific effectiveness of the DPZ in times of a general shortage in public funding.

In order to check on the effectiveness of the DPZ and to provide the management with information on the further structural developments, the departments regularly undergo evaluations conducted by the Advisory Council with the help of external experts. In 2001, the Working Group Primate Genetics was evaluated. It was set up in 1997 with the appointment of Dr. Zischler as its head for a duration of five years. The evaluation was meant to provide the Advisory Council and the management with a basis for a decision on the future of the working group. Professor Boesch from Max-Planck-Institute for Evolutionary Anthropology and Professor Brosius from University of Münster were the external experts. The experts came to the conclusion that the scientific activities of this working group were of a generally high standard in the field of molecular phylogenetics of mammals and it could even be counted as one of the leading groups on an international scale. They particularly noted the great importance of the internal cooperation with the Departments of Ethology and Ecology and came to the conclusion that the working group plays a central role in the many research projects at the DPZ and contributes to the maintenance and improvement of the international competitiveness of the DPZ through increased implementation of molecular genetic methods. In 2002 the Department of Reproductive Biology was evaluated. The Advisory Council was supported by Professor Martin from the Field Museum, Chicago and Professor Ivell from the University of Hamburg as external experts. These experts found that, in this department, two more or less independent areas had developed, namely, the areas of evolutionary endocrinology and of reproductive medicine. They came to the encouraging conclusion that both areas are capable of international top performance. Particularly in the case of the evolutionary endocrinology, they considered all the criticisms of the past to have been cleared up and underlined the importance of this work also in cooperation with other departments of the DPZ.

These two positive evaluations were reflected by corresponding structural developments. Thus, following the evaluation, Primate Genetics will become a regular research field. However, this will not be able to take place under the leadership of Dr. Zischler, because he has been offered the chair of Anthropology in the Biological Faculty at the University of Mainz and has accepted the position. The position of head of the research group Primate Genetics has been advertised and the selection procedure is underway. The separation of a research group working on reproductive medi-

cine from the Department of Reproductive Biology under the leadership of Professor Einspanier as recommended by the evaluation could not be carried out because she was offered a C3 professorship at the University of Leipzig which she accepted.

These offers to the scientists of the DPZ of appointments to professorships reflect the quality of the research they carry out, but at the same time the acceptance of a professorship is a challenge to the structural and personnel flexibility of the DPZ. In all, in the years 2001 and 2002, six of our colleagues were offered professorships. In addition to the two already mentioned to Dr. Zischler and Prof. Espanier, Dr. Kappeler was offered a C3 professorship at Leipzig University which he accepted. Prof. Hunsmann was offered the chair of Virology in the Faculty of Medicine at the University in Göttingen which he accepted. Prof. Fuchs was offered the C3 professorship of Functional Neuroanatomy at Trier University and the C3 professorship of Neurobiology in the Faculty of Medicine at Göttingen University and accepted the latter position. The last two positions, i.e. the professorships for Prof. Hunsamnn and Prof. Fuchs at the University Clinic in Göttingen allow them to continue their work at the DPZ and, therefore, very positively strengthen the integration of the DPZ into the research world in Göttingen.

In addition to the many professorships, there was a further, special prize. At the annual meeting of the Leibniz Association in November 2002, Prof. Fuchs received a prize, awarded by the Association of German Science for the first time, following the recommendation of the WGL for "Society needs Science".

Along with all these positive developments, there was a challenge or two. For example, the basic conditions under which the DPZ runs its Field Station in Madagascar became more complicated in 2002. In addition to an increasing threat to the forest and, therefore, to the primate population around the station, there was increasing political unrest in connection with the elections to the office of president of Madagascar. Fortunately the political situation has calmed down in the meantime and the management of the DPZ is planning discussions with the Madagascan politicians, public authorities and environmental protectionists with the support of the German Foreign Ministry and the Ministry for Science, among others, in order to permanently reduce the danger to the ecological system around the Field Station and to guarantee the long term scientific value. More information can be found in the report from the Department of Behavioural Science/ Ecology.

The increasing lack of public money from state and federal government presents a serious challenge. It is, therefore, a particularly gratifying situation that the authorities which provide grants recognise the special role played by the DPZ and its special function in the German scientific world and that, therefore, in the years 2001 and 2002 the DPZ showed a positive economic development. As the following report shows in detail, the successful applications for national and international external funds also played a role. However, in the next few years it will be more important than ever to preserve, to further develop and to make plain the acknowledged high efficiency of the DPZ in research and service. Here, the structure reform realised at the end of 2002 and the beginning of 2003 will help, with which the DPZ clearly illus-

brates its areas of work and competence through the organization of its scientific departments and research groups into three sections and is also preparing for the change planned for the next few years to "programme budgets".

Professor Stefan Treue  
(Scientific Manager and Director)

## **Committees of the Company and Economic Development**

The The German Primate Centre (DPZ) is a Leibniz Institute, founded in 1977 as a private limited company, whose task is to carry out scientific and medical research on and with primates as well as to keep and breed primates to supply other research institutes.

The committees of company are the company general meeting, the supervisory board and the managing directors. The scientific and technical staff of the DPZ are involved in decisions through their delegates to the supervisory board. For scientific problems, the company is advised by a scientific advisory board composed of external members.

The DPZ is a member of the incorporated Scientific Society of Gottfried Wilhelm Leibnitz e. V. (WGL). The head of the administrative department Digital Information Processing and Communication of the DPZ is chairman of the Electronic Data Processing Committee set up by the WGL. The administrative manager is a member of the steering committee as speaker of the Administrative Committee.

## **Partners**

The partners of the DPZ are according to the contract the Federal Republic of Germany represented by the Ministry for Education and Research (BMBF) and the State of Lower Saxony represented by the Ministry for Finance. The two partners hold an stock capital of 25 TDM. (The change to Euros is planned for the next alteration in the contract). The grant requirements are covered by the National Government and the State (as far as it is represented by the Ministry for Science and Culture) in a 50:50 relationship according to the "General Agreement on the Advancement of Research" from Nov. 28<sup>th</sup> 1975 and the Implementation Agreement (Implementing Statutes) from June 26<sup>th</sup> 1978. The DPZ is an institute with a service function for research.

## **Supervisory Board**

The Supervisory Board supervises the legitimacy, expediency and profitability of the management. It makes decisions on the general research aims and on important research-political and economic matters of the company. Until the changes in the contract in the year 2001, the Supervisory Board was composed of nine members, who carried out their work on a honorary basis. From these members, four are nominated by the partners. Two members are elected from the circle of scientists and technicians of the DPZ who are recommended by the staff of the DPZ at the general meeting of the partners. These are joined by two further members from the areas of economy or science who are also nominated at the general meeting. Furthermore, the current president of Göttingen University is also a member of the Supervisory Board. With the change in the contract, the chairman and the vice-chairman of the scientific advisory board have also become members of the Supervisory Board. This

change took into account the recommendation of the German Scientific Council (Wissenschaftsrat) to integrate its work more strongly into the supervisory body.

On 31.10.02 a particularly drastic change in the personnel of the Supervisory Board took place in that the vice-chairman of many years standing, Counsellor Rainer Gross retired and, therefore, left the Board. In the future, the government director Dr. Gabriele Hausdorf will represent the government on the Supervisory Board.

The partner Lower Saxony has the right to the chair of the Supervisory Board, the national government provides the vice-chairman. The Supervisory Board met four times during the period of this report (16.05.01, 04.10.01, 22.05.02 and 22.10.02). The Supervisory Board was composed of the following members during the period of this report:

- Prof. Dr. Almuth Einspanier, Göttingen
- PD Dr. Gabriele Flügge, Göttingen
- Counsellor Rainer Gross, Bonn – vice-chairman – (until 31.10.02)
- Government director Dr. Gabriele Hausdorf – vice-chairman – (from 01.11.02)
- University President Prof. Dr. Horst Kern, Göttingen
- Counsellor Dr. Axel Kollatschny, Hannover – chairman –
- Government director Corrina Kuhny, Hannover
- Counsellor PD Dr. Peter Lange, Bonn
- Prof. Dr. Gerhard Neuweiler, München
- Prof. Dr. Heiner Niemann, Mariensee (from 17.05.02)
- Prof. Dr. Werner Rathmayer, Konstanz
- Prof. Dr. Walter Stühmer, Göttingen (from 24.07.01 to 16.05.02)
- Prof. Dr. Dr. Ulrich Welsch, München (from 24.07.01)

### **The Scientific Advisory Board**

The Scientific Advisory Board is composed of ten scientists who do not belong to the company. The Scientific Advisory Board advises the company in scientific and technical matters.

Due to the fact that the company contract provides that the members of the Board may only be elected for two terms of office, considerable changes took place during the period of this report.

The Scientific Advisory Board met four times during the period of this report (03.04.01, 09.10.01, 09.04.02 and 01.10.02). The Advisory Board was composed of the following members during 2001 and 2002:

- Prof. Dr. Boesch, MPI für Evolutionäre Anthropologie, Leipzig (from 01.01.02)
- Prof. Dr. Bernhard Fleischer, Bernhard-Nocht-Institut, Hamburg
- Prof. Dr. Jens Frahm, MPI für biophysikalische Chemie, Göttingen (from 21.05.02)

- Prof. Dr. J.A.R.A.M. van Hooff, Universität Utrecht, Niederlande (until 31.02.01)
- Prof. Dr. Hans Lehrach, MPI für molekulare Genetik, Berlin
- Prof. Dr. Hans Konrad Müller-Hermelink, Universität Würzburg (until 17.05.02)
- Prof. Dr. Nikolaus Müller-Lantzsch, Universität des Saarlandes (from 21.05.02)
- Prof. Dr. Heiner Niemann, Institut für Tierzucht und Tierverhalten, Mariensee – vice-chairman –
- Prof. Dr. Andreas Pospischil, Universität Zürich, Schweiz (from 18.05.02)
- Prof. Dr. Helga Rübsamen-Waigmann, Bayer AG, Wuppertal (until 31.12.01)
- Prof. Dr. Walter Stühmer, MPI für Experimentelle Medizin, Göttingen – vice-chairman – (until 17.05.02)
- Prof. Dr. Hans-Peter Thier, Universität Tübingen (from 01.03.01)
- Prof. Dr. Dr. Ulrich Welsch, Universität München – chairman –
- Prof. Dr. Elke Zimmermann, Tierärztliche Hochschule Hannover

## **Management**

The managing directors are the legal representatives of the company and conduct the affairs according to the provisions of the law, the company contract, the decisions of the Partners' assembly and the Supervisory Board. Together with the other committees, they develop the initiative necessary for the realisation of the aims of the company in planning, coordination and supervision and ensure the effective and economic application of the funds.

With the above-mentioned changes in the contract, the management structure of the DPZ was also moderately changed. In order for the priority of the scientific management to become clear to the outside world, the scientific manager now bears the title, "Director of the DPZ," and can carry, according to company law, sole responsibility.

Prof. Dr. med. Gerhard Hunsmann (until 28.02.01)  
(Scientific-Technical Manager)

Prof. Dr. Franz-Josef Kaup (01.03.to 31.05.01)  
(Acting Manager in the absence of the Scientific-Technical Manager)

Prof. Dr. Stefan Treue (from 01.06.01)  
(Scientific Manager and Director)

Assessor jur. Michael Lankeit  
(Administrative Manager)

## Economic Development

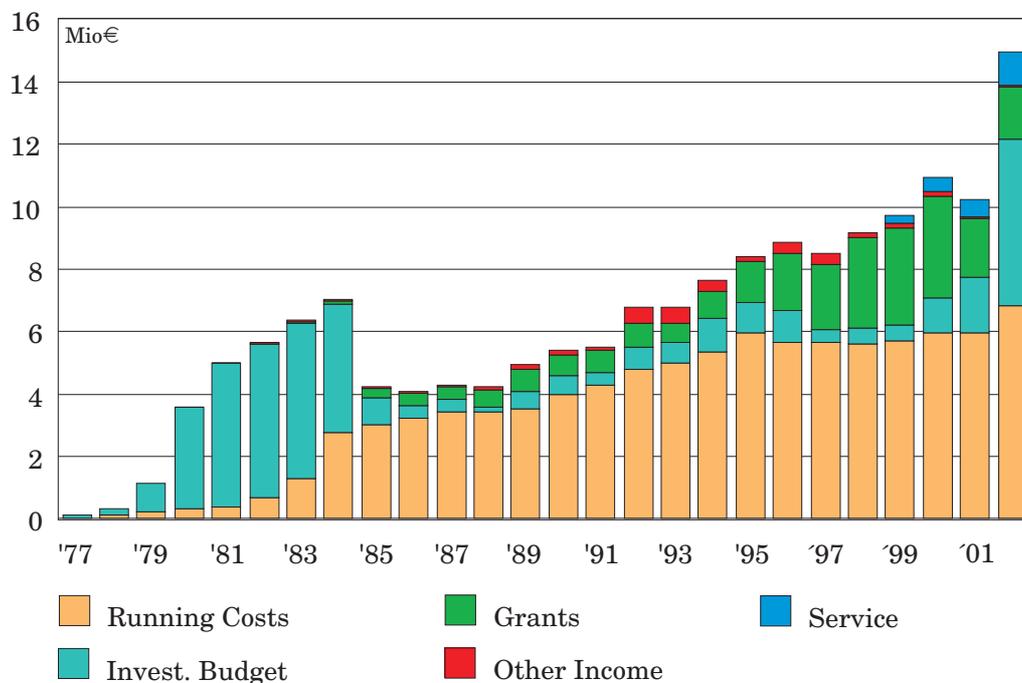
During the last two years, the economic development has fortunately continued the positive trend of the previous year. There was indeed some stagnation in 2001 but this was compensated for by the improved dynamics of 2002.

The overall budget 2001 had a volume of approximately 10.3 Mio€ which was 640 T€ less than the previous year. The main reason for this was that some of the large externally funded projects came to an end in that year and new projects had not yet been granted. The decrease was roughly 629 T€, so that the remaining budget was approximately the same as in the previous year.

In contrast, in 2002, there was a great improvement in all areas so that the overall budget grew to approximately 15.5 Mio€. This growth is a consequence of several factors which played a role in the budget of 2002.

The appointment of the new scientific manager who is at the same time head of the newly created Department of Cognitive Neurosciences Laboratory which is still being set up led to acceptance of a number of special circumstances which have partly a momentary effect but partly also a lasting effect on the budget. Particularly the personnel resources grew by approximately 814 T€ to 6928 T€ at this stage. Included in this sum is an increase in the securities to finance employment of young scientists in addition to the staff appointment scheme as well as an increase of four

Development of Income 1977 - 2002



posts. Due to the work of an additional department, higher costs for laboratory and materials occur and the materials budget was increased by about 176 T€. The necessity to provide initial equipment for the Department of Cognitive Neurosciences led to an increase in the investment securities (excluding building investment) of around 700 T€.

Finally, the start of the construction of the alternative quarters as a prerequisite for the reorganisation of the animal house led to a further increase of around 3,487 T€.

From the external financing, an increase in the income of around 332 T€ to 2,945 T€ was achieved so that the level of the highest external funding in the year 2000 has almost again been reached.

As particularly gratifying, an increase in the income from research and development contracts, services and licences can be noted. This rose from 448 T€ to a present level of 1089 T€. This is mainly due to the increased success in the area of technology transfer.

### **Renovation of the animal house**

The necessary renovation of the animal house turned out to be a difficult and complex problem. The planning and authorisation phase of the alternative quarters was already exceptionally difficult because the entire property lies in a water protection zone, and then further factors led to a partially very considerable exceeding of time and funds. Since the safety measures, which are similar to those for a waste disposal site, necessitated extensive underground engineering, periods of bad weather led to extensive loss of time. In the course of the tariff dispute in the building trade, the DPZ was also affected by the strikes. And the bankruptcy of the roofing firm led to a further loss of several weeks. All of this led to the problem that the originally planned completion date at the end of 2002 was shifted to May/June 2003.

With respect to the increase in costs, a supplemental "HU-Bau" (calculation of costs) must be developed and discussed with the authorities responsible. The DPZ is hoping that a solution will be able to be found which, on the one hand, will not endanger the project and, on the other, will not overburden the future budgets of the DPZ.

### **Technology transfer**

At the moment, the DPZ is following up three projects that promise success.

In the first one, the DPZ has developed monoclonal antibodies against the prion protein, which are being used in BSE tests by a pharmaceutical company within the framework of a non-exclusive licence. On the basis of this licence, in 2002, the DPZ

was able to achieve an income of 1.6 Mio€. Since the test is still being sold further, it can be assumed that also in the future a corresponding income can be expected. In accordance with the patent regulations in force, the income will be divided up between the inventors, the department in which the inventor worked (in this case the Department of Virology and Immunology) and the DPZ. In agreement with the Supervisory Board, the money payable to the DPZ will be put into a strategy fund from which projects for the strategic development of the DPZ will be financed.

Because the licence for the use of the antibodies was not exclusive, the DPZ is currently negotiating with a second firm as to their utilisation .

The second project has to do with the DPZ patent for virus-like-particles. A German pharmaceutical company is showing great interest in developing this principle into a saleable product. It has made an offer to a whole DPZ working group (1 head, 3 postdoctoral fellows, 2 technicians) to work in a subsidiary company in the USA which the group has accepted. The DPZ is negotiating the utilisation of the patent rights.

The third project is concerned with a DPZ patent for a nasal yellow fever vaccination. For a long time, no-one was interested in this patent, but now the DPZ is negotiating with a British company.

## **Personnel**

During the period of this report, the total numbers of employees at the DPZ on the set days 31.12 were 172 (2001) and 169 (2002). This is a clear decrease in comparison with our last report, since, on the set day 31.12.00, 180 employees were counted.

Particularly amongst the scientific staff, the decrease from 78 in 2000 to 74 in 2001 and to 54 in 2002 was significant. This is mainly a consequence of the decrease in the external resources described above due to the completion of some of the major projects. In addition, there were 34 (2001) and 27 (2002) unpaid staff members at the DPZ (diploma students, doctoral students, guests and people participating in practicals), so that at the end of 2001 there was a total of 206 staff members and, at the end of 2002, 196 at the DPZ.

As regards the annex personnel - financed by the basic budget in addition to the staff appointment scheme - there were considerable shifts in comparison with the last report as well as within the period of this report. Whereas, in 2000, there were annex personnel to an extent of 33.2 man-years, the number rose in 2001 to 39.5 man-years and fell back in 2002 to 26.7 man-years. The reason for the high number in 2001 was that there was an unusually high number of guest scientists, amounting to 22.3 man-years. The Department of Reproductive Biology had the highest share with 7.2 man-years, followed by the Department of Virology and Immunology with 6.7 man-years.

For the reasons already mentioned, the employment of externally funded personnel decreased in comparison to the year 2000 from 51.6 man-years to 41.8 man-years in 2001 and 38.9 in 2002.

On the other hand, in the staff appointment scheme there was an increase from 87 to 91 positions due to the formation of the Department of Cognitive Sciences Laboratory which is still in the process of being set up.

As regards the strengths of the departments compared to one another, a certain adjustment has taken place which is mainly due to the fact that the Department of Virology and Immunology is no longer so dominant. Their personnel capacity decreased from 52.3 man-years in 2000 to 28.8 man-years in the year 2001 and 19 man-years in 2002. The main reason is the reduction in the number of externally financed staff members from 29.8 man-years in the year 2000 to 9.2 man-years in 2001 and to 5.3 man-years in 2002.

The Department of Veterinary Medicine and Primate Husbandry has remained relatively stable. Along with 28.5 positions (2002: 29.5) mostly employed in animal care, the department was strengthened by annex and externally funded personnel by 10.2 man-years in 2001 and 11.00 man-years in 2002 (2000: 8.5 man-years).

Also the Department of Reproductive Biology showed only slight variations. To the 8.5 basically financed positions there was an addition of 14.1 man-years in 2001 and 11.4 man-years in 2002 as annex and externally funded personnel (2000: 12.2).

And also in the Department of Neurobiology there was little fluctuation. The entire capacity was 21.1 man-years in the year 2000, from which 8.4 man-years were financed externally. With 9.5 positions, the department had in 2001 a total capacity of 20.9 man-years with a external financing of 6.8 man-years. In 2002, the total capacity was 20.1 man-years with a externally funded quota of 6.0 man-years.

The two small departments, Ethology and Ecology and Primate Genetics, had with a total of 8 posts, externally funded posts of 3.5 man-years in 2001 and 3.0 man-years in 2002 (2000: 3.5 man-years), whereas the Department of Cognitive Neurosciences, still being built up, has no external funding as yet. From the annex personnel, the three departments were strengthened by a total of 6.8 man-years in 2001 and 7.0 man-years in 2002 (2000: 5.1 man-years).

Due to the legal rules at the DPZ, the extra burdens in personnel areas have grown. Because of the changes in the laws on works industrial relations schemes, the last works council had to elect 9 instead of the 7 members needed up to now from whom one member must be completely relieved of his normal duties to carry out his works council duties. In the form of a further half of a position, an equal status representative must be relieved of his regular duties in the future.

Assessor jur. Michael Lankeit  
(Administrative Manager)

**Projects supported by external funding agencies  
in the reporting period (2001-2002)**

<b>Project</b>	<b>Funding agency</b>	<b>Period</b>	<b>Total (€)</b>
<b>Department of Veterinary Medicine and Primate Husbandry</b>			
Xenotransplantation	Medizinische Hochschule Hannover	2001	25,565
Haltung von Javaneraffen ( <i>Macacca fascicularis</i> )	Forschungszentrum Jülich GmbH	01.06.01-31.12.02	22,500
PET- und MRI-Studien bei Pavianen incl. Streßbelastungen in nicht-invasiven Tierversuchen	Forschungszentrum Jülich GmbH	01.01.01-31.12.02	30,676
Eelektronenmikroskopische Untersuchungen von Rhesusaffen mit JCV-VLP incl. Tierhaltung	Jenapharm	15.08.02-14.08.03	69,307
Messung von intermolekularen Kräften zwischen Prion-Proteinen und Prion-Liganden mit der Rasterkraft-Mikroskopie	DLR	01.02.02-31.01.05	224,339
Infectivity of blood components in experimental nvCJD: Towards a risk assessment for human blood	EU	01.10.01-30.04.04	403,260
Strategies for the prevention and treatment of prion disease	EU	01.09.02-30.08.05	232,200
Immunpathogenese und Interventionsstrategien bei mukosalen Infektionen	DFG	13.09.02-2004	36,813
Intracraniale Hirndruckmessungen bei Rhesusaffen	Janssen Pharmaceutica	30.09.01-31.12.01	30,000
Stipendien ausländischer Wissenschaftler	DAAD	01.05.01-31.07.01	5,216
<b>Total</b>			<b>1,079,876</b>
<b>Department of Ethology and Ecology</b>			
Ecology of Neotropical Primates	Margot Marsh Biodiversity Foundation	12.10.01-06.11.01	3,407
3. Göttinger Freilandtage "Sexual Selection in Primates: Causes, Mechanisms, Consequences"	DFG	11.12.01-14.12.01	15,339

<b>Project</b>	<b>Funding agency</b>	<b>Period</b>	<b>Total (€)</b>
3. Göttinger Freilandtage "Sexual Selection in Primates: Causes, Mechanisms, Consequences"	MWK Hannover	11.12.01-14.12.01	4,417
Reisekosten XIXth Congress Intern. Primatological Soc., China	Flora Immerschitt	2002	1,500
Ursachen und Mechanismen des Paarlebens bei <i>Lepilemur ruficaudatus</i>	DFG	01.05.02-30.04.04	81,345
Reisekosten XIXth Congress Intern. Primatological Soc., China	DFG	2002	1,169
Determinanten der Diversität intestinaler Parasitengemeinschaften sympatischer Neuweltaffen ( <i>Saguinus mystax</i> , <i>Saguinus fuscicollis</i> und <i>Callicebus cupreus</i> )	DFG	14.06.02-13.06.03	7,462
Paarungsstrategien und Fortpflanzungserfolg beim grauen Mausmaki	DFG	01.10.02-30.09.03	31,408
IAS-Programm Würzburg-Duke	DAAD	2001	18,023
IAS-Programm Würzburg-Duke	DAAD	2002	16,810
TBA Kurs	TBA	2002	10,000
Primatologisch-tropenökologische Exkursion	DAAD	07.09.02-10.10.02	3,579
Primatologisch-tropenökologisches Freilandpraktikum	Förderkreis DPZ	07.09.02-10.10.02	300
Primatologisch-tropenökologisches Freilandpraktikum	Deutsch-Ibero-Amerikanische Gesellschaft	07.09.02-10.10.02	130
Parasiten freilebender Neuweltaffen	DAAD	01.05.02-30.04.03	21,600
<b>Total</b>			<b>216,489</b>
<b>Working Group Primate Genetics</b>			
INPRIMAT	EU	2002-2005	262,690
Molekulare Genetik der Spermium Ei-Interaktion von Primaten	DFG	01.05.02-30.04.04	44,810
Biogeographische Evolution, Populationsgenetik und -differenzierung von <i>Microcebus</i> spp. und <i>Cheirogaleus</i> spp. in Madagaskar	DFG	01.06.02-31.05.03	10,958

<b>Project</b>	<b>Funding agency</b>	<b>Period</b>	<b>Total (€)</b>
Biogeographische Evolution, Populationsgenetik und -differenzierung von <i>Microcebus</i> spp. und <i>Cheirogaleus</i> spp. in Madagaskar	DFG	01.04.02-31.03.03	43,250
Analyse von phylogenetischen Beziehungen der Primaten zu anderen Säugerordnungen mit Hilfe von Transposons als momoplasiefreie molekularkladistischer Marker	DAAD	01.01.02-31.12.02	25,156
<b>Total</b>			<b>386,864</b>
<b>Department of Reproductive Biology</b>			
Funktion von Relaxin während der Gravitation am Affenmodell	Leidenberger Müller Stiftung	01.01.01-31.12.02	72,426
Etablierung von Zell-Linien: Primaten-Granulosa- und Theka-Zellkulturen von Neuweltaffen, <i>Callithrix jacchus</i> , zum Studium biomedizinischer Grundlagenforschung und Wirkstoffscreening	Stiftung zur Förderung der Erforschung von Ersatz- und Ergänzungsmethoden zur Einschränkung von Tierversuchen (SET)	01.04.01-31.03.02	64,551
Etablierung von Zell-Linien: Primaten-Granulosa- und Theka-Zellkulturen von Neuweltaffen, <i>Callithrix jacchus</i> , zum Studium biomedizinischer Grundlagenforschung und Wirkstoffscreening	Stiftung zur Förderung der Erforschung von Ersatz- und Ergänzungsmethoden zur Einschränkung von Tierversuchen (SET)	01.04.02-31.03.03	32,500
Evaluierung des <i>in vivo</i> - Endometriosemodells in Weißbüffelaffen (Primaten, <i>Callithrix jacchus</i> )	Solvay Pharmaceuticals GmbH	01.03.01-28.02.03	37,500
Aufbau eines Endometriosemodells	Solvay Pharmaceuticals GmbH	01.03.01-28.02.03	38,250
Local economy, nature conservation and research perspectives in Siberut Island	Zoologische Gesellschaft für Arten- und Populationsschutz	01.01.01-31.12.02	48,876

<b>Project</b>	<b>Funding agency</b>	<b>Period</b>	<b>Total (€)</b>
Intrasexuelle Kompetetion und Hoden- und Gametenfunktion bei Primaten	DFG	01.07.01-30.06.02	53,332
Vaginalzytologie bei Cynomolgus	Labor für Pharma- und Toxikologie (LPT)	01.01.01-31.12.01	4,500
Ovulation und Luteinisierung auf zellulärer Ebene an einem Primatenmodell, dem Weißbüschelaffen ( <i>Callithrix jacchus</i> )	DFG	01.07.01-30.06.03	133,658
FWF-Projekt - Hormonphysiologische Charakterisierung der weiblichen Gonadenfunktionen bei Berberaffen	Universität Wien	15.10.01-31.07.02	18,822
Interaktive männliche und weibliche Fortpflanzungsstrategien in Mehrmännchen-Mehrweibchen-Primatengruppen und ihre Bedeutung für die Festlegung der Vaterschaft	DFG	01.01.01-31.12.02	50,398
Interaktive männliche und weibliche Fortpflanzungsstrategien in Mehrmännchen-Mehrweibchen-Primatengruppen und ihre Bedeutung für die Festlegung der Vaterschaft	DFG	01.01.01-15.01.02	25,234
Implementation of assisted reproductive techniques in spider monkeys ( <i>Ateles geoffroyoi</i> ) to increase reproduction in capacity	National Council for Science and Technology, Mexico	01.02.01-31.11.01	8,434
Untersuchungen der <i>in vivo</i> Follikeldynamik in Korrelation zur IGF-Expression im Weißbüschelaffen	DAAD	01.04.01-31.03.04	81,000
Diverse Kooperationen	Verschiedene Zoos und Institutionen	03.07.02	4,900
Molekulargenetische Untersuchungen zur Phylogenie und Taxonomie endemischer Makaken des Mentawai-Archipels, Indonesien	DFG-Stipendium	01.09.02-31.08.03	24,332
Endokrine Korrelate der Musth bei Afrikanischen Elefanten	Ev. Studienwerk Villigst	01.10.02-31.09.03	12,240
<b>Total</b>			<b>710,953</b>

<b>Project</b>	<b>Funding agency</b>	<b>Period</b>	<b>Total (€)</b>
<b>Department of Cognitive Neuroscience</b>			
Aufbau der Abteilung Kognitive Neurowissenschaften	Volkswagen	16.07.01-15.07.06	619,686
Promotionsprojekt "The perception of visual motion in man and monkey" im Rahmen des Promotionsprogrammes "Neurowissenschaften"	G. C. Lichtenberg-Stipendium (Land Niedersachsen)	01.10.02-30.09.03	13,500
<b>Total</b>			<b>633,186</b>
<b>Department of Neurobiology</b>			
Neuronale Aktivitäten während audio-motorischer Interaktion	DFG	01.03.01-28.02.02	61,866
Reisekosten XVIIIth Congress Intern. Primatological Soc., Australien	DFG	2001	1,774
Alarmrufe und Raubfeindvermeidung in Assoziation von Tamarinen	Ev. Studienwerk Villigst	01.12.02-31.05.03	17,340
Akustische Analysen von emotionalen und präverbalen Lautäußerungen bei hochgradig schwerhörigen Kindern	DFG	01.06.02-31.05.03	29,312
Reisekosten XIXth Congress Intern. Primatological Soc., China	DFG	2002	1,660
<b>Department of Neurobiology: Working Group Fuchs</b>			
Kooperationsprojekt mit Prof. Paulus	Klinische Neurophysiologie, Univ. Göttingen	2001	23,652
Tianeptine's action within the hippocampal neuronal network of stressed rats	Institut de Recherches Internationales Servier (I.R.I.S)	2001	36,813
Psychogenic stress-induced hippocampal volume loss in marmoset monkeys - pilot study	Institut de Recherches Internationales Servier (I.R.I.S)	2001	65,599
Doktorandin Olga Pudovkina	Solvay Pharmaceuticals GmbH	01.08.02-31.07.03	42,422

<b>Project</b>	<b>Funding agency</b>	<b>Period</b>	<b>Total (€)</b>
Antidepressant activity of substance P-receptor antagonists: their biobehavioral effectiveness investigated in psychosocially stressed male tree shrew	Merck	01.02.01-31.12.01	70,666
a) Effect of substance P-receptor antagonist L-760, 735 and clomipramine on stress-induced alterations in neurogenesis, hippocampal and major cerebral metabolites b) Effect of substance P and a NK1R antagonist on cytogenesis in the dent gyrus: <i>In vitro</i> studies on rat brain slices	Merck	2002	84,848
Zusammenarbeit mit dem Institut für Multiple-Sklerose-Forschung	Institut für Multiple-Sklerose-Forschung (IMSF)	01.07.02-13.06.05	70,000
Investigational compounds following chronic psychosocial stress in tree shrews as a model for depression and pharmacological treatment (4. Pilotstudie)	Solvay Pharmaceuticals GmbH	01.04.02-31.03.03	112,500
Forschungszentrum Molekularphysiologie des Gehirns (Universität Göttingen): Mechanisms and repair strategies in non-human primate models	DFG	01.10.02-30.09.04	185,000
Forschungszentrum Molekularphysiologie des Gehirns (Universität Göttingen): Transcriptional and functional effects of antidepressant drugs	DFG	01.10.02-30.09.04	90,400
Insight into the mechanism of action of antidepressant therapies and novel targets for development of antidepressant and mood-stabilising agents with special emphasis to neurogenesis	GSK-Medicine Research Center	02.12.02-01.12.04	122,000
Synaptische Interaktion in Neuronalen Zellverbänden	DFG	01.01.01-31.12.03	198,513
"Forschungsverbund" Dopamin produzierende Zellen in experimentellen Modellen der Parkinson Erkrankung	BMBF	01.09.01-31.08.04	378,992
Reisekostenzuschuß	Centre de Recherche en Neurosciences Cognitives	2001	500

<b>Project</b>	<b>Funding agency</b>	<b>Period</b>	<b>Total (€)</b>
Stipendium Tania Costoli	Universität Degli Studi di Parma	01.09.01-31.08.02	15,843
Projektbezogener Wissenschaftleraustausch mit Argentinien-PROALOAR	DAAD	2001	7,311
Stipendium Ana M. Perez Villalba	DAAD	2001	2,214
Transkranielle Magnetstimulation – Einfluß auf Rezeptoren und strukturelle Merkmale des Gehirns	DLR	01.01.01-31.12.01	61,729
Transkranielle Magnetstimulation – Einfluß auf Rezeptoren und strukturelle Merkmale des Gehirns	DLR	01.01.02-31.03.02	17,350
Shared Costs: Hypertension and alpha2-adrenergic receptor subtype expression	EU	01.01.01-30.04.01	20,145
Neuroplasticity: From molecules to systems	DFG	01.01.01-31.08.03	72,092
Promotionsprojekt "Transcriptional and behavioral effects of antidepressant drugs" im Rahmen des Promotionsprogrammes "Neurowissenschaften"	G. C. Lichtenberg-Stipendium (Land Niedersachsen)	01.11.02-31.12.02	2,250
Einnahmen über DPZ-Förderverein (Servier)	diverse	2001	8,098
Einnahmen über DPZ-Förderverein (Servier)	diverse	2002	2,989
<b>Total</b>			<b>1,803,878</b>
<b>Department of Virology and Immunology</b>			
Virus-like particles (VLP) - Ein neuartiges Carriersystem für therapeutische Gene	Jenapharm	01.03.01-31.08.02	259,225
Verfahren zur Behandlung von Gelenkerkrankungen	Forschungszentrum für Medizintechnik und Biotechnologie (fzmb)	01.01.01-31.12.02	35,023
Immunmodulation durch BBay55-8800	Bayer AG	24.01.02-31.12.02	17,370
Kooperation zur vorklinischen Testung des Proteasominhibitors PS-273 in SIV-infizierten Rhesusaffen	Heinrich-Pette-Institut	07.01.02-31.12.02	42,910
Vektorimmunisierung im SIV-Makakenmodell	Universität Pohang	21.02.02-16.04.03	196,003

<b>Project</b>	<b>Funding agency</b>	<b>Period</b>	<b>Total (€)</b>
Immuntherapie SIV-infizierter Makaken	Bayer AG	11.11.02-31.10.03	349,728
BSE transmission through food and blood products: a study in primates to assess the risk for humans (Acronym: BSE Transmission to Primates)	EU	01.12.02-28.11.07	1,332,646
Mucosal vaccines against human and simian immunodeficiency viruses based on dendritic cells (Short Title: MUVADEN)	EU	01.09.02-31.08.05	667,999
Genome-wide search for human-specific retrotransposon integration polymorphisms in human populations	EU	01.07.02-30.06.05	6,000
<b>Total</b>			<b>2,906,904</b>
<b>Interdepartmental Projects</b>			
<b>Veterinary Medicine and Primate Husbandry – Primate Genetics</b>			
Genetische Aspekte der TSE (SINE)	DFG	01.11.02-31.10.04	160,000
<b>Ethology and Ecology – Reproductive Biology</b>			
Sozio-endokrinologische Analyse der Fortpflanzungsstrategien freilebender Rotstirnmakis ( <i>Eulemur rufus</i> )	DFG	01.02.01-31.01.02	25,021
Paarungssystem polyandrischer Tamarin ( <i>Saguinus mystax</i> )	DFG	15.08.02-14.08.03	36,800
<b>Ethology and Ecology – Primate Genetics</b>			
Populationsgenetische Struktur und phylogenetische Beziehung von <i>Papio hamadryas</i> und <i>Papio anubis</i> in NO Afrika	DFG	01.01.02-31.12.02	14,977
Paarungsstrategien und Fortpflanzungserfolg beim grauen Mausmaki	DFG	01.10.02-30.09.03	31,408
<b>Neurobiology (WG Fuchs) – Reproductive Biology – Primate Genetics</b>			
Quality of life and management of living resources: Glucocorticoid hormone programme in early life and its impact on adult health	EU	01.11.02-31.10.06	1,188,863
<b>Total</b>			<b>1,457,069</b>
<b>Total DPZ</b>			<b>9,195,219</b>



## The DPZ Primate Colony

The primate colony is the core of the DPZ. In recent years the primate population has increased continuously. From 1992 to 1997 the number of animals was about 1000. After the establishment of the Department of Veterinary Medicine and Primate Husbandry in 1997 the population increased to 1275 animals in the year 2000 and amounted to 1444 animals at the end of 2002, additionally 121 primates were kept for external institutions.

The main focus of the primate colonies is still the rhesus monkeys (*Macaca mulatta*, 408 animals) and the marmosets (*Callithrix jacchus*, 687 animals), however, there have been some displacements in the last two years. Whilst the population of rhesus monkeys remained constant compared to the year 2000, a considerable increase of more than 180 animals compared to the year 2000 was recorded among the marmosets. The number of tree shrews (*Tupaia belangeri*), which are mainly housed in the facilities for experimental animals of the university Göttingen in Holtensen, also increased by 60 animals.

The squirrel monkey (*Saimiri sciureus*) colony was reduced by a half whereas the animal colonies of cotton top tamarins (*Saguinus oedipus*), baboons (*Papio hamadryas*) and cynomolgus monkeys (*Macaca fascicularis*) remained constant. The wanderoos (*Macaca silenus*) were made over to the zoological garden Cologne, however, they remain in the enclosures of the German Primate Center for the time being. The cotton top tamarins and the wanderoos are being further looked after within the scope of the European preservation breeding programme (EEP).

During the reporting period more than 120 animals, above all rhesus monkeys, were kept for 16 different national and international institutions. 225 animals procured from 12 different institutions, were entrusted to the DPZ. Also 324 animals were sold to 35 different scientific institutions, commercial firms and occasionally zoological gardens at home and abroad.

Primate husbandry is subdivided into the following operational fields: central primate husbandry, breeding colonies of Old and New World monkeys and the central feeding kitchen. During the reporting period veterinary services were provided by the veterinarian Susanne Rensing, who was substituted by Dr. Annette Schrod. The colony manager, the biologist, Uwe Schönmann, took care of all the organizational questions as to animal keeping, purchase and sales of animals. Apart from the breeding colonies, the Department of Veterinary Medicine and Primate Husbandry is looking after the experimental animals of the Department of Reproductive Biology, the Department of Cognitive Neurosciences and the Department of Neurobiology, the latter is equipped with animal keepers of its own. The experimental animals of the Department of Virology and Immunology build an independent functional unit with veterinarians and animal keepers of its own. As a consequence of the forthcoming redevelopment of the animal buildings and the outsourcing of the animal stocks in the newly built accommodation early in 2003, restructuring of the pri-

*The DPZ Primate Colony*

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mate husbandry department will be started. The aim is to centralize primate husbandry as a "Cost-Center" with a transparent cost analysis and an organizational fusion of the different animal keeping units in order to meet the increased demands of internal and external scientists and also to optimize the keeping of experimental animals under the aspects of animal protection. In this context the building up of macaque colonies, free of Herpes B has also been started.

**Total primate numbers at the DPZ on 31.12.2001 (total: 1417)**

Species	Adult			Juvenile				Total
	m	w	Total	m	w	x	Total	
<i>Tupaia belangeri</i>	69	90	159	26	10	0	36	195
<i>Callithrix jacchus</i>	185	178	363	119	140	0	259	622
<i>Saguinus oedipus</i>	20	14	34	0	1	4	5	39
<i>Saimiri sciureus</i>	18	22	40	16	7	1	24	64
<i>Macaca mulatta</i>	43	176	219	150	56	3	209	428
<i>Macaca fascicularis</i>	1	28	29	12	7	3	22	51
<i>Papio hamadryas</i>	3	5	8	5	5	0	10	18

m = male; w = female; x = sex unknown

**Total primate numbers at the DPZ on 31.12.2002 (total: 1444)**

Tierart	Adult			Juvenile				Total
	m	w	Total	m	w	x	Total	
<i>Tupaia belangeri</i>	49	90	139	26	24	0	50	189
<i>Callithrix jacchus</i>	178	175	353	146	188	0	334	687
<i>Saguinus oedipus</i>	12	13	25	6	6	2	14	39
<i>Saimiri sciureus</i>	14	16	30	17	9	0	26	56
<i>Macaca mulatta</i>	103	165	268	77	63	0	140	408
<i>Macaca fascicularis</i>	2	30	32	14	6	0	20	52
<i>Papio hamadryas</i>	1	9	10	2	1	0	3	13

m = male; w = female; x = sex unknown

**DEPARTMENT OF VETERINARY MEDICINE AND PRIMATE HUSBANDRY**

**Head of Department:** Prof. Dr. F.-J. Kaup

**General research objectives**

The Department of Veterinary Medicine and Primate Husbandry is the central service and infrastructure department of the German Primate Center. In addition to general infrastructure tasks, the department is engaged in research in the field of primate pathology. Both spontaneous diseases and animal models from infection medicine are worked on scientifically. The experimental work centers on: SIV-infections and their effect on the intestinal tract, experimental infections with *Helicobacter pylori* and diseases belonging to the transmissible spongiform encephalopathies. In the field of pathomorphological diagnostics selected cases are worked on scientifically.



*Foreign body in the kidney of a baboon (*Papio hamadryas*). The foreign body consists of bedding material which has drifted into the kidney after oral intake and perforation of the large intestine.*

**Structure of the department**

The Department of Veterinary Medicine and Primate Husbandry is divided into two areas of work, pathology and primate husbandry. The working group **Pathology**, on the one hand, deals with scientific projects in the field of infection medicine and, on the other hand, with various veterinary diagnostic tasks. Diagnostics include pathology with histology, bacteriology, parasitology and laboratory diagnostics. Moreover the central electron microscopy laboratory, which is manned by one scientist, belongs to this area. At the end of 2002, two additional scientists were employed in this group. The working group is supported by five technical assistants (one of them employed part-time) and a necropsy assistant. Five PhD students, two of them as scholarship holders of the Göttingen college of graduates "Perspectives in Primatology", are also part of this group.

In the area of **Primate Husbandry** with the infrastructural facilities, feeding kitchen, animal housing and pharmacy, two veterinary practitioners, one of them with a permanent position, deal with all veterinary aspects of husbandry and care in the breeding colonies. Their job is, furthermore, the professional care of the experimental animals of the Departments of Reproductive Biology, Neurobiology and Cognitive Neurosciences. This section is headed by a biologist who as colony manager is responsible for organisational tasks including the acquisition and sale of animals. They are furthermore supported by 15 technical assistants and animal keepers, who are supplemented by temporary employees and trainees.

Scientists

Prof. Dr. Walter Bodemer (01.06.01-)  
Dr. A. Floto (01.06.01-)  
Dr. Uwe Hahmann (-31.05.01)  
Dr. Kerstin Mätz-Rensing

Veterinary care

Susanne Rensing  
Dr. Annette Schrod (01.09.01-,  
part-time)  
Dr. Monika Ziegler (-31.05.01)

Colony management

Uwe Schönmann

Further employees

Dr. Karin Hampe (-30.06.01)  
Dr. Christina Schlumbohm (01.11.02-)  
Alexander Strom (01.12.02-)

Secretary

Ingrid Rossbach (part-time)

Technicians: Pathology

Helga Gilhaus (-31.05.01)  
Jutta Gloth (01.01.-01.10.02, part-time)  
Erna Hackenbroich  
Wolfgang Henkel  
Karin Kaiser-Jarry (part-time)  
Nadine Knöchelmann  
Elke Lischka  
Hafiza Zuri

Technicians and animal keepers:

Primate Husbandry

Henry Benseler  
Nadine Bertram  
Holger Bölling

Martin Brüggemann (-30.06.01)

Silvia Casper (-31.07.01)

Yvonne Dierich

Ilona Dix

Gerhard Fleckenstein

Jürgen Gans

Heike Giller

Melanie Henne

Eduard Herdt

Annette Husung

Stephanie Jockel (01.08.01-)

Heinz-Josef Knöchelmann

Andre Krückeberg (-31.12.01)

Silke Küster (-31.08.01, part-time)

Karl-Heinz Lambrecht

Ramona Lenzner-Pollmann (part-time)

Tamara Meyer-Burhenne (13.06.02-)

Susanne Passek

Nadine Rudolph

Helmut Rumpeltin (-22.06.02)

Norbert Schwandt (01.08.01-)

Petra Stöfer

Trainees, retrainees

Silke Becker (01.08.01-)

Sarah Blume

Kathrin Grell (01.08.02-)

Janine Henrici (-01.10.02)

Patrick Soppa (01.08.01-30.09.02)

PhD students

Karin Bingger

Anja Blankenburg

Christiane Kott (01.01.02-)

Andrea Quohs

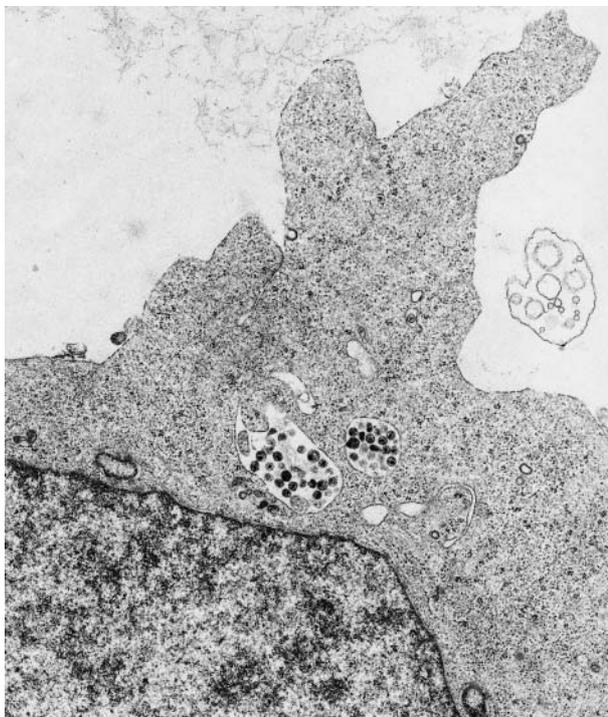
Frank Runge (01.10.02-)

Jarno Marius Schmidt (01.08.02-)

### **Progress during the year**

After the fusion of the working groups "Experimental Pathology", "Breeding and Keeping" and the "Department of Pathology and Veterinary Services" to one department, "Veterinary Medicine and Primate Husbandry", a central infrastructure department was created. Corresponding to the guidelines of the scientific council the department's aim is to ensure and to optimize the service assignment of the DPZ. The service tasks comprise the breeding, acquisition and sales of animals, quarantine, and veterinary care with associated veterinary-diagnostic services, such as pathology, bacteriology and parasitology as well as the veterinary pharmacy. Moreover, the head of the department, observes the legally prescribed tasks as representative for the protection of animals and for the protection of infections. Despite the loss of a further scientifically established post, performance increased and the service tasks were further optimized and adapted to the KLR-system.

During the reporting period, infection research in the department has changed considerably. The previous spectrum with **SIV-reasearch**, main area gastro-intestinal tract, and the primate model for **Helicobacter pylori-infections** has been considerably widened by investigations on **transmissible spongiform encephalopathies (TSE)**. These areas of research are supplemented by investigations on the **pathology of spontaneous primate diseases**.



*C 8166 cell with intracytoplasmic vacuole containing accumulations of SIV particles. The permanent lymphoid cell line C 8166 serves virus propagation. Eight days after the infection, the production of particles reaches a peak level.*

### **SIV-research**

Investigations on primary SIV-induced lymphomas, pathogenetic processes in opportunistic infections and on virus spreading in the gastro-intestinal tract of rhesus monkeys (*Macaca mulatta*) were continued, however, their scope was reduced. After termination of the AIDS-research network Würzburg-Göttingen the department participated in the foundation of a clinical research group at the FU Berlin. In 2001 the research group with the subject "Immunopathogenesis and intervention strategies in mucosal infections" filed an application (meanwhile granted) for support with the DFG (AZ 60665-01-50/00), the department is participating with two projects.

The project entitled, "SIV-infection of the mucosa: characterization of the migration of CD4+ T-cells and mucosal T-cell response against attenuated poliovirus (vaccine virus)", deals with two problems of mucosal immunodeficiency in the SIV-model. On the one hand, the migration behaviour of lymphocytes into the intestinal mucosa before and after SIV-infection is investigated. For this purpose autologous lymphocytes, which are gained at present, are marked *in vitro* with fluorescent dyes (5-, 6-carboxyfluorescein-diacetate-succinimidylester, CFSE) and are reinjected. It is intended to look for CFSE-marked cells *in vivo* before and after SIV-infection by means of intestinal biopsies and in peripheral blood and to compare their behaviour. In the second part of the experiments the mucosal cellular immune response to attenuated poliovirus before and after an SIV-induced immunosuppression will be investigated. Following an antiretroviral treatment, the regeneration of a polio-specific immunoresponse will be checked. These experiments have been started with the collection of autologous lymphocytes for a pool.

In investigations on the intestinal spread of virus and the passage of the virus through the rectal intestinal barrier we succeeded in specifically proving SIV antigen immuno-electron microscopically by means of a silver-enhanced gold technique using ultra-small gold particles. This method was established light- and electron microscopically using C8166 cell cultures and was transferred to intestinal biopsies of SIV-infected rhesus monkeys (times of extraction 1 min to 48 hs p.i.). In fact, it was possible to present gold particles in the biopsies but virus particles could not be found ultrastructurally. Perhaps the virus concentration applied to the rectum is too low to detect SIV-particles or corresponding antigen in the very limited extent of a biopsy. Thus the question of whether SIV particles pass through the rectal barrier, including participating cell types, still remains unanswered. In this context it also has to be mentioned that the M-cell, at present favoured for the entry, could not be found in the biopsies. It is not possible to gather selected lymphofollicular structures of the rectum with associated epithelium, including M-cells, by means of the endoscopy technique.

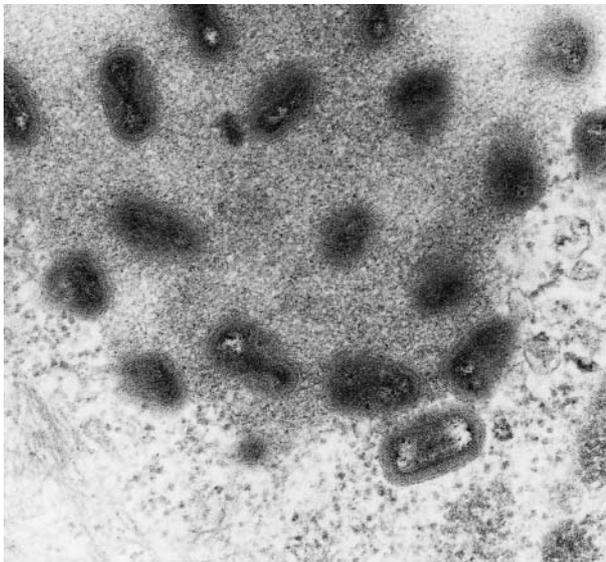
### **TSE-research**

Already before the onset of the BSE crisis we had negotiated with Messrs. Baxter, Vienna, on the taking over of a TSE research project with rhesus monkeys. The project is supported by the EU, participating scientists are Prof. Collinge, London, Prof. Aguzzi, Zurich, and Prof. Dittami, Vienna. After the taking over and the coordination of the project early in 2001 the Department of Veterinary Medicine and Primate Husbandry was completed by Prof. Bodemer, a scientist who since then has started

several projects on transmissible spongiform encephalopathies (TSE). At present the following projects are being carried out:

The infection of rhesus monkeys with prions of sporadic CJD, the variant CJD and BSE

- Molecularbiological and physical investigations on the interaction of prion protein molecules and its ligands
- Moleculargenetical experiments on the regulation of the prion protein synthesis by SINE



*Intracytoplasmic accumulation of pox viruses in epithelium cells of the skin. The viruses are unusual cow pox viruses, which have resulted in numerous deaths in a population of New World monkeys with *Callithrix* sp. and *Saguinus* sp. (TEM, 60.000x).*

### **The infection of rhesus monkeys with prions of sporadic CJD, the variant CJD and BSE**

Since May 2001, our department has been coordinating on EU-supported project on this problem. After the receipt of 18 rhesus monkeys from Messrs. Baxter, Vienna, we inoculated the animals intraperitoneally with brain material of a sCJD, a vCJD patient and of cattle suffering from BSE. Our experimental approach focusses on the determination of when and where in the organism prions responsible for transmissibility and infectivity of prion diseases are formed. We are not only interested in the transmission and evidence of prion proteins (PrP) in their normal physiological form or in pathogenetically relevant PrP molecules. We also include behavioural-biological investigation methods in our concept in order to detect early disturbances in the behaviour and especially in the activity rhythm of an animal, i.e. shortly after the prion infection. For this purpose the corresponding transmitters for a telemetric surveillance have been implanted. From this approach we expect evidence on if and how it will be possible to prove behavioural disturbances in the



*Multiple older fractures and glass bones due to a secondary hyperparathyroidism. Front limbs of a common marmoset (*Callithrix geoffroyi*).*

course of a prion infection. The telemetric data supply us with the respective individual behavioural pattern of each animal, perhaps they will allow us to draw conclusions from behavioural activities, e.g. the sleeping rhythm of men, too. These investigations are routinely realized at the DPZ by the working group of Prof. Dittami, Vienna. So far no significant deviations of the norm can be observed.

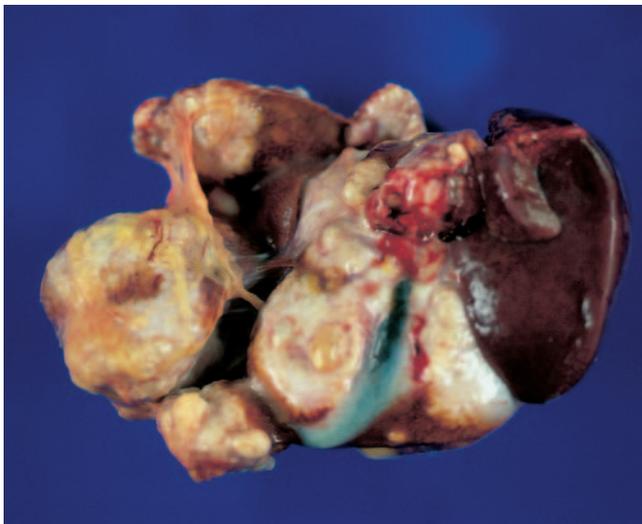
In the first few months after inoculation of the animals, we collected blood and blood cells and have started to determine the transcription of an indicative TSE gene in rhesus monkeys and in parallel in men. In order to prove pathologically relevant prion protein our collected sample material is processed and determined with the latest techniques (ELISA, Delfia, CIE). Next year, we are planning experiments and transmission studies relevant to infections together with our partners Profs. Aguzzi and Collinge in Zurich and in London. During the reporting period, one animal infected with vCJD unfortunately had to be euthanized because of a cornifying tessellated epithelium carcinoma of the tongue with metastases into the regional lymph nodes.

#### **Molecular biological and physical investigations on the interaction between prion protein molecules and their ligands**

The investigations related to the rhesus monkey model have been extended by a Rasterkraft-analysis of prion protein molecules and their ligands. On the basis of single molecules, molecular basics of behaviour of solutions under particular pH- and salt conditions and the aggregation capability of prion proteins can be studied. This very biophysically orientated TSE project is realized in cooperation with Dr. Metze, Institute for Bioprocessing and Analytical Measurement Techniques (iba), Heiligenstadt, and Prof. Sklaviadis, Aristoteles University, Thessaloniki. These investigations are supported by the TSE-therapy program of the BMBF.

In the project we intend to gather basics on molecular interactions of experimental candidate molecules and of possible therapeutically effective substances. Our

earlier work on monoclonal antibodies suggests using these as binding partners for prion proteins with different structures in Rasterkraft (atomic-force-microscopy) investigations. In the first eight months of the funding period we succeeded in finding an optimal carrier for the piling up of prion protein. The solubility and the aggregation behaviour of prion proteins under fixed conditions, such as pH and ion strength, were tested. In cooperation with Prof. Sklaviadis the quality of the recombinant prion protein used was confirmed by two-dimensional gel electrophoresis. In competition experiments, binding and displacement of monoclonal antibodies by ligand molecules were checked. For the next few months, further investigations on the reversible aggregation and solution of prion protein molecules are planned. The Rasterkraft investigations are carried out at the Institute for Bioprocessing and Analytical Measurement Techniques in Heiligenstadt.



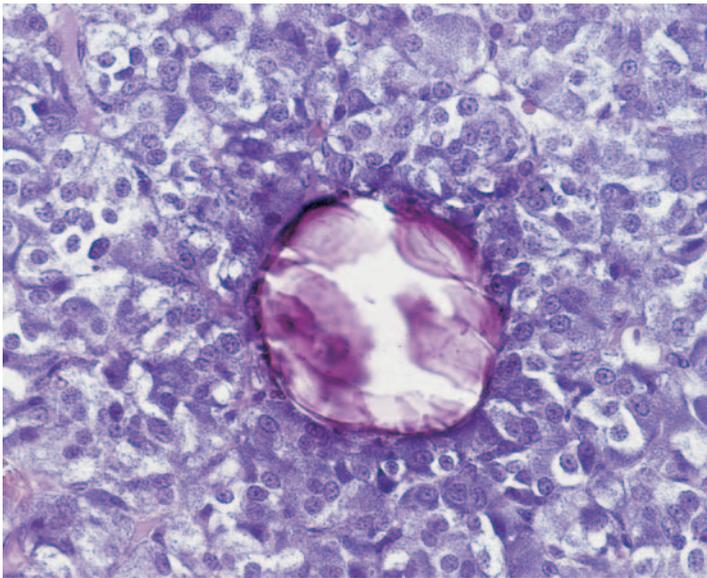
*Severe liver alterations in a cynomolgus monkey (*Macaca fascicularis*) due to echinococcosis. Infestation with measles of the fox tapeworm *Echinococcus multilocularis* is one of the population problems of the DPZ with animals kept in outdoor facilities.*

### **Molecular genetic experiments on the regulation of the prion protein synthesis by SINE**

In cooperation with Prof. Zischler, we are dealing with a molecular genetic question concerning the regulation of the prion protein synthesis in relation to the building of Short Interspersed Nuclear Elements = SINEs. This project is carried out within the scope of a DFG research group around Prof. Geldermann, University Hohenheim. The synthesis of the cellular prion protein is considered to be the condition for pathophysiological alterations in prion diseases with causal amyloid formation of insoluble prion protein molecules. Here the question arises as to whether the quantity of available prion protein is reached by an increase in protein biosynthesis in the cells. Following a hypothesis of T. Gibson, EMBO Heidelberg, an increased number of transcripts of short interspersed nuclear elements (SINE), to which the well known alu-sequences belong, could intervene in the protein synthesis of the cell and subsequently result in an increased translation of prion protein mRNA. The in-

duction of the transcription of alu-elements has already been found in connection with viral infections. However, no experiments have been reported in which selected cellular genes, or their gene products, have been checked with respect to an increased synthesis. It is known of adenoviruses and herpes viruses that virus encoded genes comparable to the alu-sequences and their transcripts do exist (e.g. adena VARNAs and EBER from EBV). Both cause a strengthening of the virus-specific protein synthesis by an interaction with the cellular protein kinase PKR. The aim of our project is to check this hypothetical connection between SINE-transcription and formation of prion protein. We can work experimentally with cell cultures, which are well accessible for the SINE transcript analysis and the determination of prion proteins. As we have investigation material from prion diseases of man and animal at our disposal, we are able to extend our research approach into the sick organism.

Supplementary to the mentioned projects, Prof. Bodemer in cooperation with Prof. Pfaff, BFAV Tübingen, is in charge of investigations within the scope of an EU-project (coordinator Prof. Collinge, London) on the immune modulation of TSE in mice.



*Calcification in the threshold of the cortex of the suprarenal gland to the suprarenal mark. The pathogenesis of such calcifications is still unclear, they regularly appear in rhesus monkeys (*Macaca mulatta*) as incidental findings.*

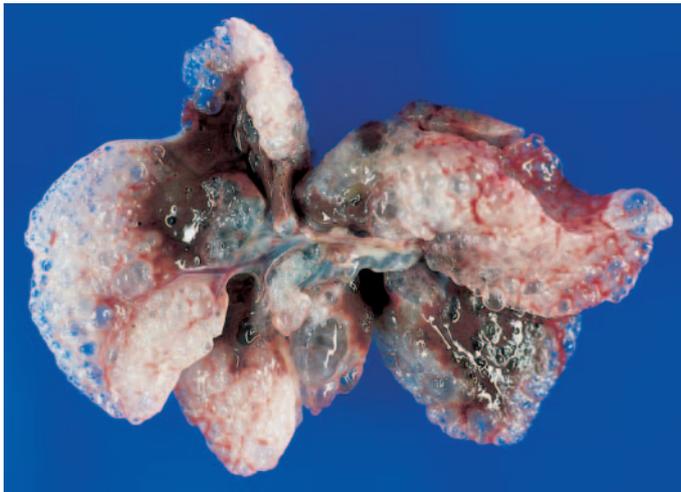
### **Primate model *Helicobacter pylori***

The establishing stage of the primate animal model of *Helicobacter (H.) pylori*-infection in rhesus monkeys (*Macaca mulatta*) is completed. In cooperation with a working group of the University Würzburg (Prof. Suerbaum), three rhesus monkeys were experimentally infected with different human pathogenic isolates. The animals are continuously screened and stomach biopsies are regularly taken, which are systematically elaborated histologically, immunohistologically, electron microscopically, microbiologically and molecular biologically. Up to now, the infection strains

could be re-isolated, therefore a defined permanent infection can be assumed. We are particularly interested in a mucosal immune response in the course of the infection. Moreover, Dr. Ignatius, Institute of Infection Medicine of the FU Berlin, is carrying out investigations on the mucosal immune response by re-injection of autologous dendritic cells loaded with antigen. Dendritic cells of rhesus monkeys are very similar to those of man. After the characterization of the peripheral and the mucosal immune response, several possibilities for the antigen load of dendritic cells are investigated in our chronically infected animals. At present, these experiments are in the early stage. Later on, autologous dendritic cells of monkeys free from *Helicobacter pylori* will be loaded with selected antigens and will be injected into the animals. After evaluation of the induced immune response the animals will be exposed to a virulent strain and the protection achieved will be analyzed.

### **Pathology of primates**

In the field of diagnostics, casuistries of scientific interest arise regularly, which are systematically worked on and published. These activities were continued successfully during the reporting period.



*Distinct cystic liver, presumably as congenital abnormality in a cotton top marmoset (*Saguinus oedipus*).*

### **Involvement into national and international research**

The following cooperations exist in the diverse fields of research of the department:

- SIV animal model in primates: DFG research group on the immunopathogenesis and intervention strategies in mucosal infections: Prof. Zeitz and Prof. Schneider, University Clinical Center Benjamin Franklin, Berlin.
- TSE-animal models in primates: EU-research project in co-operation with Prof. J. Collinge (MRC Prion Unit, Inst. of Neurology, Univ. College, London, GB), Dr. I. Machatschke, Prof. J. Dittami (Zoological Inst., Univ. Vienna, A), Prof. A. Aguzzi

(Inst. for Neuropathology, Univ. Zürich, CH); BMBF-Project with Dr. J. Metze (Inst. für Bioprozess- und Analysenmesstechnik, Heiligenstadt).

- *H. pylori*-model of infections: Prof. Suerbaum and Dr. C. Kraft (Inst. für Hygiene und Mikrobiologie, Univ. Würzburg); DFG research group on immunopathogenesis and intervention strategies in mucosal infections: Dr. Ignatius, Inst. f. Infektionsmedizin, FU Berlin.
- Pathology of primates: Dr. R. Plesker, Paul Ehrlich Institut, Langen; Dr. E. Buse, Messrs. Covance, Münster.

Apart from our own research activities, we are in charge of several projects of external partners (service-orientated). These include among others:

In co-operation with the Medizinische Hochschule, Hannover, Prof. Winkler: Xenotransplantation of kidneys of transgenic pigs to cynomolgus monkeys (*Macaca fascicularis*).

With the Kernforschungszentrum Jülich: Testing of imaging procedures at the CNS of baboons (*Papio hamadryas*).

In co-operation with the Klinikum Aachen (Prof. Flöge): Pathogenesis of Nephropathies in marmosets (*Callithrix jacchus*) as a model for human kidney diseases.

In co-operation with Prof. Hunsmann, DPZ, and the EU-project on the risk potential of bovine spongiform encephalopathies coordinated by him: J. Löwer (Paul-Ehrlich-Institute, Langen), P. Bierke (SIIDC, Stockholm, S), D. Dormont (CEA, Fontenay-aux-Roses, F), M. Pocchiari (ISS, Rome, I).

### Projects and partners in co-operation

(I: interdepartmental projects, E: external co-operation; A: project completed, L: current project)

<b>Projects and partners of the Department of Veterinary Medicine and Primate Husbandry</b>		
<b>SIV-infections of the rhesus monkey: Pathogenesis of intestinal alterations</b> <b>F.-J. KAUP, K. MÄTZ-RENSING, K. BINGGER, A. FLOTO, M. ZEITZ, T. SCHNEIDER</b> (Universitätsklinikum Benjamin Franklin, Berlin), <b>P. RACZ</b> (Bernhard-Nocht-Institute, Hamburg), <b>C. STAHL-HENNIG, N. STOLTE</b> (Dept. of Virology and Immunology, DPZ)	E,I	L
<b>Experimental Helicobacter-infections of rhesus monkeys (<i>Macaca mulatta</i>)</b> <b>K. MÄTZ-RENSING, F. RUNGE, S. SUERBAUM, C. KRAFT</b> (Inst. for Hygiene and Microbiology, Univ. Würzburg), <b>M. EISENBLAETTER, R. IGNATIUS</b> (Inst. for Medicine of Infections, Free Univ., Berlin), <b>F.-J. KAUP</b>	E	L
<b>Pathology of spontaneous diseases of primates</b> <b>K. MÄTZ-RENSING, A. FLOTO, F.-J. KAUP</b>		L

<b>Projects and partners of the Department of Veterinary Medicine and Primate Husbandry</b>		
<b>On the occurrence of spontaneous tumors in primates</b> <b>A. FLOTO, K. MÄTZ-RENSING, F.-J. KAUP</b>		L
<b>Investigations on the occurrence of the marmoset-wasting-syndrome in marmosets (<i>Callithrix jacchus</i>) at the DPZ</b> <b>A. QUOHS, F.-J. KAUP</b>		L
<b>Echinococcosis in nonhuman primates</b> <b>A. BLANKENBURG, K. MÄTZ-RENSING, S. RENSING, K. BREHM, M. FROSCH</b> (Inst. for Hygiene und Microbiology, Univ. Würzburg), <b>U. SAUERMAN</b> (Dept. of Virology and Immunology, DPZ), <b>F.-J. KAUP</b>	E,I	L
<b>Expression of HER-2 receptors in mamma carcinomas</b> <b>C. KOTT, F.-J. KAUP</b>		L
<b>Infectivity of blood components in experimental NVCJD: Towards a risk assessment for human blood</b> <b>F.-J. KAUP, W. BODEMER, J. COLLINGE</b> (MRC Prion Unit, Inst. of Neurology, Univ. College London, GB), <b>I. MACHATSCHKE, J. DITTAMI</b> (Zoological Inst., Univ. Vienna, A), <b>A. AGUZZI</b> (Inst. for Neuropathology, Univ. Zürich, CH)	E	L
<b>Small Interspersed Nuclear Elements (SINEs) as predisposing genomic marker and cofactor for a TSE of man and animal</b> <b>W. BODEMER, H. ZISCHLER</b> (Working Group Primate Genetics, DPZ)	I	L
<b>Measurement of intermolecular forces between prion protein and prion protein-ligands with Rasterkraft-microscopy</b> <b>W. BODEMER, J. METZE</b> (Inst. für Bioprocess- und Analysenmesstechnik, Heiligenstadt)	E	L
<b>Investigations on the risk potential of bovine spongiform encephalopathies</b> <b>G. HUNSMANN</b> (Dept. of Virology and Immunology, DPZ), <b>F.-J. KAUP, J. LÖWER</b> (Paul-Ehrlich-Institute, Langen), <b>P. BIERKE</b> (SIIDC, Stockholm, S), <b>D. DORMONT</b> (CEA, Fontenay-aux-Roses, F), <b>M. POCCHIARI</b> (ISS, Rome, I)	E,I	L
<b>PET- and MRI-studies in baboons including stress pressures in non-invasive animal experiments</b> <b>H. MÜHLENSIEPEN, A. BAUER</b> (Forschungszentrum Jülich, Jülich), <b>S. RENSING</b>	E	L
<b>Immunohistochemical investigations of the cytoskeleton of dogs and cats with various syndromes</b> <b>S. Neumann</b> (Veterinary Inst., Univ. Göttingen), <b>F.-J. KAUP</b>	E	L

<b>Projects and partners of the Department of Veterinary Medicine and Primate Husbandry</b>		
<p><b>Xenotransplantations of kidneys of transgenic pigs to cynomolgus monkeys</b></p> <p>M. Winkler (Klinik für Abdominalchirurgie, Medizinische Hochschule, Hannover), <b>K. MÄTZ-RENSING, S. RENSING, F.-J. KAUP</b></p>	E	L
<p><b><i>Callitrichid herpesvirus 3 (CalHV3) and lymphoma genesis in marmosets (Callithrix jacchus)</i></b></p> <p><b>K. MÄTZ-RENSING, W. BODEMER, A. FLOTO, K. BORCHERS</b> (Free Univ., Berlin), B. EHLERS, M. GLOTZ (Robert-Koch-Institute, Berlin)</p>	E	L
<p><b>Endoparasitic strain on sympatric tamarins (<i>Saguinus mystax, Saguinus fuscicollis</i>)</b></p> <p>E. HEYMANN (Dept. of Ethology and Ecology, DPZ), <b>K. MÄTZ-RENSING, C. EPE</b> (Inst. for Parasitology, Tierärztliche Hochschule, Hannover)</p>	E,I	L
<p><b>Xenotransplantations in baboons</b></p> <p>D. BRANDEL (Klinikum Großhadern, Univ. München), <b>S. RENSING</b></p>	E	L
<p><b>Pathogenesis of nephropathies in marmosets (<i>Callithrix jacchus</i>) as a model for human kidney diseases</b></p> <p>F. EITNER, J. FLÖGE (Medizinische Klinik II, Universitätsklinikum Aachen), <b>S. RENSING</b></p>	E	L
<p><b>Microbiological and immunological characterization of Helicobacter-infections</b></p> <p><b>K. MÄTZ-RENSING, E. KUNZ, F.-J. KAUP, S. SUERBAUM</b> (Inst. for Hygiene and Mikrobiology, Univ. Würzburg), B. KNAPP (Chiron-Behring Werke, Marburg), H. J. MONSTEIN (Div. Clinical Microbiology, KMÖ, Linköping, S), C. KRAFT (Univ. Würzburg), G. FELDMANN (Dept. of Virology and Immunology, DPZ)</p>	E,I	A
<p><b>Investigations on the pathogenesis of primary and secondary alterations in different organs of SIV-infected rhesus monkeys</b></p> <p><b>F.-J. KAUP, K. MÄTZ-RENSING, P. HOFMANN, N. STOLTE, C. STAHL-HENNIG</b> (Dept. of Virology and Immunology, DPZ)</p>	I	A

### Scientific contributions

#### Doctoral theses

RODE, G.: Zur Pathogenese von Zahnstein bei Hunden. Tierärztliche Hochschule Hannover (2001).

BINGGER, K.: Licht- und elektronenmikroskopische Untersuchungen zum Nachweis von SIV (Simian Immunodeficiency Virus) im Rektum experimentell infizierter Rhesusaffen (*Macaca mulatta*). Tierärztliche Hochschule Hannover (2002).

### Congress contributions

19<sup>th</sup> Jena Symposium "Respiratorisches System", Jena, 19.-21.03.01,  
KAUP, F.-J., MÄTZ-RENSING, K., HOFMANN, P.: SIV-assoziierte pulmonale Alterationen bei Rhesusaffen.

KAUP, F.-J., RENSING, S., MÄTZ-RENSING, K., RENSING, H.: Untersuchungen zur Tuberkuloseproblematik bei Totenkopffaffen unter Verwendung verschiedener Nachweisverfahren.

31<sup>st</sup> Seminar on experimental animals and animal experiments, Berlin, 21.-22.05.01, KAUP, F.-J.: Forschung an und mit Primaten: Haltungskonzepte in der biomedizinischen Forschung am Deutschen Primatenzentrum.

2<sup>nd</sup> European Wildlife and Zoo Animal Pathology Workshop, Berlin, 30.05.-01.06.01, MÄTZ-RENSING, K., RENSING, S., STAHL-HENNIG, C., BRACK, M., KAUP, F.-J.: Critical evaluation of different diagnostic methods for tuberculosis in squirrel monkeys.

44<sup>th</sup> Conference of the specialist group pathology in the DVG, Münster, 05.-06.06.01, BINGGER, K., MÄTZ-RENSING, K., HOFMANN, P., RENSING, S., KAUP, F.-J.: Zystische Leberveränderungen in einer Lisztaffenkolonie.

11<sup>th</sup> International Workshop on Campylobacter, Helicobacter and related organisms, Freiburg, 01.-05.09.01, KRAFT, C., MÄTZ-RENSING, K., KUNZ, E., KAUP, F.-J., SUERBAUM, S.: Genetic stability of *H. pylori* strains during experimental infection of rhesus macaques.

39<sup>th</sup> Conference of the Soc. Lab. Anim. Science (GV-SOLAS), Ulm, 10.-13.09.01, MÄTZ-RENSING, K., KUNZ, E., KRAFT, C., LORENZEN, D., SUERBAUM, S., KAUP, F.-J.: Experimental *Helicobacter pylori* infection of rhesus macaques.

7<sup>th</sup> Congress of the Primatological Society, Zürich, CH, 30.09.-04.10.01, BINGGER, K., MÄTZ-RENSING, K., HOFMANN, P., BRUNO, S.F., BOGA, J.A., KAUP, F.-J.: Morphological detection of SIV within tissue from SIV-infected rhesus monkeys (*Macaca mulatta*).

BLANKENBURG, A., SAUERMAN, U., KAUP, F.-J.: Spontaneous echinococcosis in a colony of lion-tailed macaques (*Macaca silenus*).

3<sup>rd</sup> Göttingen Symposium: Primates in biomedical research – diseases and pathology, DPZ, Göttingen, 25.-26.10.01

BINGGER, K., MÄTZ-RENSING, K., HOFMANN, P., BRUNO, S.F., BOGA, J.A., KAUP, F.-J.: Morphological detection of SIV within tissue from SIV-infected rhesus monkeys (*Macaca mulatta*).

BLANKENBURG, A., SAUERMAN, U., KAUP, F.-J.: Morphological and genetic examinations of spontaneous echinococcosis in a colony of lion-tailed macaques (*Macaca silenus*).

MÄTZ-RENSING, K., JENTSCH, D., RENSING, S., NIPHUIS, H., KAUP, F.-J.: Fatal *Herpes simplex*-infection in a group of common marmosets (*Callithrix jacchus*).

BODEMER, W.: Model substances for a therapy of transmissible spongiform encephalopathies.

30<sup>th</sup> Seminar on environmental hygiene, Hannover, 22.02.02, BODEMER, W., KAUP, F.-J.: Grundlagen zur Übertragbarkeit der BSE auf den Menschen.

4<sup>th</sup> Meeting European Association of Zoo and Wildlife Veterinarians, Heidelberg, 08.05.02

KAUP, F.-J.: Biology and Diseases of Primates.

KAUP, F.-J., QUOHS, A., MÄTZ-RENSING, K., AHREND, F.: Wasting marmoset syndrome (WMS) in a *Callithrix geoffroyi* monkey: Case report.

BODEMER, W., FLOTO, A., MÄTZ-RENSING, K., KAUP, F.-J.: Gene expression in B-cell lymphoma of SIV-infected rhesus monkeys (*Macaca mulatta*). An overview.

FLOTO, A., MÄTZ-RENSING, K., BODEMER, W., KAUP, F.-J.: Malignant lymphomas in SIV-infected rhesus monkeys (*Macaca mulatta*).

BINGGER, K., MÄTZ-RENSING, K., HOFMANN, F., RENSING, S., KAUP, F.-J.: Three cases of cystic liver alterations in a colony of cotton top tamarins (*Saguinus oedipus*).

MÄTZ-RENSING, K., JENTSCH, K.D., NIPHUIS, H., RENSING, S., KAUP, F.-J.: Case report of a fatal herpes simplex infection in a group of common marmosets (*Callithrix jacchus*).

BLANKENBURG, A., MÄTZ-RENSING, K., DINKEL, A., SAUERMAN, U., KAUP, F.-J.: Spontaneous echinococcosis in a colony of lion-tailed macaques (*Macaca silenus*).

FELASA-Annual Meeting, Aachen, 17.-20.06.02, KUNZ, E., MÄTZ-RENSING, K., STOLTE, N., HAMILTON, P.B., KAUP, F.-J.: Reactivation of *T. cruzi* in a SIV-immunocompromised rhesus monkey.

5<sup>th</sup> International Workshop on Pathogenesis and Host Response in Helicobacter Infections, Helsingør, DK, 04.-07.07.02, KRAFT, C., FALUSH, D., STACK, A., FOX, J.G., SCHLAPBACH, R., MÄTZ-RENSING, K., MEYER, T.F., ACHTMANN, M., SUERBAUM, S.: Frequent genetic changes during long-term colonization with *Helicobacter pylori*.

### Seminars

CDU district Göttingen, Lenglern, 27.01.01, KAUP, F.-J.: Prionenerkrankungen bei Mensch und Tier.

Association of veterinarians, Friesoythe, 01.02.01, KAUP, F.-J.: Grundlagen zu BSE und anderen Prionenerkrankungen.

CDU-national committee, Göttingen, 02.02.01, KAUP, F.-J.: Zur Problematik der bovinen spongiformen Encephalopathien.

Association of young farmers, Rottal/Inn, Pfarrkirchen, 15.02.01, KAUP, F.-J.: Zur Problematik der bovinen spongiformen Encephalopathien.

Hessian farmer's association, Bad Hersfeld, 02.03.01, KAUP, F.-J.: Grundlagen zu BSE und anderen Prionenerkrankungen.

Medical association of the district Reutlingen, 03.03.01, BODEMER, W.: BSE – der aktuelle Stand.

CDU district Braunschweig, 12.03.01, KAUP, F.-J.: Grundlagen zu BSE und anderen Prionenerkrankungen.

Junge Union Neustadt/Rbge., 13.03.01, KAUP, F.-J.: Grundlagen zu BSE und anderen Prionenerkrankungen.

District association B90/Die Grünen Landkreis Eichsfeld, Leinefelde, 23.03.01, KAUP, F.-J.: Grundlagen zu BSE und anderen Prionenerkrankungen.

Biosensor Symposium, University Tübingen, 01.04.01, BODEMER, W.: Prionenerkrankungen von Mensch und Tier.

Bundesforschungsanstalt für Ernährung, Karlsruhe, 02.04.01, BODEMER, W.: Prionen, BSE und die neu aufgetretene variante Creutzfeldt-Jakob-Krankheit.

Agricultural conference of the district Northeim, Uslar, 04.04.01, KAUP, F.-J.: BSE und MKS: Hintergründe zu zwei Tierkrankheiten und Auswirkungen auf die deutsche Tierseuchenbekämpfung.

Messrs. Intervet International, Boxmeer, NL, 10.05.01, KAUP, F.-J.: Diagnostic electron microscopy: applications and limitations in infectious biology.

Environment committee of the city of Goslar, 16.05.01, KAUP, F.-J.: BSE im Überblick.

Veterinary faculty of the University Leipzig, 30.05.01, KAUP, F.-J.: Der Gastrointestinaltrakt als Zielorgan einer Infektion mit dem simiären Immundefizienzvirus (SIV).

TSE Co-ordinators meeting "Follow up the TSE Action Plan" of the European Commission DG Research, Brussels, B, 01.06.01, KAUP, F.-J.: Infectivity of blood components in experimental nvCJD: towards a risk assessment for human blood.

Ursulinengymnasium, Köln, 12.06.01, KAUP, F.-J.: Das Deutsche Primatenzentrum Göttingen – Arbeitsmöglichkeiten in der biomedizinischen Grundlagenforschung.

Lionsclub Celle, 02.08.01, KAUP, F.-J.: Biomedizinische Forschung an und mit Primaten: Das Deutsche Primatenzentrum und seine Aufgaben.

Academy for further education of veterinarians, Hannover, 27.09.01, KAUP, F.-J.: Primaten als Versuchstiere.

Dermatological clinic Dresden, medical further education, Dresden, 10.-11.10.01, BODEMER, W.: TSE – Epidemiologie und Diagnostik von TSE  
BODEMER, W.: Antikörper als Therapeutikum für Prionkrankheiten

Rural women's association, Neustadt/Rbge., 16.10.01, KAUP, F.-J.: BSE – Grundlagen und aktueller Kenntnisstand.

Students association Saxo-Silesia, Hannover, 06.11.01, KAUP, F.-J.: Wildkrankheiten als Biotopstörung.

DPZ-Colloquium, Göttingen, 05.12.01, BODEMER, W.: Die physiologische Rolle des Prionproteins.

Studium generale, Eberhard Karls University, Tübingen, 24.01.02, BODEMER, W.: BSE und andere Prionerkrankungen von Mensch und Tier: Ursache, Diagnose, Forschung.

Westphalian veterinarians working group "Diseases of pigs", Ibbenbüren, 25.04.02, KAUP, F.-J.: Die Normalstruktur der Darmbarriere.  
KAUP, F.-J.: Die Pathophysiologie der Diarrhoe.

Veterinary University, Vienna, A, 03.05.02, BODEMER, W.: Wirts- und erregerspezifische Komponenten der Prionerkrankungen.

Institute for Ethology, University Vienna, A, 06.05.02, BODEMER, W.: Übertragung und Pathomechanismen von Prionerkrankungen.

European Primate Expert Group Meeting "Animal Welfare", Göttingen, 07.05.02, KAUP, F.-J.: The keeping and breeding systems of the DPZ.  
KAUP, F.-J.: The tasks of the animal welfare officer according to the German Animal Welfare Act.

Tierärztliche Hochschule Hannover, 15.05.02, KAUP, F.-J.: Das Deutsche Primatenzentrum Göttingen: Forschung an, mit und für Primaten.

Doping conference, Bundesinstitut für Sportwissenschaften, Bonn, 10.07.02, BODEMER, W.: Transduktion mittels viraler Vektoren.

District Duchy Lauenburg, Ratzeburg, 06.09.02, KAUP, F.-J.: Wildkrankheiten und Wildbrethygiene.

11<sup>th</sup> Heiligenstadt Colloquium "Technische Systeme für Biotechnologie und Umwelt", Inst. für Bioprozesse und Analysetechnik, Heiligenstadt, 30.09.-02.12.02,

BODEMER, W.: Grenzen und Anwendungspotentiale der Chip-Technologie in der Molekularbiologie.

Robert-Koch-Institute, Berlin, 09.12.02, MÄTZ-RENSING, K.: Zoonotic risk of alpha herpesviruses.

Messrs. Covance, Münster, 21.11.02, FLOTO, A.: Zoonosen bei nicht menschlichen Primaten.

## **Publications**

### **Chapters in collected editions**

HUNSMANN, G., KAUP, F.-J.: The role of non-human primates for the development of an HIV/AIDS vaccine. In: SCHAUER, A.J., SCHREIBER, H.-L., RYN, Z., ANDRES, J. (eds.): Ethics in Medicine. Verlag Vandenhoeck & Ruprecht (2001).

### **Reviewed papers**

ASPER, M., HOFMANN, P., OSMANN, C., FUNK, J., METZGER, C., BRUNS, M., KAUP, F.-J., SCHMITZ, H., GÜNTHER, S.: First outbreak of callitrichid hepatitis in Germany: Genetic characterization of the causative lymphocytic choriomeningitis virus strains. *Virology* (2001) 284: 203-213.

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BODEMER, W., FLOTO, A., MÄTZ-RENSING, K., KAUP, F.-J.: Molecular assessment of gene expression in B-cell lymphoma of SIV infected rhesus monkeys (*Macaca mulatta*). An introduction. *Primate Report* (2002) 62: 61-68.

BODEMER, W., KAUP, F.-J.: Grundlagen zur Übertragbarkeit der BSE auf den Menschen. *Dtsch. Tierärztl. Wschr.* (2002) 109: 338-341.

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### Abstracts

BINGGER, K., MÄTZ-RENSING, K., HOFMANN, P., BRUNO, S.F., BOGA, J.A., KAUP, F.-J.: Morphological detection of SIV within tissue from SIV infected rhesus monkeys (*Macaca mulatta*). Folia Primatol. (2001) 72: 155.

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LOSS, M., VANGEROW, B., SCHMIDTKO, J., KUNZ, R., HECKER, J., SCHRÖDER, C., RUCKHOLT, H., KAUP, F.-J., SOIN, B., COZZI, E., PIEPENBROCK, S., KLEMPNAUER, J., WHITE, D. J., WINKLER, M.: Acute vascular rejection of h-DAF transgenic porcine kidneys in immunosuppressed cynomolgus monkeys is associated with systemic and intragraft complement activation. Transplant. Proc (2001) 33: 715.

*Veterinary Medicine and Primate Husbandry*

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<b>Publications</b>	<b>2002</b>	<b>2001</b>	<b>2000</b>
1. Books	0	0	0
2. Publications of collected editions	0	0	0
3. Chapters in collected editions	0	1	0
4. Reviewed papers	8	10	13
5. Non-reviewed papers	13	1	4
Total 1 - 5	<b>21</b>	<b>12</b>	<b>17</b>
6. Editorials	0	0	0
7. electronic publications	0	0	0
8. Abstracts	2	4	<b>8</b>
<b>Publications altogether</b>	<b>23</b>	<b>15</b>	<b>25</b>

**Other scientific activities**

**F.-J.Kaup**

- Diplomate of the European College of Veterinary Pathology.
- Diplomate of the European College of Laboratory Animal Medicine.
- Authorized to give further education to the specialist veterinarian for pathology.
- Consultant in support through official channels for different organisations and authorities.
- Consultant for the Deutsche Forschungsgemeinschaft (DFG).
- Editorial Board Journal of Veterinary Medicine B, referee for J. Med. Primatol., Verh. Erkr. Zootiere, Moll. Cell. Probes, Exp. Tox. Pathol.

**W. Bodemer**

- Consultant in BMBF-prion research networks.
- Member of the German TSE platform.
- Exploratory group of BSE-research in the ministries for science of Baden-Württemberg and Saxony-Anhalt.
- Consultant for the DFG and the Bundesinstitut für Sportwissenschaft.
- Referee for different scientific journals.

**Important activities and functions**

**F.-J. Kaup**

- Deputy in the absence of the director of the DPZ (01.03.-30.05.01).
- Since 05.12.01 deputy of the director of the DPZ
- Secretary of the primatological society.

- Deputy member of the commission for the protection of animals of the Bezirksregierung Braunschweig.
- Animal welfare officer of the DPZ and animal welfare expert of the primatological society.
- DPZ officer for the prevention of infections.
- Member of the Lower Saxonian Chamber of Veterinarians, 13<sup>th</sup> elective period: board member and member in the committee for animal welfare.
- Committee for experimental animals of the Federal Chamber of Veterinarians.
- Member of the Managing Board European Primate Resources Network (EUPREN).

**S. Rensing**

- German representative of the European Marmoset Research Group (EMRG).

**U. Schönmann**

- Representative of the EFAT (European Association of Animal Technology) in the European Primate Group (PEG).

**A. Husung**

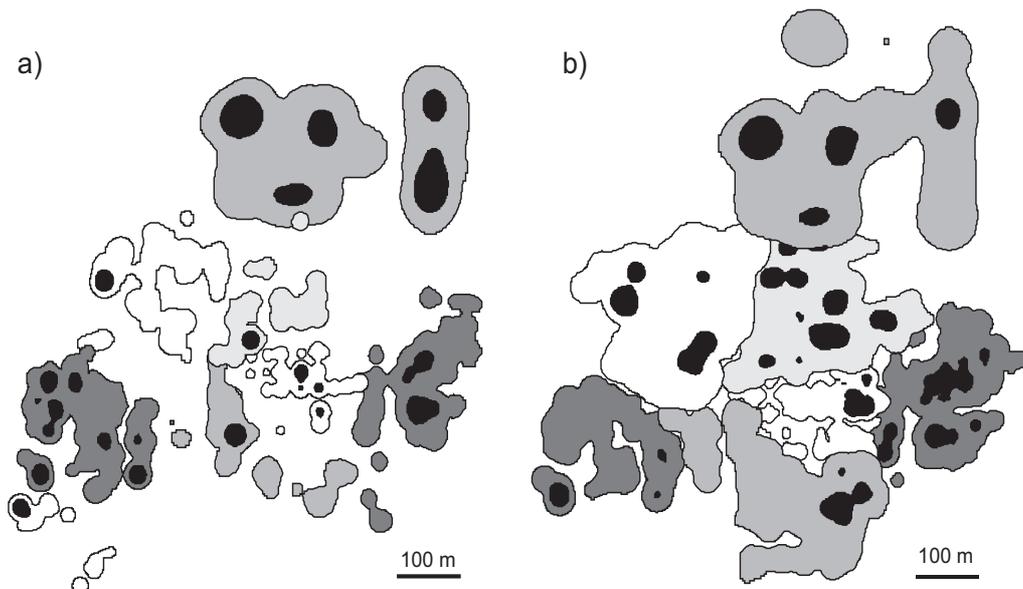
- Board member of the interest group of the animal keepers in the Society for Laboratory Animals (IGtP-GV Solas).

**DEPARTMENT OF ETHOLOGY AND ECOLOGY**

**Head of Department:** PD Dr. Peter M. Kappeler

**General research objectives**

Within the broad fields of behavior and ecology, the current research activities of our department focus on two central topics: primate social systems and community ecology. We conduct comparative field studies on these topics with lemurs in Madagascar and tamarins in Peru. Field projects are multidisciplinary and involve internal and external collaborations to examine behavioral, endocrinological and genetic questions. By addressing similar questions in these different projects within a common theoretical framework, we create a platform for identifying basic processes and mechanisms underlying the evolution of primate behavior and ecology. Together with theoretical analyses, our results are being used to test hypotheses on the evolution of primate communities and to develop recommendations for conservation projects.



*Kernel projection (95 % probability; black: 50 % probability) of home ranges of a) adult female and b) adult male fork-marked lemurs (*Phaner furcifer*) from June 1999 to August 2000. Home-range outlines of single males overlap well with those of one single female each which implies that fork-marked lemurs live in pairs. From Schülke & Kappeler (2003) *Anim. Behav.* 65: 331-343.*

**Structure of the department**

At the end of the reporting period, the department consisted of the provisional head of the department, two scientists, one doctoral student supported by DPZ,

seven doctoral students supported through external grants, and one technical assistant. The field sites in Madagascar and Peru are being operated by a total of three local doctoral students.

Scientists

PD Dr. Eckhard W. Heymann  
Dr. Dietmar Zinner

Marcos Roland Oversluijs Vasquez

Jenni Perez Yamacita  
Tina Plasil

Technicians

Ulrike Walbaum

Veromaritra Raharimanantsoa

Romule Rakotondravony

Odon Rakotonirainy

Emilienne Rasoazanabary

David Rasolofoson

PhD Students

Manfred Eberle

Tina Fredsted

Roland Hilgartner

Maren Huck

Iris Leinfelder

Petra Löttker

Britta Müller

Julia Ostner

Léonard Razafimanantsoa

Oliver Schülke

Trainees

Toralf Borchert

Georgia Erdmann

Isabel Formella

Barbara Kremeyer

Jennifer Kröger

Angelika Oppelt

Alicia Pérez-Melis

Maribel Recharte Uscamaita

Michaela Rentsch

Livia Schäffler

Friederike Scholz

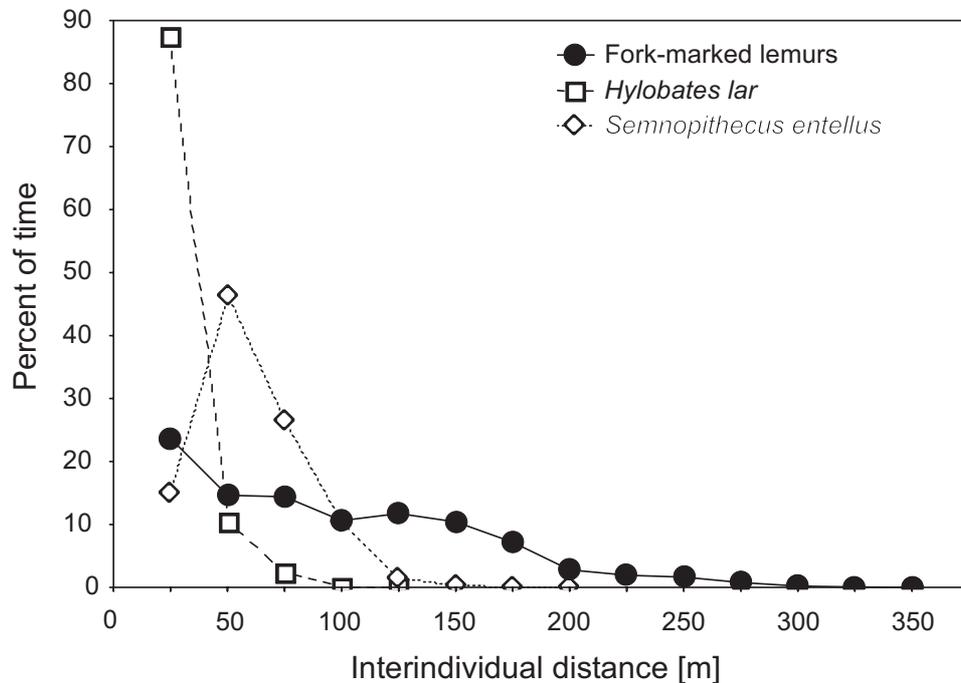
Sabine Schulze

Cécilia Wentrup

Tine Wiedemann

**Progress during the year**

As in the preceding two years, work of the department was characterized by the uncertainties for planning with regard to the head of the department, e.g., through the appointment to the C3-professorship for Behavioral Ecology and the University of Leipzig received by the provisional head of the department. This uncertainty is particularly detrimental for the planning of long-term field projects, but should be resolved in the foreseeable future through the advertisements in 2002 for the heads of the Ethology and Ecology, and Sociobiology and Anthropology, respectively. The scientific highlight of the reporting period was the 3<sup>rd</sup> Göttinger Freiländertage in December 2001, which addressed the topic of sexual selection in primates. This now well-established international conference once again attracted more than 200 participants and strengthened DPZ's image as a European center for organismic primate biology. A book with selected congress contributions is in press at Cambridge University Press; the proceedings of the 2<sup>nd</sup> Göttinger Freiländertage have been published in the meantime by the University of Chicago Press. Another scientific highlight was the 5<sup>th</sup> Kirindy-Symposium in August 2002, where more than 50 users of the field station in Madagascar discussed the results of the research.

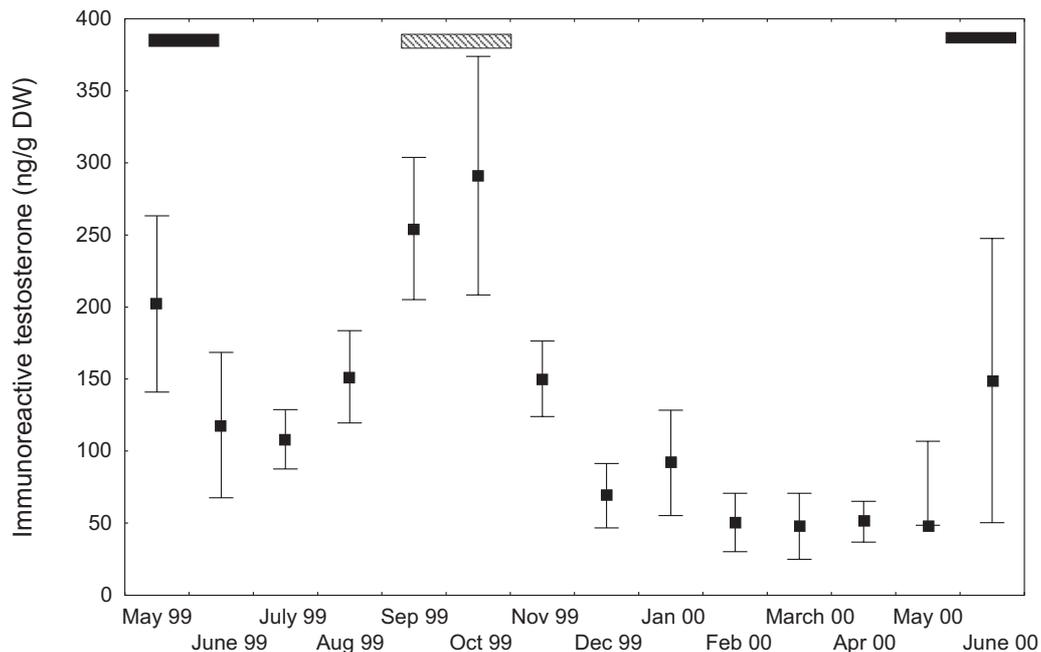


*Cohesiveness between pair-partners during regular activities. Comparison of fork-marked lemur (*Phaner furcifer*) pairs with gibbon (*Hylobates lar*) pairs and the most distant members of a Hanuman langur (*Semnopithecus entellus*) group; all distance classes contain a 25 m range (e.g. 25: 0–25 m, 50: 25–50 m). While gibbon pair-partners spend about 80 % of their time LESS than 25 m from each other, fork-marked lemur males and females spend about 80 % of their time MORE than 25 m from one another. The cohesive pairs of gibbons are now differentiated from the dispersed pairs of fork-marked lemurs to account for the variation in cohesiveness among pair-living primates. From Schülke & Kappeler (2003) *Anim. Behav.* 65: 331-343.*

The scientific work of the members of the department was characterized by a number of intensive internal co-operations. These co-operative projects were highly successful in attracting external grants and thus underline the importance of the accumulation of primatological know-how at DPZ. This competence was also illustrated by the election of the provisional head of the department as president of the Gesellschaft für Primatologie and of the European Federation for Primatology.

Field work in Madagascar has been hampered by several months of political instability. However, due to the enthusiasm of Dr. Rodin Rasoloarison, Léonard Razafimanantsoa and our field assistants, the basic field work could be continued uninterrupted. Since the summer of 2002, our activities in Madagascar take place within the framework of a second collaboration treaty with Prof. Dr. Daniel Rakotondravony at the Département Biologie Animale of the University of Antananarivo. The temporary political instability in Madagascar also led to local problems with illegal logging within the Kirindy forestry concession. In response, several governmental

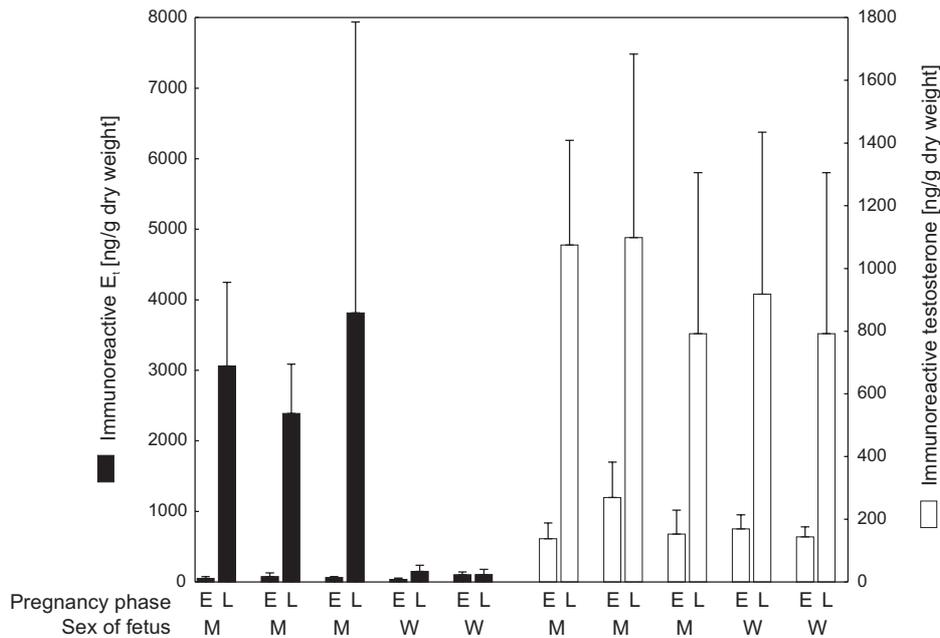
and non-governmental institutions and organizations, including the DPZ, formed a local *Platfôrme pour la conservation du Menabe* whose activities contributed to the reduction of illegal activities and the development of sustainable conservation and development perspectives for the region and its people. In this context, the DPZ also established contacts with German governmental agencies to explore possibilities for potential German development projects in the region.



*Seasonal variation of fecal androgen excretion of six redfronted lemur males over 14 months. As expected for a seasonal breeding species androgen excretion was significantly elevated during the mating season in May - June (black bars). However, birth season values (hatched bar) even exceeded those from the mating season. The possibility of infanticide may promote elevated androgen levels in males as a means of supporting aggressive behavior against infanticidal males. From Ostner, J., Kappeler, P.M. & Heistermann, M. *Behav. Ecol. Sociobiol.* 52: 485-495, 2002.*

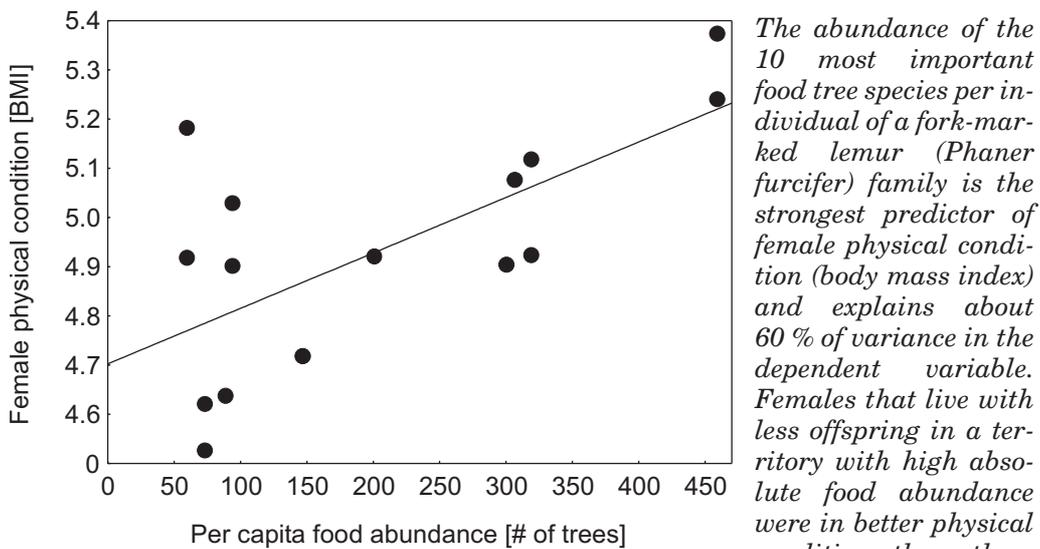
To increase and intensify our conservation activities in the Menabe region, DPZ has also established a strategic partnership with Durrell Wildlife. This British NGO has a strong tradition in species conservation and extensive experience in the Menabe region, so that our areas of expertise mutually complement each other. The conservation efforts in the region were further enhanced by the first field course of the Tropical Biology Association (TBA, Cambridge) in Madagascar, conducted in Kirindy in November 2002. This course introduced 20 European and African students to the ecology of this fragile dry forest ecosystem. Support from the TBA was used to improve the camp infrastructure. In addition, establishment of a third grid system was initiated in 2002, which will further enhance the logistical capacities of our Malagasy field station.

Scientific work in Kirindy was dominated by four doctoral dissertation projects and the associated diploma thesis and trainee work. In December 2002 Julia Ostner turned in her DFG-funded PhD thesis "Sex-specific reproductive strategies of red-fronted lemurs (*Eulemur fulvus rufus*, Lemuridae, Primates)" at the University of Würzburg. In cooperation with the Department of Reproductive Biology Julia Ostner investigated reproductive strategies of this group-living Malagasy lemur using a combination of detailed behavioral observations with non-invasive endocrine analyses from feces samples. Characterization of ovarian cycles was not possible, however, because of a high day-to-day variability in excreted hormones, which is probably caused by ecological factors. Nevertheless, the study provided reliable information on gestation and cycle length as well as endocrine changes associated with gestation. Additionally, a method for prenatal sex determination was established using maternal fecal samples collected during late gestation. Analysis of the seasonal variation in male androgen excretion revealed an increase in androgen levels during the mating season, as expected for a seasonal breeding primate. However, highest levels were obtained during the birth season, which may be part of a male



*Fecal estrogen excretion in redfronted lemur females during the late phase of gestation is strongly correlated with the sex of the fetus. Females carrying a male fetus show a 30-60 fold increase in estrogen levels until birth whereas levels of female-carrying mothers remain at baseline levels. In contrast, levels of excreted androgens are similar in all females irrespective of fetal sex. These results allow non-invasive prenatal sex determination in redfronted lemurs and may have important implications for the evolution of genital masculinization and female dominance in lemurs. From: Ostner, J., Heistermann, M. & Kappeler, P.M. Naturwiss. in press.*

strategy to remain aggressive during this period of high infanticide risk by non-resident males. Dominant and subordinate males did not differ in their androgen excretion, indicating that dominant males did not suppress the endocrine function of subordinate rivals. Red-fronted lemurs live in groups with an even adult sex ratio, which is unexpected considering that males compete over access to mates. While females derive benefits from a high number of co-resident males, males should generally try to monopolize access to a group of females and expel rival males from the group. Analysis of demographic data collected between 1996 and 2002 re-



*The abundance of the 10 most important food tree species per individual of a fork-marked lemur (Phaner furcifer) family is the strongest predictor of female physical condition (body mass index) and explains about 60 % of variance in the dependent variable. Females that live with less offspring in a territory with high absolute food abundance were in better physical condition than those living with many off-*

*spring in poor or small territories. These data are the first to show a strong group size effect on female physical condition in a pair-living primate.*

vealed that birth and mortality rates were not sex-biased and that males migrated considerably more frequently than females, providing no proximate explanation for the unusual sex ratio. Females in this study may proximately regulate group composition by synchronizing their fertile periods, which was inferred indirectly from the temporal distribution of births within groups. Both males and females benefit from a high number of co-resident males because the number of males per group is the main predictor of takeover rate and, thus, infanticide risk. Because males and females both benefit from a high number of males the conflict of interest between the sexes is considerably defused in this species. In this study the feasibility of non-invasive hormone analyses in red-fronted lemurs was tested, sex-specific reproductive strategies were investigated and causes for the unusual, even sex ratio were provided.

The project "Socioecology of the fork-marked lemur" funded by the DPZ and conducted in co-operation with the working group Primate Genetics was finished when Oliver Schülke turned in his dissertation thesis "Living apart together – Patterns, ecological basis, and reproductive consequences of life in dispersed pairs of fork-

marked lemurs (*Phaner furcifer*, Primates)" at the University of Würzburg in December 2002. Cohesiveness between members of a social unit is a defining characteristic of animal social organization. Dispersed social organizations, where members of a social unit spend the main part of their activity period apart, have only recently been distinguished from cohesive social organizations and are still poorly understood with respect to their ecological basis and reproductive consequences. The ecological settings determine the mode of food competition within and between social units and have shaped the social system of fork-marked lemurs in several ways. Intense within-group competition for food (scramble and contest) may have ultimately led to female intra-sexual avoidance and range exclusivity which represents an evolutionary precursor of pair-living. Although why females ultimately associate with single males remains elusive, patterns of within-group contest competition for food can explain why pair partners avoid each other during nocturnal activity and spend 75 % of their time more than 25 m apart. The limited number of food resources (mainly *Terminalia* tree exudates) that is used in repetitive fashion and incomplete knowledge about the pair partners position explain why pair partners meet relatively often and why most encounters involve agonistic conflict. Rigid feeding itineraries characteristic of exudate feeders are likely to pose high costs to offspring dispersing to unfamiliar areas. Feeding ecology can, therefore, also explain why parents tolerate delayed natal dispersal despite a negative group size effect on actual female reproductive success. Dispersed social organization in itself, i.e. low cohesion between pair partners, cannot explain the high incidence of high extra-pair paternity found. It has been proposed instead that several other factors common to most primates living in dispersed pairs constrain mate guarding and lead to high EPP. In conclusion, the present study successfully applied existing socio-ecological theory to a new area of research, refined a recent evolutionary model and contributed important comparative data to our understanding of dispersed pairs in particular and primate and animal societies in general.

The main aim of the study of Manfred Eberle on reproductive strategies in gray mouse lemurs was to establish detailed knowledge of their social organization and their mating and breeding behavior in order to test predictions about their mating and breeding system. Gray mouse lemurs are nocturnal solitary foragers with extensively overlapping home ranges among and between sexes. In Kirindy Forest their mating system is characterized by seasonally, but asynchronously receptive females, with matings annually limited to a four week period when each female becomes receptive only for a few hours during a single night. They show a seasonally fluctuating dimorphism in body mass and males have relatively large testes. These traits suggest, according to sexual selection theory, pronounced scramble and weak contest competition. During the day males mostly sleep alone whereas females usually form sleeping groups of variable size, giving the potential for cooperative breeding.

Over 300 animals were trapped regularly and individually marked and in a cooperation with the working group Primate Genetics genetic relationships between all animals were determined precisely. Most males in the study area were immigrants whereas all females were native and formed stable groups of closely related animals. During the brief mating season, males regularly encountered pre-estrous females and up to 12 males were observed in the vicinity of receptive females. In to-

tal, 98 matings were observed. Females mated with 1-7 males up to 11 times without exhibiting any obvious mate choice. Most males applied mating plugs. After matings, however, females either escaped into the vegetation or into a tree hole. Females staying less time in shelters mated with more, different males. Females in tree holes were guarded successively by 1-7 males between 1 and 11h. Guarding males were regularly harassed by other males and either aggressively chased rivals among successfully or were displaced by them. As a result most litters had multiple paternity (17/26) but, age, absolute body weight and relative mating time predicted male reproductive success. This effect of relative mating time could also be confirmed in mating experiments, carried out in the course of a cooperation with Martine Perret, Laboratoire d'Ecologie Générale, CNRS, Paris, France. Thus, the mating system of this species is indeed characterized by scramble competition polygyny but, in contradiction to the morphological evidence, males are able to aggressively monopolize access to females. Male monopolization potential, however, largely depends on female behavior. Most males in the study area were immigrants whereas all females were native and formed stable groups of closely related animals. To determine whether females in a sleeping group cooperate in infant rearing, five breeding groups of 2-3 females were filmed inside their nests with infrared equipment for a total of 410 h. All



*Female mouse lemur carrying an infant to a new sleeping site. Female mouse lemurs transport exclusively their own offspring. They form, however, stable sleeping groups of closely related females and regularly nurse and groom all pups of such a group.  
(Photo: Manfred Eberle).*

females within a breeding group gave birth and regularly groomed offspring other than their own. Allonursing could be filmed in three groups. However, females carried only their own offspring between nest sites, demonstrating their discrimination ability. In three groups, females successfully adopted young of relatives who had died before weaning their offspring. This study could show for the first time that (1) males have a mixed mating strategy and, (2) closely related females form groups in which they rear their young cooperatively.

The objectives of the study of red-tailed sportive lemurs (*Lepilemur ruficaudatus*) by Dr. Dietmar Zinner and Roland Hilgartner can be looked at on three increasing geographical scales. On the first level, the genetical population structure and the so-

cial and mating systems of *Lepilemur ruficaudatus* in the Kirindy Forest will be analyzed. This part of the project constitutes the doctoral thesis of Roland Hilgartner and is funded by the DFG. The focus population of this first part will be then used as a baseline in a subsequent comparative study on a broader geographical scale. On this level, we will concentrate on the genetic (phylo-geographical) relationships among populations of sportive lemurs in central western Madagascar between the Bemaraha reserve in the North and the Onalivy river in the South. On the third level we will investigate the phylo-geographical relations of populations of red-tailed sportive lemurs with populations of other sportive lemur taxa. By the end of 2002, 62 individuals of red-tailed sportive lemurs had been caught in- and outside the main research area in the Kirindy Forest. Tissue samples from all of these individuals are available for subsequent genetical analyses. 28 individuals within the focus area have been equipped with radio collars. These animals have been radio-tracked and systematically observed since May 2001 by R. Hilgartner.

Finally, two new studies on mouse lemurs and fat-tailed lemurs have started during the last two years in Kirindy: Melanie Dammhahn started her master's thesis with the first study on the social system of the smallest living primate, the pygmy mouse lemur (*Microcebus berthae*), still known only in Kirindy. The study was founded by the Christian-Vogel Fonds of the Gesellschaft für Primatologie. Tina Fredsted, funded by the Danish government, started her PhD thesis on the impact of mating systems on the genetic structure of populations of mouse lemurs and fat-tailed lemurs.

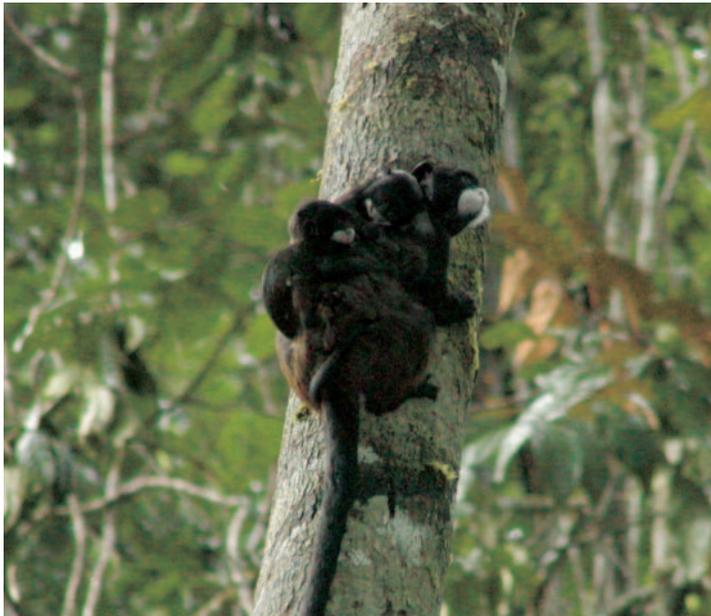
The project on population genetics of hamadryas baboons in Eritrea was extended into a project on the phylo-geography of baboons. This project was funded by the DFG. Collection of samples is completed and a total of 357 feces and tissue samples of *Papio* have now been included in the analysis. Samples stem from Eritrea, Ethiopia, Tanzania, Guinea, Ivory Coast, Nigeria, Malawi und Saudi Arabia. The collection of samples was made possibly through a network of international collaborations. From the samples, we have successfully extracted 310 mitochondrial DNA sequences (D-loop, Hyp I and Cytb). The retrieved sequence information will be used for phylogenetical reconstructions and for an analysis of the phylo-geographical re-



*What are the evolutionary causes and mechanisms which lead to the exaggeration of sexual swellings in females of many Old World primate species?*

relationships within the genus *Papio*. A second part of the baboon project was completed with the doctoral thesis of Iris Leinfelder from the University of Antwerp. She did her thesis in the Antwerp Zoo on female – female relationships in hamadryas baboons. With this thesis she laid the basis for another ongoing doctoral thesis including free-ranging baboons in Eritrea. Rebecca Deleu from the University of Antwerp is continuing with this project for her doctoral thesis. She carried out a pilot study in Eritrea in 2001 and went back to Eritrea in December 2002 for a longer time period.

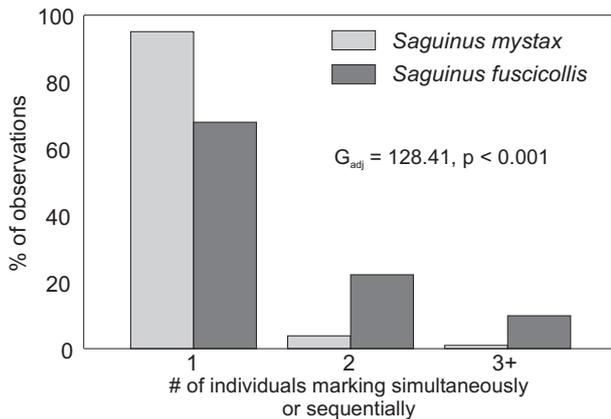
As in the previous reporting period, research at the field site in Peru was mainly carried out within the framework of internal co-operations. In December 2001, Maren Huck and Petra Löttker concluded their 15-month field phase of the DFG-funded project on the proximate regulation and genetic consequences of the mating system of moustached tamarins, *Saguinus mystax* (co-operation: Department Ethology and Ecology, Department Reproductive Biology, Working Group Primate Genetics). The background of this project is the polyandrous mating system of tamarins,



*Adult male moustached tamarin (Saguinus mystax) carrying 4 week old twins. Twin births are the rule in all callitrichids (except Goeldi's monkey, Callimico goeldii), and adult males contribute to infant care through carrying and food sharing. In tamarins, adult males are the principal carriers of infants. (Foto: J. Diegmann)*

which is unique amongst primates. In such a system, a single adult female monopolizes reproduction in a group, but usually mates with more than one adult male. Furthermore, males are the principal caregivers for infants (except for lactation). So far, the role of genetic relationships between group members and the consequences of mating with multiple males for paternity as well as the regulation of reproductive monopolization by a single female are unknown. Therefore, detailed behavioral data on social and sexual interactions and on infant care, and fecal samples for genetic and hormonal analyses were collected during the field phase of the project. In the subsequent laboratory phase, genetic analyses were carried out. Thus, for the first

time data are available on genetic relationships and paternities from wild tamarins. Within the framework of this project, a Peruvian undergraduate student from the Universidad Nacional de la Amazonía Peruana (UNAP) in Iquitos collected data on the vigilance behavior.



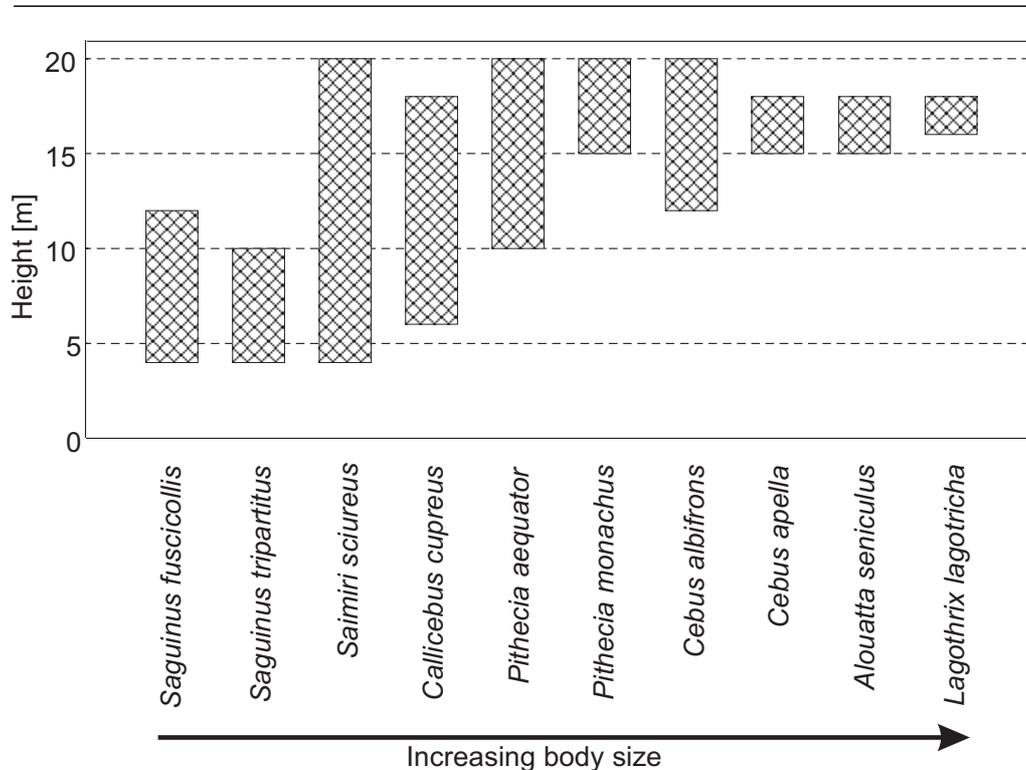
*Olfactory communication plays an important role in the social life of callitrichids. Our studies on moustached and saddle-back tamarins (*Saguinus mystax* und *Saguinus fuscicollis*) were the first systematic field studies on this behavioral complex. The two species differ substantially in the structure of their scent-marking behavior. In saddle-back tamarins two or more individuals scent mark simultaneously or sequentially at the same place much more often than moustached tamarins.* From Heymann (2001) *Folia Primatol* 72: 253-267.

*taneously or sequentially at the same place much more often than moustached tamarins. From Heymann (2001) Folia Primatol 72: 253-267.*

Janna Kirchhof continued her studies on the role of alarm calls in interspecific associations of moustached and saddle-back tamarins (co-operation: Department Neurobiology, Department Ethology and Ecology) and worked at the field station in Peru for two more field phases. Apart from recording the spontaneous reactions and vocalizations of tamarins in the presence of predators, she also carried out experiments by presenting playback of alarm calls and predator models (snake, ocelot), and documented the tamarins' responses on video for later detailed analyses. The aim is to investigate whether tamarin alarm calls are referential signals or whether the code "response urgency" and whether the two tamarin species differ in this respect. Furthermore, the project examines whether the alarm behavior in general is similar or different in the two tamarin species which live in stable mixed-species troops.

In May 2002, Britta Müller started the field work for the project "Comparative ecological-parasitological study of moustached and saddle-back tamarins" (cooperation: Department of Ethology and Ecology, Department of Veterinary Medicine and Primate Husbandry). As in other projects, detailed behavioral studies are combined with non-invasive sample collection (fecal samples). The aim of this project is to examine the influence of niche segregation (differential use of micro-habitats, different prey components) between the tamarin species on the spectrum of endoparasites. A grant from the DFG made it possible to include a third primate species, red titi monkeys, *Callicebus cupreus*, in the study. This will allow us to separate ecological factors from phylogenetic factors. The observations on the red titi monkeys are mainly carried out by a Peruvian undergraduate student, who also collects basic data on the ecology of this little known primate species.

*Ethology and Ecology*



*Body size and differential height use are structuring factors for neotropical primate communities. With increasing body size, species prefer higher strata of the rain forest for their activities. From Heymann & Canaquin (2002) Int J Primatol 23:191-201.*

The studies of olfactory communication in tamarins were preliminarily concluded through a comparative analysis of interspecific differences in scent-marking behavior of moustached and saddle-back tamarins. With these studies, this aspect of behavior was examined systematically for the first time in wild tamarins. It became clear that considerable interspecific differences exist in the structure of scent-marking behavior, which is most likely associated with hitherto unknown subtle differences in social organization and mating patterns.

In the studies of neotropical primate communities, additional evidence was obtained for the role of body size as a structuring factor. With increasing body size, higher strata of the rainforest are preferred for activities. For species living on the same trophic level, such differences can be critical for the avoidance or reduction of interspecific competition.

Supported by a grant from the Margot Marsh Biodiversity Foundation, the field station in Peru was expanded and intensively used for the training of students. Within the framework of two field courses in 2001 and 2002, which were supported by the Margot Marsh Biodiversity Foundation, the German Academic Exchange Service (DAAD) and the Förderkreis des Deutschen Primatenzentrums, Dr. Eck-

hard W. Heymann trained German and Peruvian students in the foundations of field work on primate biology and tropical ecology. A number of German and Peruvian trainees stayed at the field site for several weeks to several months. Furthermore, the field site was used by visiting scientists from the USA.

### **Integration into national and international research**

Research by members from the Department Ethology and Ecology is not only strongly linked with other departments within DPZ through internal co-operations, but also characterized by a number of bi- and multi-lateral national and international co-operations. These co-operations are listed in the following table.

### **Projects and partners in co-operation**

(I: interdepartmental projects, E: external co-operation; A: project completed, L: current project)

<b>Projects and Partners of the Department of Ethology and Ecology</b>		
<b>Conservation biology of Malagasy lemurs and New World monkeys</b> B. RAKOTOSAMIMANANA, D. RAKOTONDRAVONY (Univ. Antananarivo, Madagascar), J.U. GANZHORN (Inst. of Zoology, Univ. Hamburg), S. GOODMAN (FMNH Chicago & WWF Madagascar), J. DURBIN (Durrell Wildlife, GB), F. ENCARNACIÓN (Univ. Nacional Mayos San Marcos, Lima, Peru), H. VALDERRAMA FREYRE, R. PEZO (Univ. Nacional Amazonia Peruana, Iquitos, Peru), J.K. HODGES ( Dept. of Reproductive Biology, DPZ), H. ZISCHLER, A. HAPKE, C. ROOS (Working Group Primate Genetics, DPZ), <b>P.M. KAPPELER, E.W. HEYMANN, D. ZINNER</b>	E,I	L
<b>Social organization of red-tailed sportive lemurs</b> <b>P.M. KAPPELER, D. ZINNER, R. HILGARTENER</b>		L
<b>Sexual selection in female primates</b> <b>D. ZINNER</b> , C. NUNN (Univ. of California, Davis, CA, USA), D. STAHL (MPI for Evolutionary Anthropology, Leipzig)	E	L
<b>Phylo-geography of <i>Papio</i></b> <b>D. ZINNER</b> , H. ZISCHLER, A. HAPKE, C. ROOS (Working Group Primate Genetics, DPZ)	I	L
<b>Structure of neotropical primate communities</b> <b>E.W. HEYMANN</b> , J.U. GANZHORN (Inst. of Zoology, Univ. Hamburg)	E	L

<b>Projects and Partners of the Department of Ethology and Ecology</b>		
<p><b>Taxonomy and biogeography of Cheirogaleidae</b></p> <p>R. RASOLOARISON (Univ. Antananarivo, Madagascar), S. GOODMAN (FMNH Chicago &amp; WWF Madagascar), A. YODER (Northwestern Univ., USA), J.U. GANZHORN (Inst. of Zoology, Univ. Hamburg), H. ZISCHLER, A. HAPKE, C. ROOS (Working Group Primate Genetics, DPZ), <b>P.M. KAPPELER</b></p>	E,I	L
<p><b>Feeding ecology and seed dispersal by sympatric tamarins</b></p> <p>C. SMITH (Univ. Stirling, GB), C. KNOGGE (free lance collaborator), E.R. TIRADO HERRERA (Facultad de Biología, Univ. Nacional Amazonía Peruana, Iquitos, Peru), <b>E.W. HEYMANN</b></p>	E	L
<p><b>Socio-endocrinology of group-living lemurs</b></p> <p>M. HEISTERMANN, J.K. HODGES (Dept. of Reproductive Biology, DPZ), <b>J. OSTNER, P.M. KAPPELER</b></p>	I	A
<p><b>Adaptation of visual systems in diurnal and nocturnal primates</b></p> <p>L. PEICHL (MPI for Brain Research, Frankfurt), A. RANDRIANJAFY (Parc Botanique et Zoologique de Tsimbazaza, Madagascar), H.M. BUCHANAN-SMITH (Univ. Stirling, GB), N. MUNDY (Univ. Oxford, GB), <b>P.M. KAPPELER, E.W. HEYMANN</b></p>	E	L
<p><b>Genetic analysis of lemur mating systems</b></p> <p>D. TAUTZ (Univ. Köln), H. ZISCHLER, A. HAPKE (Working Group Primate Genetics, DPZ), <b>M. EBERLE, O. SCHÜLKE, B. WIMMER, D. ZINNER, P.M. KAPPELER</b></p>	E,I	L
<p><b>Proximate regulation and genetic consequences of the mating system of polyandrous tamarins</b></p> <p>M. HEISTERMANN, J.K. HODGES (Dept. of Reproductive Biology, DPZ), U.-R. BÖHLE, C. SCHWIEGK (Working Group Primate Genetics, DPZ), <b>P. LÖTTKER, M. HUCK, E.W. HEYMANN</b></p>	I	L
<p><b>Female-female relationships among hamadryas baboons in Eritrea</b></p> <p><b>D. ZINNER</b>, F. PELÁEZ (Univ. Autónoma Madrid, E), I. LEINFELDER, R. DELEU (Univ. Antwerp, RUCA, B), J. SHOSHANI (Dept. of Biology, Univ. Asmara, Eritrea)</p>	E	L
<p><b>Comparative aspects of lemur socio-ecology</b></p> <p>M. PERRET (MNHN, Laboratoire d'Ecologie, Brunoy, F), H. ERKERT (Univ. Tübingen), C. DIRAC (Univ. Neuchatel, CH), <b>M. EBERLE, R. HILGARTNER, P.M. KAPPELER, J. OSTNER, O. SCHÜLKE, D. ZINNER</b>, H. ZISCHLER, A. HAPKE, C. ROOS (Working Group Primate Genetics, DPZ)</p>	E,I	L

<b>Projects and Partners of the Department of Ethology and Ecology</b>		
<b>Acoustic communication in lemurs</b> C. FICHTEL, K. HAMMERSCHMIDT (Dept. of Neurobiology, DPZ), <b>P.M. KAPPELER</b>	I	A
<b>Predator avoidance of tamarins: function of alarm calls and their employment in polyspecific associations</b> J. KIRCHOF, K. HAMMERSCHMIDT (Dept. of Neurobiology, DPZ), <b>E.W. HEYMANN</b>	I	L
<b>Lemur population biology and genetics</b> T. FREDSTED, J. OLESEN (Univ. Aarhus, DK), J.U. GANZHORN (Inst. of Zoology, Univ. Hamburg), C. ROOS, A. HAPKE, H. ZISCHLER (Working Group Primate Genetics, DPZ), <b>M. EBERLE, P.M. KAPPELER</b>	E,I	L
<b>Behavioral ecology and evolution of interspecific associations in callitrichids</b> H.M. BUCHANAN-SMITH (Univ. Stirling, GB), <b>E.W. HEYMANN</b>	E	L
<b>Phylogeny of New World primates</b> S. SINGER, H. ZISCHLER (Working Group Primate Genetics, DPZ), <b>E.W. HEYMANN</b>	I	L
<b>Comparative ecological-parasitological studies of sympatric New World primates</b> K. MÄTZ-RENSING (Dept. of Veterinary Medicine and Primate Husbandry, DPZ), C. EPE (School of Veterinary Medicine Hannover), <b>B. MÜLLER, E.W. HEYMANN</b>	E,I	L
<b>Geographic distribution and taxonomic status of tamarins</b> A.B. Rylands (Conservation International, Washington, USA), <b>E.W. HEYMANN</b>	E	L
<b>Social evolution of primates: sexual selection and life history</b> C.P. VAN SCHAIK (Duke Univ., USA), T. BIRKHEAD (Univ. Sheffield, GB), A.P. MOLLER (Univ. Paris, F), P. LEE (Cambridge Univ., GB), <b>P.M. KAPPELER</b>	E	L

**Stays of DPZ scientists in other institutions**

<b>Name/Institute/Duration</b>	<b>Project</b>
Manfred Eberle Laboratoire d'Ecologie Générale, CNRS, Paris, F 30.07.-20.08.01	Sperm competition in gray mouse lemurs ( <i>Microcebus murinus</i> )

Visited institution	Duration of stay (2001/2002)		
	< 1 month	1 - 3 months	> 3 month
German universities, research or service institutions	0	0	0
European universities, research or service institutions	1	0	0
Universities, research or service institutions outside Europe	0	0	0
<b>Altogether</b>	<b>1</b>	<b>0</b>	<b>0</b>

### Scientific Contributions

#### Doctoral thesis

LEINFELDER, I.: The social life of hamadryas baboons in captivity: female subtlety in response to male conspicuousness. Faculteit Wetenschappen, Universiteit Antwerpen (2001).

#### Diploma theses

BRAND, S.: Social behavior and olfactory communication in family groups of white-faced sakis (*Pithecia pithecia pithecia*). University of Göttingen (2002).

HILGARTNER, R.: Vigilance behavior of free-ranging red-fronted lemurs (*Eulemur fulvus rufus*). University of Ulm (2001).

RAHARIMANANTSOA, V.: Etude comparative de la communication olfactive entre les sexes et entre les groupes chez *Eulemur fulvus rufus*. Département de Paléontologie & Anthropologie Biologique, Université d'Antananarivo, Madagascar (2001).

RAKOTONIRAINY, O.: Etude de la prédation entre *Mirza coquereli* et *Microcebus murinus* dans la forêt dense sèche de Kirindy. Département de Paléontologie & Anthropologie Biologique, Université d'Antananarivo, Madagascar (2002).

RASOAZANABARY, E.: Stratégie adaptative chez les males de *Microcebus murinus* pendant la saison sèche, dans la forêt de Kirindy, Morondava. Département de Paléontologie & Anthropologie Biologique, Université d'Antananarivo, Madagascar (2001).

RASOLOFOSON, D.: Stratégies anti-predatrices de l'*Eulemur fulvus rufus* dans la forêt de Kirindy, Morondava. Département de Paléontologie & Anthropologie Biologique, Université d'Antananarivo, Madagascar (2002).

**Congress contributions**

XVIII<sup>th</sup> Congress of the International Primatological Society, Adelaide, Australien, 07.-12.01.01,

LEE, P.C., KAPPELER, P.M.: Phenotypic plasticity in primate life histories: comparative analyses of social and ecological influences.

SCHMID, J., KAPPELER, P.M.: Physiological adaptations to seasonality in nocturnal prosimians.

14<sup>th</sup> Annual Meeting of the Society of Tropical Ecology, Bremen, 13.-16.02.01, HEYMANN, E.W., FELDMANN, M.: Tamarin seed dispersal influences the natural regeneration of *Parkia panurensis*.

Annual Meeting of the Association in Vision and Ophthalmology (ARVO), Ft. Lauderdale, FL, USA, 29.04.-04.05.01, PEICHL, L., RAKOTONDRAPARANY, F., KAPPELER, P.M.: Photoreceptor types and distributions in nocturnal and diurnal Malagasy lemurs.

Seminario Etología de Primates, Universidad International Menéndez Pelayo, Valencia, E, 25.-29.06.01, PELÁEZ, F., ZINNER, D.: Distribution and habitat of primates in Eritrea.

28<sup>th</sup> Göttinger Neurobiologen Tagung, Göttingen, 07.-10.07.01, PEICHL, L., RAKOTONDRAPARANY, F., KAPPELER, P.M.: Photoreceptor types and distributions in nocturnal and diurnal Malagasy primates.

8<sup>th</sup> International Theriological Congress, Sun City, South Africa, 12.-17.08.01, SHOSHANI, J., HUTTERER, R., LAGERLOF, J., ZINNER, D., SHANKARAIAH, K.: Small mammals recovered from barn owl pellets, Asmara, Eritrea.

SHOSHANI, J., MEDHANIE, G., TESFAMICHAEL, E., GHEBRU, M.W., TEWODROS, W., GHEBREAB, W., BERAKHI, O., YOHANNES, H., YOHANNES, Y., ZINNER, D.: Biogeography in Eritrea: observations toward testing an ecotonal hypothesis.

Workshop "Monogamy – Partnerships in birds, humans and other mammals", MPI for Evolutionary Anthropology, Leipzig, 14.-18.08.01,

HEYMANN, E.W.: Monogamy in New World primates: what can communication patterns tell us?

VAN SCHAİK, C.P., KAPPELER, P.M.: Male-female association and relationships in primates: precursors to monogamy.

27<sup>th</sup> International Ethological Conference, Tübingen, 22.-29.08.01,

EBERLE, M., KAPPELER, P.M.: Cooperative breeding in grey mouse lemurs (*Microcebus murinus*).

ZINNER, D., TIMMANN, I.: Grooming in hamadryas baboons – a test of the biological markets theory.

KAPPELER, P.M., ERKERT, H.G.: Correlates and determinants of cathemeral activity in wild redfronted lemurs (*Eulemur fulvus rufus*).

7<sup>th</sup> Congress of the Society for Primatology, Zürich, CH, 30.09.-04.10.01,  
FELDMANN, M., HEYMANN, E.W.: The effect of tamarin seed dispersal on the recruitment of *Parkia panurensis*.

HEYMANN, E.W.: Phenology and the scarcity of folivory in New World primates.

HEYMANN, E.W.: Thoughts on the future of primate behavioural ecology.

HEYMANN, E.W.: The role of sleeping habits for malaria infection rates in Amazonian primates.

OSTNER, J., KAPPELER, P.M.: Determinants of group composition in redfronted lemurs (*Eulemur fulvus rufus*).

SCHÜLKE, O., KAPPELER, P.M.: Protection from infanticide, male resource defense, overdispersed females and the evolution of pair-living in a nocturnal lemur, *Phaner furcifer*.

3<sup>rd</sup> Göttinger Freilandtage, Göttingen, 11.-14.12.01,

EBERLE, M., KAPPELER, P.M.: Male and female mating strategies in gray mouse lemurs (*Microcebus murinus*): who decides?

HEYMANN, E.W.: Scent marking and sexual selection in neotropical primates.

HILGARTNER, R., ZINNER, D., PIETSCH, T., WALBAUM, U., KAPPELER, P.M., GANZHORN, J.U.: Pair-living and stable territoriality in red-tailed sportive lemur (*Lepilemur ruficaudatus*).

OSTNER, J., KAPPELER, P.M.: Unusual sex ratio and male life history in red-fronted lemur groups.

SCHÜLKE, O., ZISCHLER, H., KAPPELER, P.M.: The potential for sexual selection in a pair-living nocturnal primate.

ZINNER, D., KNOGGE, C., HEYMANN, E.W., KAPPELER, P.M.: Large primate aggregations: limits to female – female networks?

ZINNER, D., NUNN, C.L., VAN SCHAİK, C.P., KAPPELER, P.M.: Sexual swellings: the female primates' peacock tail?

15<sup>th</sup> Annual Meeting of the Society of Tropical Ecology, Göttingen, 20.-23.02.02,  
KNOGGE, C., HEYMANN, E.W.: Seed- and pulp characteristics as determinants of the dispersal probability of tamarin dispersed seeds.

HEYMANN, E.W., KNOGGE, C.: Do larger animals disperse larger seeds? A test of Mack's hypothesis with primates.

HEYMANN, E.W., KNOGGE, C.: Estación Biológica Quebrada Blanco – opportunities for tropical ecology research in northeastern Peru.

OSTNER, J., KAPPELER, P.M.: Unusual sex ratio and male life history in red-fronted lemur groups.

SCHÜLKE, O., KAPPELER, P.M.: Female fertility is determined by family size rather than by territory size or food abundance in pair-living fork-marked lemurs.

15<sup>th</sup> Congresso d'Associazione Primatologica Italiana, Rome, I, 30.05.-01.06.02,

SPIEZIO, C., RIGAMONTI, M., KAPPELER, P.M., POLI, M.: A study of hand preference in wild sifakas (*Propithecus verreauxi verreauxi*).

RIGAMONTI, M., SPIEZIO, C., KAPPELER, P.M., POLI, M.: Functional asymmetries and locomotion in two species of lemurs: *Indri indri* and *Propithecus verreauxi verreauxi*.

International Symposium "The Role of Research in Nation Building", University of Asmara, Asmara, Eritrea, 15.–18.06.02, Eritrea,

ZINNER, D.: Primate research in Eritrea.

SHOSHANI, J., MICHAEL, A., SEIFE, B., YOSEPH, L., REID, R., HAGOS, Y., YOHANNES, Y., WALTER, R.C., ZINNER, D.: Proboscideans in Eritrea: extinct and living elephants, their relatives and history.

SHOSHANI, J., ERMIAS, T.A., GHEREHIWET, M., OGBAGEBRIEL, B., TEKLEAB, M., WILKUND, C., ZINNER, D.: Biogeography and biodiversity in Eritrea: a possible ecotonal hypothesis.

XIX<sup>th</sup> Congress of the International Primatological Society (IPS), Beijing, China, 04.-09.08.02,

EBERLE, M., KAPPELER, P.M.: Cooperative breeding in gray mouse lemurs (*Microcebus murinus*).

KAPPELER, P.M.: Male-male competition in wild white sifakas (*Propithecus verreauxi*).

SPIEZIO, C., RIGAMONTI, M., KAPPELER, P.M., POLI, M.: Laterality of the manual function in wild sifakas (*Propithecus verreauxi*).

V<sup>th</sup> Kirindy Symposium, DPZ, Göttingen, 23.08.02,

EBERLE, M.: Testing the model: mixed mating strategies and cooperative breeding in gray mouse lemurs.

KAPPELER, P.M., ERKERT, H.: Cathemeral activity of redfronted lemurs.

OSTNER, J.: Data dropping out of the trees: how hormone analysis from feces can deepen our understanding of redfronted lemur reproductive strategies.

SCHÜLKE, O.: To breed or not to breed: food competition and other factors involved in female breeding decisions in the pair-living nocturnal fork-marked lemur (*Phaner furcifer*).

ZINNER, D., HILGARTNER, R.: Territoriality and pair-living in red-tailed sportive lemurs (*Lepilemur ruficaudatus*).

## **Seminars**

Faculty of Biological Sciences, University of Leipzig, 10.01.01, KAPPELER, P.M.: Evolution of the mating systems of Malagasy primates.

Departamento de Psicología, Universidad Autónoma de Madrid, E, 25.01.01, HEYMANN, E.W.: Olfactory communication in callitrichids.

MPI for Evolutionary Anthropology, Leipzig, 03.05.01, KAPPELER, P.M.: Social evolution in lemurs.

Department of Anthropology, State University New York at Stony Brook, USA, 09.05.01,

OSTNER, J.: Redfronted lemurs – just small anthropoids?

SCHÜLKE, O.: Fork-marked lemurs - The how and why of pair-living at night.

Key program of the Deutsche Forschungsgemeinschaft: "Genetic Analysis of Social Systems", Thurnau, 24.-26.05.01, KAPPELER, P.M., EBERLE, M.: Genetic structure of lemur societies.

Institute for Zoo and Wildlife Research, Berlin, 22.06.01, KAPPELER, P.M.: Socioecology of nocturnal lemurs.

Zoo Ueckermünde, 14.08.01, ZINNER, D.: Dying branches at the pedigree of humans. Threat of extinction towards our closest living relatives through commercial hunting and bush meat trade.

German-Ibero-American Society, Frankfurt, 22.01.02, HEYMANN, E.W.: Amongst pygmy monkeys of the Amazon – Field research of tamarins in north-eastern Peru.

Zoological Research Institute and Museum Alexander Koenig, Bonn, 06.02.02, ZINNER, D.: Field research at the Horn of Africa – Hamadryas baboons in the deserts and mountains of Eritrea.

Graduating meeting of the study group Evolutionary Biology of the German Society of Zoology, Regensburg, 08.-10.02.02, EBERLE, M.: Scramble and contest competition: mixed mating strategies and multiple paternity in a natural population of gray mouse lemurs (*Microcebus murinus*).

Volkswagen Foundation, "Friendship and Kinship: Catenation and Relevance of two Systems of Relationship", Bielefeld, 08.-10.02.02, KAPPELER, P.M.: Kinship in non-human primates.

Institute and Museum of Anthropology, University of Zürich, CH, 13.05.02, SCHÜLKE, O.: The socioecology of fork-marked lemurs (*Phaner furcifer*).

Institute of Zoology, University of Zürich, CH, 13.06.02, EBERLE, M.: Mixed mating strategies and multiple paternity in a small primate, the gray mouse lemur (*Microcebus murinus*).

Department of Ethology, University of Bielefeld, 18.06.02, HUCK, M., LÖTTKER, P.: Amongst pichicos: field research of tamarins in the Amazona rain forest of north-eastern Peru.

Zoological Institute and Museum, University of Hamburg, 20.06.02, EBERLE, M.: Reproductive strategies of gray mouse lemurs (*Microcebus murinus*).

Department of Behavioral Biology, University of Münster, 11.07.02, LÖTTKER, P., HUCK, M.: Amongst pichicos: field research of tamarins in the Amazona rain forest of north-eastern Peru.

Department of General Zoology/Genetics, University of Essen, 11.07.02, EBERLE, M.: Reproductive strategies of gray mouse lemurs (*Microcebus murinus*).

Zoo Osnabrück, exhibition opening "Unique, but threatened by extinction – the golden-headed lion tamarin", 14.07.02, KNOGGE, C.: Diversity, endangerment and conservation of the Brazilian Atlantic Rain Forest.

Facultad de Biología, Universidad Nacional de la Amazonía Peruana, Iquitos, Peru, 07.10.02, HEYMANN, E.W.: Introduction to ethological methods for primate field studies.

### **List of Publications**

#### **Books**

MAESTRIPIERI, D., KAPPELER, P.M. (eds.): Evolutionary Theory and Primate Behavior. Int. J. Primatol., Special Issue (2002).

#### **Chapters in collected editions**

KAPPELER, P.M.: Lemurs: Cheirogaleidae, Lepilemuridae, Daubentoniidae, Indridae and Lemuridae. In: MACDONALD, D.W. (ed.): Encyclopedia of Mammals, 2<sup>nd</sup> edition. Andromeda Press (2001): 309-323.

KAPPELER, P.M.: Primate biogeography. In: PAGEL, M. (ed.): Encyclopedia of Evolution. Oxford University Press, Oxford (2002): 939-942.

#### **Reviewed papers**

BORRIES, C., KOENIG, A., WINKLER, P.: Variation of life history traits and mating patterns in female langur monkeys (*Semnopithecus entellus*). Behav. Ecol. Sociobiol. (2001) 50: 391-402.

DONATI, G., LUNARDINI, A., KAPPELER, P.M., BORGOGNINI TARLI, S.M.: Nocturnal activity in the cathmeral red-fronted lemur (*Eulemur fulvus rufus*), with observations during a lunar eclipse. Am. J. Primatol. (2001) 53: 69-78.

EBERLE, M., KAPPELER, P.M.: Mouse lemurs in space and time: a test of the socioecological model. Behav. Ecol. Sociobiol. (2002) 51: 131-139.

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- HEYMANN, E.W., ENCARNACIÓN, F., CANAQUIN, J.E.: Primates of the Río Curaray, Northern Peruvian Amazon. *Int. J. Primatol.* (2002) 23: 191-201.
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- KAPPELER, P.M.: Sexual selection in primates: New and comparative perspectives. *Evol. Anthropol.* (2002) 11: 173-175.
- KAPPELER, P.M., VAN SCHAIK, C.P.: The evolution of primate social systems. *Int. J. Primatol.* (2002) 23: 707-740.
- KAPPELER, P.M., WIMMER, B., ZINNER, D., TAUTZ, D.: Hidden matrilineal group structure of a solitary lemur: Implications for primate social evolution. *Proc. R. Soc. B* (2002) 269: 1755-1763.
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FREDSTED, T.: Lemurer- de fantastiske aber fra Madagaskar. *Naturens Verden* (2002) 11/12: 53-61.

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KAUMANN, W., SCHMID, P., SCHWITZER, C., HUSUNG, A., KNOGGE, C.: The European population of lion-tailed macaques (*Macaca silenus*): Status and problems. *Primate Report* (2001) 59: 65-75.

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ZINNER, D., PELÁEZ, F., BERHANE, D., TORCLER, F.: Mantelpaviane in Eritrea. *Z. Kölner Zoo* (2001) 44: 65-80.

### **Editorials**

SCHWIBBE, M., SINGH, M., KAUMANN, W., KNOGGE, C. (eds.): Proceedings of the Fifth International Symposium on Lion-tailed Macaque, Mysore, India (Part 2). Primate Report (2001) 59.

KAPPELER, P.M., KNOGGE, C., SCHWIBBE, M. (eds.): 3. Göttinger Freilandtage: Sexual Selection in Primates: Causes, Mechanisms, Consequences. Primate Report (2001) 60-1.

### **Abstracts**

DONATI, G., LUNARDINI, A., KAPPELER, P.M., BORGOGNINI TARLI, S.M.: Nocturnal activity in the cathmeral red-fronted brown lemur (*Eulemur fulvus rufus*): Variations during a lunar eclipse. Folia Primatol. (2001) 72: 147.

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GIL-BURMANN, C., PELÁEZ, F., ZINNER, D.: Research and teaching with the free-ranging baboons in Cádiz. Folia Primatol. (2001) 72: 355.

EBERLE, M., KAPPELER, P.M.: Male and female mating strategies in gray mouse lemurs (*Microcebus murinus*): Who decides? Primate Report (2001) 60-1: 19-20.

HEYMANN, E.W.: Phenology and the scarcity of folivory in New World primates. Folia Primatol. (2001) 72: 166.

HEYMANN, E.W.: Thoughts on the future of primate behavioral ecology. Folia Primatol. (2001) 72: 167.

HEYMANN, E.W.: Scent marking and sexual selection in neotropical primates. Primate Report (2001) 60-1: 24.

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ZINNER, D., TIMMANN, I.: Grooming in hamadryas baboons – a test of the biological markets theory. *Adv. Ethol.* (2001) 36: 293.

<b>Publications</b>	<b>2002</b>	<b>2001</b>	<b>2000</b>
1. Books	0	0	0
2. Publication of collected editions	1	0	1
3. Chapters in collected editions	1	1	9
4. Reviewed papers	19	14	14
5. Non-reviewed papers	5	8	4
<b>Total: 1 - 5</b>	<b>26</b>	<b>23</b>	<b>28</b>
6. Editorials	0	2	0
7. Electronic publications	0	0	0
8. Abstracts	0	19	16
<b>Publications altogether</b>	<b>26</b>	<b>44</b>	<b>44</b>

#### **Other scientific activities**

- **E.W. Heymann** and **D. Zinner** are members of the IUCN/SSC Primate Specialist Group.
- **E.W. Heymann** is a member of the editorial boards of *Folia Primatologica* and *Neotropical Primates*.
- **E.W. Heymann** organized the DPZ seminar series in the winter term 2001/02 together with W. Bodemer (Dept. of Veterinary Medicine and Primate Husbandry).
- **E.W. Heymann** was reviewer for the Volkswagenstiftung and for numerous scientific journals.
- **P.M. Kappeler** is associated editor of *Behavioral Ecology and Sociobiology* and *Current Anthropology* and reviewer for the DAAD.
- **P.M. Kappeler** was reviewer for the DFG, the Swiss National Fond, the Nederlandse Organisatie voor Wetenschappelijk Onderzoek, the National Science Foundation, Plenum Press, Springer Verlag and for numerous scientific journals.
- **D. Zinner** was reviewer for the Leakey Foundation and for numerous scientific journals.

#### **Important activities and functions**

- **P.M. Kappeler** is the president of the Gesellschaft für Primatologie and of the European Federation for Primatology.
- **E.W. Heymann** is a member of the Scientific Advisory Board of the Gesellschaft für Tropenökologie.

#### **Awards**

- **Julia Ostner** won the 2<sup>nd</sup> place of the young scientist competition of the 7th Congress of the Gesellschaft with her talk on the potential causes of the unusual sex-ratios in groups of red-fronted lemurs.

## **WORKING GROUP PRIMATE GENETICS**

**Head of Working Group:** Prof. Dr. H. Zischler

### **General research objectives**

The Primate Genetics Group was founded in 11/97 and was evaluated by the scientific advisory board in 10/2001. As a result of this evaluation the board proposed permanent installation of the research field "primate genetics" at the DPZ and to appoint the current group leader for another period. With the appointment of the group leader as director of the Institute of Anthropology at the University of Mainz, starting from 9/2002, the genetics group leader position at the DPZ was advertised at the end of 2002. In essence, the projects of the proposed thematic areas already started were, therefore, brought to an end in the period under report. With respect to the organisational and administrative level, the thematic area of "Immunogenetics" formerly a part of the primate genetics group was shifted into the Department of Virology and Immunology starting from 1/2002. Their work is therefore described in the Virology and Immunology section of the annual report.

The thematic focus of the Working Group Primate Genetics can be partitioned in two main areas. One area deals with primate-relevant phylogenetic issues and applies molecular genetic methodology. In the second area of interest, we characterize highly polymorphic mitochondrial and nuclear, tandem repetitive DNA markers that are used in the analysis of non-human primate social systems and genetic diversity, a prerequisite for species survivability over evolutionary time scales.

### **Primate phylogeny**

In this thematic area the group examines the two classical orientations of molecular evolutionary research - "pattern and process". On the one hand, our goal is to clarify the mechanisms that create genetic variability. To this end, we analyse different aspects of non-homologous recombinations, especially nuclear integrations of mitochondrial DNA, and the sequence evolution of mitochondrial DNA. On the other hand, we aim to use the observed genetic diversity to deduce estimations on the phylogenetic affiliations among members of non-human primate taxa. Our interest covers all taxonomic levels in the order of primates, thus, we concentrate on infraspecific phylogenetic questions as well as on the deep splitting events in primate phylogeny, e.g. the phylogenetic affiliations of primates to other eutherian orders. The aim of the group is to contribute to the solution of primate-relevant phylogenetic issues by combining molecular phenetic and cladistic analyses. The relevance of the phylogeny-related work of our group arises from the fundamental meaning of phylogeny for the study of character evolution in the field of comparative biology and medicine. Uncovering the phylogenetic affiliations of different taxa allows us to discriminate between homology and analogy in molecular, morphological, physiological and sociobiological character evolution. Moreover a phylogenetic framework is an indispensable prerequisite for any conclusion on the biogeography

of a taxon. In spite of this central meaning of phylogenetic research in comparative biological and biomedical primatology, there are numerous unanswered questions related to the phylogeny of primates, which concern recent divergences as well as the deep splitting events, e.g. the origin of primates. Thus, work on primate phylogeny is not only an interesting subject in itself, but is rather an essential field of post-genomic research, which in the end sets the stage for the huge field of functional genomics.

Merely on the basis of an undisputed phylogenetic framework, we are able to delineate the dynamics of the primate DNA-turnover, which in turn provides a basis to define adequate models of sequence evolution, to develop algorithms for sequence-based phylogenetic reconstructions and to search for the molecular principles of the DNA-turnover. The comparative analysis of nuclear integrations of mitochondrial DNA and their mitochondrial paralogues enables us to study the compartment-specific sequence evolution in homologous DNA regions and to estimate the influence of selection and compartment-specific mutational mechanisms on the evolution of sequences. Since nuclear DNA-stretches generally evolve at a slower rate compared to their mitochondrial counterparts, nuclear integrations of mitochondrial DNA represent molecular fossils, that allow us to estimate ancestral mtDNA sequences that came about during primate divergence.

### **Population genetics**

In this thematic area, a combined approach of genetic and field work is undertaken with the aim of understanding the ecological, phylogenetic, and social factors, that determine the great diversity of different social organisations and mating systems observable in non-human primates. We, moreover, wish to answer the questions of how spatial isolation of subgroups, their effective population sizes and gene flow between them are influenced by the respective social systems and ecological parameters of the habitats. In this way we try to gather fundamental information about microevolutionary forces like drift and migration. Primates display - in contrast to other mammalian orders - a multitude of different forms of social organisation which are realized in a species. To determine the forms of these social organisations themselves and their determinates, genetic as well as reproductive biological data represent an indispensable complement to the field work. At the German Primate Center, the field work expertise (Dept. of Ethology and Ecology, Dept. of Reproductive Biology, DPZ) is combined with the molecular know-how of the primate genetics group. As a consequence of the analysis of representatives pertaining to different primate infraorders which all display different forms of social systems, it is possible to estimate ancestral character states and changes in the social organisation that occurred during primate divergence. In biological terms our work therefore contributes to the test of social evolution models by analysing taxa that are closely related to humans. With respect to the genetic aspect of our work, the obtained data are relevant for the connectivity of social system and population genetic make up, since every form of genetic differentiation - even massive differences in the genomes of two taxa e.g. presence/absence of complete transposon families - are, in the end, strongly influenced by population parameters such as effective population sizes, migration rates, gender-biased dispersal, that largely determine the fixation probabil-

ity of an allele. Likewise, different forms of social organisation influence the genetic structuring and heterogeneity of a taxon, which is an important factor for the survivability of a taxon over evolutionary time scales. All knowledge about a social system, therefore, bears direct relevance to the conservation of the respective taxon. This aspect is becoming more important since about 50% of all currently recognised species are of conservation concern to different extents.

### **Structure of the department**

In the period under review the group consisted of a maximum of 5 scientists, 5 PhD students, 1 diploma student and 4 technical assistants, with 2 scientists, 4 PhD students and two technical assistants financially supported by external funding.

#### Scientists

Dr. Uta-Regina Böhle  
Dr. Holger Herlyn (01.06.01-)  
Dr. Ulrike Sauermann (-31.12.01)  
Dr. Jürgen Schmitz

#### Technicians

Mareike Hausmann (-31.12.01)  
Martina Ohme  
Claudia Schwiegk (-31.08.02)  
Nathalie Vignon

#### PhD students

Anja Blankenburg (-31.12.01)  
Andreas Hapke  
Thorsten Mühl (-31.12.01)  
Christian Roos  
Silke Singer (-31.03.01)  
Oliver Piskurek (01.10.01-)

#### Undergraduate students

Jelka Cimermann  
Oliver Piskurek (-30.09.01)

### **Progress during the year**

#### **Phylogeny**

In the year under report, the group mainly worked on the inter- and infraordinal phylogenetic affiliations of primate taxa applying classical sequence analyses as well as pursuing a molecular-cladistic approach.

#### *Primates and their closest relatives*

With regards to the taxonomical hierarchy, one of the most fundamental questions in primate evolution pertains to the phylogenetic affiliation of primates to other eutherian orders, i.e. to clarify the origin of primates. Gregory (1910) proposed embracing primates, together with Dermoptera, Chiroptera and the genera of *Tupaia* and *Ptilocercus*, two taxa that are assembled in the modern order of Scandentia, in a superorder "Archonta". Members of the palaeocene plesiadapiforms are currently regarded as an extinct sister taxon to the "archaic" primates. Several synapomorphic – mostly postcranial – characters hint at a close phylogenetic affiliation of extant dermopterans and the plesiadapiform taxa. This interpretation is a matter of dispute mainly because of the scarcity of the fossil record, which is directly relevant for the question of the extant sister group of primates. In order to complement the fossil evidence by molecular analyses, the group sequenced and phylogen-

etically analysed another complete mitochondrial genome from a supposedly close relative of primates, *Cynocephalus variegatus*. Surprisingly, all phylogenetic tree reconstructions regardless of which algorithms were applied or sequence evolution models assumed displayed a close relationship of dermopterans to the anthropoid primates (New World monkeys, Old World monkeys and hominoids). This close phylogenetic affiliation, rendering the primates a paraphyletic group, had already been postulated by other groups and is strikingly discordant with all hitherto formulated hypotheses on the phylogenetic position of the dermopterans. To corroborate or disprove this interpretation we have obtained retropositional evidence: The fact, that 7SL-derived Alu-elements are completely absent from dermopterans and present in high copy number in all primates, even in strepsirrhines and tarsiers that split off early in primate divergence, clearly shows on a multilocus level, that the mtDNA-based hypothesis is completely at odds with the retropositional evidence. This observation is corroborated by single copy analyses i.e. the presence/absence pattern of SINEs at orthologous loci. Therefrom the question arises of why a correct dermopteran to primates relation could not be uncovered on a mtDNA-basis. This problem is apparently not only restricted to the origin of primates, it also holds true for the phylogenetic position of tarsiers in the primate tree. To set the stage for a reasonable comparison of the mt-genomes among different primates and with *Cynocephalus*, we sequenced the complete mitochondrial genome of *Tarsius bancanus* in

		.10	.20	.30	.40	.50	.60	
AF135280	1:	AGAGA GAA	CAC C C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135281	1:	AGAGA GAA	CAC C C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135350	1:	AGAAA GAA	CACCC C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135314	1:	AGAGA GAA	CACCC C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135316	1:	AGAGA GAA	CAC C C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135282	1:	AGAGA GAA	CAC C C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135362	1:	AGAGA GAA	CAC C C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135286	1:	AGAGA GAA	CACCC C CC	AGGGCAA	CAGAAGAAAGC	ACC AAC	CCACCACC	AAACA : 59
AF135364	1:	AGAGA GAA	CAC C C CC	AGGG AA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135315	1:	AGAAA GAA	CACCC C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135365	1:	AGAGA GAA	CAC C C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135337	1:	AGAAA GAA	CACCC C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135363	1:	AGAGA GAA	CAC C C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135277	1:	AGAGA GAA	CAC C C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135351	1:	AGAAA GAA	CACCC C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135341	1:	AGAAA GAA	CACCC C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135342	1:	AGAAA GAA	CACCC C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135287	1:	AGAGA GAA	CAC C C CC	AGGG AA	CAGAAGAAAG	A C C	CCACCACC	AAACA : 59
AF135325	1:	AGAGA GAA	CAC C C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135343	1:	AGAAA GAA	CACCC C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135292	1:	AGAGA GAA	CAC C C CC	AGGGCAA	CAGAAGAAAG	ACC A C C	CCACCACC	AAACA : 59
AF135335	1:	AGAGA GAA	CAC C C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135353	1:	AGAAA GAA	CACCC C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135288	1:	AGAGA GAA	CAC C C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135305	1:	AGAGA GAA	CAC C C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135302	1:	AGAGA GAA	CAC C C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135347	1:	AGAAA GAA	CACCC C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135338	1:	AGAAA GAA	CACCC C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135291	1:	AGAGA GAA	CACCC C CC	AGGGCAA	CAGAAGAAAGC	ACC AAC	CCACCACC	AAACA : 59
AF135346	1:	AGAAA GAA	CACCC C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135354	1:	AGAGA GAA	CAC C C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135357	1:	AGAGA GAA	CAC C C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135360	1:	AGAGA GAA	CACCC C CC	AGGGCAA	CAGAAGAAAGC	ACC AAC	CCACCACC	AAACA : 59
AF135289	1:	AGAGA GAA	CACCC C CC	AGGGCAA	CAGAAGAAAGC	ACC AAC	CCACCACC	AAACA : 59
AF135313	1:	AGAGA GAA	CAC C C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59
AF135309	1:	AGAGA GAA	CAC C C CC	AGGGCAA	CAGAAGAAAG	ACC AAC	CCACCACC	AAACA : 59

1. To further analyse the sequence information, homologous positions from sequences of different individuals are ordered below each other. Each line therefore represents a part of the sequence information of an individual, each column the positions in these sequences. Identical character states are coloured. The diversity of the sequences forms the basis for estimation of the phylogenetic affiliations of the respective individuals.

the period under review. A more detailed comparative analysis of both mitochondrial genomes from *Cynocephalus* and *Tarsius* to the mitochondrial genomes of other primates and eutherians disclosed a considerable plasticity of the mtDNA-composition of single genomes on the lineage to primates and after the rodents split off. The reason for this is not clear, the same phenomenon, however, could be observed in the mtDNAs of other eutherians e.g. the hedgehog. As a consequence of the changing nucleotide composition, the codon usage becomes altered e.g. there are more amino acids used, which are encoded by AT-rich codons. This means that the phylogenetic tree reconstruction on the basis of mtDNA sequences does not necessarily lead to the true evolutionary history of certain taxa, it could rather display a close relationship between two taxa simply because of a similar nucleotide composition. This, moreover, shows that it is absolutely necessary to gather – beside mtDNA data- further evidence preferably molecular-cladistic, to more exactly estimate the phylogenetic affiliation of primates to other eutherian orders.

The presence of a high copy number of Alu-elements is restricted to the order of primates. Thus an effective approach to the solution of the interordinal phylogenetic affiliations of primates is only possible by exploiting the complete genome information of human and mouse and using other types of SINEs (e.g. MIR-sequences). In the period under review we have, therefore, started to directly detect SINE elements in the dermopteran genome. By this approach we have not obtained any hint that dermopteran genomes harbour 7SL-derived SINEs in a high copy number. However, we could describe the first SINEs for this eutherian order. These elements are also transcribed by Pol III and display a close relation to the tRNA isoleucine. Apparently these elements occur in differentially reiterated forms as mono, -di and trimers.

### *Primate infraordinal phylogenetic relationships*

The strategic approach of using both retropositional evidence as well as sequence analyses in combination to clarify phylogenetic questions was carried out in the period under report both on the level of New World monkeys and strepsirrhines. On the basis of currently available sequence data, it can be supposed for both groups that no massive variations of the mtDNA composition appear within the infraorders. Therefore, for the strepsirrhines, mtDNA fragments were sequenced in addition to retroposon analysis and analysed comparatively.

The predominantly nocturnal strepsirrhines represent the most ancestral group of primates. They are characterised by some "primitive" features as, for example, the existence of a tapetum or an open orbita, both shared with some other mammalian orders to the exclusion of higher primates. The suborder of the strepsirrhines comprises about 80 species that are geographically distributed over extended parts of Africa, Asia and Madagascar. Based on the enormous biodiversity and the different distribution zones, many questions concerning the evolution and biogeography of these taxa are still a mystery. In order to clarify some of these issues, two different molecular genetic methods were used:

1. By sequencing the 1140 bp spanning cytochrome b gene, a first overview over the molecular evolution of the strepsirrhines was generated. To this end, a number of different materials such as faecal, hair or tissue samples were utilised as starting material for DNA-isolation. This sample list was expanded by museum skins because it was not possible to obtain the above mentioned materials for some

taxa. The subsequently applied laboratory procedures were mainly standardised ones e.g. PCR and sequencing. Phylogenetic tree reconstructions were done applying routine computer programs (PHYLIP, PUZZLE, PAUP). In the period under report, all strepsirrhine genera and almost all currently recognised species of strepsirrhines were sequenced at this locus.

2. Based on the phylogenetic information obtained from sequencing the mitochondrial cytochrome b gene, some principal questions of the strepsirrhine evolution were tackled by analysing molecular cladistic markers. One of these issues focuses on the question of the aye-aye's (*Daubentonia madagascariensis*) phylogenetic position and the associated question of the colonisation history of Madagascar, as well as the evolutionary relationships among the Loriformes Lorisidae, Perodicticidae and Galagonidae. Regarding both of these issues, whether morphology or zoogeography reflects the authentic evolutionary history of these primates is questionable.

Transposable elements such as SINEs that transpose in a LINE-dependent fashion proved to be especially suited for these studies. Based on their random and irreversible mode of integration into the genome, they represent perfect cladistic markers in a Hennigian sense, since the character state at a locus can simply be defined as "SINE present" and therefore derived or as "SINE absent" and ancestral.

In the period under report, SINEs described for strepsirrhines were sought in publicly accessible databases. The already published short interspersed elements were described for *Propithecus*, *Lemur* and *Eulemur* (Alu) as well as for *Galago* (tRNA derived SINEs). In order to check the presence of these elements in other strepsirrhine families, Southern blot analyses were carried out. The results thereof show that the 7SL-derived Alu element is present in all strepsirrhines and a further (not 7SL-derived) SINE in all Loriformes. This can be interpreted as proof of the monophyly of all strepsirrhines and all Loriformes, respectively. Based on this knowledge, five size-enriched genomic libraries were generated for *Daubentonia*, *Lemur*, *Propithecus*, *Perodicticus* and *Loris* and screened for the corresponding SINEs. SINE-containing loci were subsequently PCR-checked for a broad taxonomic sampling and auspicious PCR products were sequenced later. Based on this procedure, 49 cladistic markers were defined, which were able to clarify important issues of strepsirrhine phylogeny such as the monophyly of the Lemuriformes or the order of consecutive separation within the Loriformes.

For the New World monkeys, retropositional evidence was be acquired in a similar manner in the period under report. Based on the fact that New World monkeys probably diverged displaying an adaptive radiation, the retropositional evidence was consolidated by further sequence analyses. This was necessary to minimise false interpretations, based on possible unequal distributions of ancestral polymorphism into the progeny lineages. Essential statements emerging from these investigations were retropositional evidence for the monophyly of the callithrichids including *Callimico*, the sister group relationship of the genera *Callithrix* and *Cebuella* and the close phylogenetic relationship of the genera *Cebus*, *Saimiri* and *Aotus* to the callithrichids.

### Population genetics

In the field of population genetics, the group also works on two thematic orientations - "pattern and process" in infraspecific phylogeny. On the one hand, neutral

marker systems are applied to work on population genetic and biogeographic phenomena of different primate species. Moreover, we try to contribute to the elucidation of the molecular mechanisms of speciation by analysing the evolution of the sperm-egg interaction.

Our population genetic work focuses on the two geographical regions Indochina and Madagascar.

*Population genetics and biogeography of Indochinese langurs and crested gibbons*

The bioregion of Indochina (Vietnam, Laos, Cambodia, Southern China) is known for its huge number of endemic plant and animal species. Even within the order of primates, a multitude of species e.g. douc langurs, crested gibbons and Francois' langurs exclusively have become inhabit this region. Because of poaching and habitat loss, a lot of primate species got highly endangered and close to extinction (7 species are in the Top 25 of the "most endangered primate species" in the meantime).



*Booth of a "healer" in the neighbourhood of the Phong Nha-Ke Bang national park, Vietnam. Wildlife conserved in alcohol, including protected primate species are frequently utilized in traditional Vietnamese medicine. Besides poaching, the wildlife of Indochina is predominantly threatened by habitat loss.*

In close collaboration with Vietnamese colleagues and conservation organisations, a number of samples including all species of Indochinese gibbons, langurs and slow lorises were collected in the recent years and genetically analysed. Based on the sequences of the mitochondrial cytochrome b gene, the phylogenetic affiliations within the specific groups were determined precisely. A special "highlight" result of this study was the first molecular evidence for the existence of a fourth species of crested gibbons (*Nomascus nasutus*) in northeastern Vietnam. Furthermore, the data yield evidence for the existence of three species of douc langurs as well as for four species of Francois' langurs.

After the fundamental questions on the phylogeny of the specific primate groups were clarified, we started to generate a "genetic distribution map" for Indochina in the period under report. To this end, a fragment of the mitochondrial control region was sequenced from a multitude of individuals. First analyses permit the conclusion

that grey-shanked douc langurs (*Pygathrix cinerea*) are genetically highly variable, however, this variability is not linked to their distribution. In contrast to this, a clear correlation between genetic structuring and geographic distribution is recognisable for the red-shanked (*P. nemaus*) and black shanked douc langurs (*P. nigripes*). A similar picture emerges for the crested gibbons; however, the especially interesting question of the distribution boundaries of *N. leucogenys siki* has still not been definitively clarified.

*Population genetics of Microcebus spp. and Cheirogaleus spp. in Southeast Madagascar*

The region around Fort Dauphin in Southeast Madagascar displays a unique diversity of different ecological landforms in close vicinity. In this region the eastern Malagasy rainforest zone merges with the southern spiny forest zone forming a dramatic rainfall gradient. In addition, there is a string of littoral forests that is unique in Madagascar. The distribution of different species of the primate family of the Cheirogaleidae is accordingly multifaceted. In many locations, displaying strikingly different types of vegetation, each two to three different species occur in sympatry. The landscape is strongly structured by anthropogenic and natural habitat modifications and barriers such as savannahs, agriculturally used areas, swamps, rivers and lakes. In particular the littoral forests make up a string of numerous fragments with each being up to 700 ha in size. In the project carried out in the period under review, we analysed the influence of these ecological-geographic parameters on the population genetic structuring of *Cheirogaleus medius*, *Microcebus griseorufus*, *Microcebus murinus* and *Microcebus rufus* applying population genetic molecular techniques. To this end we separately analysed maternally transmitted mitochondrial DNA and biparentally transmitted nuclear markers, to take the different social systems of these taxa, in particular the gender biased dispersal, into account.

In 2001 and 2002 the fieldwork in Southeast Madagascar was continued in two periods for a duration of altogether nine months. During this time, 155 *Microcebus* sp. individuals and 78 *Cheirogaleus* sp. individuals were trapped at 14 different locations, analysed and subsequently set free again. Tissue material for genetic analyses was taken from all trapped individuals. Beside this, a morphometric analysis of 12 parameters was carried out and photographs were taken from each individual. Currently, altogether tissue as well as DNA-samples from 420 *Microcebus* sp., 86 *Cheirogaleus medius* und 39 *Cheirogaleus major* individuals stemming from 22 locations of different vegetation types constitute the collection held by our group.

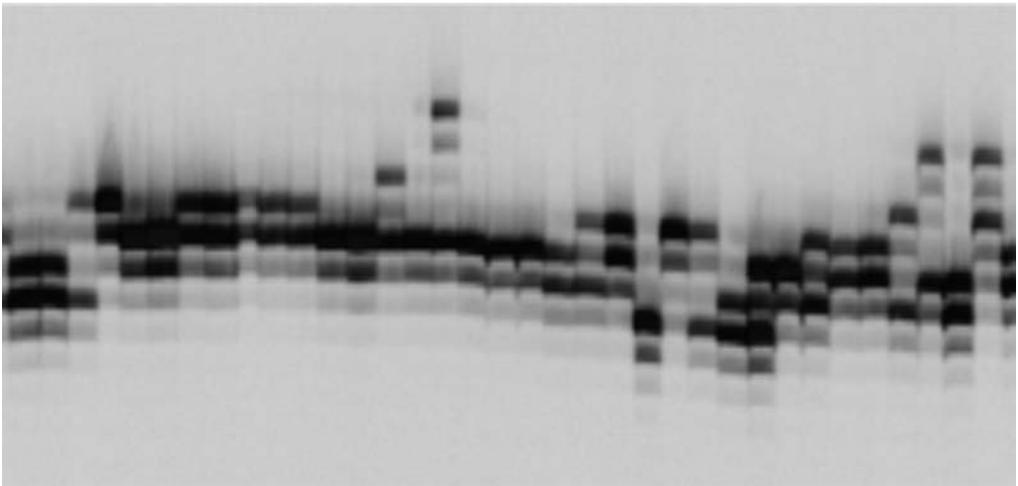
Plasmid DNA-libraries were constructed for *Cheirogaleus medius* and *Microcebus murinus* and 16 polymorphic microsatellites were isolated (Hapke et al., in press). In addition already published microsatellite markers (Fietz et al. 2000) were used. As a fast method to type mitochondrial markers a primer system for direct sequencing of the hypervariable region I of *Microcebus* sp. und *Cheirogaleus* sp. was developed and applied. In the meantime, the bulk of samples has already been typed at 8-13 microsatellite loci. Initial phylogenetic reconstructions on the basis of the mitochondrial sequence data show that the sampled forest fragments are isolated from each other to a varying extent. The data show, in part, surprising connections between the single locations and allow an interpretation of a very complex colonisation history of the respective habitats, especially of the littoral forest fragments. At pres-



*The outstanding diversity of different types of forests in close vicinity in the region around Fort Dauphin, South-east Madagascar:*

- *humid littoral forest, Ste Luce, habitat of the Brown Mouse Lemur (*Microcebus rufus*) (above),*
- *deciduous forest in the rainy mountain range Vo-himena (middle),*
- *spiny forest in the dry season, Ifotaka (below).*

ent a joint population genetic and statistical analysis is being carried out for both mitochondrial as well as nuclear microsatellite data to unravel the genetic variability of the populations that are isolated to a different degree and to gain information on the influence of the different kinds of barriers separating the habitats. At the time of planning the urgently required protection actions for the region of Fort Dauphin, these types of data are of prime importance. The characterisation of the microsatellite markers was done in a joint co-operation with the Dept. of Ethology and Ecology, DPZ (M. Eberle, O. Schülke). The markers characterised in this co-operation were subsequently applied in projects of both departments.



*Microsatellite-PCR-products are separated in a polyacrylamide gel electrophoresis to determine their molecular weights. Because microsatellite loci contain length polymorphic sequence stretches, each allele of an individual can be determined in this way. The respective data are used for paternity tests and population genetic analyses.*

#### *Population genetic structure of Eritrean hamadryas baboons*

In this project, executed in a period from 1998 to 2000, we carried out a population genetic analysis on faeces samples from free ranging hamadryas baboons (D. Zinner – Dept. of Ethology and Ecology, DPZ). Among the Old World monkeys, hamadryas baboons represent a rare exception to the predominant pattern of female philopatry and male dispersal. Most adult male baboon individuals stay in the social group in which they were born, which contrasts to most other Old World monkey taxa. Beside this, there are some observations of female individuals migrating between social groups. It is hitherto not clear, to which extent female migration occurs in hamadryas baboons and how this phenomenon influences the population genetic structure. In our genetic analyses, the maternally transmitted mitochondrial hypervariable region I was employed as a genetic marker. Phylogenetic tree reconstructions as well as population genetic and statistical analyses (AMOVA, estimation of genetic distances between populations, mantel-correlations of genetic and geogra-

phic distances) clearly show that maternally transmitted haplotypes are exchanged between social groups on a broad geographic scale and due to female migration.

#### *Molecular genetics of the sperm-egg interaction*

The term sperm-egg interaction summarises all phenomena that lead to a fusion of the sperm and egg cells. The sperm-egg interaction is of central importance for biology, since the functioning of this interaction decides on the reproduction of two individuals, whereas the malfunction contributes to an effective separation of two populations by building up a reproductive barrier between them.

Hitherto, the molecular mechanisms that are relevant for the evolution of the sperm-egg interaction, were merely analysed for some receptor-ligand systems of marine Echinozoa and molluscs. In this way it was shown, that the sperm-ligands - probably caused by an adaptation to egg receptor systems that evolve in a concerted fashion - evolve remarkably fast. This pattern of protein evolution presumably represents a strategy to avoid interspecific hybrids between closely related and sympatric taxa.

In contrast to this, only scarce relevant sequence information is available for organisms showing an internal fertilisation e.g. mammalia, which do not allow meaningful sequence comparisons due to considerable genetic distances between the taxa (e.g. mouse and humans). It is, therefore, not clear, in what manner the sperm-egg interaction evolves in organisms that display an internal fertilisation and different social systems. To tackle these questions, we started the project "Molecular genetics of the sperm-egg interaction in primates" by midyear 2001, which has been supported by the DFG since the middle of 2002. In a first step, we determine the sequences of functionally different domains of several sperm-ligands of as many primate taxa as possible, to delineate the sequence evolution in the light of the respective functional aspects. In a second step, we intend to determine the infraspecific variability of particularly rapidly evolving exons, to disclose possible correlations between social system and sequence evolution.

#### **Integration into national and international research**

The research of the Working Group Primate Genetics is tied into the the interdepartmental cooperations of the DPZ. Furthermore several bi- and multilateral cooperations exist with groups in Germany and abroad, e.g. the EU-initiative INPRIMAT. The respective cooperations are listed in the following table.

**Projects and partners in co-operation**

(I: interdepartmental projects, E: external co-operation; A: project completed, L: current project)

<b>Projects and Partners of the Working Group Primate Genetics</b>		
<p><b>Conservation Biology of Malagasy lemurs and New World monkeys</b>                      B. RAKOTOSAMIMANANA, D. RAKOTONDRAVONY (Univ. Antananarivo, Madagascar, ), J.U. GANZHORN (Zoological Inst., Univ. Hamburg), S. GOODMAN (FMNH Chicago &amp; WWF Madagascar), J. DURBIN (Durrell Wildlife), F. ENCARNACIñN (Univ. Nacional Mayos San Marcos, Lima, Peru), H. VALDERRAMA FREYRE, R. PEZO (Univ. Nacional Amazonia Peruana, Iquitos, Peru), K. HODGES (Dept. of Reproductive Biology, DPZ), P.M. KAPPELER, E.W. HEYMANN, D. ZINNER (Dept. of Ethology and Ecology, DPZ), <b>H. ZISCHLER, A. HAPKE, C. ROOS</b></p>	E,I	L
<p><b>Phylogeography of <i>Papio</i></b>                      D. ZINNER (Dept. of Ethology and Ecology, DPZ), <b>H. ZISCHLER, A. HAPKE, C. ROOS</b></p>	I	L
<p><b>Taxonomy and Biogeography of Cheirogaleids</b>  <b>R. RASOLOARISON</b>, S. GOODMAN (FMNH Chicago &amp; WWF Madagascar), A. YODER (Northwestern Univ., USA), J.U. GANZHORN (Zoological Inst., Univ. Hamburg), P.M. KAPPELER (Dept. of Ethology and Ecology, DPZ), <b>H. ZISCHLER, A. HAPKE, C. ROOS</b></p>	E	L
<p><b>Genetic analysis of lemur mating systems</b>                      D. TAUTZ (Univ. Köln), M. EBERLE, O. SCHÜLKE, B. WIMMER, D. ZINNER, P.M. KAPPELER (Dept. of Ethology and Ecology, DPZ), <b>H. ZISCHLER, A. HAPKE</b></p>	E	L
<p><b>Proximate Regulation and genetic consequences of the mating system of polyandric tamarins</b>                      M. HEISTERMANN, K. HODGES (Dept. of Reproductive Biology, DPZ), P. LÖTTKER, M. HUCK, E.W. HEYMANN (Dept. of Ethology and Ecology, DPZ), <b>U.-R. BÖHLE, C. SCHWIEGK</b></p>	I	L
<p><b>Comparative aspects of lemur socio-ecology</b>                      M. PERRET (MNHN, Laboratoire d'Ecologie, Brunoy, F), H. ERKERT (Univ. Tübingen), C. DIRAC, M. EBERLE, R. HILGARTNER, P.M. KAPPELER, J. OSTNER, O. SCHÜLKE, D. ZINNER (Dept. of Ethology and Ecology, DPZ), <b>H. ZISCHLER, A. HAPKE, C. SCHWIEGK</b></p>	E,I	L
<p><b>Phylogeny and Biogeography of Asian Lorisiidae</b>                      K.A.I. NEKARIS (Univ. Oxford Brookes, GB), H. SCHULZE (Univ. Bochum), U. STREICHER (EPRC, Vietnam), <b>C. ROOS, H. ZISCHLER</b></p>	E	L

<b>Projects and Partners of the Working Group Primate Genetics</b>		
<b>Phylogeny and Biogeography of Mentawai-Macacques</b> T. ZIEGLER, C. ABEGG, K. HODGES (Dept. of Reproductive Biology, DPZ), <b>C. ROOS, H. ZISCHLER</b>	I	L
<b>Population genetics and biogeography of Indochinese colobines and gibbons</b> T. NADLER (EPRC, Vietnam), T. GEISSMANN (Tierärztliche Hochschule, Hannover), VU NGOC THANH (Univ. Hanoi, Vietnam), B. (WWF Indochina, Hanoi), Flora & Fauna International Indochina (Hanoi, Vietnam), Frontier (Hanoi, Vietnam), Conservation International, IEBR (Hanoi, Vietnam), <b>C. Roos</b>	E	L
<b>Population genetics of <i>Cheirogaleus</i> and <i>Microcebus</i> in Southeast-Madagascar</b> J. U. GANZHORN (Zoological Inst., Univ. Hamburg), B. RAKOTOSAMI-MANANA, G. RANDRIA (Univ. Antananarivo, Madagascar), J.B. RAMANAMANJATO (QIT Madagascar Minerals, Madagascar), WWF Madagascar, ANGAP, Réserve Naturelle de Berenty (Société H.A.H. de Heaulme), Réserve Naturelle Domaine de la Cascade (Madagascar), <b>A. HAPKE, H. ZISCHLER</b>	E	L
<b>Sperm-egg interaction</b> K. HODGES, A. EINSPANIER (Dept. of Reproductive Biology, DPZ), <b>H. HERLYN, H. ZISCHLER</b>	I	L
<b>Gene Bank of Primates</b> K. MÄTZ-RENSING (Dept. of Veterinary Medicine and Primate Husbandry, DPZ), K. HODGES (Dept. of Reproductive Biology, DPZ), <b>C. ROOS</b>	I	L
<b>Phylogeny and biogeography of the lemuriformes</b> Y. RUMPLER (Univ. Strasbourg, F), P.M. KAPPELER (Dept. of Ethology and Ecology, DPZ), J.U. GANZHORN (Zoological Inst., Univ. Hamburg), <b>C. ROOS, A. HAPKE, H. ZISCHLER</b>	E,I	L
<b>Population biology and –genetics of lemurs</b> T. FREDSTED, J. OLESEN (Univ. Aarhus, DK), J. GANZHORN (Zoological Inst., Univ. Hamburg), M. EBERLE, P.M. KAPPELER (Dept. of Ethology and Ecology, DPZ), <b>H. ZISCHLER, A. HAPKE, C. ROOS</b>	E,I	L
<b>New World monkey phylogeny</b> E.W. HEYMANN (Dept. of Ethology and Ecology, DPZ), <b>S. SINGER, H. ZISCHLER</b>	I	L

## Stays of DPZ scientists in other institutions

Name/Institute/Duration	Project
Dipl. Biol. Oliver Piskurek Tokyo Institute of Technology Faculty of Bioscience and Biotechnology, Japan 01.10.01-30.09.02	Retroposon analyses in eutherian phylogeny

Visited institution	Duration of stay (2001/2002)		
	< 1 month	1 - 3 months	> 3 months
German universities, research or service institutions	0	0	0
European universities, research or service institutions	0	0	0
Universities, research or service institu- tions outside Europe	0	0	1
<b>Altogether</b>	<b>0</b>	<b>0</b>	<b>1</b>

## Scientific Contributions

### Diploma theses

PISKUREK, O.: Molecular evolution of mitochondrial ribosomal RNA: Comparison of gene and pseudogene in primates. Fachbereich Biologie der Georg-August-Universität Göttingen (2001).

CIMERMANN, J.: Molecular mechanisms of reproductive isolation in primates: Sequence evolution of the sperm surface proteins PH-20 and P47. Fachbereich Biologie der Georg-August-Universität Göttingen (2003).

### Congress contributions

Symposium "Primate Evolution: Phylogenetic, Physiological and Behavioural Aspects", 06.02.01, DPZ, Göttingen, ROOS, C., ZISCHLER, H.: Molecular Phylogeny of the Strepsirhini (Primates).

Anthropoid Origins Symposium, 20.-21.04.01, Powdermill Nature Reserve, USA, SCHMITZ, J., ZISCHLER, H.: Molecular cladistic markers and the infraordinal phylogenetic relationships of primates.

7<sup>th</sup> Kongress der Gesellschaft für Primatologie, 30.09.-04.10.01, Zürich, CH, ROOS, C., NADLER, T., ZHANG, Y.P., ZISCHLER, H.: Molecular evolution and distribution of the superspecies *Trachypithecus francoisi*.

Annual internal meeting of the Biology Department of the University of Poitiers, F, October 2001, SOLER, C., DI TOMMASO, A., ROOS, C., KITZIS, A., LADEVÈZE, V.: Evolution du locus *ink4a* chez les primates.

SMBE Meeting on Molecular Evolution (Evolution, Genomics, Bioinformatics) Sorrento (Naples), I, 13.-16.06.02, SCHMITZ, J., ZISCHLER, H.: Mammalian Phylogeny: Convergence in mitochondrial nucleotide composition shapes the mammalian phylogenetic tree.

XIX<sup>th</sup> Congress of the International Primatological Society, 04.-09.08.02, Beijing, China,.

NADLER, T., ROOS, C.: Systematic position, distribution and status of douc langurs (*Pygathrix*) in Vietnam.

NADLER, T., ROOS, C.: Systematic position, distribution and status of langurs within the genus *Trachypithecus* in Vietnam.

V<sup>th</sup> Kirindy-Symposium, DPZ, Göttingen, 23.08.02,

HAPKE, A.: Population Genetics.

HAPKE, A.: Biogeography of mouse lemurs and dwarf lemurs in south-east Madagascar.

### Seminars

QIT Madagascar Minerals Fort Dauphin, 11.01.01, HAPKE, A.: Cheirogaleid population genetics (1).

DPZ-Colloquium, Göttingen, 21.03.01, HAPKE, A.: Population genetics of hamadryas baboons in Eritrea.

Anthropological Institute and Museum, University of Zürich, CH, 08.05.01, ZISCHLER, H.: Molecular cladistics in primate phylogeny

QIT Madagascar Minerals Fort Dauphin, Madagascar, 22.11.01, HAPKE, A.: Cheirogaleid population genetics (2)

Jahr der Lebenswissenschaften: "Leben ist Vielfalt", Senckenbergmuseum, Frankfurt, 26.11.-02.12.01, ZISCHLER, H.: Auch wir haben mal klein angefangen.... Eine Klettertour am Stammbaum der Primaten.

DPZ-Colloquium, Göttingen, 20.03.02, ROOS, C.: Molecular evolution of strepsirrhines (Strepsirrhini).

Dept. of Human Genetics, Homburg, 22.04.02, ZISCHLER, H.: Molecular evolution of primates

Seminar of the Dept. of Conservation and Ecology at the Zoological Institute, Univ. Hamburg, 25.04.02, HAPKE, A.: Population genetics of *Cheirogaleus* and *Microcebus* in SE-Madagascar.

Institut für Zoologie der LMU München, 26.04.02, ZISCHLER, H. Molecular Taxonomy of primates.

Jahr der Geowissenschaften: "Leben und Erde", Naturkundemuseum, Dresden, 20.11.02, ZISCHLER, H.: Auch wir haben mal klein angefangen.... Eine Klettertour am Stammbaum der Primaten.

DPZ, Göttingen, 03.12.02, ROOS, C.: Auch wir haben mal klein angefangen.... Eine Klettertour am Stammbaum der Primaten.

## **List of publications**

### **Reviewed papers**

BÖHLE, U.-R., ZISCHLER, H. Polymorphic microsatellite loci for the mustached tamarin (*Saguinus mystax*) and their cross-species amplification in other New World Monkeys. *Mol. Ecol. Notes* (2002) 2: 1-3.

HAPKE, A., ZINNER, D., ZISCHLER, H.: Mitochondrial DNA variation in Eritrean hamadryas baboons (*Papio hamadryas hamadryas*): Life history influences population genetic structure. *Behav. Ecol. Sociobiol.* (2001) 50: 483-492.

REUS, K., MAYER, J., SAUTER, M., ZISCHLER, H., MÜLLER-LANTZSCH, N., MEESE, E.: HERV-K (OLD): Ancestor Sequences of the Human Endogenous Retrovirus Family HERV-K(HML-2). *J. Virol.* (2001) 75: 8917-8926.

ROOS, C., GEISSMANN, T.: Molecular Phylogeny of the Major Hylobatid Divisions. *Mol. Phylogenet. Evol.* (2001) 19: 486-494.

SCHMITZ, J., OHME, M., ZISCHLER, H.: SINE insertions in cladistic analyses and the phylogenetic affiliations of *Tarsius bancanus* to other primates. *Genetics* (2001) 157: 777-784.

SCHMITZ, J., OHME, M., ZISCHLER, H.: The complete mitochondrial sequence of *Tarsius bancanus*: Evidence for an extensive nucleotide compositional plasticity of primate mitochondrial DNA. *Mol. Biol. Evol.* (2002) 19: 544-553.

SCHMITZ, J., OHME, M., SURYOBROTO, B., ZISCHLER, H.: Colugo (*Cynocephalus variegatus*, Dermoptera): The primates gliding sister? *Mol. Biol. Evol.* (2002) 19: 2308-2311.

### **Non-reviewed paper**

ROOS, C., NADLER, T.: Molecular evolution of the Douc Langurs. *Zool. Garten (N.F.)* (2001) 71(1): 1-6.

## Abstracts

ROOS, C., NADLER, T., ZHANG, Y.P., ZISCHLER, H.: Molecular evolution and distribution of the superspecies *Trachypithecus [francoisi]*. *Folia Primatol.* (2001): 181-182.

NADLER, T., ROOS, C.: Systematic position, distribution and status of douc langurs (*Pygathrix*) in Vietnam. Abstracts of the XIXth Congress of the International Primatological Society, 4<sup>th</sup>-9<sup>th</sup> August 2002, Beijing, China: 301.

NADLER, T., ROOS, C.: Systematic position, distribution and status of langurs within the genus *Trachypithecus* in Vietnam. Abstracts of the XIXth Congress of the International Primatological Society, 4<sup>th</sup>-9<sup>th</sup> August 2002, Beijing, China: 302-303.

SCHÜLKE, O., ZISCHLER, H., KAPPELER, P.M.: The potential for sexual selection in a pair-living nocturnal primate. *Primate Report* (2001) 60-1: 39.

<b>Publications</b>	<b>2002</b>	<b>2001</b>	<b>2000</b>
1. Books	0	0	0
2. Publication of collected editions	0	0	0
3. Chapters in collected editions	0	0	0
4. Reviewed papers	3	4	8
5. Non-reviewed papers	0	1	3
<b>Total: 1 - 5</b>	<b>3</b>	<b>5</b>	<b>11</b>
6. Editorials	0	0	0
7. Electronic publications	0	0	0
8. Abstracts	2	2	0
<b>Publications altogether</b>	<b>5</b>	<b>7</b>	<b>11</b>

## Other scientific activities

### C. Roos

- Supervisor of "Gene Bank of Primates"
- Member of the IUCN/SSC Primate Specialist Group, Section Asia
- Reviewer for *Folia Primatologica*

**H. Zischler** is reviewer for several journals

## DEPARTMENT OF REPRODUCTIVE BIOLOGY

**Head of Department: Prof. J. K. Hodges**

### **General research objectives**

The overall aim of the Department is to explore mechanisms underlying key reproductive processes in non-human primates. The broad-based research programme is designed to generate basic information relevant to i) better understanding of problems of human reproductive health and disease, ii) better understanding of reproductive variation and factors influencing reproductive success in natural primate populations, and iii) the development and application of technologies to improve breeding and management of primates for research and conservation.

Research is carried out in the following main areas:

#### *Follicular and gametogenic function*

Studies utilize *in vitro* and *in vivo* methodologies to explore the cellular and molecular basis of follicle and gamete maturation, oocyte-somatic cell interactions and the processes of ovulation and luteinization. The information obtained is of potential practical value in the development of new approaches to fertility regulation, such as induction of ovulation and contraception based on immunisation against *Zona pellucida*.

#### *Fertilization and embryo-maternal dialogue*

Areas of investigation are IVF, mechanisms controlling *corpus luteum* function, development of the pre-implantation embryo, mechanisms of implantation, embryo-maternal communication and angiogenic supply of the early pregnant reproductive tract. Research is being carried out using a range of *in vitro* techniques as well as functional *in vivo* methodologies, such as ultrasonographic investigations using colour doppler. Studies focus on addressing problems underlying infertility (e.g. disorders in the process of implantation) but are also useful for providing marmoset blastocysts for embryonic stem cell research.

#### *Field endocrinology*

Based on the use of non-invasive endocrine methodologies (urinary and faecal hormone analysis) this research area is providing new opportunities for exploring proximate mechanisms underlying behavioural variation and for testing hypotheses concerning the evolutionary significance of primate mating systems. The main objective is to use field endocrinology as part of an integrated approach to a better understanding of the relative roles of male and female reproductive strategies in determining mating outcome (i.e. paternity) in natural primate populations.

#### *Genome Resource Bank*

A number of aspects of the work of the Department are contributing to the establishment and operation of a functional genetic resource bank for primates. Key areas include i) the development of various reproductive technologies to support the collec-

tion, storage and utilization of gametes and embryos (e.g. non-invasive reproductive assessment, semen collection, *in vitro* oocyte maturation, IVF, cryopreservation) and ii) generation of a bank of reproductive organs, tissues (normal and pathological), cells and cell lines.

Within the framework set out by the departmental research objectives and in line with the 1998 recommendations of the German Science Council, the following recent initiatives have helped to both consolidate and expand the research capabilities of the department:

*Animal alternatives*

The establishment of permanent ovarian and uterine cell lines as well as follicle/embryo culture systems in the marmoset are not only important for our basic research, but also provide opportunities for applied studies aimed at testing physiological and pharmacological substances. Various cell lines have been characterized and developed to the stage of initial testing by external cooperation partners. The development and utilization of cell lines in reproductive biology is also potentially important in contributing towards a reduction in the use of animals for research, although work along these lines is still at an early stage.

*Field endocrinology*

The establishment and validation of a range of non-invasive endocrine methodologies for quantifying gonadal and adrenal steroid output in primates provides the basis for a question-driven approach by which data on endocrinology, behaviour and genetics are combined to study reproductive processes in natural primate populations. In addition to a range of projects based on collaborations with field workers in and outside of DPZ, we have now established our own programme of field-based research.

*Conservation management*

Two new international collaborative programmes in primate conservation have recently been established. One of these is the Gibraltar Barbary Macaque Project (GBMP), a programme of scientific research and education designed to improve understanding of the biology of the Barbary macaque and to support effective conservation of the species in Gibraltar and in the wild. The programme, co-ordinated by this Department and the Gibraltar Ornithological and Natural History Society, involves a network of participating institutes from Europe and North America. The second is a project of scientific and technical collaboration between DPZ and Bogor Agricultural University to promote wildlife biology research and conservation in Indonesia. According to our Memorandum of Understanding, the main objectives include i) exchange of scientific and graduate students, ii) information and technology transfer, and iii) co-operative research and human resource development in wildlife biology and conservation.

*Disease models*

The marmoset has been further established as a model for human diseases, e.g. in studies on disorders in ovulation and implantation, endometriosis and mammary

cancer. Furthermore, in collaboration with various partners, we are establishing the marmoset as a model species for Alzheimer's and Parkinson's disease and are providing marmoset blastocysts from which embryonic stem cells as a potential therapeutic approach can be produced.

### **Structure of the department**

The work of the department is organized in three groups. Ovarian Physiology, led by Prof. Almuth Einspanier, comprises one postdoctoral scientist, three technical assistants (one supported by the DPZ; two by the DFG) and ten PhD students.

In the Gamete Biology group, two DPZ funded technicians and four PhD students support the work of the group leader Dr. Penelope Nayudu.

Dr. Michael Heistermann runs the Comparative Endocrinology group, which currently comprises three scientists (two in part time positions), two DPZ financed technicians and ten PhD students. The work of the Department is also supported by a secretary and by numerous students providing animal caretaking help.

In April 2002 Dr. Bettina Husen finished her research work in the Ovarian Physiology group and took on a new position at Solvay Pharmaceuticals GmbH, Hannover. She obtained her Habilitation at the Hannover School of Veterinary Medicine in November 2002. Dr. Husen was replaced by Dr. Martina Blaschke, who has been working here since April 2002. In September 2001, Ellen Wiese took over the secretarial work of the Department from Sabine Stuber.

Ines Frait passed her examination to become a biology technician. Christelle Ademmer obtained her Diploma in Biology in 2002 and Ingo Schwabe (2001), Ulrike Möhle (2001), Thomas Ziegler (2001) and Annette Schrod (2002) were awarded their PhD's. Congratulations are due to Dr. Almuth Einspanier who was appointed to an extraordinary professor at the Hannover School of Veterinary Medicine. She was also offered a position as C3 professor at the University of Leipzig, which she will begin in February 2003.

#### Scientists

Dr. Martina Blaschke (part time, 01.04.02-)  
Prof. Dr. Almuth Einspanier  
Dr. Michael Heistermann  
Dr. Bettina Husen (-30.04.02)  
Kai Lieder (30.05.01-)  
Dr. Ulrike Möhle (part time, 14.07.01-)  
Dr. Penelope Nayudu  
Dr. Ann-Kathrin Oerke (part time)  
Dr. Annette Schrod (part time, 28.11.02-)  
Dr. Thomas Ziegler (31.10.01-)

#### Secretary

Sabine Stuber (-30.09.01)  
Ellen Wiese (24.09.01-)

#### Technicians

Kerstin Fuhrmann  
Andrea Heistermann  
Jutta Hagedorn  
Andreas Kues  
Alexandra Marten  
Angelika Jurdzinski  
Matthias Schulz (01.04.01-30.09.02)  
Nicole Umland

#### PhD Students

Jorgelina Barrios de Tomasi  
Nicola Beindorff  
Katja Bogner  
Angela Brüns (01.01.02-)  
Tobias Deschner

PhD Students

Karin Reichert  
Antje Engelhardt  
André Ganswindt  
Leonor Hernandez (06.02.-30.11.01)  
Frauke Hegermann  
Hanan Kennich  
Stefan Kuhnert  
Julia Ostner  
Ulrike Möhle (-13.07.01)  
Petra Löttker  
Maren Huck  
Ellen Preußing  
Alessandra Quaggio Augusto (01.04.01-)  
Alexander Schneiders  
Christina Simon (15.08.02-)  
Ingo Schwabe (-30.11.01)  
Annette Schrod (-27.11.02)  
Jan Stumper  
Iris-Nadine Tillmann

Svenja Verhagen  
Ekaterina Vorobieva  
Nicola Wolff  
Thomas Ziegler (-30.10.01)

Undergraduate Students  
Christelle Ademmer (-25.01.02)

Trainees

Ines Frait (-31.01.01)  
Angela Reipert (01.02.-30.04.02)  
Anna Hermann (01.05.-01.11.01)  
Britta Schönnagel (17.02.-31.03.02)  
Saskia Teuteberg (25.11.-06.12.02)

Student assistants

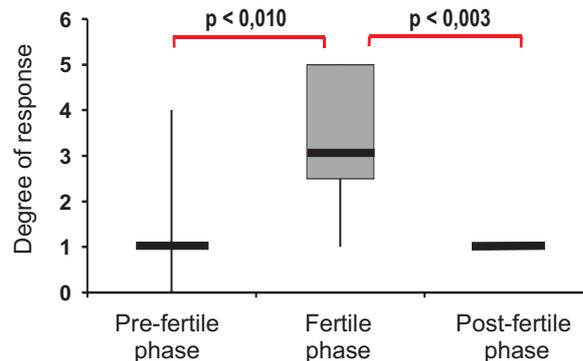
Andrea Quohs (01.04.-31.09.01)  
Dirk Beimforde (01.01.-15.03.02)  
Christiane Kott (03.04.-22.05.02)

**Progress during the year**

One focus of the studies of the Comparative Endocrinology group on male and female reproductive strategies and their adaptive significance in wild primate populations is to determine the extent to which females are able to conceal the time of ovulation from males. One line of investigation has been to examine the functional significance of perineal swellings in free-ranging chimpanzees on the Ivory Coast as part of a collaboration with the Max Planck Institute for Evolutionary Anthropology, Leipzig. Using urinary endocrine analysis for assessment of female reproductive status we have investigated the relationship between perineal swelling patterns and timing of ovulation in order to test hypotheses on the value of the swelling as a reliable signal of the female fertile phase. Our data set on 36 cycles from 12 females showed that i) the maximum swelling period was highly variable (6-18 days), ii) ovulation usually occurred during the second half of the maximum swelling phase, although its timing both in relation to the onset and end of maximum swelling varied considerably and iii) despite variation, there was a well-defined peak in probability of ovulation on day 7. The findings support the hypothesis that sex skin swelling in chimpanzees is a probabilistic or graded signal of the female fertile phase which might enable the female to manipulate male mating activities and paternity outcome. Our results have also an important practical implication in that they demonstrate that field researchers should not rely on the last two days of maximum tumescence to represent the likely time of ovulation as is currently the usual practice when approximating the periovulatory period in free-ranging chimpanzees.

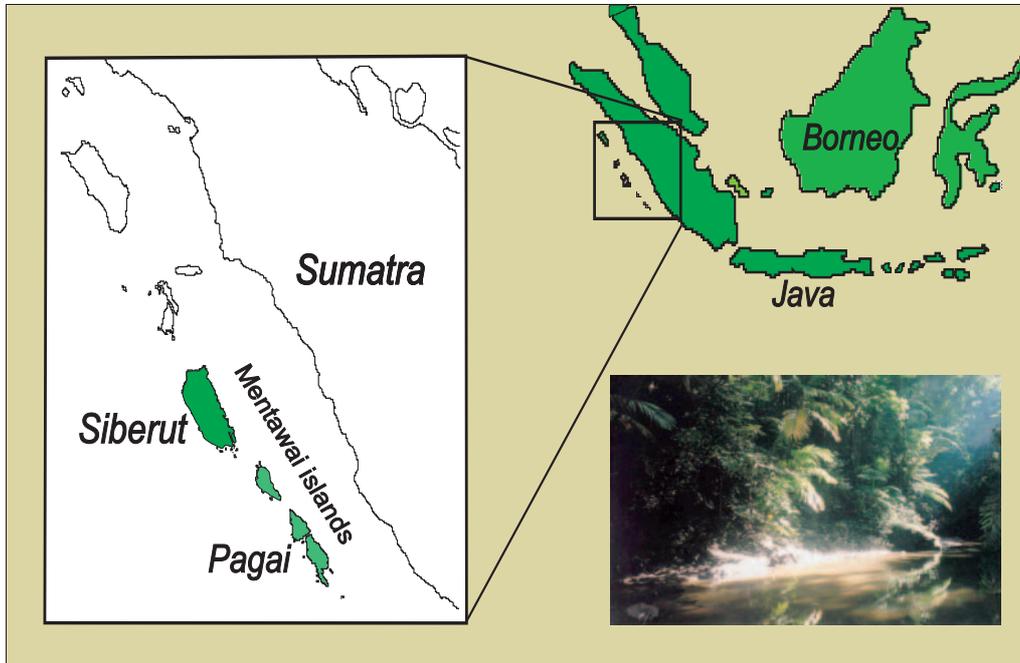
Pursuing the question of reproductive strategies and factors determining paternity from a different perspective, we have used an experimental approach to test whether males are able to discern the female fertile phase in a population of free-

ranging long-tailed macaques in West Java, Indonesia. In this study, we used a playback experiment in which the response of subordinate males to a constant auditory signal (female copulation call) was determined in relation to the female reproductive status as assessed by faecal hormone analysis. As a second measure of male interest in the female, timing of mate-guarding by  $\alpha$ -males was assessed throughout the female cycle. We found that i) the pattern of  $\alpha$ -male monopolization and male response to the copulation call was strongly correlated with the female oestrogen levels, ii) male interest in females was strongest during the fertile phase and iii) both  $\alpha$ - and subordinate males are better able to recognize the fertile phase in cycles in which conception had occurred. The results suggest that male long-tailed macaques have a higher ability to discern the female fertile phase compared, for instance, to male Hanuman langurs, the only other primate species for which such data on free-ranging populations are available. The factors underlying these species differences are not clear. In contrast to female Hanuman langurs, however, long-tailed macaque females appear to possess a variety of characteristics (e.g. perineal swelling, copulation call, olfactory signals) which males might be able to use as signals to discern female reproductive status. How this affects male and female reproductive strategies and ultimately paternity outcome is currently being investigated.

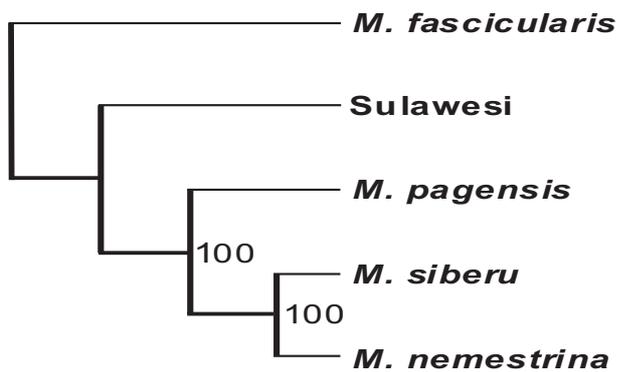


*Using a playback experiment we could show that in free-ranging long-tailed macaques (left) subordinate males showed the highest and fastest response towards a constantly played female copulation call during the fertile phase of the female cycle (right). The increased interest of the males during this particular period is providing evidence that male long-tailed macaques are better able to discern the female fertile phase than for example Hanuman langurs.*

The Biology and Conservation of the Mentawai island macaques is one of the key projects within our new programme of Conservation Management. The Mentawai island group off Sumatra's west coast is not only of special interest to the study of macaque evolution, it is also of major importance in terms of biodiversity conservation. It has at least four unique (and endangered) primate species, representing one of the highest degrees of endemism with regard to land surface, anywhere. Our project (Siberut Conservation Project, SCP) which is carried out as an international collaboration between institutes in Germany, France, Indonesia, USA and Canada has



Based in the Peleonan forest (photo above) in North Siberut, our project aims to study and preserve the Mentawai Islands unique primate fauna. Of special interest are the Mentawai macaques, whose evolutionary history and taxonomy are poorly understood. Our initial genetic data suggest a paraphyletic origin of these macaques and the existence of two distinct species [*Macaca siberu* (photo below) and *Macaca pagensis*].

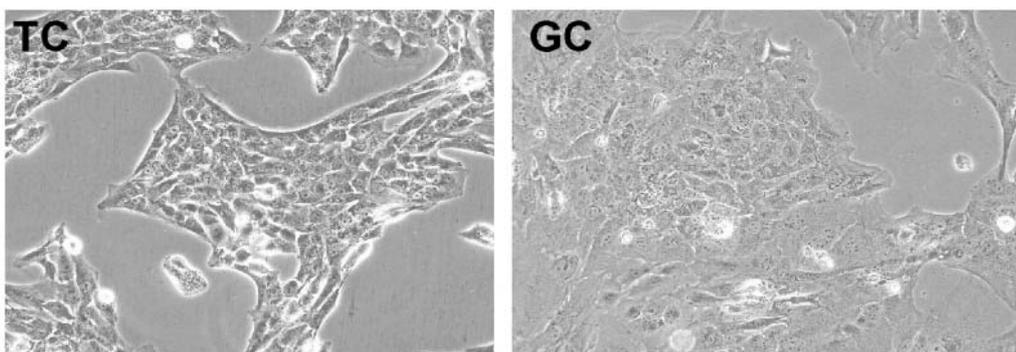


the following main objectives: i) to clarify the taxonomic status of the island's macaques and explore evolutionary mechanisms influencing macaque radiation ii) to study the biology and promote conservation of Mentawai primates and iii) to help sustainable economic development in Siberut as an alternative to logging. After two surveys (2000; 2001), a suitable study site has been found in a strategic location in the Peleonan forest in northern Siberut. All essential contacts (both local and institutional) have been established and official permission obtained to enable us to begin construction of a field site for research at this location. We have also recently begun a transport improvement scheme (provision of boats, boat engines and training) as part of a plan to assist local inhabitants to market fruits and vegetables as an alternative to logging a means of generating cash income.

As part of our initial efforts to elucidate the evolutionary history and taxonomy of the Mentawai macaques, sequence analysis of part of the cytochrome b gene from faecal samples collected from individuals from Siberut and the other Mentawai islands as well as mainland Sumatra was carried out. Preliminary results are highly interesting, suggesting a paraphyletic origin of the Mentawai macaques, with the Siberut population being more closely related to *Macaca nemestrina* from Sumatra, than it is to populations from the other Mentawai islands. This opens up the unexpected possibility of two unrelated colonization events on these remote islands. Furthermore, the data also suggest the existence of two separate species of macaque: one from Siberut (*Macaca siberu*) and one from the more southern islands of Sipora and Pagai (*Macaca pagensis*).

Additional details on the SCP project are available under [www.siberutisland.org](http://www.siberutisland.org). Information on our activities in the project on the Biology and Conservation of the Barbary Macaque (GBMP) can be found under [www.gibnet.gi/~gonhs/gibraltar/index.htm](http://www.gibnet.gi/~gonhs/gibraltar/index.htm).

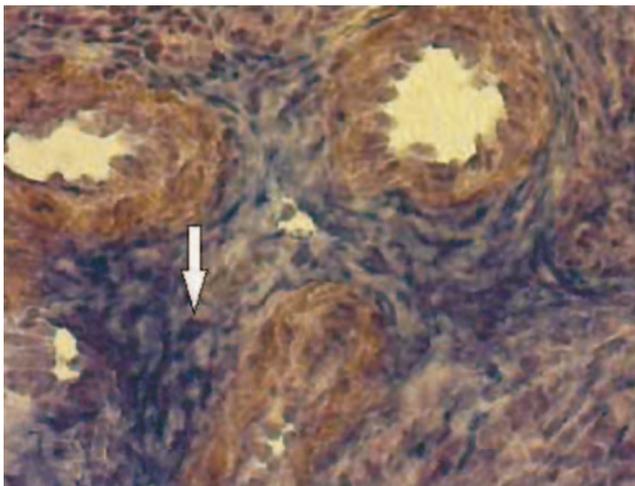
One of the main objectives of the work of the Ovarian Physiology group during the last two years has been the establishment of immortalized primate cell lines for both basic research and for the testing of pharmacological substances. 15 granulosa and 13 theca cell lines from the marmoset monkey (*Callithrix jacchus*) have been



Light microscopic picture (200x) of adherent theca- and granulosa cells (TC/GC) following their immortalization. After having reached the stage of confluence, the cells are enzymatically detached from the surface and cultured for further cell expansions and isolation of RNA and protein.

successfully established. Through DNA and protein characterization and the demonstration of specific markers, the developmental status of these ovarian cells has been characterized. The specific properties of the cell lines were not markedly affected by the immortalization process and the attributes of the various ovarian cells was comparable to *in vivo* cells characterising different stages of follicular development, ovulation and luteinization. We hope that the production of cell lines and their use will make an important contribution towards a reduction in the number of animals used for research in the not-too-distant future.

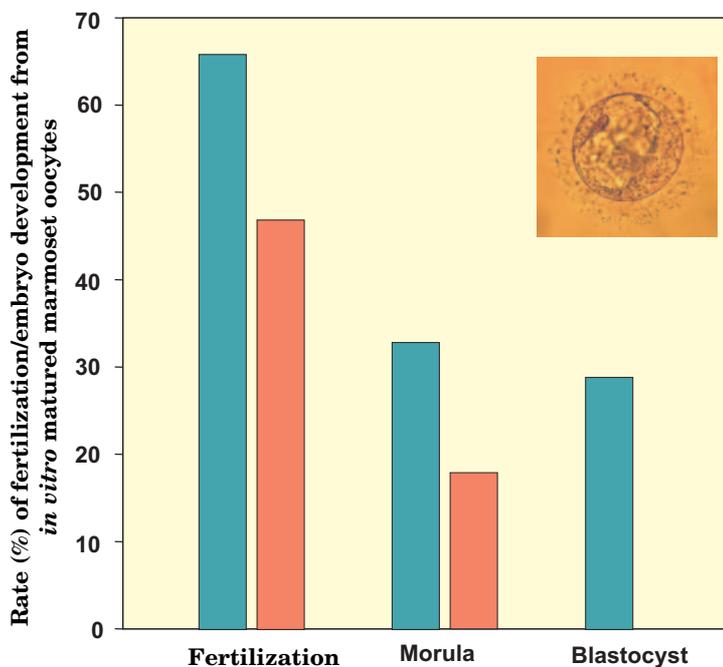
In a second important area, which focuses on the characterization of the marmoset relaxin receptor, we have been able to successfully characterize the receptors LGR7 and LGR8. In addition, we have demonstrated the existence of these receptors in both reproductive (e.g. ovary, uterus, testis) as well as non-reproductive (e.g. liver, kidney, brain) tissues. Following the development of marmoset specific probes, we have also verified the local expression of both receptors. In addition, we have demonstrated a massive up-regulation of both receptors at the time of implantation, when relaxin levels in blood also increase significantly. Our findings are thus in line with the hypothesis that relaxin is an important factor for implantation and maternal-fetal dialogue in primates.



*In-situ hybridisation (300x) of uterine tissue in the marmoset using a DIG-labelled probe to demonstrate RNA expression of the relaxin receptor. The cells which express LGR7 mRNA are stained blue. The picture clearly demonstrates the local expression of the relaxin receptor in some stroma cells (white arrow).*

A major goal of the research activities in the Gamete Biology group over the last two years has been the development and testing of an improved IVF and embryo development protocol using *in vitro* matured oocytes harvested from antral follicles from unstimulated cyclic female marmosets. The production of embryos has now reached a degree of success comparable to that in macaques, making *in vitro* maturation systems a practical method for investigating gamete function and developmental competence in the marmoset. Oocytes from small and medium sized antral follicles can be matured to produce an expansion of the surrounding cumulus cell mass at a rate of 80 %. Cumulus cell expansion is important for the final pre-fertilization changes of the sperm, thereby promoting successful gamete fusion. The

current fertilization rate of the matured oocytes averages 65 %. Of the fertilized oocytes, around 30 % develop to advanced morula stage and 30 % of these develop to blastocysts. This improvement in *in vitro* fertilization and embryo development success depends not only on enhanced *in vitro* oocyte maturation and fertilization conditions, but also on the optimization of sperm collection (e.g. using vibrostimulation) and preparation (e.g. density gradient sperm washing and *in vitro* capacitation). Oocyte quality, however, seems to be a major limiting factor in the success rate and appears to be strongly influenced by numerous factors, such as age, weight, endocrine status, stress level, health status, and treatments undergone. One example of a treatment apparently having a negative effect over the long term is regular application of a PGF2alpha analogue (a standard cycle control method for the marmoset) which leads to reduction in oocyte quality as evaluated by capacity to undergo fertil-



*Proportion of in vitro embryo production obtained from marmosets after a single PGF 2alpha analogue treatment cycle (blue-green bars) compared to those undergoing more than eight treatment cycles (red bars). The results indicate that, using newly developed culture methods, high embryo development rates can be achieved with in vitro matured oocytes from antral follicles. They also show, however, that high embryo development rates are only achievable with healthy oocytes.*

*One factor, shown here, having a negative effect both on oocyte quantity and quality is the prolonged application of PGF 2alpha analogue which is routinely used to control the ovarian cycle of the marmoset.*

ization and embryo development.

On the male gamete side, a newly established technique of key importance is a density gradient sperm washing method. This effectively removes seminal plasma and coagulum, and improves the quality of sperm samples by removing dead sperm as well as bacteria and viruses. The technique is important in that it i) ensures clean conditions for *in vitro* culture and ii) can prevent disease transmission when sperm samples from males of unknown disease status are used for artificial insemination

(AI), a particular danger from sperm banks intended for use with endangered species. It is a critical technique in the production of specific pathogen free (SPF) genetically defined primates for biomedical research because it allows the use of non-SPF males of appropriate genetic background as sperm donors for SPF females.

### **Integration into national and international research**

The department is considered to be one of the leading groups in reproductive biology, due to its broad spectrum of methodologies and comparative approach to both basic and applied aspects of primate research. In all main areas of the departmental work, research is largely carried out as part of bi- or multilateral national and international collaborations. The partners of these collaborations come mainly from Universities, either within Germany (e.g. University of Göttingen, Hannover Veterinary School, Universities of Münster, Giessen, Bayreuth) or abroad (e.g. Netherlands, Belgium, England, Slovenia, Indonesia, Mexico, Brazil, Australia) as well as from non-university research institutions (e.g. Max Planck Institutes, IHF Hamburg, Howard Florey Institute, Australia). Members of the Department are also involved in an EU-funded project on "Glucocorticoid hormone programming in early life and its impact on adult health" which is carried out together with the Department of Neurobiology, the Working Group Primate Genetics and other national and international institutions. Together with the "Gibraltar Ornithological and Natural History Society", the Department is coordinating an international research network on "The Biology and Conservation of the Barbary Macaques", which to date includes the Chicago Field Museum, USA, the Anthropological Institute of Zürich University, the Department of Ethology, University of Vienna and the Department of Biological Anthropology of the University Toronto, Canada. Finally, there are various cooperations with national and international industrial partners (e.g. Schering AG, Solvay Pharmaceuticals), particularly in areas of applied research relevant to human reproductive medicine.

The department is also involved in a range of interdepartmental projects with other DPZ scientists. Socio-endocrinological studies on free-ranging primate populations are being carried out together with the Department of Ethology and Ecology and the Working Group Primate Genetics. Close collaborations also exist with the Department of Veterinary Medicine and Primate Husbandry in various projects investigating reproductive abnormalities in the common marmoset and the causes and consequences of pathological processes of the reproductive tract. In a collaboration with the Department of Virology and Immunology, reproductive cell lines of the marmoset are being established.

**Projects and partners in co-operation**

(I: interdepartmental projects, E: external co-operation; A: project completed, L: current project)

<b>Projects and Partners of the Department of Reproductive Biology</b>		
<b>Examination of serum relaxin concentrations in breast cancer patients</b> C. BINDER (Dept. of Haematology/Oncology, Univ. Göttingen), L. BINDER, L. GURLIT (Clinical Chemistry, Univ. Göttingen), D. BERKOVIC (Dept. of Haematology/Oncology, Univ. Göttingen), <b>A. EINSPANIER</b>	E	A
<b>Detection of serum relaxin during early pregnancy in different races of bitches</b> <b>A. EINSPANIER</b> , B. WÜNSCH, A. GÜNZEL-APEL (School of Veterinary Medicine, Hannover)	E	A
<b>Examination of tumors in the female reproductive tract of primates</b> <b>A. EINSPANIER</b> , F.-J. KAUP (Dept. of Veterinary Medicine and Primate Husbandry, DPZ)	I	A
<b>IGF-BPI expression in the uterus of the marmoset monkey</b> A. FAZTEBAS (Dept. of Obstetrics and Gynecology, Univ. Illinois, USA), <b>B. HUSEN</b> , <b>A. EINSPANIER</b>	E	L
<b>The influence of relaxin application on the process of implantation and pregnancy in the marmoset monkey</b> <b>A. EINSPANIER</b> , N. BEINDORFF, K. FUHRMANN, <b>A. MARTEN</b> , E. UNEMORI (Connective Therapeutics, USA)	E	A
<b>Relaxin: an important factor for implantation in the common marmoset monkey</b> <b>A. EINSPANIER</b> , K. FUHRMANN, <b>A. MARTEN</b> , <b>A. JURDZINSKI</b> , D.O. SHERWOOD (Univ. Illinois, Chicago, USA), E. UNEMORI (Connective Therapeutics, USA)	E	A
<b>Regulation of estradiol-synthesis by 17<math>\beta</math>-hydroxysteroid dehydrogenases type 1 and type 7 in the ovary and placenta of the marmoset monkey</b> <b>I. SCHWABE</b> , <b>B. HUSEN</b> , <b>A. EINSPANIER</b> , J. ADAMSKI (Inst. for Experimental Genetics, Research Centre for Environment and Health, Neuherberg)	E	A
<b>Sex- and tissue-specific expression of 17<math>\beta</math>-hydroxysteroid dehydrogenases in the marmoset monkey</b> <b>B. HUSEN</b> , <b>I. SCHWABE</b> , K. FUHRMANN, <b>A. EINSPANIER</b>		A

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<b>Projects and Partners of the Department of Reproductive Biology</b>		
<b>Luteinisation of the preovulatory follicle in the common marmoset monkey</b> <b>A. EINSPANIER, A. MARTEN, A. JURDZINSKI</b>		A
<b>Regulation of the expression of estradiol-inactivation enzymes throughout the reproductive cycle in the uterus of the marmoset monkey</b> <b>B. HUSEN, A. EINSPANIER, J. ADAMSKI</b> (Inst. for Experimental Genetics, Research Centre for Environment and Health, Neuherberg)	E	A
<b>Primate relaxin physiology: comparative studies on the cellular level and in relation to whole animal physiology</b> <b>A. EINSPANIER, K. FUHRMANN, B. HUSEN, A. JURDZINSKI</b>		A
<b>Effect of extracellular matrix on the process of luteinisation in the common marmoset monkey</b> <b>A. EINSPANIER, A. MARTEN, B. HUSEN</b>		L
<b>Aging in the female and male reproductive tract of primates</b> <b>A. EINSPANIER, B. HUSEN, R. IVELL</b> (Inst. of Hormone and Fertility Research, Hamburg)	E	L
<b>Establishment of ovarian and uterine cell lines</b> <b>B. HUSEN, K. LIEDER, W. LÜKE, H. PETRY</b> (Dept. of Virology and Immunology, DPZ), <b>A. EINSPANIER</b>	I	L
<b>Collection of blastocysts in the marmoset monkey using surgical flushing</b> <b>E. PREUSSING, A. EINSPANIER, P. NAYUDU, M. HEISTERMANN</b>		A
<b>Expression pattern of steroid receptors, relaxin and enzymes in uterus and ovary of the baboon</b> <b>B. HUSEN, A. EINSPANIER, A. FAZLEABAS</b> (Univ. Illinois, Chicago, USA)	E	L
<b>Ovulation, perineal swelling and reproductive strategies in the bonobo (<i>Pan paniscus</i>)</b> <b>M. HEISTERMANN, K. REICHERT</b> (Univ. Bayreuth), <b>G. HOHMANN</b> (MPI for Evolutionary Anthropology, Leipzig), <b>J.K. HODGES</b>	E	A
<b>Socio-endocrinology of group-living lemurs</b> <b>M. HEISTERMANN, J. OSTNER</b> (Dept. of Ethology and Ecology, DPZ), <b>J.K. HODGES, P.M. KAPPELER</b> (Dept. of Ethology and Ecology, DPZ)	I	L
<b>Non-invasive endocrine assessment of female and male reproductive status in the Sumatran rhinoceros</b> <b>M. AGIL</b> (Univ. Bogor, Indonesia), <b>M. HEISTERMANN, J.K. HODGES</b>	E	L

<b>Projects and Partners of the Department of Reproductive Biology</b>		
<p><b>Studies on the genetic and reproductive status and parasite load of lion-tailed macaques living in fragmented populations: biological basis for the development of <i>in situ</i> und <i>ex situ</i> conservation programmes</b></p> <p>W. KAUMANN (Cologne Zoo), A. KUMAR, M. SINGH (Salim Ali Centre for Ornithology and Natural History, Coimbatore, India), A. SCHREIBER, P. SCHMITT (Univ. Heidelberg), <b>C. KNOGGE, M. HEISTERMANN, J.K. HODGES</b></p>	E	A
<p><b>Development and application of non-invasive endocrine methodology for assessing gonadal status in male non-human primates</b></p> <p><b>U. MÖHLE, M. HEISTERMANN, R. PALME</b> (Inst. of Biochemistry, Univ. Vet. Medicine, Vienna, A), <b>J.K. HODGES</b></p>	E	A
<p><b>Proximate regulation and genetic consequences of mating systems in polyandrous tamarins</b></p> <p>E.W. HEYMAN, M. HUCK, P. LÖTTKER (Dept. of Ethology and Ecology, DPZ), U.-R. BÖHLE, G. SCHWIEGK (Working Group Primate Genetics, DPZ), <b>M. HEISTERMANN, J.K. HODGES</b></p>	I	L
<p><b>Socio-endocrinological studies on male quality, mate choice and reproductive strategies in free-ranging Thomas langurs</b></p> <p>S. WICH, L. STERCK (Projectgroup of Ethology and Socio-Ecology, Univ. Utrecht, NL), <b>M. HEISTERMANN</b></p>	E	A
<p><b>Influence of female reproductive status on female mate choice in long-tailed macaques (<i>Macaca fascicularis</i>)</b></p> <p>E. NIKITOPOULOS, L. STERCK (Projectgroup of Ethologie and Socio-Ecology, Univ. Utrecht, NL), <b>M. HEISTERMANN</b></p>	E	L
<p><b>Significance of male and female reproductive strategies for the determination of paternity in free-ranging long-tailed macaques (<i>Macaca fascicularis</i>)</b></p> <p>A. ENGELHARDT, C. NIEMITZ (Univ. Berlin), P. NUERNBERG (Charité Berlin), <b>J.K. HODGES, M. HEISTERMANN</b></p>	E	L
<p><b>Socio-endocrinological studies on the functional significance of female sexual swelling in free-ranging chimpanzees (<i>Pan troglodytes</i>)</b></p> <p>T. DESCHNER (MPI for Evolutionary Anthropology, Leipzig), <b>M. HEISTERMANN, J.K. HODGES, C. BOESCH</b> (MPI for Evolutionary Anthropology, Leipzig)</p>	E	L
<p><b>Reconciliation and stress in bonobos (<i>Pan paniscus</i>)</b></p> <p>B. MEULEMANN, L. VAN ELSACKER (Royal Zoological Society of Antwerp, B), <b>J.K. HODGES, M. HEISTERMANN</b></p>	E	A

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<b>Projects and Partners of the Department of Reproductive Biology</b>		
<b>Socio-endocrinological studies on the function of anogenital swellings in free-ranging Barbary macaques</b> U. MÖHLE, V. REINBERG, J. DITTAMI (Univ. Wien, A), M. HEISTERMANN, J.K. HODGES	E	L
<b>Studies on the significance of social and ecological factors on adrenal function in free-ranging male sifakas</b> C. FICHTEL (Dept. of Neurobiology, DPZ), M. HEISTERMANN	I	A
<b>Comparative endocrine characterisation of pregnancy in lemurs</b> P. GERBER (Inst. of Anthropology, Univ. Zürich, CH), P. MOISSON (Mulhouse Zoo, F), M. HEISTERMANN	E	L
<b>Endocrine and behavioural studies on the effects of socio-dynamic processes on adrenal function in male cotton-top tamarins</b> F. PELAEZ, M. SUAREZ, C. GIL BURMAN (Univ. Madrid, E), M. HEISTERMANN	E	A
<b>Population genetics and demography in wild Barbary macaques</b> L. MODOLO (Inst. of Anthropology, Univ. Zürich, CH), U. MÖHLE, J.K. HODGES, R.D. MARTIN (Chicago Field Museum, USA)	E	L
<b>Studies on the interrelationship between social status, mating activities and endocrine gonadal and adrenal function in the Tonkean macaque</b> B. THIERRY (Centre de Primatologie, Strasbourg, F), J.K. HODGES, M. HEISTERMANN	E	L
<b>Intra-sexual competition and testis and gamete function in primates</b> J.K. HODGES, G. WEINBAUER (Inst. of Reproductive Medicine, Univ. Münster), A. SCHNEIDERS, A. SCHROD, J. WISTUBA, M. LÜTJENS, H. ASLAM (Inst. of Reproductive Medicine, Univ. Münster)	E	L
<b>Studies on the interrelationships between androgen status and behaviour in male and female bonobos</b> A. SANNEN, L. VAN ELSACKER (Royal Zoological Society of Antwerp, B), J.K. HODGES, M. HEISTERMANN	E	L
<b>Endocrine and behavioural correlates of musth in the African elephant</b> A. GANSWINDT, M. ACOSTA (Carbaceno Elephant Research Project, E), U. BECHERT (Oregon State Univ., USA), L.E.L. RASMUSSEN (Oregon Graduate Inst., USA), H. RASMUSSEN (Univ. Oxford, UK), N. SACHSER (Univ. Münster), M. HEISTERMANN, J.K. HODGES	E	L

<b>Projects and Partners of the Department of Reproductive Biology</b>		
<b>Comparative studies on the endocrine correlates of dominance and reproductive success in male great apes</b> E. VOROBIEVA, H. ZISCHLER (Working Group Primate Genetics, DPZ), E. ZIMMERMANN (School of Vet. Medicine, Hannover), M. HEISTERMANN, J.K. HODGES	E,I	L
<b>Behavioural and endocrine measures of stress and gonadal status in male gorillas living in all male groups</b> N. WOLFF, M. BÖER (School of Vet. Medicine, Hannover), M. HEISTERMANN, J.K. HODGES	E	L
<b>Non-invasive assessment of female reproductive status and adrenal function in Douc langurs</b> C. ADEMMEER (Univ. Köln), W. KAUMANN (Cologne Zoo), M. HEISTERMANN, J.K. HODGES	E	A
<b>Endocrine characterisation of pregnancy in free-ranging <i>Procolobus verus</i></b> R. NOE, A. BRAMLEY (Univ. Strasbourg, F), M. HEISTERMANN	E	L
<b>Evolution, behaviour and conservation of Mentawai island primates</b> C. ABEGG, T. ZIEGLER, B. THIERRY (Centre de Primatologie, Strasbourg, F), R.D. MARTIN (Chicago Field Museum, USA), U. BECHERT (Oregon State Univ., USA), J.K. HODGES	E	L
<b>Molecular phylogeny of the Mentawai macaques</b> C. ABEGG, C. ROOS, H. ZISCHLER (Working Group Primate Genetics, DPZ), T. ZIEGLER, J.K. HODGES	I	L
<b>Development of an optimised protocol for <i>in vitro</i> fertilization and embryonic cell culture from <i>in vitro</i> matured marmoset oocytes</b> P.L. NAYUDU, N. UMLAND, A. KUES		L
<b>Influence of FSH und LH concentrations and temperature on <i>in vitro</i> oocyte maturation in <i>Callithrix jacchus</i></b> E. ISACHENKO (IVF-Lab., Univ. Cologne), P.L. NAYUDU, H.-W. MICHELMANN (Working Group of Reproductive Medicine, Univ. Göttingen)	E	A
<b>Characterization of follicular dynamics and ovarian productivity during natural and controlled ovarian cycles in the marmoset</b> E. ISACHENKO (IVF Lab. Univ. Cologne), H.-W. MICHELMANN (Working Group of Reproductive Medicine, Univ. Göttingen), R. GILCHRIST (Univ. Adelaide, Australia), M. WICHEREK, M. HEISTERMANN, A. EINSPANIER, P.L. NAYUDU	E	A

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<b>Projects and Partners of the Department of Reproductive Biology</b>		
<b>Development of a culture system for the production of mature and functional oocytes from preantral follicles of the marmoset monkey</b> J. WU, P.L. NAYUDU, H.W. MICHELMANN (Working Group of Reproductive Medicine, Univ. Göttingen)	E	A
<b>Studies on chromosomal integrity of <i>in vitro</i> matured oocytes of the marmoset monkey</b> S. DELIMITREVA (Dept. of Biology, Sofia, BG), P.L. NAYUDU, H.W. MICHELMANN (Working Group of Reproductive Medicine, Univ. Göttingen)	E	L
<b>Collection of marmoset blastocysts for development of embryonic stem cell lines</b> A. EINSPANIER, A. MANSURI (MPI for Biophysical Chemistry, Göttingen), P.L. NAYUDU, E. FUCHS (Dept. of Neurobiology, DPZ), M. HEISTERMANN	E	L
<b>Development and application of rapid freezing methods for oocytes, ovaries and ovary pieces of new born marmoset monkeys</b> E. ISACHENKO (IVF-Lab., Univ. Cologne), H.-W. MICHELMANN (Working Group of Reproductive Medicine, Univ. Göttingen), P.L. NAYUDU	E	L
<b>Further development of a culture system for the production of mature and functional oocytes from early developmental stages of the marmoset monkey and the human</b> P.L. NAYUDU, H.-W. MICHELMANN (Working Group of Reproductive Medicine, Univ. Göttingen)	E	L
<b>Correlation of age, body weight, health and cycle status on ovarian productivity in the marmoset monkey</b> E. ISACHENKO (IVF-Lab., Univ. Cologne), H.-W. MICHELMANN (Working Group of Reproductive Medicine, Univ. Göttingen), P.L. NAYUDU	E	L
<b>Stage specific role of FSH isoforms for the development of ovarian follicles <i>in vitro</i></b> J. BARRIOS DE TOMASI, P.L. NAYUDU, A. ULLOA-AGUIRRE (Reproductive Medicine Unit, Mexican Inst. for Social Security, Mexico City, Mexico)	E	L
<b>Development of a primate sperm wash technique based on density gradient centrifugation, for the removal of bacterial and viral contamination</b> N. UMLAND, A. KUES, L. HERNANDES, P.L. NAYUDU		L

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<b>Projects and Partners of the Department of Reproductive Biology</b>		
<b>Development and application of a rapid freezing method using sperms collected by vibrostimulation from the marmoset monkey and other species</b> N. UMLAND, A. KUES, L. HERNANDES, P.L. NAYUDU		L
<b>Investigation of genetic control of coagulation promoting seminal plasma proteins in the New World monkey</b> A. LUNDWALL, C. VALTONEN-ANDRÉ (Dept. of Laboratory Medicine, Lund Univ., Univ. Hospital, Malmö, S), N. UMLAND, A. SCHROD, P.L. NAYUDU	E	L
<b>Investigation of gene expression in the immature and <i>in vitro</i> matured marmoset oocyte</b> C. WRENZYCKI, H. NIEMANN (Biotechnology Group, Inst. of Animal Breeding and Animal Behaviour, Neustadt), P.L. NAYUDU	E	L
<b>Investigation of the DAZL gene in marmoset ovarien tissue</b> P. VOGT (Inst. Humangenetic, Univ. Heidelberg), P.L. NAYUDU	E	L
<b>Investigation of the composition and development of the marmoset zona pellucida with particular emphasis on ZP2</b> K. BOGNER, S. KUHNERT, E. HINSCH (Centre for Dermatology and Andrology, Univ. Gießen), P.L. NAYUDU	E	L
<b>Establishment of a non-invasive method for the collection of embryos of the marmoset monkey (<i>Callithrix jacchus</i>)</b> E. PREUSSING, A. EINSPANIER, P.L. NAYUDU, M. HEISTER-MANN, S. RENSING, M. ZIEGLER (Dept. of Veterinary Medicine and Primate Husbandry, DPZ)	I	L

**Stays of DPZ scientists in other institutions**

<b>Name/Institute/Duration</b>	<b>Project</b>
Bettina Husen GSF Centre for Research, Inst. Exp. Genetics, Neuherberg, 01.-30.04.01	Analysis of patterns of HSD expression and production of microarray
Nicola Beindorff Veterinary School, Cambridge, UK 23.-31.03.01	Training in tumorigenesis
Nicola Beindorff School of Veterinary Medicine, Hannover 08.-19.01.01	Participation in a course on animal experiments

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<b>Name/Institute/Duration</b>	<b>Project</b>
Alessandra Quaggio Augusto School of Veterinary Medicine, Hannover 04.-12.03.02	Participation in a course on preparing for examination
Almuth Einspanier Connections Cooperation, Boston, USA 03.-10.07.02	Participation in the Serono Symposium "Embryo Implantation – Relaxin in Primates"
Ulrike Möhle Center for Life Science Study, Agricultural Univ. Bogor, Indonesia 31.01.-28.02.01	Set up of a hormone laboratory
Andre Ganswindt Univ. Münster 12.-30.11.01; 22.04.-07.06.02	Practical courses in behavioural biology
Andre Ganswindt Inst. of Biochemical, Veterinary med. Univ. Vienna, A 15.-21.04.02	HPLC analysis of glucocorticoid metabolites in the African elephant
Antje Engelhardt IPB Agricultural Univ. of Bogor, Indonesia 10.-26.06.02	Co-operation with Balikpapan Orang Utan Reintroduction Project and assistance in semen collection from primates
Annette Schrod IPB Agricultural Univ. of Bogor, Indonesia 05.-26.06.02	Semen collection and analysis in Indonesian Primates
Ann-Kathrin Oerke Research camp Samburu, Kenia 21.06.-04.09.02	Studies on distribution, association and movement patterns of male African elephants
J.K. Hodges IPB Agricultural Univ. of Bogor, Indonesia 18.02.-13.03.01;05.-26.06.02	Establishment and continuation of cooperative projects and assistance in semen collection in primates
J.K. Hodges Gibraltar Ornithological and Natural History Society (GOHNS), Gibraltar 09.-19.04.01; 10.-15.11.01; 18.-24.04.02	Establishment and continuation of the Gibraltar Barbary Macaque Project
J.K. Hodges Parque de la Naturaleza de Cabarceno, E 19.-23.04.01	Cabarceno Elephant Research Project Co-ordinations
J.K. Hodges Save the Elephants, Nairobi, Kenia 09.-16.02.02	Establishment of research collaboration with Save the Elephants
Andre Ganswindt Research Camp Samburu, Kenia 06.-13.09.02	Data collection for the project "Endocrine and behavioural correlates of musth in free ranging African elephants"

Name/Institute/Duration	Project
Antje Engelhardt Inst. of Medical Genetics, Charité, Humboldt Univ. Berlin 29.11.-13.12.02	Genetic paternity analyses in free-ranging long-tailed macaques

Visited institution	Duration of stay (2001/2002)		
	< 1 month	1 - 3 months	> 3 month
German universities, research or service institutions	4	2	0
European universities, research or service institutions	4	0	0
Universities, research or service institutions outside Europe	7	2	0
<b>Altogether</b>	<b>17</b>	<b>4</b>	<b>0</b>

### Scientific Contributions

#### Doctoral theses

MÖHLE, U.: Metabolism and excretion of testosterone in male non-human primates and its significance for the development of non-invasive methods for assessing male gonadal activity. Faculty of Biology, Univ. Hamburg (2001).

SCHROD, A.: Comparative analyses of sperm motility, morphology and morphometry in non-human primates with different mating systems. Department of Reproductive Medicine, School of Veterinary Medicine, Hannover (2002).

SCHWABE, I.: Significance of estradiol synthesis by 17 $\beta$ -hydroxysteroid dehydrogenase type1 and type7 in the ovary and placenta of the marmoset monkey. Department of Reproductive Medicine, School of Veterinary Medicine, Hannover (2001).

ZIEGLER, T.: Socio-endocrine studies on reproductive strategies of female Hanuman langurs (*Semnopithecus entellus*) in Nepal. Faculty of Biology, Univ. Giessen (2001).

#### Diploma theses

ADEMMER, C.: Reproduction and stress in Douc langurs (*Pygathrix nemaeus*): non-invasive assessment of endocrine status. Faculty of Biology, Univ. Köln (2002)

#### Habilitation theses

HUSEN, B.: Possibilities for direct cell-cell interactions by integrins: Influence on fertilization, implantation and embryogenesis. School of Veterinary Medicine, Hannover (2002).

**Congress contributions**

XVIII<sup>th</sup> Congress of the International Primatological Society, Adelaide, Australia, 07.-14.01.01,

ZIEGLER, T., HEISTERMANN, M., HODGES, J.K.: Socio-endocrine studies on paternity confusion in a multi-male group of seasonally breeding wild Hanuman langurs (*Presbytis entellus*).

EIBL, K., HEISTERMANN, M., HODGES, J.K., HOHMANN, G., BOESCH, C.: Are genital swellings of female bonobos an honest signal of ovulation?

DE VLEESCHOUWER, K., VAN ELSACKER, L., LEUS, K., HEISTERMANN, M.: Melengestrol acetate (MGA) implants as a population control method in *Leontopithecus chrysomelas*.

Symposium "Primate Evolution: Phylogenetic, Physiological and Behavioural Aspects", Göttingen, 06.02.01, VOROBIEVA, E., HEISTERMANN, M., HODGES, J.K.: Endocrine correlates of dominance and mating success in male Great apes.

Meeting of the "European Elephant Keeper and Manager Association", Rotterdam, NL, 07.-09.02.01, OERKE, A.-K.: Hormonal studies in elephant urine.

34<sup>th</sup> Congress "Physiology and Pathology of Reproduction", Giessen, 22.-23.02.01, BOGNER, K., NAYUDU, P. L., HINSCH, E., HINSCH, K.: Localization and function of a ZP2 epitope (ZP2-20) in the marmoset monkey.

BEINDORFF, N., VERHAGEN, S., EINSPANIER, A.: Lutetotropic effect of relaxin in the marmoset monkey.

Annual Meeting of the Zoological Society of Germany, Bielefeld, 05.-08.06.01, REYES, R., SOMMER, S., HEISTERMANN, M., HODGES, J.K., GANZHORN, J.: Comparison of the hormone levels of captive and free-living Malagasy giant jumping rats, *Hypogeomys antimena* (Rodentia, Nesomyinae).

International Symposium on Research in Elephants and Rhinos, Wien, A, 07.-11.06.01,

GANSWINDT, A., HEISTERMANN, M., HODGES, J.K.: Faecal glucocorticoid and androgen metabolite excretion in male African elephants (*Loxodonta africana*).

AGIL, M., RIYANTO, M.A., SUMAMPAK, T., HODGES, J.K., VAN STRIEN, N.J.: A program of managed breeding for the Sumatran rhinoceros at the Sumatran Rhino Sanctuary (SRS) Way Kamba National Park Lampung, Indonesia.

OERKE, A.K., HEISTERMANN, M., HODGES, J.K.: Reproductive characteristics of the European elephant population: Long-term cycle and pregnancy data based on non-invasive methodology.

34<sup>th</sup> Meeting of the Society for the Study of Reproduction, Ottawa, Canada, 28.07.-02.08.01,

EINSPANIER, A., UNEMORI, E., JURDZINSKI, A., FUHRMANN, K.: Relaxin supports implantation and early pregnancy in the common marmoset monkey.

HUSEN, B., SCHWABE, I., EINSPANIER, A.: Estradiol synthesizing 17 $\beta$ -hydroxysteroid dehydrogenases in reproductive tissues of the marmoset monkey.

XXVII<sup>th</sup> International Ethological Conference, Tübingen, 22.-29.08.01, EIBL, K., BOESCH, C., HEISTERMANN, M., HODGES, J.K., HOHMANN, G.: Do genital swellings in bonobos conceal or signal ovulation?

Annual Conference of EAZA, Prag, CZ, 20.-21.09.01, GANSWINDT, A., HEISTERMANN, M., HODGES, J.K.: Endocrine and behavioural correlates of musth in captive African elephants (*Loxodonta africana*).

10<sup>th</sup> Congress on Alternatives to Animal Experiments, Linz, A, 28.-30.09.01, HUSEN, B., LIEDER, K., MARTEN, A., JURDZINSKI, A., PETRY, H., LÜKE, W., EINSPANIER, A.: Immortalization of ovarian granulosa and theca cells of the marmoset monkey (*Callithrix jacchus*).

43<sup>rd</sup> International Meeting of the European Tissue Culture Society, Granada, E, 29.09-03.10.01, HUSEN, B., LIEDER, K., MARTEN, A., JURDZINSKI, A., PETRY, H., LÜKE, W., EINSPANIER, A.: Immortalization of ovarian granulosa and theca cells from the New World monkey *Callithrix jacchus*.

7<sup>th</sup> Congress of the Society of Primatology, Zürich, CH, 30.09.-04.10.01, VOROBIEVA, E., HEISTERMANN, M., HODGES J.K.: Endocrine correlates of dominance and mating behaviour in male pygmy chimpanzees.  
HEISTERMANN, M., HODGES, J.K.: Non-invasive endocrine assessment: methods and applications for monitoring reproductive status and studying physiological mechanisms underlying primate behaviour.

Congress of the DFG Graduate Programme "Cell-Cell Interaction in Reproduction", Giessen, 19.-20.10.01, NAYUDU, P.L: *In vitro* cultivation of ovarian follicles: A tool for understanding follicle development.

Rolduc Symposium, Kloster Rolduc, NL, 09.-11.11.01, EINSPANIER, A.: Follicular-genesis in primates.

3. Göttinger Freilandtage, Göttingen, 11.-14.12.01, ENGELHARDT, A., PFEIFER, J.B., HEISTERMANN, M., HODGES, J.K., NIEMITZ, C.: Do male long-tailed macaques (*Macaca fascicularis*) know when females are most likely to conceive?

Maribor Workshop: 40 years of infertility treatment at Maribor, Slovenia, 01.02.02. NAYUDU, P.L.: How can we improve oocyte *in vitro* maturation for human?

35<sup>th</sup> Annual Meeting of Physiology and Pathology of Reproduction, Leipzig, 14.-15.02.02,  
PREUSSING, E., NAYUDU, P.L., SCHROD, A., HEISTERMANN, M., EINSPANIER, A.: Surgical flushing in common marmosets (*Callithrix jacchus*).  
QUAGGIO AUGUSTO, A., JURDZINSKI, A., EINSPANIER, A.: Effect of growth factor IGF-I on follicle development of marmoset monkeys (*Callithrix jacchus*).  
SCHROD, A., SCHNEIDERS, A., HEISTERMANN, M., HODGES, J.K.: Comparative aspects of sperm morphology and morphometrics in nonhuman primates.

Congress of the Society of Endocrinology of Germany, Göttingen, 27.02.-02.03.02, HUSEN, B., LIEDER, K., GIEBEL, J., FUHRMANN, K., JUDZINSKI, A., MARTEN, A.: Characterization of immortalized primate granulosa and theca cell lines. BEINDORFF, N., EINSPANIER, A.: Lutetotrophic action in non-pregnant versus early pregnant primate corpora lutea.

EINSPANIER, A., UNIMORI, E., JURDZINSKI, A., FUHRMANN, K., BEINDORFF, N.: Supportive effect of relaxin during implantation and early pregnancy in the common marmoset monkey.

HAGEMANN, T., EINSPANIER, A., SCHULZ, M., TRÜMPER, L., BINDER, C.: Relaxin-induced upregulation of matrix metalloproteases and enhanced *in vitro* invasiveness of breast cancer cell lines.

ASAB 2002 Easter Conference, Bristol, UK, 15.-17.04.02, ENGELHARDT, A., PFEIFER, J.B., HEISTERMANN, M., HODGES, J.K., VAN HOOFF, J.A.R.A.M., NIEMITZ, C.: Should I stay or should I go? What male long-tailed macaques (*Macaca fascicularis*) know about a female's fertile phase.

European Primate Veterinarian Symposium, Paul-Ehrlich-Institut, Langen, 24.-25.05.02, SCHROD, A., BITTRICH, B., HUSUNG, A., SCHÖNMANN, U., RENSING, S.: Inguinal hernia in lion-tailed macaques.

1<sup>st</sup> European Conference on Behavioural Biology, Münster, 31.07.-03.08.02.

HEISTERMANN, M.: Field endocrinology in primates: the use of non-invasive endocrine methods for assessing physiological status and studying hormone-behaviour interactions in the wild.

GANSWINDT, A., HEISTERMANN, M., BORRAGAN, S., HODGES, J.K.: Faecal androgen metabolites in African elephants.

4<sup>th</sup> International Symposium on Physiology and Ethology of Wild and Zoo animals. Berlin-Erkner, 30.09.-03.10.02,

GANSWINDT, A., HEISTERMANN, M., PALME, R., BORRAGAN, S., HODGES, J.K.: Non-invasive assessment of adrenal function in the male African elephant (*Loxodonta africana*) and its relation to musth.

DEHNHARDT, M., SZDZUY, K., HEISTERMANN, M., MÖSTL, E.: Monitoring of adrenocortical activity in elephants by measuring urinary cortisol metabolites.

Joint European Conference on Reproduction, Université of François Rabelais, Tours, F, 19.-21.12.02, BARRIOS DE TOMASI, J., ULLOA-AGUIRRE, A., NAYUDU, P.L.: Is intact follicle culture a good model for the *in vivo* effects of FSH isoforms?

### Seminar lectures

Scientific colloquium for PhD students, School of Veterinary Medicine, Hannover, 11.05.01, VOROBIEVA, E.: Endocrine correlates of dominance and reproductive success in male common (*Pan troglodytes*) and pygmy (*Pan paniscus*) chimpanzees.

*Reproductive Biology*

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Inst. of Neurobiology and Behavioural Biology, Univ. Münster, 24.05.01, GANSWINDT, A.: Endocrine and behavioural correlates of musth in captive African elephants (*Loxodonta africana*).

Co. Solvay Pharmaceuticals, Hannover, 28.05.01, EINSPANIER, A.: The marmoset monkey, *Callithrix jacchus*, as a model in research in reproductive biology.

HUSEN, B.: Regulation of oestrogen metabolism in primates.

School of Veterinary Medicine, Hannover, 7.11.01, VOROBIEVA, E.: Endocrine correlates of dominance and mating behaviour in male pygmy chimpanzees (*Pan paniscus*).

Inst. of Neurobiology and Behavioural Biology, Univ. Münster, 08.11.01, GANSWINDT, A.: Faecal androgen and glucocorticoid metabolite excretion in captive and free-ranging male African elephants in various reproductive conditions.

IHF, Hamburg, 06.-07.12.01, EINSPANIER, A.: Physiological effects of the hormone relaxin in a primate model.

Schering Co., Berlin, 13.12.01, NAYUDU, P.L.: Working with nature: Fertility modulation versus fertility control.

DPZ-Seminar, Göttingen, 13.01.02, HEISTERMANN, M.: Field endocrinology: what hormones in faeces can tell us about the biology and behaviour of non-human primates.

General Hospital Maribor, Slowenien, 31.01.-03.02.02, NAYUDU, P.L.: How we make IVM more effective in Human ART.

DPZ-Seminar, Göttingen, 03.04.02, EINSPANIER, A.: Ovulation: the promising end of a follicle.

DPZ, Göttingen, 21.05.02, EINSPANIER, A.: Biomedical research in reproduction: possibilities and perspectives.

Centre of Dermatology and Andrology, Giessen, 11.06.02, NAYUDU, P.L.: Follicle development *in vitro* and *in vivo*.

Center for Life Sciences Study (IPB), Bogor Agricultural University, Bogor, Indonesia, 05.-26.06.02,

HODGES, J.K.: Genetic resource banking for wildlife conservation.

SCHROD, A., HODGES, J.K.: Collection, storage and assessment of primate semen for the establishment of a genetic resource bank.

Workshop: SCHROD, A.: Computer assisted semen evaluation.

Schering Co., Berlin, 08.-09.08.02, EINSPANIER, A.: Relaxin: a multitalent in reproductive biology.

Department of Anthropology and Human Biology, FU Berlin, 28.11.02, ENGELHARDT, A.: Reproductive strategies in free-ranging long-tailed macaques (*Macaca fascicularis*).

Inst. of Neurobiology and Behavioural Biology Univ. of Münster, 19.12.02, GANSWINDT, A.: Musth in African elephants: a short look behind the scenes of daily field work.

### **List of Publications**

#### **Chapters in collected editions**

BINDER, C., BINDER, L., GURLIT, L., EINSPANIER, A.: High serum concentrations of relaxin correlate with dissemination of breast cancer. In: TREGGEEAR, W., IVELL, R., BATHGATE, R.A., WADE, J.D. (eds): Relaxin 2000. Kluwer Academic Publisher (2001): 429-435.

DEHNHARD, M., HEISTERMANN, M., GÖRITZ, F., HERMES, R., HILDEBRANDT, T. B., STRAUSS, G., WEISGERBER, C., HABER, H.: Demonstration of volatile C19-steroids in the urine of female Asian Elephants, *Elephas maximus*. In: MARCHLEWSKA-KOJ, A., LEPRI, J.J., MÜLLER-SCHWARZE, D. (eds): Chemical Signals in Vertebrates 9. Kluwer Academic/Plenum Publishers, New York (2001): 125-132.

EINSPANIER, A.: Relaxin is an important factor for uterine differentiation and implantation in the marmoset monkey. In: TREGGEEAR, W., IVELL, R., BATHGATE, R. A. WADE, J.D. (eds): Relaxin 2000. Kluwer Academic Publishers (2001): 73-82.

FRENCH, J.A., DE VLEESCHOUWER, K., BALES, K., HEISTERMANN, M.: Lion Tamarin Reproductive Biology. In: KLEIMAN, D.G., RYLANDS, A.B. (eds.): Lion Tamarins, Biology and Conservation. Smithsonian Institution Press, Washington and London (2002): 133-156.

HODGES, J.K.: Reproductive technologies necessary for successful application of genetic resource banking. In: WATSON, P.F., HOLT, W.V. (eds.): Cryobanking the genetic resource. Taylor & Francis, London (2001): 85-111.

MORRELL, J.M., HODGES, J.K.: Germplasm cryopreservation and non-human primates. In: WATSON, P.F., HOLT, W.V. (eds.): Cryobanking the genetic resource. Taylor & Francis, London (2001): 407-426.

VERHAGEN, S., EINSPANIER, A.: Relaxin: a lutetrophic factor in the marmoset corpus luteum. In: TREGGEEAR, W., IVELL, R., BATHGATE, R.A., WADE, J.D. (eds): Relaxin 2000. Kluwer Academic Publisher (2001): 139-144.

**Reviewed papers**

ABEGG, C., THIERRY, B.: Macaque evolution and dispersal in insular south-east Asia. *Biol. J. Linn. Soc.* (2002) 75: 555-576.

ANDERSEN C.Y., LEONARDBSEN, L., ULLOA-AGUIRRE, A., BARRIOS-DE-TOMASI, J., KRISTENSEN, K.S., BYSKOV, A.G.: Effect of different FSH isoforms on cyclic-AMP production by mouse culumus-oocyte-complexes: A time course study. *Mol. Hum. Reprod.* (2001) 7: 129-135.

ASLAM, H., SCHNEIDERS, A., PERRET, M., WEINBAUER, G.F., HODGES, J.K.: Quantitative assessment of testicular germ cell production and kinematic and morphometric parameters of ejaculated spermatozoa in the grey mouse lemur, *Microcebus murinus*. *Reproduction* (2002) 123: 323-332.

BARRIOS-DE-TOMASI, J., TIMOSSO, C., MERCHANT, H., QUINTANAR, A., AVALOS, J.M., ANDERSEN, C.Y., ULLOA-AGUIRRE, A.: Assessment of the *in vitro* and *in vivo* biological activities of the human follicle-stimulating isohormones. *Mol. Cell. Endocrinol.* (2002) 186: 189-198.

BINDER, C., HAGEMANN, T., HUSEN, B., SCHULZ, M., EINSPANIER, A.: Relaxin enhances *in vitro* invasiveness of breast cancer cell lines by upregulation of matrix metalloproteases. *Mol. Hum. Reprod.* (2002) 8: 789-796.

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EINSPANIER, A., MÜLLER, D., LUBBERSTEDT, J., BARTSCH, O., JURDZINSKI, A., FUHRMANN, K., IVELL, R.: Characterization of relaxin binding in the uterus of the marmoset Monkey. *Mol. Hum. Reprod.* (2001) 7: 963-970.

GANSWINDT, A., HEISTERMANN, M., BORRAGAN, S., HODGES, J.K.: Assessment of testicular endocrine function in captive African elephants by measurement of urinary and fecal androgens. *Zoo Biology* (2002) 21: 27-36.

GILCHRIST, R.B., WICHEREK, M., HEISTERMANN, M., NAYUDU, P.L., HODGES, J.K.: Changes in follicle-stimulating hormone and follicle populations during the ovarian cycle of the common marmoset. *Biol. Reprod.* (2001) 64: 127-135.

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#### **Non-reviewed papers**

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ADEMMER, C., KLUMPE, K., VON MARAVIC, J., KÖNIGSHOFEN, M., SCHWITZER, C.: Nahrungsaufnahme und Hormonstatus von Kleideraffen (*Pyathrix n. nemaus* Linnaeus 1771) im Zoo. Zeitschrift des Kölner Zoo (2002) 45: 129-136.

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STEINMETZ, H.W., KAUMANN, W., DIX, I., HEISTERMANN, M., FOX, M., KAUP, F.-J.: Influence of housing condition and stress status on coat condition in captive rhesus macaques (*Macaca mulatta*). Verhber. Erkr. Zootiere (2001) 40: 213-219.

#### **Editorials**

SCHWIBBE, M.H., ZIEGLER, T. (eds.): Mixed Species Exhibits in German Zoological Gardens (Part 1). Special References on Primates. Primate Report (2002) 64.

#### **Electronic publications**

NAYUDU, P.L., VITT, U.A., BARRIOS DE TOMASI, J., PANCHARATNA, K., ULLOA-AGUIRRE, A.: Intact follicle culture: What can it tell us about the roles of FSH glycoforms during follicle development? *Reproductive Biomedicine Online* (2002) 5: 240-253.

#### Abstracts

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- ENGELHARDT, A., PFEIFER, J.-B., HEISTERMANN, M., HODGES, J.K., VAN HOOFF, J.A.R.A.M., NIEMITZ, C.: Do male long-tailed macaques know when females are most likely to conceive? *Primate Report* (2001) 60: 20.
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VOROBIEVA, E., HEISTERMANN, M., HODGES, J.K.: Endocrine correlates of dominance and mating behaviour in male pygmy chimpanzees (*Pan paniscus*). Folia Primatol. (2001) 72: 153-154.

<b>Publications</b>	<b>2002</b>	<b>2001</b>	<b>2000</b>
1. Books	0	0	0
2. Publication of collected editions	0	0	0
3. Chapters in collected editions	1	6	1
4. Reviewed papers	15	12	10
5. Non-reviewed papers	3	2	0
<b>Total: 1 - 5</b>	<b>19</b>	<b>20</b>	<b>11</b>
6. Editorials	1	0	0
7. Electronic publications	1	0	1
8. Abstracts	12	12	22
<b>Publications altogether</b>	<b>33</b>	<b>32</b>	<b>34</b>

### **Other scientific activities**

Staff members attended the following meetings:

- Seminar for scientists on successful fundraising as part of the EU FTE-Programme, Brüssel, B, 09.-10.05.01 und 26.06.01.
- Symposium of European Association of Zoo and Wildlife Veterinarians, Rotterdam, 23.-27.05.01.
- Symposium "Harmony and conflict", Univ. Utrecht, NL, 09.06.01.
- ESHRE-Congress, Lausanne, CH, 01.-06.07.01.
- 7<sup>th</sup> Congress of the Society of Primatology, Univ. Zürich, CH, 01.-04.10.01.
- 2<sup>nd</sup> Congress of DFG Graduiertenkolleg "Zell-Zell-Interaktion im Reproduktionsgeschehen", Gießen, 19.-20.10.01.
- ZOO-kunft 2002, Leipzig, 22.-24.02.02.
- Congress of the German Society of Endocrinology, Hannover, 27.02.-02.03.02.
- European Primate Veterinarian Symposium, Langen, 24.-25.05.02.
- 19<sup>th</sup> EAZA Conference, Pompeu Fabra University, Zoo Barcelona, E, 17.-22.09.02.
- Winter Meeting of the Primate Society of Great Britain, Roehampton Institute London, UK, 28.11.-02.12.02.

- 4<sup>th</sup> Symposium on Physiology and Behaviour of Wild and Zoo animals, Institute for Zoo and Wildlife Research, Berlin, 02.10.02.
- Staff members of the Department of Reproductive Biology review manuscripts for numerous journals including American Journal of Primatology, Animal Reproduction Science, Animal Science, Behavioural Ecology and Sociobiology, Biology of Reproduction, Cell & Tissue, Conservation Biology, Ethology, Fertilität, General and Comparative Endocrinology, Journal of Endocrinology, Journal of Medical Primatology, Reproduction, Journal of Zoology, Reproduction in Domestic Animals and Zoo Biology. Reviews are also carried out for funding organizations: German Research Council, Leakey Foundation und Wellcome Trust (UK), National Science Foundation (USA) and the Swiss National Research Council.

### **Important activities and functions**

- **Prof. Hodges** is member of the research committee of the European Association of Zoos and Aquaria (EAZA). He is also a member of the editorial board of the journals "Reproduction" and "Zoo Biology".
- **Prof. Einspanier** is member of the supervisory board of the German Primate Centre and has held the position of visiting professor at the School of Veterinary Sciences Hannover since July 2002. She is also a member of the appointment commission for the C4-professorship in Anthropology and Sociobiology of the University of Göttingen.
- **Dr. Heistermann** is commissioner for radiation protection of the Department and coordinator of radiation protection within the institute.
- **Dr. Oerke** is member of the committee of the European Endangered Species (EEP) programme of the Asian and African elephant.
- **Mrs Hagedorn** and **Mrs Jurdzinski** are members of the works council of the German Primate Centre. Mrs Hagedorn is also a member of the safety board of the institute and was until the beginning of 2002 responsible for the education of laboratory assistants in biology.

### **Awards**

During the last two years the following PhD students were awarded prizes for their poster presentations held at various congresses:

- **Nicola Beindorf** (Ovarian Physiology Group): 1<sup>st</sup> prize at the 34. Annual Meeting on Physiology and Pathology of Reproduction, Giessen.
- **Karin Reichert** (Comparative Endocrinology Group): 2<sup>nd</sup> prize at the XXVII International Ethological Conference, Tübingen.
- **Ekaterina Vorobieva** (Comparative Endocrinology Group): 3<sup>rd</sup> prize at the 7<sup>th</sup> Congress of the Society of Primatology, Zürich, CH.



## **COGNITIVE NEUROSCIENCE LABORATORY**

**Head of Department:** Prof. Dr. Stefan Treue

### **General research objectives**

The central theme of the laboratory is the neuronal basis of visual perception. The special focus within this theme is the processing and perception of visual motion information and the influence of attention on these processes.

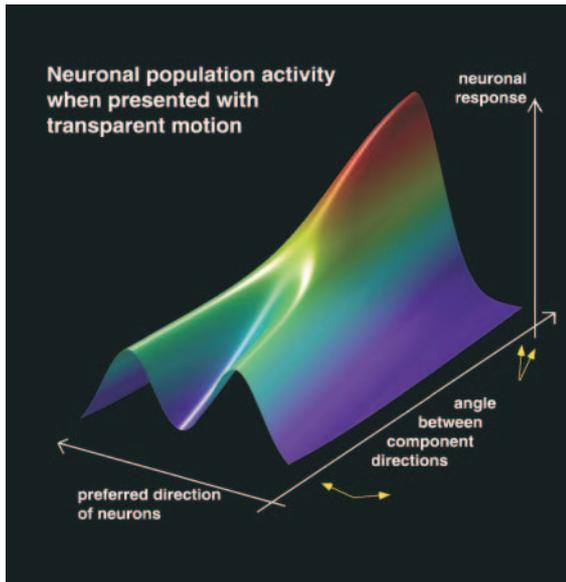
The precise representation of visual motion in the environment is one of the most important tasks of the visual system. An analysis of the direction and speed of motion in the environment provides the organism with important information about its own movement in space and about the movement of others, both friend and foe. The relative motion of objects as well as their own motion allows inferences about their spatial arrangements and their three-dimensional structure and it helps in visually segmenting objects from the background. However, despite its great importance the perception of movement is not without errors. There are illusions, for both the perception of directions and speeds, i.e. systematic miperceptions whose analysis allows inferences about the mechanisms of perception. Understanding these mechanisms is important because vision is an active process that encompasses much more than the passive reflection of our environment. Along the pathway from the eyes to the cortex, visual information is processed and modified by a multitude of processes. These processes do not only provide specific analysis and interpretation of different aspects such as motion information. Rather, additional selection mechanisms such as attention allow us to suppress irrelevant information and to concentrate the processing capacity of the brain on important information. In the recent past it has become increasingly obvious that attentional mechanisms exert their influence early on in the processing of sensory information. One can show that most of the information that the eyes receive never reaches consciousness. The importance of attention becomes clear if one considers the great problems that arise if the attentional system is disturbed as it is in ADHD (Attention Deficit Hyperactivity Disorder) and in a multitude of other neurological diseases that create attentional deficits.

Within the Cognitive Neuroscience Laboratory the study of the perception of visual motion and of attentional phenomena are tightly linked. Because of the plethora of information critical for survival that can be derived from an analysis of visual motion almost every animal with a visual system is able to perceive movement. Because of this widespread use, movement perception is particularly well suited as a model system for sensory information processing and its modulation by cognitive factors such as attention. Research concentrates on the neuronal basis i.e. the understanding of the structures and processes in the brain that are the basis of the sensory information processing and its modulation by the current behavioral relevance of the visual stimuli.

### *Scientific methods*

So far, the Cognitive Neuroscience Laboratory has concentrated on two techniques. One approach is to use electrophysiological techniques to record extra-

cellular signals from individual cells in the visual cortex of rhesus monkeys, the other is to employ psychophysical techniques, i.e. the measurement of human perceptual performance based on observable behavioral data (reaction times and error rates).



*Model of the activity of a population of direction-selective cells to moving stimuli that contain two directions of motion.*

*The combination of different directions within the same spatial area poses the difficult task for the visual system to keep those directions separate to allow their independent perception. This figure shows an idealized population activity across direction-selective neurons. The activity in the population caused by a particular combination of directions is shown along lines that run from right to left across the surface. Following the axis that traverses from front to back, the possible combinations of directions within the stimulus are plotted. In the part of*

*the surface closer to the observer it can clearly be seen that the population activity that is created by two superimposed motions with a relatively large angle has two peaks. Each of the two peaks represents one of the directions of motions within the stimulus. As can be seen from this plot as well as from corresponding experiments, our perception of two superimposed directions is possible even when the population activity contains only a single peak (as in the back part of the surface corresponding to small angles between the directional components).*

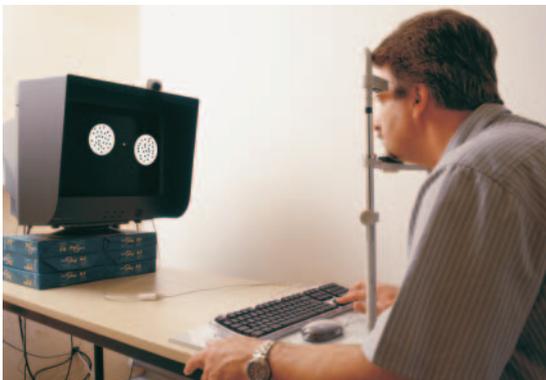
In the future, it is planned to expand the array of methods by the following two approaches.

Computational neuroscience, i.e. approaches that concentrate on theoretical aspects of sensory information processing. With the aid of mathematical models and computer simulations neuronal processes can be described and investigated.

Functional imaging of the brain, i.e. non-invasive methods for measuring the activity of various brain regions. This is primarily functional magnetic resonance imaging (fMRI) that allows us to visualize the large scale distribution of activities. Because the necessary technical devices are not available at the Primate Center the Cognitive Neuroscience Laboratory is co-operating with the university clinic and Max-Planck-Institutes in Göttingen and Tübingen.



*A member of the laboratory pictured controlling computer-based psychophysical experiments (top panel) and a subject during the psychophysical measurement (lower panel). The chin and head rest is used to keep a defined and constant distance between the subject and the computer monitor on which the visual stimuli are presented. Using the computer keyboard the subject answers questions on the stimulus presentation.*



### Structure of the department

Reflecting the array of methods used, the laboratory is divided into three sections. The larger section entitled Neurophysiology investigates information processing in the visual cortex with the help of electrophysiological techniques. Section Psychophysics concentrates on the performance of the visual system in humans. This is also where the work on the functional imaging of the brain is located. The section Computational Neuroscience develops theoretical models for the interpretation of physiological and psychophysical data as well as quantitative hypotheses that can be verified experimentally. Because in the year 2002 the laboratory was still in the process of being set up, in each of these three sections there were vacant positions and the sections had not reached their planned personnel structure or their planned spectrum of competence.

#### Technicians

Kurt Fahrner (01.09.01-)  
Dirk Prüße (01.02.02-)

#### Secretary

Sabine Stuber (01.01.02-)

#### PhD Students

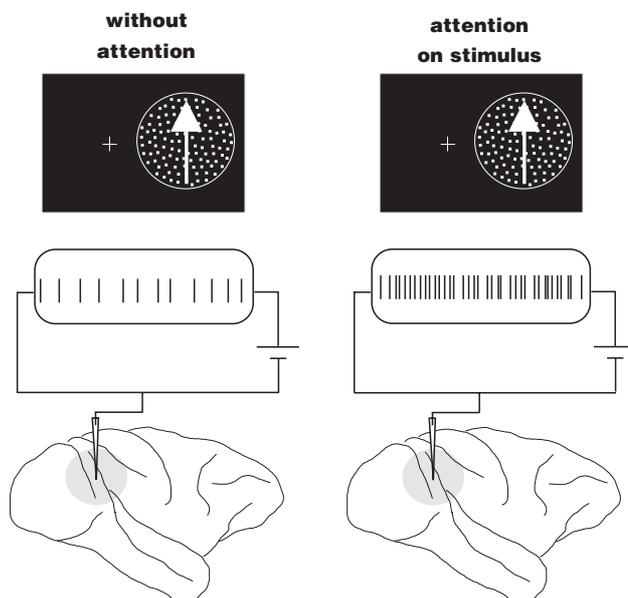
Pinar Boyraz (01.10.02-)  
Laura Busse (01.12.02-)  
Steffen Katzner (01.01.02-)  
Florian Pieper (01.01.02-)  
Thilo Womelsdorf (01.01.02-)

### Progress during the year

The Cognitive Neuroscience Laboratory was founded with the appointment of Prof. Stefan Treue as the director of the German Primate Center and as head of laboratory in the summer of 2001. After the necessary construction the laboratory was able to start working in preliminary space at the beginning of 2002. In 2003 a move into a building is planned which is being constructed as part of the building necessary to provide additional housing during the renovation of the Primate Center's animal house.

Correspondingly, the current report only refers to the year 2002. This year the focus was on putting together the laboratory both in terms of personnel and technical equipment. Despite the complexity of the technical equipment the first studies began in 2002. Nevertheless, the data that were presented at the Annual Meeting of the Federation of European Neuroscience Societies in Paris in July 2002 were based on investigations in Tübingen.

The relatively short set up time for the psychophysical studies in humans enabled a series of experiments whose results were presented at the most important international neuroscience conference, the Annual Meeting of the American Society of Neuroscience in Orlando, USA.



*The lower part of the figure shows a sideview of the cortex of rhesus monkeys. Using electrophysiological recordings the activity of single cells can be determined and can be plotted as a series of individual impulses on an oscilloscope (middle panel of the figure), or on a computer. The frequency of these so-called action potentials is a measure for the activity of a nerve cell. In the depicted example the reaction of a nerve cell to a visual movement is shown under two conditions. In the left panel the stimulus is behaviorally meaningless for the animal and is therefore ignored. The right hand panel*

*shows the condition where the animal has directed its attention toward the stimulus. Even though the stimulus conditions are identical in the two cases the cell responds more strongly in the right hand case (more impulses). This means that the activity of the neuron is not only determined by the stimulus but also by the current relevance of the stimulus for the animal, i.e. by allocation of attention.*

In this study on healthy human subjects it was possible to show the influence of a reduced allocation of attention on the perceptual performance in motion detection and discrimination tasks. Interestingly, these studies also demonstrated conditions in which a heightened level of attention led to drops in performance. These seemingly paradox results could be explained based on a model inspired by electrophysiological data from the laboratory.

Because of the necessary training for the experimental animals (which takes several months) the neurophysiological experiments are still only at the beginning. During this phase the animals learn visual behavioral tasks. The laboratory has used this training time to establish a complex new multi-channel recording system and to develop the necessary computer software. When the training of the animals is completed this system can be used to record the activity of individual neuron cells from the visual cortex during performance of various visual tasks.

### **Integration into national and international research**

Göttingen is one of the leading centers of neuroscience in Germany with a broad scientific spectrum. The systems and behaviorally oriented neurosciences profit from a number of local advantages. They include the numerous departments and laboratories, both at the university and also at the Max-Planck-Institutes and the German Primate Center (DPZ). This allows research approaches that reach from invertebrates to primates and on to humans. Additionally, the system and behavior oriented neurosciences in Göttingen profit from the presence of traditionally strong cellular and molecular biological neurosciences. In contrast to the other areas of neuroscience, the size and the competence of the systems and behavior oriented neuroscience in Göttingen is not reflected in its import on in the science community or in corresponding structures. This has changed in 2002. Partially because of the strengthening of system oriented neurosciences in Göttingen through the establishment of the Cognitive Neuroscience Laboratory at the DPZ the Center for the Neurobiology of Behavior (ZNV) was founded. It encompasses approximately thirty groups from the clinic and the various institutes of the university, from three Max-Planck-Institutes and from the German Primate Center. The Cognitive Neuroscience Laboratory is closely linked with the Center for the Neurobiology of Behavior and exerts an active influence on it especially through the role of Prof. Treue as the speaker of the Center for the Neurobiology of Behavior. The Center for the Neurobiology of Behavior offers good possibilities of co-operation for all parts of the Cognitive Neuroscience Laboratory. There is already a collaboration with the Department of Prof. Frahm at the Max-Planck-Institute for Biophysical Chemistry in the area of functional brain imaging. Additionally, there is a large overlap with psychological laboratories in the Department of Biology in the field of psychophysics of attention, with laboratories for neurology and psychiatry at the university clinic in the area of pathology of attention, and with the department of Prof. Geisel at the Max-Planck-Institute for Fluid Dynamics in the area of Computational Neuroscience.

The Cognitive Neuroscience Laboratory together with the Department of Neurobiology at the DPZ is a member of the DFG Graduate College "Perspectives of Primatology: Integration of Genetic, Neurobiological and ethological Sciences" that is led

by Prof. Hunsmann, and with the DFG Graduate College "Neuroplasticity: From Molecules to Systems", that is led by Prof. Paulus from the university clinic. In the context of the latter there is a co-operation with Dr. Husain at University College London, that includes psychophysical investigations in healthy humans, in rhesus monkeys and in neurological patients with specific brain lesions.

### Projects and partners in co-operation

(I: interdepartmental projects, E: external co-operation; A: project completed, L: current project)

<b>Projects and Partners of the Cognitive Neuroscience Laboratory</b>		
<b>Theoretical and psychophysical issues in the modulation of visual motion processing by attention</b> M. HUSAIN (King' s Cross Hospital, London, UK), <b>S. TREUE</b>	E	L
<b>fMRI studies of attentional modulation in visual cortex</b> N. LOGOTHETIS (MPI for Biological Cybernetics, Tübingen), J. FRAHM (MPI for Biophysical Chemistry, Göttingen), <b>S. TREUE</b>	E	L
<b>Neural network models of attentional modulation in primate visual cortex</b> H. WILSON (Center for Vision Research, York Univ., Toronto, CDN), <b>S. TREUE</b>	E	L

### Congress contributions

3<sup>rd</sup> Forum of European Neuroscience, Paris, F, 13.-17.07.02,  
MARTINEZ-TRUJILLO, J.C., WILSON, H.R., TREUE, S.: Modeling attentional effects in cortical areas MT and MST of the macaque monkey through feedback loops.  
TREUE S., EICHSTÄDT, B.: The influence of attention and contrast on direction discrimination and detection of visual motion in humans.  
PIEPER, F., JÜRGENS, U.: Pre-vocal neuronal activity and the external and dorsal nuclei of the inferior colliculus (ICx; ICd).

32<sup>nd</sup> Meeting of the Society for Neuroscience, Orlando, USA, 02.-07.11.02, KATZNER, S., PIEPER, F., TREUE, S.: Effects of attention and contrast on detection and discrimination of visual motion: Evidence from psychophysics.

### Seminars

Max-Planck-Institute for Fluid Dynamics, Göttingen, 05.03.02, TREUE, S.: To see or not to see - The influence of attention on visual information processing.

DPZ-Colloquium, Göttingen, 06.03.02, TREUE, S.: Von der Einzelzelle zur visuellen Wahrnehmung - Methoden der Abteilung Kognitive Neurowissenschaften.

Graduate College "Neuroplasticity: From Molecules to Systems", University of Göttingen, 21.03.02, TREUE, S: To see or not to see - The influence of attention on visual information processing.

University clinics Aachen, 05.06.02, Talk to Lecture Series "Das Gehirn und sein Bewusstsein", TREUE, S.: Attention and visual perception.

Experimental Medicine Lecture Series, Max-Planck-Institute for Experimental Medicine, Göttingen, 13.09.02, TREUE, S.: The influence of attention on visual information processing.

## **List of Publications**

### **Reviewed papers**

MARTINEZ-TRUJILLO, J.C., TREUE, S.: Attentional modulation strength in cortical area MT depends on stimulus contrast. *Neuron* (2002) 35: 365-370.

MERBOLDT, K.-D., BAUDEWIG, J., TREUE, S., FRAHM, J.: Functional MRI of self-controlled stereoscopic depth perception. *Neuroreport* (2002) 13 (14): 1721-1725.

### **Abstracts**

KATZNER, S., PIEPER, F., TREUE, S.: Effects of attention and contrast on visual motion detection and discrimination thresholds. *Society for Neuroscience Abstracts* (2002): 28.

ROTENSTEIN, A., MARTINEZ-TRUJILLO, J. C., TREUE S., TSOTSOS, J., WILSON, H.R.: Modeling attentional effects in cortical areas MT and MST of the macaque monkey through feedback loops. *Society for Neuroscience Abstracts* (2002): 28.

MARTINEZ-TRUJILLO, J. C., WILSON H. R., TREUE, S.: Modeling attentional effects in cortical areas MT and MST of the macaque monkey through feedback loops. *Federation of European Societies Abstracts 1* (2002): 124.18.

TREUE, S., EICHSTÄDT, B.: The influence of attention and contrast on direction discrimination and detection of visual motion in humans. *Federation of European Societies Abstracts 1* (2002): 124.27.

PIEPER, F., JÜRGENS, U.: Pre-vocal neuronal activity and the external and dorsal nuclei of the inferior colliculus (ICx; ICd). Federation of European Societies Abstracts 1 (2002): 093.10.

<b>Publications</b>	<b>2002</b>
1. Books	0
2. Publication of collected editions	0
3. Chapters in collected editions	0
4. Reviewed papers	2
5. Non-reviewed papers	0
<b>Total: 1 - 5</b>	<b>2</b>
6. Editorials	0
7. Electronic publications	0
8. Abstracts	<b>5</b>
<b>Publications altogether</b>	<b>7</b>

#### **Other scientific activities**

- **Prof. Treue** is member of both Graduate Colleges, "Neuroplasticity: From Molecules to Systems", and "Perspectives of Primatology: Integration of Genetic, Neurobiological and ethological Sciences" of the University of Göttingen, and he is a member of the Center for the Neurobiology of Behaviour, Göttingen. He is a reviewer for the Commission of the European Union, German Research Foundation (DFG), German-Israeli Foundation for Scientific Research & Development, Dutch Research Council, National Science Foundation, USA, Swartz Foundation, USA, and the Wellcome Trust, UK, and is reviewing scientific contributions to following journals: Cerebral Cortex, Current Biology, European Journal of Neuroscience, Experimental Brain Research, Journal of Neurophysiology, Journal of Neuroscience, Journal of Neuroscience Methods, Nature, Nature Neuroscience, Nature Reviews Neuroscience, Naturwissenschaften, Neuron, Neuropsychologia, Perception, Perception & Psychophysics, Science, Trends in Cognitive Sciences, Visual Neuroscience, Vision Research.

#### **Important activities and functions**

- **Prof. Treue** is speaker of the Center for the Neurobiology of Behaviour, Göttingen.

## DEPARTMENT OF NEUROBIOLOGY

**Head of Department: Prof. Dr. Uwe Jürgens**

### General research objectives

The research program of the Neurobiology Department comprised three subjects: 1) the neuroethology of vocal communication, 2) the neurobiology of stress and 3) the establishment of primate models for the study of neurological diseases.

1) In the first field, our work follows three lines:

- a) One line is centred on the questions of which brain structures are involved in the motor control of phonation, and which specific functions these structures play in vocal pattern generation.
- b) The second line seeks to unravel the neuroanatomical connections underlying the vocal control mechanism.
- c) The third line is devoted to the acoustic analysis of emotional vocal expression, with the aim of clarifying the phylogenetic basis of human emotional intonation and non-verbal emotional utterances. The animals under investigation are mainly squirrel monkeys. In addition, rhesus monkeys, chacma baboons, saddle-back tamarins and tree shrews are used. The methodological approaches range from neuroanatomical and single-unit recording techniques to psychoacoustic experiments and classical ethological studies.

2) In the second field, the aim of our research is to elucidate basic neurobiological mechanisms induced by psychosocial stress and their consequences for physiology and behaviour. We study effects of chronic psychosocial stress in tree shrews (*Tupaia belangeri*), a species phylogenetically closely related to primates. During chronic social stress, these animals develop physiological and behavioural symptoms that resemble those of depressive human patients. Using molecular techniques, we investigate changes in central nervous transmitter and modulator systems and compare them to cognitive capabilities and behaviour of the animals. Pharmacological interventions are used to clarify the specific roles of neurotransmitters and their receptors in distinct behavioural paradigms. Stress-induced neurodegenerative as well as antidepressant-induced regenerative processes are analyzed with morphometric techniques. These studies can provide a basis for therapeutical attempts to cure stress-induced, depression-like changes in the central nervous system.

3) The evaluation of new therapeutic strategies for neuroprotection and neuroregeneration in non-human primate models is a prerequisite before such therapeutical approaches can be applied in patients. Thus, the goal of the third research area in our department is to establish in marmoset monkeys models of i) Parkinson's disease and ii) multiple sclerosis. This work integrates input from other groups of researchers, both on the national and international level, with the ultimate aim of de-

veloping animal test systems and new therapeutic strategies for neurodegenerative disorders in non-human primate models.

### **Structure of the department**

The department consisted of two working groups. One was headed by Prof. U. Jürgens, dealing with the neuroethology of vocal communication; the other is headed by Prof. E. Fuchs, dealing with the neurobiology of stress and primate models of neurological disorders. The department's staff is as follows:

#### Scientists

Dr. Boldizar Czéh  
Dr. Gabriele Flügge  
Dr. Claudia Fichtel (01.07.01-30.06.02)  
Prof. Dr. Eberhard Fuchs  
Dr. Kurt Hammerschmidt (-31.07.01)  
Dr. Roland Tammer

Elisabeth Scheiner

Kristina Simonyan  
Keneoue Thinyane (08.10.02-)  
Marieke van der Hart (01.02.01-)  
Marja van Kampen (-31.03.02)  
Gesa Vollmann-Honsdorf (-30.09.01)

#### PhD Students

Nashat Abumaria (24.04.02-)  
Gabriel de Biurrun  
Tania Costoli (29.11.01-03.12.02)  
Eva Dujardin  
Frank Düsterhöft  
Nuria Estape (12.11.01-11.11.02)  
Claudia Fichtel (-30.06.01)  
Anja Fischer  
Steffen Hage (01.10.01-)  
Stefanie Hannig  
Urs Heilbronner (01.10.01-)  
Jeanine Keuker  
Janna Kirchhof  
Maarten Kole  
Lisa Kotthaus (-16.03.02)  
Lutz Lütke (-22.08.01)  
Monika Palchaudhuri (-31.12.01)  
Olga Pudovkina (05.08.02-)

#### Undergraduate Students

Florian Pieper (-31.09.01)  
Silvana Siebert (-30.11.02)

#### Secretary

Elena Nomikos (part time)  
Ursula Buchhorn (part time, 01.10.02-)

#### Technicians

Ludwig Ehrenreich  
Stefanie Gleisberg  
Anna Hoffmann (01.08.02-)  
Heino Hartung  
Cornelia Heckmann (15.10.02-)  
Andreas Heutz  
Achim Lück  
Simone Lüert (part time)  
Manuela Sorge (part time)  
Miriam Vorwald (part time, -16.07.02)

### **Progress during the year**

#### **Vocal communication studies**

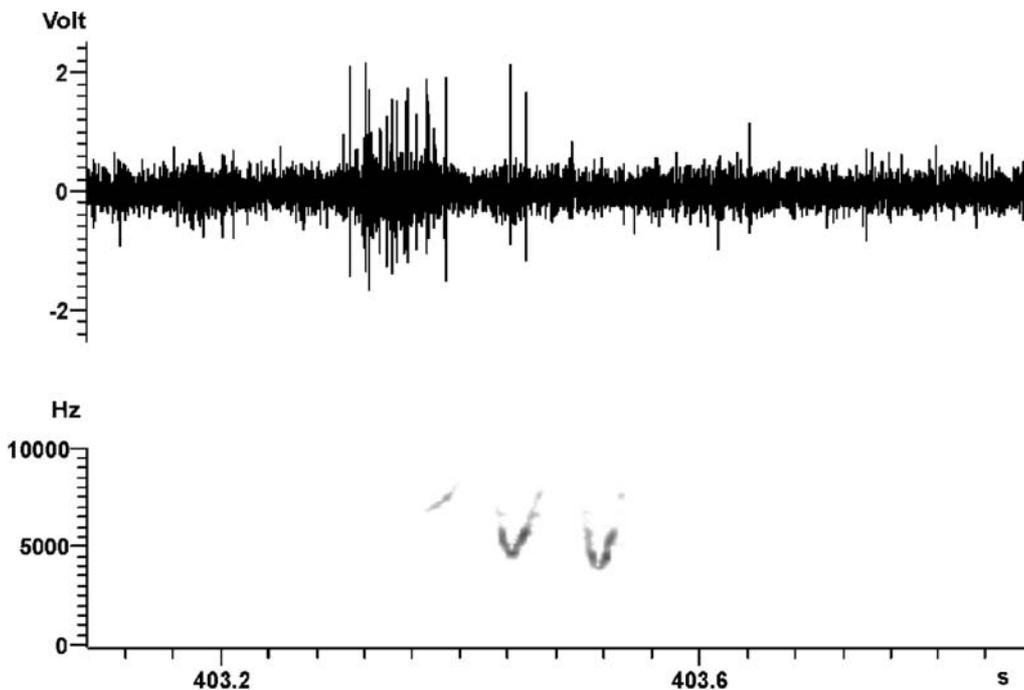
During the period under record, a number of projects were completed. One of these projects was devoted to the question of which role the periaqueductal grey of the midbrain (PAG) plays in vocal motor coordination. From earlier studies, it was

known that the PAG does play a role in vocal control, as its electrical and pharmacological stimulation yields vocalization and its destruction causes mutism. It has remained unclear, however, which specific role the PAG plays in this task. In order to answer this question, we have recorded the neuronal activity in the PAG during spontaneous vocal communication in the squirrel monkey. For this purpose, a telemetric recording technique was used which allowed the registration of the electrical activity of single neurones in freely moving, socially living animals. The study revealed 1) that the PAG contains neurones with vocalization-related activity; 2) that most of these neurones fired immediately before vocalization onset, but not during vocalization itself; 3) those neurones that were active during vocalization did not change their discharge rate during changes of fundamental frequency or intensity; 4) vocalization-correlated activity was always limited to specific call types, and 5) the PAG contains neurones which are active in the interval between a perceived vocalization and the self-produced vocal response. These observations suggest that the PAG rather serves to couple vocalization-eliciting stimuli to the vocal motor-coordinating apparatus than to carry out vocal motor-coordination itself.

In a second single-unit recording study, we wanted to find out whether the inferior colliculus contains neurones that are able to distinguish self-produced vocalizations from externally produced vocalizations. Such a distinction is necessary to avoid responding to one's own vocalization. A possible mechanism that might serve this purpose, is feedforward from a vocal control structure to the auditory system, informing the latter about the forthcoming (self-produced) acoustic event. If such a mechanism exists, there should be neurones receiving input from vocal control structures as well as auditory structures and behaving differently from self-produced vocalization and external acoustic stimuli. The inferior colliculus was chosen as it represents an auditory structure, receiving a direct input from the PAG, a vocal control structure. The study showed that the external, but not the central nucleus of the inferior colliculus contains neurones that, on the one hand, react to external acoustic stimuli and fire in advance of self-produced vocalization: on the other hand, it contains neurones that are activated by external acoustic stimuli, but do not react to self-produced vocalizations. These findings suggest that the peripheral part of the inferior colliculus is involved in the distinction between self-produced and external vocalization.

In order to gain an overview of brain structures potentially involved in the control of vocalization, we have, in addition, carried out a 2-deoxyglucose study in the squirrel monkey. In this study, we compared the regional cerebral glucose consumption between animals made to vocalize by electrical stimulation of the PAG and animals stimulated in the PAG without eliciting vocalization. Evaluation was made by quantitative autoradiography, using digital image analysis procedures. It turned out that vocalizing in comparison to non-vocalizing animals showed an increased glucose consumption in the primary motor cortex, supplementary motor area, cingulate gyrus, dorsomedial and dorsolateral prefrontal cortex, rostral claustrum, perifornical hypothalamus, periaqueductal grey, intercollicular region, midbrain tegmentum, substantia nigra, peripeduncular nucleus, nucleus ruber, paralemniscal area, spinal trigeminal nucleus, solitary tract nucleus, medullary reticular formation, nucl. retroambiguus and nucl. hypoglossus. For some of these structures, there is also evidence from other studies that they might be involved in vocal control. For

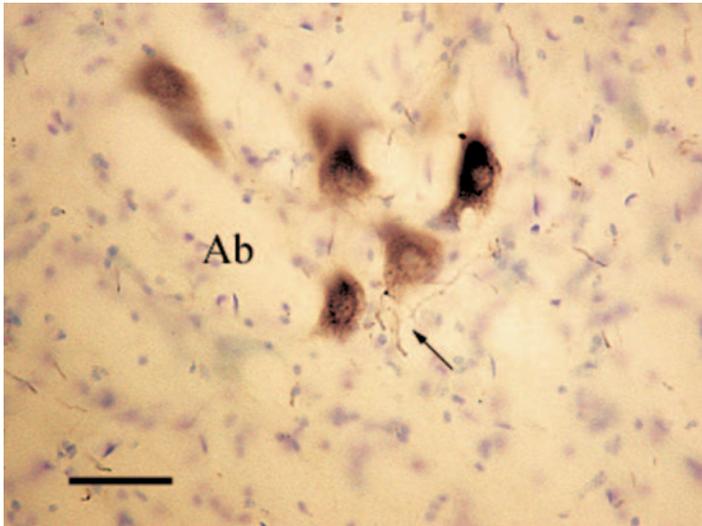
other structures, the present study offers the first evidence. These structures deserve further investigation with more specific methods, such as single-unit recording.



Vocalization-correlated activity in the brainstem (ventral paralemniscal area) of a squirrel monkey (*Saimiri sciureus*). Upper trace: neuronal activity; lower trace: spectrographic representation of a vocalization uttered during recording of the neuronal activity.

In a comparative neuroanatomical study, we have analysed the connections between motor cortex and hypoglossal nucleus. The latter is the site of the motoneurons innervating the tongue. The tongue is the most important articulatory organ in humans. In non-human mammals, in contrast, the tongue does not play an important role in the differentiation of vocalizations. From this, the question arises of why lingual movements play such a different role in human and non-human vocal communication. One possible reason could be differences in the neuroanatomical connections of higher lingual motor control centres. In order to test this hypothesis, we have analysed the efferent connections of the motorcortical tongue area in four species, related to man to different degrees. The aim of this study was to find out, whether there is a systematic trend in the projections, in the sense that the closer a species is related to man, the more intense are its cortico-motoneuronal projections. The following species were used: tree shrew (*Tupaia belangeri*) as a representative of a non-primate order closely related to primates, saddle-back tamarin (*Saguinus fuscicollis*) and squirrel monkey (*Saimiri sciureus*) as representatives of the infra-

order New World primates, and rhesus monkey (*Macaca mulatta*) as a representative of the same infraorder as man, namely Old World primates. The study was carried out with the anterograde tracer biotin dextranamine. The results show that tree shrews and saddle-back tamarins lack direct cortico-hypoglossal connections completely. In the squirrel monkey, some animals show a weak connection. The rhesus monkey shows a moderate projection in all animals. In humans, other authors using different methods have reported a distinct cortico-hypoglossal projection. All species investigated show a direct projection of the motorcortex to the medullary reticular formation beneath the hypoglossal nucleus, and from there to the hypoglossal nucleus itself. This suggests that during evolution from lower primates to man, indirect cortico-reticulo-motoneuronal connections changed into progressively stronger direct connections. This more direct control of the motorcortical tongue area over lingual motoneurons in man might be one of the prerequisites for speech capacity.



*Brain section of the squirrel monkey, showing retrogradely labeled laryngeal motoneurons and anterogradely labeled axon terminals in the nucleus ambiguus. Ab: nucl. ambiguus. Scale: 50  $\mu$ m.*

Squirrel monkeys have a very large vocal repertoire with hundreds of call variants. It is unclear to which degree these variants can be discriminated by the animals and thus transmit different information. We have, therefore, started to characterize the auditory perceptive capabilities of the squirrel monkey. After having determined the hearing curve and frequency discrimination thresholds in previous years, last year we studied the intensity discrimination. The study was carried out by using the conditioned eye-blink reaction. A tone of a definite intensity was presented in regular intervals over a long time. Occasionally, one of these standard tones was replaced by a tone of the same frequency and duration, but with higher intensity. Only these test tones were followed by a short air-puff against the eye. After the animals had learned to close their eyes exclusively during the representation of the test tone, the intensity difference between standard tone and test tone was reduced until no reaction occurred anymore. The study showed that the lowest abso-

lute intensity discrimination thresholds are found between 2000 and 4000 Hz; they have a value of 3 dB. The frequencies, reaching 6 dB at 16.000 Hz and 9 dB at 300 Hz. The lowest relative intensity discrimination thresholds were also found between 2000 and 4000 Hz, and had a value of 7.5 %. The thresholds reached 15 and 16% at 16.000 and 300 Hz, respectively.

Two further projects investigated the question of how emotions influence voice quality. We were especially interested in the way aversive emotional states differ in their vocal expression from non-aversive ones. One project was carried out in squirrel monkeys, the other in human infants in their first year of life. It turned out that in both species, an increase in aversiveness is accompanied by an increase in frequency range (i.e., difference between maximal and minimal frequency at a given time) and by an upward shift of the energy peak in the power spectrum (i.e., peak frequency). The fact that an increase in aversiveness is expressed in both species in the same way suggests that the vocal expression of emotional states in humans has deep-reaching phylogenetic roots. Evidence for a genetic basis of emotional vocal expression comes also from another study finished in the period under record. In this study, we compared the vocal development in normally raised squirrel monkeys with that of Kaspar-Hauser animals, that is, animals with no opportunity to hear conspecifics, and with animals born deaf. Acoustic analyses revealed that there are no significant differences in the vocalizations between the three groups.

In cooperation with the Department of Ethology and Ecology, DPZ, the Max-Planck-Institute of Evolutionary Anthropology, Leipzig, and the University of Pennsylvania, Philadelphia, furthermore, several studies on vocal alarm behaviour were carried out. The investigated species were red-fronted lemurs (*Eulemur fulvus*), sifakas (*Propithecus verreauxi*), saddle-back tamarins (*Saguinus fuscicollis*), moustached tamarins (*Saguinus mystax*), Barbary macaques (*Macaca sylvanus*) and chacma baboons (*Papio cynocephalus*). The studies showed that referential alarm calls, signalling a specific predator, are wide-spread among primates. They also made clear that categorical encoding of alarm signals does not exclude simultaneous graded encoding according to urgency.

In the last two years, three new projects have been begun. In one of these projects, we would like to find out whether the production of a species-specific vocal pattern depends upon the intactness of the PAG. For this purpose, we test the effects of PAG inactivation on the electrical elicibility of vocalization from the brainstem. PAG inactivation is brought about by the intracerebral injection of the GABA agonist muscimol. In the second project, we record the neuronal activity in the paralemniscal area during vocal communication of the squirrel monkey. The paralemniscal area was chosen, as lesions in this area have been shown in a previous study to block PAG-induced vocalizations. The third project deals with emotional intonation in human speech. Its aim is to characterize various emotional intonations with the non-verbal emotional vocal utterances of human infants on the one hand and monkey calls on the other.

### **Stress studies**

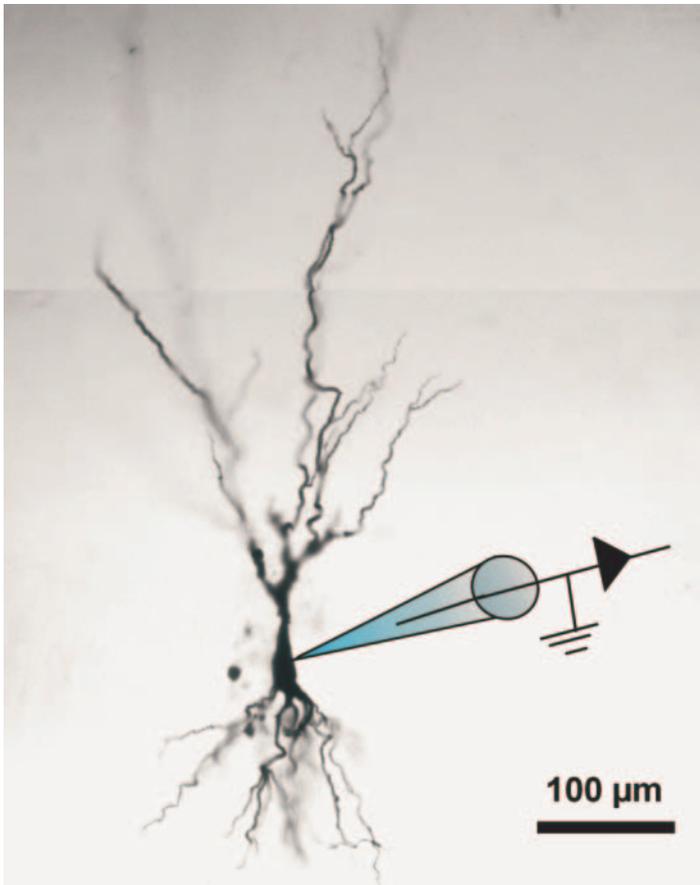
Stress-induced structural remodeling in the adult hippocampus that involves debranching and shortening of dendrites as well as suppression of neurogenesis pro-

vides a cellular basis for understanding the impairment of neural plasticity in the hippocampus of depressed human patients. Accordingly, reversal of certain processes of structural remodeling may be a desirable goal for antidepressant therapy. In collaboration with the Institut International des Recherches Servier, Courbevoie, France, we investigated the effect of tianeptine, a modified tricyclic antidepressant, in the chronic psychosocial stress model of adult male tree shrews. Animals were subjected to a 7-day period of psychosocial stress to elicit stress-induced endocrine and central nervous alterations before the onset of daily oral administration of tianeptine. The psychosocial stress continued throughout the treatment period of 28 days. In collaboration with the group of Prof. Jens Frahm, we determined brain metabolite concentrations *in vivo* by proton magnetic resonance spectroscopy. Chronic psychosocial stress significantly decreased *in vivo* concentrations of *N*-acetyl-aspartate, creatine and phosphocreatine, as well as choline-containing compounds. Cell proliferation in the dentate gyrus was quantified using bromodeoxyuridine (BrdU) immunohistochemistry, and the hippocampal volume was measured *post mortem*. The proliferation rate of the granule precursor cells in the dentate gyrus was significantly reduced in the stressed animals. These stress effects were prevented by the simultaneous administration of tianeptine. In stressed animals treated with tianeptine, the hippocampal volume tended to re-normalize. These findings provide a cellular and neurochemical basis for evaluating the effects of antidepressant treatments with regard to possible reversal of structural changes in brain that have been reported to occur in depressive disorders (Czéh et al., 2001).

The efficacy of current antidepressant medications is limited because with all drugs that are currently used in the clinic, there is a considerable time delay before the full onset of the therapeutic response. In addition, a substantial number of patients do not respond to the medication, and there might be considerable side effects. Therefore, there is an urgent need to develop new antidepressant drugs, and the establishment of neuropharmacological profiles for new compounds with putative antidepressant action is an important field of preclinical research. The neuropeptide substance P and its neurokinin 1 receptor (NK<sub>1</sub>R) have been proposed as possible targets for new antidepressant therapies. In cooperation with Merck & Co, Whitehouse Station, USA, we tested a new substance, L-760,735, that blocks the NK<sub>1</sub>R. Similar to the study with tianeptine and the tricyclic antidepressant clomipramine, this antagonist prevented stress-induced changes. These results suggest that - despite a different neurochemical profile - L-760,735 has a neuropharmacological efficacy comparable to tricyclic antidepressants such as clomipramine or tianeptine (van der Hart et al., 2002).

Recent hypotheses on the action of antidepressants imply a modulation of excitatory amino acid transmission. Using an established model for stress in rats, we analyzed the effects of a long-term tianeptine application on hippocampal CA3 glutamate receptors employing the whole-cell patch-clamp technique. Stress increased the deactivation time-constant and amplitude of the *N*-methyl-D-aspartate (NMDA) receptor-mediated excitatory postsynaptic currents (EPSCs), but did not affect the  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazole propionate (AMPA)/kainate receptor-mediated EPSCs. The concomitant pharmacological treatment of stressed animals with tianeptine resulted in a normalized scaling of the amplitude ratio of NMDA receptor to AMPA/kainate receptor-mediated currents and prevented the stress-induced at-

tenuation of NMDA-EPSCs deactivation. In all animals, both controls and stressed, tianeptine treatment strengthened the slope of the input-output relation of EPSCs. The enhancement of EPSCs could be blocked by the intracellular presence of the kinase inhibitor staurosporine, suggesting the involvement of a postsynaptic phosphorylation cascade rather than presynaptic release mechanisms at CA3 commissural/associational synapses. These results indicate that tianeptine physiologically targets the phosphorylation-state of glutamate receptors at those synapses. The modulation of this signal transduction process may provide an explanation for how tianeptine exerts its neuroprotective properties and/or antidepressant activity (Kole et al., 2002).



*Single pyramidal neuron of the cornu ammonis of the hippocampal formation.*

*Electrophysiological recordings were performed on this neuron which is located in a brain slice. At the very end of the experiment the neuron was loaded with the stain biocytin via the patch-electrode (blue). In a second step the stain was visualized by immunocytochemistry. Experiment by M. Kole et al.*

A chronic hyperactivity of the central noradrenergic system has been suspected to induce depressive disorders in humans. Chronic psychosocial stress leads to long-term or repetitive activation of noradrenergic neurons in the brain and concomitantly, to changes in the noradrenergic receptor system. Since episodes of depression often occur some time after a stress experience, we investigated whether

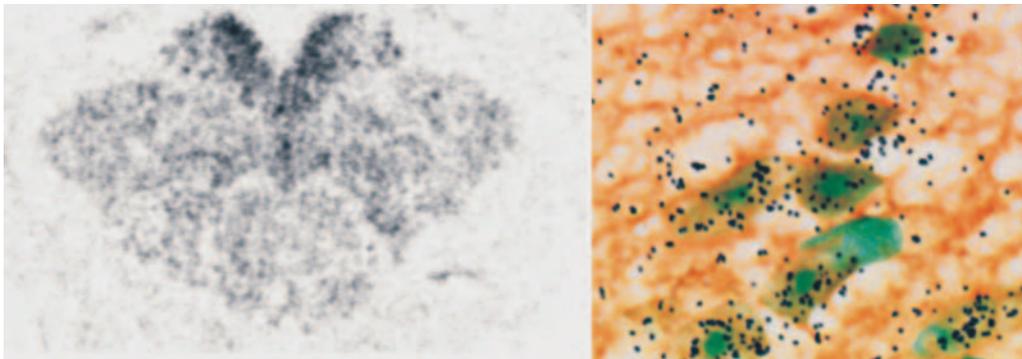
stress-induced changes in the  $\alpha_2$ -adrenoceptor system persist throughout a *post*-stress recovery period. Brains of male tree shrews were analyzed after 6 weeks of chronic psychosocial stress and after a subsequent recovery period of 10 days. Expression of RNA for  $\alpha_{2A}$  and  $\alpha_{2C}$ -adrenoceptors was quantified by *in situ* hybridization, and receptor binding was determined by *in vitro* receptor autoradiography.

Analysis of peripheral hormones (urinary cortisol and noradrenaline) showed that activities of the sympathetic nervous system and of the hypothalamo-pituitary-adrenal axis were increased during chronic stress but normalized during recovery. In the locus coeruleus, the main noradrenergic center in the brain, presynaptic  $\alpha_{2A}$ -adrenoceptor autoreceptor expression was not significantly altered after the long-term stress and recovery period but showed only a slight tendency towards downregulation. In contrast, postsynaptic expression of  $\alpha_{2A}$ -heteroreceptor in glutamatergic neurons was increased after both stress and recovery (e.g. in the lateral reticular nucleus by 29 and 17 %, respectively). In the dorsal motor nucleus of vagus, subtype A expression was enhanced after recovery (by 33 %). This finding of an upregulation of postsynaptic  $\alpha_{2A}$ -receptors indicates low rather than high concentrations of noradrenaline. Expression of postsynaptic  $\alpha_{2C}$ -adrenoceptors in caudate nucleus and putamen was elevated by the stress (by 5 and 4 %, respectively) but normalized during recovery. Our data thus show (1) that chronic psychosocial stress differentially regulates expression of  $\alpha_2$ -adrenoceptor subtypes A and C, (2) that subtype A heteroreceptor expression is persistently upregulated, whereas (3) subtype C upregulation is only transient. The present findings coincide with *post mortem* studies in depressed patients revealing upregulation of  $\alpha_{2A}$ -adrenoceptors and support the hypothesis that depression is related to a 'deficit' in central nervous noradrenaline (Flügge et al., 2003).

The hippocampus has been shown to be involved in several learning and memory processes. Being integrated into the limbic-hypothalamus-pituitary-adrenal axis, the hippocampus also plays an active role in the regulation of the stress response. Long lasting elevated levels of glucocorticoids resulting from a prolonged stress exposure affect hippocampal functions and structure, inducing deficits in learning and memory and suppressing cell proliferation in the dentate gyrus. Male tree shrews exposed to chronic psychosocial stress were tested repeatedly on a holeboard apparatus using two different learning tasks devised to evaluate hippocampal-dependent and hippocampal-independent cognitive functions. We found that chronic stress enhanced learning in animals performing the hippocampal-dependent task, whereas no stress-induced effect was found in the hippocampal-independent task. In addition, after four weeks of stress, cell proliferation was reduced in the hippocampal dentate gyrus. These results indicate that during chronic stress specific memory processes may not only remain intact, but indeed be facilitated despite elevated cortisol levels and suppressed hippocampal cell proliferation (Bartolomucci et al., 2002).

Numerous efforts have been made to answer the question of whether neuronal loss in the hippocampal formation and entorhinal cortex can, at least in part, account for age-related decline in cognitive processes such as learning and memory. To investigate whether or not aging of nonhuman primates is accompanied by a region-specific neuron loss in the hippocampal formation, we used the optical fracti-

onator technique to obtain stereological estimates of neuron numbers of the hippocampi of young (0-4 years) and aged (18-31 years) male rhesus monkeys (*Macaca mulatta*). Brain tissue blocks including the entire hippocampal formation from one side of the brain were obtained from autopsies of male rhesus monkeys from the Wisconsin Regional Primate Research Center (Madison, USA). Our results show a preservation of neurons in all subfields of the hippocampal formation. These results confirm a previous stereological study in rhesus monkeys, in which age also had no effect on neuron numbers in the hippocampus. These findings are in conflict with data from humans, showing age-dependent region-specific alterations in the hippocampal formation (Keuker et al., in press).



*Expression of alpha2B-adrenoceptors in the thalamus of tree shrews. Left: The overview shows the distribution of the receptors (in situ-hybridization). Right: This light microscopic picture shows glutamatergic neurons (brown) expressing alpha2B-adrenoceptors (black dots; emulsion autoradiography). Experiments by U. Heilbronner et al..*

Repetitive transcranial magnetic stimulation (rTMS) is being increasingly used as a therapeutic tool for various neurological and psychiatric disorders and has been demonstrated to attenuate the activity of the stress hormone system. However, the mechanism underlying its clinically observed antidepressant effect is still unknown. Stress-induced structural remodeling in the adult hippocampus may provide a cellular basis for understanding the impairment of neural plasticity in depressive illness. Accordingly, reversal of structural remodeling may be a desirable goal for antidepressant therapy. In collaboration with Dr. M. Keck (MPI for Psychiatry, Munich), we investigated the effect of chronic psychosocial stress and concomitant rTMS treatment on stress hormone regulation and hippocampal neurogenesis in rats.

As expected, chronic psychosocial stress resulted in a significant increase in stress hormone levels and potently suppressed the proliferation rate and survival of newly generated hippocampal granule cells. Concomitant rTMS treatment normalized the stress-induced elevation of stress hormones. However, despite the normalized activity of the hypothalamic-pituitary-adrenal (HPA)-system, the decrement of hippocampal cell proliferation was only mildly attenuated by rTMS, while the survival rate of BrdU-labeled cells was further suppressed by the treatment. These re-

sults support the notion that attenuating hyperactivity of the HPA-system is an important mechanism underlying the clinically observed antidepressant effect of rTMS. However, our experiments did not reveal beneficial effects of rTMS on adult hippocampal neurogenesis (Czeh et al., 2002).

In a collaborative project with the department of Clinical Neurophysiology, University of Göttingen and the Biomedizinische NMR Forschungs GmbH at the MPI of Biophysical Chemistry, Göttingen, we studied safety aspects of chronic rTMS in rats. We used a novel small stimulation coil, specifically designed for rats, and investigated brain tissue using *in vivo* localized proton magnetic resonance spectroscopy (MRS) as well as *post mortem* histological analysis. Histology was based on a modified stereology method in combination with immunohistochemistry to detect any microglial and/or astrocytic activation 48 hours after the last TMS session. Our data provide support for the safety of chronic rTMS. However, they do not exclude acute changes in neurotransmitter systems or other physiologic responses during or directly after the rTMS treatment (Liebetanz et al., in press). The studies on the central effects of rTMS were conducted within the consortium 'Gepulste Magnetstimulation des Gehirns in der Therapie neuropsychologischer Erkrankungen' supported by BMBF.

### Neurological models

Parkinson's disease (PD) is characterized by a progressive slowness of movements, rigidity and tremor. It is the second most common neurodegenerative disorder with an age-dependent prevalence of 1 % in the age group above 60 years and approximately 3 % in the population of over 80 years. The disease is caused by a progressive and selective loss of dopamine producing neurons in the pars compacta of the substantia nigra. Preventing this cell loss through early intervention would be the optimal solution. Current treatment strategies are substitutions for the dopaminergic deficit with levo-DOPA and/or dopamine agonists to rebalance the neurotransmitter systems, but when applied chronically, the dopamine system often becomes insensitive to the drugs. One new approach is to generate *ex vivo* genetically modified cells which produce dopamine and transplant these cells into the striatum. This line of research is supported by the BMBF in the co-operative group grant *Dopamine producing cells in experimental models of Parkinson's disease*. Within the consortium, our group's task is to investigate the functional integration of transplanted dopaminergic stem cells in pre-clinical models of PD. The fate of the engineered stem cells within the recipient brain tissue, their survival and integration into the host neuroarchitecture will be analysed. Should these approaches be successful in rodents, we will perform similar experiments in marmoset monkeys. The experiments in non-human primates will answer the question of whether this curative vehicle can be transferred to the clinic to develop novel therapeutic strategies in the treatment of PD.

Multiple sclerosis (MS) is an inflammatory and demyelinating disease of the central nervous system with a relapsing-remitting or chronic disease course. It is commonly described as a combined autoimmune attack by T- and B cells against myelin sheaths leading to focal lesions in the CNS.

Within the lesion or plaque as a hallmark of the disease, there is an infiltrate of T lymphocytes and macrophages, damage to the blood-brain barrier and myelin loss. The loss of the myelin sheath results in a conduction block across this portion of the axon, which can be compensated by redistribution of ion channels or repaired by remyelination through oligodendrocytes or their precursor cells. The clinical correlate is a relapsing-remitting disease course.

In the Institute of Multiple Sclerosis Research (supported by the Gemeinnützige Hertie-Stiftung), the molecular mechanisms and repair strategies of demyelination and axonal damage in MS are investigated. Experimental autoimmune encephalomyelitis (EAE) is the principal model of MS. In cooperation with B. 't Hart, Biomedical Primate Research Center, Rijswijk, a non-human primate EAE model in marmoset monkeys will be established and evaluated with electrophysiological and immunohistochemistry/molecular biology methods provided by the Department of Neurology, University of Göttingen (Prof. M. Bähr) and the Neuroimmunology Research Group at the ENI (Dr. H. Neumann) as well as high resolution magnetic resonance imaging of CNS pathology (Prof. J. Frahm).

The DFG Research Center of Molecular Physiology of the Brain (CMPB) is a cooperative network between laboratories in Göttingen including the Institute for Multiple Sclerosis Research, the Max-Planck-Institutes for Experimental Medicine and Biophysical Chemistry our Laboratory of Clinical Neurobiology at the German Primate Center and departments involved in neurobiological research at the School of Medicine, University of Göttingen. Within the CMPB our group is involved in two projects. One is investigating non-human primate models for neurodegenerative disease. The second is analyzing the effect of stress and antidepressant treatment on gene transcription (cooperation with the Clinic of Psychiatry).

Within an European network of excellence, EUROLIFE, the research project GLUCOCORTICOID HORMONE PROGRAMMING IN EARLY LIFE AND ITS IMPACT ON ADULT HEALTH (EUPEAH) was granted by the European Commission. The EUPEAH consortium is built around the DPZ and coordinated by Prof. Fuchs. The partner institutions (University of Zürich; University of Edinburgh; Karolinska Institutet; BPRC, Rijswijk and the Medical School, University of Göttingen) represent a multidisciplinary consortium of top European scientists in their respective fields. The ultimate goal of this concerted effort is to quantify the impact of prenatal dexamethasone treatment on the regulation of various genes involved in the metabolic syndrome (hypertension, diabetes, kidney failure, cardiovascular disorders, osteoporosis, impaired fertility, obesity and lipid related disorders), modulating immune competence, programming brain structure and function and behaviour.

The underlying mechanisms of prenatal programming by glucocorticoids have mainly been elucidated to date in the rat. However, since the rat is a far from ideal model of primate pregnancy and since ethical constraints restrict direct investigations in humans, the main objective of the project is to elucidate the fundamental biological role of prenatal glucocorticoid overexposure in a non-human primate model closely related to humans in evolutionary terms. We use this model to investigate the link between events during the prenatal phase of life and severe and crippling diseases in later life such as hypertension, cardiovascular disorders, diabetes, obesity, kidney failure, osteoporosis, neurological disorders and behavioural disturbances, that represent major health problems both in the European population as

well as worldwide. The collaboration of basic researchers and clinically active physicians within the consortium is of great advantage for the transfer of basic knowledge from 'bench to clinic' and is supposed to provide synergistic effects beyond its critical mass.

Milestones and expected results are the generation and implementation of a key non-human primate model for prevalent human disorder, a European non-human primate bank (EPTB) for tissues and body fluids, and a marmoset-specific cDNA microarray (EUMAMA).

### **Integration into national and international research**

The vocal communication group has national cooperations with the Institute of Music Physiology and Musician Medicine of the School for Performing Arts, Hannover, the Max-Planck-Institute for Evolutionary Anthropology, Leipzig, and the Universities of Tübingen and Witten/Herdecke. With the Institute of Music Physiology and Musician Medicine, there was a method transfer. A piece of apparatus, developed at the DPZ for testing squirrel monkeys psychoacoustically, was transferred to Hannover for experiments on audiomotor processing in piano players. With the Max-Planck-Institute of Evolutionary Anthropology, there was a common project on vocal communication in Barbary macaques. Due to the move of a former co-worker of the department (Dr. Hammerschmidt) to Tübingen, cooperations take place with the University of Tübingen in the field of acoustic analyses of human emotional intonation. A joint project is also in progress with the Department of Phoniatrics and Pedaudiology of the University of Witten/Herdecke. With the help of this department, we recruit human infants with severe hearing impairments for our studies on the vocal expression of emotions. International cooperations take place with Yale University, New Haven, University of Pennsylvania, Philadelphia, Harvard University, Cambridge (USA) and University of Odense, Denmark. With Yale University, a joint project on the cerebral glucose consumption during vocalization was carried out. Together with the University of Pennsylvania, the vocal behaviour of chacma baboons was studied in Botswana. The cooperation with Harvard University and the University of Odense concentrates on biomechanical properties of the squirrel monkey larynx, using high-speed videography.

The working group Fuchs is intimately involved in a number of local, national and international research networks. On the local level a number of active cooperations exist with departments of the Medical School and the Max-Planck-Institutes for Experimental Medicine and Biophysical Chemistry. This is clearly documented by projects within the DFG-Research Center of Molecular Physiology of the Brain (CMPB), the Institute for Multiple Sclerosis Research, the SFB 406 "Synaptische Interaktionen in neuronalen Zellverbänden" and the DFG-Graduate School "Perspektiven der Primatologie: Integration genetischer, neurobiologischer und ethologischer Forschungsansätze" as well as the international Graduate School "Neuroplasticity: From Molecules to Systems". On the national level, we are participating in the BMBF supported research networks "Gepulste Magnetstimulation des Gehirns in der Therapie neuropsychologischer Erkrankungen" and "Dopamine producing cells in experimental models of Parkinson's disease". Moreover, we are actively cooperating with research groups at the MPI Psychiatry, Munich, and the Depart-

ment for Experimental Psychology at the University of Düsseldorf. On the international level, Prof. Fuchs is coordinating the EC project EUPEAH (Glucocorticoid hormone programming in early life and its impact on adult health), PD Dr. Flügge is project leader of the EC project HARSE (Hypertension and Alpha2-Adrenoceptor Subtype Expression). To establish models for neurological disorders in marmoset monkeys we have close collaborations with the BPRC, Rijswijk, The Netherlands and the University of Cambridge. We have ongoing joint research projects with the Universities of Parma, Leiden, Groningen, Amsterdam, the Harlow Primate Laboratory, University of Wisconsin, the Rockefeller University and the Department of Psychology, Princeton University. In addition, we have collaborations with pharmaceutical companies in Italy (GlaxoSmithKline), France (Servier), the Netherlands (Solvay) and Great Britain (Merck & Co). Originally initiated through a grant from the DAAD, we have a strong collaboration with the University of Buenos Aires and the Instituto de Investigaciones Biotecnológicas, Universidad Nacional de General San Martín.

**Projects and partners in co-operation**

(I: interdepartmental projects, E: external co-operation; A: project completed, L: current project)

<b>Projects and partners in co-operation Department of Neurobiology</b>		
<b>Vocalization-correlated neuronal activity in the periaqueductal grey of squirrel monkeys</b> <b>F. DÜSTERHÖFT, U. HÄUSLER, U. JÜRGENS</b>		A
<b>Anterograde projections of the motorcortical tongue area in the squirrel monkey</b> <b>M. ALIPOUR-DIDERHOSHAN, U. JÜRGENS</b>		A
<b>Neuronal activity in the pericentral colliculus inferior during vocal utterances</b> <b>F. PIEPER, U. JÜRGENS</b>		A
<b>Psychoacoustic measurements in the squirrel monkey</b> <b>A. WIENICKE, U. HÄUSLER, U. JÜRGENS</b>		A
<b>Vocal ontogeny of the squirrel monkey</b> <b>T. FREUDENSTEIN, K. HAMMERSCHMIDT, U. JÜRGENS</b>		A
<b>Vocal expression of emotional states in the squirrel monkey</b> <b>C. FICHTEL, K. HAMMERSCHMIDT, U. JÜRGENS</b>		A
<b>Characterization of the vocal repertoire of the brown lemur (<i>Lemur fulvus rufus</i> and <i>sifaka</i>, <i>Propithecus verreauxi verreauxi</i>)</b> <b>C. FICHTEL, K. HAMMERSCHMIDT, P. KAPPELER (Dept. of Ethology and Ecology, DPZ)</b>	I	A

<b>Projects and partners in co-operation Department of Neurobiology</b>		
<b>Studies on audiomotor integration in piano players using the conditioned eye blink reflex</b> M. BANGERT, E. ALTENMÜLLER (Inst. for Music Physiology and Musician Medicine, School for Performing Arts, Hannover), U. HÄUSLER	E	A
<b>Functional neuroanatomy of vocalization using the 2-deoxyglucose method in the squirrel monkey</b> L. EHRENREICH, U. JÜRGENS, N. DE LANEROLLE (Yale Univ., New Haven, USA)	E	A
<b>Construction of an MRI-compatible platform for electrophysiological experiments</b> R. TAMMER, T. MICHAELIS (Biomed. NMR Forschungs GmbH, Göttingen)	E	A
<b>Function and structure of the vocal repertoire of the chacma baboon (<i>Papio cynocephalus ursinus</i>)</b> K. HAMMERSCHMIDT, J. FISCHER, R. SEYFARTH, D. CHENEY (Dept. of Psychology, Dept. of Biology, Univ. Pennsylvania, Philadelphia, USA)	E	A
<b>Meanings in the Barbary macaque vocalizations (<i>Macaca sylvanus</i>)</b> K. HAMMERSCHMIDT, J. FISCHER (MPI for Evolutionary Anthropology, Leipzig)	E	A
<b>Telemetric recording in the inferior colliculus during vocal communication in the squirrel monkey</b> R. TAMMER, L. EHRENREICH, U. JÜRGENS		L
<b>Neuronal activity in the ventrolateral pons during audio-vocal interaction</b> S. HAGE, U. JÜRGENS		L
<b>Afferent connections of the periaqueductal vocalization area in the squirrel monkey</b> E. DUJARDIN, U. JÜRGENS		L
<b>Anterograde projections of the ventral paralemniscal zone in the squirrel monkey</b> S. HANNIG, U. JÜRGENS		L
<b>Localization of the vocal pattern generator</b> S. SIEBERT, U. JÜRGENS		L
<b>Anterograde connections of the cortical larynx area in the rhesus monkey</b> K. SIMONYAN, U. JÜRGENS		L

<b>Projects and partners in co-operation Department of Neurobiology</b>		
<b>MRI demonstration of microelectrode tracts in the squirrel monkey</b> R. TAMMER, L. EHRENREICH, T. MICHAELIS, S. BORETIUS, O. NATT, T. WATANABE, J. FRAHM (Biomed. NMR Forschungs GmbH, Göttingen)	E	L
<b>Diffusion tensor MRI in the squirrel monkey</b> S. BORETIUS, O. NATT, T. WATANABE, J. FRAHM, T. MICHAELIS (Biomed. NMR Forschungs GmbH, Göttingen), R. TAMMER, L. EHRENREICH	E	L
<b>Laryngeal movements during frequency-modulated vocalizations</b> T. FITCH (Dept. of Psychology, Harvard Univ., Cambridge, USA), O.N. LARSEN (Inst. of Biology, Univ. Odense, Denmark), U. JÜRGENS	E	L
<b>Acoustical analyses of nonverbal emotional vocal utterances of normally hearing and severely hearing-impaired human infants</b> E. SCHEINER, K. HAMMERSCHMIDT (Univ. Tübingen), U. JÜRGENS, P. ZWIRNER (Univ. Witten/Herdecke)	E	L
<b>Acoustic analysis of human emotional intonation</b> K. HAMMERSCHMIDT (Univ. Tübingen), U. JÜRGENS	E	L
<b>Predator avoidance of tamarins in the Amazon rain forest of Peru: Function of alarm calls and their use in interspecific associations</b> J. KIRCHHOF, K. HAMMERSCHMIDT (Univ. Tübingen), U. JÜRGENS, E. HEYMANN (Dept. of Ethology and Ecology, DPZ)	E,I	L
<b>Glucocorticoid hormone programming in early life and its impact on adult health (EUPEAH)</b> G. MÜLLER, R. NAU, M. OELLERICH, W. WUTTKE (Univ. Göttingen), C. PRYCE, J. FELDON (Eidgenössische Technische Hochschule (ETH), Zürich, CH), B. T'HART (Biomedical Primate Research Centre (BPRC), Rijswijk, NL), R. DE KLOET (Univ. Leiden, NL), J. SECKL, S. HILLIER, P. SAUNDERS (Univ. Edinburgh, UK), H. FORSSBERG (Karolinska Inst., Stockholm, S), E. FUCHS, F.-J. KAUP (Dept. of Veterinary Medicine and Primate Husbandry, DPZ), A. EINSPANIER (Dept. of Reproductive Biology, DPZ), H. ZISCHLER (Working Group Primate Genetics, DPZ)	E,I	L
<b>Primate models for neurological disorders and therapy</b> M. BÄHR, W. BRÜCK, J. FRAHM, H. NEUMANN (Univ. Göttingen), P. NOMIKOS (Univ. Göttingen), E. FUCHS, B. CZÉH, C. HECKMANN, F.-J. KAUP (Dept. of Veterinary Medicine and Primate Husbandry, DPZ)	E,I	L
<b>Transcriptional and functional effects of antidepressant drugs</b> U. HAVEMANN-REINECKE, J. LANDGREBE (Univ. Göttingen), G. FLÜGGE	E	L

<b>Projects and partners in co-operation Department of Neurobiology</b>		
<b>New approaches in the therapy of multiple sclerosis</b> M. BÄHR, J. FRAHM, K. NAVE, H. NEUMANN, F. ZIPP (Univ. Berlin), O. BRÜSTLE (Univ. Bonn), B. THART (Univ. Rijswijk, NL), <b>E. FUCHS,</b> <b>B. CZÉH, C. HECKMANN, F.-J. KAUP</b> (Dept. of Veterinary Medicine and Primate Husbandry, DPZ)	E,I	L
<b>Functional neuroanatomy of dopamin-producing cell transplants</b> P. GRUSS (MPI for Biophysical Chemistry, Göttingen) W. PAULUS (Clinical Neurophysiology, Univ. Göttingen), W. WURST (GSF, Munich), <b>G. FLÜGGE, E. FUCHS, B. CZÉH</b>	E	L
<b>Hypertension and alpha2-adrenoceptor subtype expression</b> C. FLORDELLIS (Patras, GR), M. SCHEININ (Univ. Turku, FIN), H. Paris (Univ. Toulouse, F), <b>G. FLÜGGE</b>	E	A
<b>External steroids and the dopaminergic system</b> S. PARMIGIANI, P. PALANZA, F. MORELLINI (Univ. Parma, I), <b>G. FLÜGGE, E. FUCHS, M.J. MIJNSTER, E. ISOVICH</b>	E	A
<b>Neurobiological characterisation of rats with different levels of aggression</b> A. SGOIFO, T. COSTOLI (Univ. Parma, I), <b>G. FLÜGGE, E. FUCHS</b>	E	L
<b>MHC-class-I-genes of the common marmoset monkey (<i>Callithrix jacchus</i>) and their expression in the brain</b> L. WALTER (Univ. Göttingen), <b>E. FUCHS</b>	E	L
<b>Glucocorticoid receptors in the brains of nonhuman primates</b> P. LUCASSEN (Univ. Amsterdam, Netherlands), <b>E. FUCHS,</b> <b>J. KEUKER, U. MEYER, B. CZÉH</b>	E	L
<b>Stereological analysis of brain sections</b> M. RICKMANN (Anatomical Institute, Univ. Göttingen), <b>E. FUCHS,</b> <b>J. KEUKER, A. FISCHER, B. CZÉH</b>	E	L
<b>Modulation of proliferation rates of neural precursor cells in the hippocampal formation</b> E. GOULD (Princeton Univ., USA), O. ALMEIDA (MPI for Psychiatry, Munich), <b>B. CZÉH, G. FLÜGGE, E. FUCHS</b>	E	L
<b>Stress-induced alterations of central dopamin receptors</b> R. LANDGRAF, M. ENGELMANN (MPI for Psychiatry, Munich) <b>E. FUCHS, G. FLÜGGE, E. ISOVICH, M. J. MIJNSTER</b>	E	L
<b>Neurobiological basis of transcranial magnetic stimulation</b> W. PAULUS, S. FAUSER (Clinical Neurophysiology, Univ. Göttingen), M. KECK (MPI for Psychiatry, Munich), F. DANKWART (Erich Jaeger GmbH, Höchberg), <b>E. FUCHS, B. CZÉH</b>	E	A

<b>Projects and partners in co-operation Department of Neurobiology</b>		
<b>Stress- induced electrophysiological and structural changes in hippocampal neurons</b> M. KOLE, J. KOOLHAAS, P. LUITEN (Dept. Animal Physiology, Univ. Groningen, NL), E. FUCHS	E	L
<b>Glia in the brains of of tree shrews and non-human primates</b> J. COLOMBO (Univ. Buenos Aires, Argentina), E. FUCHS	E	L
<b>Psychosocial stress and cortisol: Effect on central gene expression in tree shrews</b> A.C. FRASCH, J. ALFONSO, G. POLLEVIK (Inst. Investigaciones Biotecnologicas, Univ. Nacional de General San Martin, San Martin, Argentina), G. FLÜGGE, E. FUCHS	E	L
<b>Neurobiological basis of depression</b> E.R. DE KLOET (Univ. Leiden, NL), H. DEN BOER (Univ. Groningen, NL), C. MUNOZ (Servier, Courbevoie, F), N. RUPNIAK (Merck & CO, Harlow, GB), M. HESSELINK (Solvay, Weesp, NL), E. DOMENICI (GSK, Verona, I), C.HIEMKE (Dept. of Psychiatry, Univ. Mainz), E. FUCHS, G. FLÜGGE, M.VAN KAMPEN, M. VAN DER HART, B. CZÉH	E	L
<b>NMDA-receptors in the brain of a mutant mouse</b> W. ENGEL (Inst. of Hygiene and Human Genetics, Univ. Göttingen), L. KOTTHAUS, G. FLÜGGE	E	L
<b>Housing and breeding of tree shrews</b> K. NEBENDAHL (Anatomical Inst. and Central Animal Facilities of the Univ. Göttingen), E. FUCHS	E	L
<b>Aging processes in the brains of tree shrews and non-human primates</b> P. LUITEN (Dept. Animal Physiol., Univ. Groningen, NL), M. WITTER (Univ. Amsterdam, N), E. FUCHS, G. DE BIURRUN, J. KEUKER	E	L
<b>Impact of chronic psychosocial stress on alpha<sub>2</sub>-adreneroreceptors in the brain of tree shrews</b> G. FLÜGGE, U. HEILBRONNER. H. MEYER, M. PALCHAUDHURI		L
<b>Adrenal steroids as modulators of molecular parameters and structure of neural cells</b> U. MEYER, G. VOLLMANN-HONSDORF, G. FLÜGGE, E. FUCHS		L
<b>Stress-induced modulation of cognitive processes</b> G. DE BIURRUN, A. BARTOLOMUCCI, E. FUCHS		A
<b>MRI investigations in tree shrews and marmoset monkeys</b> T. MICHAELIS, J. FRAHM (Biomed. NMR Forschungs GmbH, Göttingen), G. DE BIURRUN, E. FUCHS	E	L

**Stays of DPZ scientists in other institutions**

<b>Name/Institute/Duration</b>	<b>Project</b>
Dr. Claudia Fichtel Duke Univ., Durham, N.C., USA June 01-August 31, 2002	Acoustic communication in lemurs
Kristina Simonyan National Institute of Neurological Disorders and Stroke, Bethesda, MD, USA May 07-July 03, 2001	Central control of vocal fold movements
Prof. E. Fuchs, Dr. B. Czéh Univ. Cambridge, GB September 24-28, 2001	Primate models of Parkinson's Disease
Dr. B. Czéh Univ. Pécs, Hungaria December 10-20, 2001, May 06-17, 2002	Quantitative analysis of brain sections (Neurogenesis) via confocal microscopy
J. Keuker Univ. Groningen, NL November 04-22, 2002	Serotonergic innervation of selected brain areas: Experiments and analysis of age-related alterations.

<b>Visited institution</b>	<b>Duration of stay (2001/2002)</b>		
	<b>&lt; 1 month</b>	<b>1 - 3 months</b>	<b>&gt; 3 months</b>
German universities, research or service institutions	0	0	0
European universities, research or service institutions	4	0	0
Universities, research or service institutions outside Europe	0	2	0
<b>Altogether</b>	<b>4</b>	<b>2</b>	<b>0</b>

**Scientific Contributions**

**Doctoral theses**

FICHTEL, C.: Emotional correlates in vocalizations of primates. Fachbereich Biologie, Chemie, Pharmazie, Freie Univ. Berlin (2001).

LÜTHE, L.: Elektrophysiologische Untersuchungen zur Vokalisationskontrolle beim Totenkopffaffen (*Saimiri sciureus*). Naturwissenschaftliche Fakultät, Techn. Univ. Braunschweig (2001).

VAN KAMPEN, M.: Chronic psychosocial stress in male tree shrews. Univ. Leiden, NL (2002).

Vollmann-Honsdorf, G.: Lichtmikroskopische und ultrastrukturelle morphologische Veränderungen in der Hippocampusformation von Tupaia (*Tupaia belangeri*) als Folge von chronisch psychosozialen Stress. Biologische Fakultät Univ. Bielefeld (2001).

#### Diploma theses

PIEPER, F.: Neuronale Aktivität im Mesencephalon und angrenzendem Pons während Vokalisation. Eine Einzelzellstudie am Totenkopffaffen (*Saimiri sciureus*). Biologische Fakultät, Univ. Göttingen (2001)

SIEBERT, S.: Die Bedeutung des periaquädukten Graus für die Auslösbarkeit von Vokalisation vom unteren Hirnstamm bei Totenkopffaffen. Biologische Fakultät, Univ. Göttingen (2002)

#### Habilitation theses

FLÜGGE, G.: Funktionen des noradrenergen Systems. Medizinische Fakultät, Univ. Göttingen (2002).

#### Congress contributions

18<sup>th</sup> Congress of International Primatological Society, Adelaide, Australia, January 07-12, 2001, JÜRGENS, U.: On the neurobiology of vocal communication.

Annual BCN Poster Session, Groningen, NL, January 18, 2001, KOLE, M.H.P., KOOLHAAS, J.M., LUITEN, P.G.M., FUCHS, E.: Structural and functional characterization of hippocampal neurons after chronic psychosocial stress.

80<sup>th</sup> Annual Congress, German and Scandinavian Physiol. Society, Berlin, March 10-13, 2001, KOLE, M.H.P., KOOLHAAS, J.M., LUITEN, P.G.M., FUCHS, E.: Electrophysiological and morphological characterization of hippocampal CA1 and CA3 neurons after chronic psychosocial stress.

Symposium "Neurorepräsentation und Psyche" of the Siemens-Foundation, Munich, April 20, 2001, JÜRGENS, U.: Vom Affenlaut zum Menschenwort: eine stammesgeschichtliche Reise.

9<sup>th</sup> Annual Meeting of the International Society for Magnetic Resonance in Medicine, Glasgow, GB, April 21-27, 2001, MICHAELIS, T., DE BIURRUN, G., WATANABE, T., FRAHM, J., VAN KAMPEN, M., FUCHS, E., HIEMKE, C., VAN T HART, B., BROK, H., BARTOLUMUCCI, A., MUNOZ, C.: Brain and immune changes in response to psychosocial stress are reversed by tianeptine.

5<sup>th</sup> Dutch Endo-Neuro-Meeting, Doorwerth, NL, June 05-08, 2001, LUCASSEN, P., VOLLMANN-HONSDORF, G., GLEISBERG, M., CZÉH, B., DE KLOET, R.,

FUCHS, E.: Chronic psychosocial stress differentially influences apoptosis in hippocampal subregions and cortex of the adult tree shrew.

4<sup>th</sup> Meeting of the German Neuroscience Society, Satellite Symposium "Neuroplasticity: From Molecules to Systems", Göttingen, June 06, 2001,

FLÜGGE, G.: Dynamics of central nervous monoamine receptors: *in vivo* studies.

FUCHS, E.: Tianeptine reverses stress-induced central nervous changes.

28<sup>th</sup> Göttingen Neurobiology Conference, 4<sup>th</sup> Meeting of the German Neuroscience Society, Göttingen, June 07-10, 2001,

CZÉH, B., FISCHER, A.K., ERHARDT, A., SCHMITT, W., WELT, T., TOSCHI, N., KECK, M.E., FUCHS, E.: Chronic psychosocial stress and concomitant repetitive transcranial magnetic stimulation: effects on neurogenesis and stress hormone levels.

EHRENREICH, L., JÜRGENS, U.: Brain activity during vocalization – A 2-DG study in the squirrel monkey.

FISCHER, A.K., CZÉH, B., BURIC, R., VON ROSENSTIEL, P., ALMEIDA, O., FUCHS, E.: The effect of the mineralocorticoid aldosterone on adult hippocampal cell proliferation.

FLÜGGE, G., VAN KAMPEN, M., FUCHS, E.: Stress-induced alpha<sub>2</sub>-adrenoceptor downregulation is reversible: rebound effects.

HAGE, S., EHRET, G.: Electrophysiological mapping of linear frequency sweeps in the inferior colliculus of the mouse (*Mus domesticus*).

HANNIG, S., JÜRGENS, U.: Efferent projections of the ventral paralemniscal area in the squirrel monkey.

JÜRGENS, U., HÄUSLER, U., LÜTHE, L.: Vocalization-correlated neuronal activity in the lower brainstem of the squirrel monkey.

KEUKER, J., LUITEN, P., FUCHS, E.: Differential anterior-posterior neuronal densities in rhesus monkey hippocampal subfields.

KOLE, M.H.P., KOOLHAAS, J.M., LUITEN, P.G.M., FUCHS, E.: Psychosocial stress-induced electrophysiological and morphological alterations in hippocampal CA3 neurons.

MICHAELIS, T., DE BIURRUN, G., WATANABE, T., FUCHS, E., FRAHM, J.: Time courses of cerebral metabolite levels after psychosocial stress and oral cortisol.

MICHAELIS, T., DE BIURRUN, G., WATANABE, T., FRAHM, J., VAN KAMPEN, M., MUNOZ, O.: Synaptic plasticity and stablon: structural regulation.

The Voice Foundation's 30<sup>th</sup> Annual Symposium, Philadelphia, USA, June 13-17, 2001, ZWIRNER, P., SCHEINER, E., HAMMERSCHMIDT, K., JÜRGENS, U.: Acoustic analyses of emotional correlates in the preverbal vocalizations of infants.

Orage 2001, Aix-en-Provence, F, June 17-22, 2001, JÜRGENS, U.: On the vocal expression of emotion. A multi-parametric acoustical analysis in a non-human primate.

7<sup>th</sup> World Congress of Biological Psychiatry, Berlin, July 01-06, 2001, FUCHS, E.: Stress regulates neurogenesis.

7<sup>th</sup> Armenian World Medical Congress, Toronto, Canada, July 04-08, 2001, SIMONYAN, K., JÜRGENS, U.: Efferent projections from the motorcortical larynx area to the basal ganglia in the rhesus monkey.

6<sup>th</sup> Int. Congress of Neuroethology, Bonn, July 29-August 03, 2001, JÜRGENS, U.: Vocal control in primates  
JÜRGENS, U.: Organization of the symposium "Neural mechanisms of sound production: A comparative approach".  
FITCH, W.T., LARSEN, O.N., ANDERSEN, B.B., NEUBAUER, J., JÜRGENS, U., HÄUSLER, U.: High-speed video endoscopy of vocalizing squirrel monkeys (*Saimiri sciureus*).

27<sup>th</sup> Int. Ethological Conference, Tübingen, August 22-29, 2001, JÜRGENS, U.: Neurobiology of primate vocal communication.  
SCHEINER, E., HAMMERSCHMIDT, K., JÜRGENS, U., ZWIRNER, P.: Expression of emotions in the preverbal vocalizations of infants.  
FICHTEL, C., HAMMERSCHMIDT, K.: Information content of redfronted lemur (*Eulemur fulvus*) alarm calls.  
HAMMERSCHMIDT, K., FICHTEL, C.: "Call pitch" as an indicator of the intensity of affective states.

33<sup>th</sup> Annual General Meeting of European Brain and Behaviour Society, Marseille, F, September 09-12, 2001, DE BIURRUN, G., MICHAELIS, T., WATANABE, T., FRAHM, J., FUCHS, E.: Stress-induced alterations of cortisol, memory and cerebral metabolites: gender differences in tree shrews.

2<sup>nd</sup> Int. Workshop on Models and Analysis of Vocal Emission for Biomedical Applications, Florence, I, September 13-15, 2001, JÜRGENS, U.: The squirrel monkey as a model in the study of the central control of vocalization.

18<sup>th</sup> Annual Meeting of the German Society for Phoniatics and Pedaudiology, Frankfurt/Main, September 28-30, 2001, SCHEINER, E., HAMMERSCHMIDT, K., JÜRGENS, U., ZWIRNER, P.: Informationsgehalt präverbaler Lautäußerungen von Säuglingen.

31<sup>st</sup> Annual Meeting of the Society for Neuroscience, San Diego, USA, November 10-15, 2001, ISOVICH, E., FLÜGGE, G., FUCHS, E.: Alpha<sub>2b</sub>-adrenoceptor expression in the tree shrew thalamus.  
MIJNSTER, M.J., VAN DER HART, M.G.C., CREMERS, T.I.F.H., BOSKER, F.J., WESTERINK, B.H.C., FUCHS, E.: Measuring dopamine in freely moving tree shrews: a pilot microdialysis study.  
BOSKER, F.J., JONGSMA, M., CREMERS, T.I.F.H., VAN DER HART, M.G.C., KORF, J., WESTERINK, B.H.C., DEN BOER, J.A., FUCHS, E.: Do 5-HT<sub>1b</sub> auto-receptors desensitize following chronic treatment with citalopram?  
KEUKER, J.I.H., LUITEN, P.G.M., FUCHS, E.: Stereological estimation of neuron numbers in hippocampal subfields of aging rhesus monkeys.

MICHAELIS, T., WATANABE, T., FRAHM, J., FUCHS, E.: Manganese-enhanced MRI of rat retinal projections *in vivo*.

CZÉH, B., MICHAELIS, T., WATANABE, T., FRAHM, J., DE BIURRUN, G., VAN KAMPEN, M., BARTOLOMUCCI, A., MUNOZ, C., FUCHS, E.: Tianeptine prevents stress-induced changes in cerebral metabolites, hippocampal volume and cell proliferation.

New Year Meeting, School of Behaviour and Cognitive Neuroscience (BCN), Groningen, NL, February 2002, KOLE, M.H.P., SWAN, L., FUCHS, E.: Tianeptine persistently modulates glutamate receptor current of the hippocampal CA 3 associational-commissural synapse in chronically stressed rats.

Philippe Laudat Conference on "Neuronal stem cells: from development to the clinic", Aix-les-Bains, F, February 18-21, 2002, CZÉH, B.: Internal and external factors regulating proliferation and survival of neural progenitor cells in the adult dentate gyrus.

46<sup>th</sup> Annual Meeting of the German Society of Endocrinology, Göttingen, February 27-March 02, 2002,

MICHAELIS, T., DE BIURRUN, G., WATANABE, T., FRAHM, J., FUCHS, E.: Temporal relationship of stress and cortisol treatment on brain metabolism analyzed *in vivo* by localized proton magnetic resonance spectroscopy.

FLÜGGE, G., VAN KAMPEN, M., FUCHS, E.: Cortisol and noradrenaline during chronic stress and recovery.

Elba Summerschool and Workshop on "Neurobiology of Stress in Health and Disease", Marina di Campo, I, May 04-10, 2002,

HEILBRONNER, U., FLÜGGE, G.: Alpha2B-Adrenoceptor in the thalamus of tree shrews (*Tupaia belangeri*).

KOLE, M.H.P., KOOLHAAS, J.M., LUITEN, P.G.M., FUCHS, E.: Psychosocial stress-induced changes in membrane properties and neurotransmitter responsiveness of hippocampal CA3 pyramidal neurons of the tree shrew.

10<sup>th</sup> Scientific Meeting of the International Society for Magnetic Resonance in Medicine, Honolulu, May 18-24, 2002,

MICHAELIS, T., LIEBETANZ, D., WATANABE, T., CZÉH, B., PAULUS, W., FUCHS, E., FRAHM, J.: Protons MRS of rat brain after chronic repetitive transcranial stimulation.

MICHAELIS, T., WATANABE, T., NATT, O., BORETIUS, S., VAN DER HART, M., CZÉH, B., DE BIURRUN, G., FUCHS, E., FRAHM, J.: Antidepressants prevent stress-induced reductions of cerebral metabolites.

DFG-Colloquium "Akustische Kommunikation von Affekten bei nonhumanen Säugetieren und dem Menschen: Produktion, Wahrnehmung und neurale Verarbeitung", Hannover, June 05, 2002, JÜRGENS, U.: Untersuchungen zum stimmlichen Ausdruck emotionaler Zustände bei Totenkopffaffe und Mensch.

- 3<sup>rd</sup> Forum of European Neuroscience, Paris, F, July 13-17, 2002,  
COSTOLI, T., FLÜGGE, G., FUCHS, E., SGOIFO, A.: Autonomic stress responsivity in rats: Relationship with aggression.
- CZÉH, B., DE BIURRUN, G., VAN DER HART, M., BARTOLOMUCCI, A., VAN KAMPEN, M., FUCHS, E.: Antidepressant treatment can prevent chronic psychosocial stress-induced suppression of cell proliferation in the adult hippocampal dentate gyrus.
- DE BIURRUN, G., BARTOLOMUCCI, A., CZÉH, B., VAN KAMPEN, M., FUCHS, E.: Chronic psychosocial stress selectively enhances spatial learning.
- JÜRGENS, U., HÄUSLER, U., LÜTHE, L.: Vocalization-correlated neuronal activity in the lower brainstem of the squirrel monkey.
- KOLE, M., LUITEN, P., FUCHS, E.: NMDA receptor currents at the CA3 commissural-associational synapse are up-regulated by chronic restraint stress.
- PIEPER, F., JÜRGENS, U.: Pre-vocal neuronal activity in the external and dorsal nuclei of the inferior colliculus (ICx; ICd).
- Summer Lecture Course, Brain Science Institute, Riken, Tokio, Japan, July 14-August 04, 2002, SIMONYAN, K.: Cortico-cortical projections from the laryngeal motorcortex in the rhesus monkey.
- XIX<sup>th</sup> Congress of the International Primatological Society, Peking, China, August 04-09, 2002, JÜRGENS, U.: Psychoacoustic measurements in the squirrel monkey.
- 15<sup>th</sup> European College of Neuropsychopharmacology, Barcelona, E, September 05, 2002, FUCHS, E.: Synaptic plasticity and tianeptine: structural regulation. Symposium "A new pharmacology of depression: the concept of synaptic plasticity".
- 10<sup>th</sup> Meeting of the European Neuroendocrine Association, Munich, September 12-14, 2002, FUCHS, E.: Images from small brains provide neuroendocrine markers.
- 19<sup>th</sup> Annual Meeting of the German Society for Phoniatics and Pedaudiology, Erlangen, September 14-16, 2002, SIMONYAN, K.: Subcortical efferent projections from the laryngeal motorcortex in the rhesus monkey.
- XIV<sup>th</sup> World Congress of the International Federation of Otorhinolaryngological Societies, Kairo, Egypt, September 27-October 03, 2002, SIMONYAN, K.: Cortico-cortical projections from the motorcortical larynx area in the rhesus monkey.
- Symposium of the Royal Danish School of Pharmacy "Stem cell base therapeutics: Future medical revolution or fairy tale?", Copenhagen, Denmark, October 11, 2002, FUCHS, E.: Stress, dentate cell proliferation, and neuropsychiatric disorders.
- 32<sup>nd</sup> Annual Meeting of the Society for Neuroscience, Orlando, Florida, USA, November 02-07, 2002,  
CZÉH, B., BARTOLOMUCCI, A., DE BIURRUN, G., VAN KAMPEN, M., FUCHS, E.: Marked enhancement of spatial learning during chronic stress despite suppressed cell proliferation in the dentate gyrus.

HEILBRONNER, U., FLÜGGE, G.: Alpha-2B adrenoceptor expression in the thalamus of tree shrews (*Tupaia belangeri*): Co-localization with GABA- and glutamate-like immunoreactivity.

FUCHS, E., LUCASSEN, P.J., CZÉH, B.: The antidepressant tianeptine prevents apoptosis in the hippocampus in a subregion specific manner.

KOLE, M.H.P., SWAN, L., FUCHS, E.: Stress-protecting effects of tianeptine by glutamate receptor activation.

SCHINDEHÜTTE, J., BAIER, P.C., THINYANE, E., FUCHS, E., FLÜGGE, G., PAULUS, W., TRENKWALDER, C., GRUSS, P.: Transplantation of dopaminergic neurons derived from murine embryonic stem cells in unilateral 6-OHDA lesioned rats.

SIMONYAN, K., JÜRGENS, U., ZIMMERMANN, E.: Descending projections of the laryngeal motorcortex in the rhesus monkey.

VAN DER HART, M., CZÉH, B., DE BIURRUN, G., MICHAELIS, T., WATANABE, T., NATT, O., FRAHM, J., FLÜGGE, G., FUCHS, E.: The NK<sub>1</sub> receptor antagonist L-760,735 and clomipramine prevent stress-induced changes in cerebral metabolites, cell proliferation in the dentate gyrus and hippocampal volume.

Final Graduate Meeting of the DFG-Schwerpunktprogramm "Sensomotorische Integration" Bochum, November 28-30, 2002, JÜRGENS, U., TAMMER, R., HAGE, S.: Elektrophysiologische Untersuchungen zur audiovokalen Interaktion beim Totenkopffaffen.

### Seminar lectures

Interdisziplinäres Kolleg 2001, Günne am Möhnesee, March 02-09, 2001, JÜRGENS, U.: Wie steuert das Gehirn Sprache und den nonverbalen akustischen Ausdruck?

Neuropediatrics Department of Women & Child Health, Karolinska Institute, Stockholm, S, April 10, 2001, FUCHS, E.: Stressful life events – effects on brain structure and function.

Institute of Psychology, Univ. Gießen, April 15, 2001, FUCHS, E.: Psychosozialer Stress – seine Auswirkungen auf Gehirn und Verhalten.

Dept. of Psychiatry and Psychotherapy, Univ. Göttingen, June 16, 2001, FLÜGGE, G.: Anpassungsvorgänge an Stress.

Dipartimento di Biologia Evolutiva e Funzionale, Univ. Parma, I, June 20-21, 2001, FUCHS, E.: Stress and the brain (two lectures).

Biological Institute, Univ. Stuttgart, Stuttgart, October 23, 2001, FUCHS, E.: Psychosozialer Stress – seine Auswirkungen auf Gehirn und Verhalten.

Max-Planck-Institute of Evolutionary Anthropology, Leipzig, November 19, 2001, SCHEINER, E.: Acoustic analyses of developmental changes and emotional expression in the preverbal vocalizations of human infants.

Dept. of Psychiatry, Freie Univ. Berlin, April 29, 2002, FUCHS, E.: Psychosoziale Belastung als Auslöser molekularer und struktureller Veränderungen im Gehirn.

"Elba Summerschool and Workshop on Neurobiology of Stress in Health and Disease", Marina di Campo, I, May 04-10, 2002, FUCHS, E.: Tree shrews in chronic stress.

DPZ-Colloquium, Göttingen, May 15, 2002, KEUKER, J.: Der Hippocampus in allen Lebensabschnitten.

Institute of Behavioural Biology, Freie Univ. Berlin, June 06, 2002, KIRCHHOF, J.: Raubfeindvermeidung bei Tamarinen im Amazonas-Regenwald von Peru: Funktion von Alarmrufen und deren Einsatz in polyspezifischen Assoziationen.

Clinic for Nervous Diseases, Univ. Rostock on the occasion of the Graduate Program "Interzelluläre Kommunikation und Signaltransduktion bei pathophysiologischen Prozessen", Rostock, June 20, 2002, KOLE, M.H.P.: Functional analysis of stress-induced changes of the CA3 neuron.

Dept. of German Philology, Univ. Göttingen, July 02, 2002, SCHEINER, E.: Entwicklung und Gefühlsausdruck nonverbaler Säuglingslaute.

Dept. of Behavioural Biology, Univ. Bielefeld, July 04, 2002, SCHEINER, E.: Prä-verbale Lautentwicklung und vokaler Ausdruck von Emotionen bei Säuglingen.

Institute of Zoology, School of Veterinary Medicine, Hannover, July 12, 2002, DUJARDIN, E.: Vokalisationsrelevante Afferenzen des zentralen Höhlengraus bei Totenkopffaffen (*Saimiri sciureus*).

PhD seminar of the MSc/PhD Program Neuroscience, Max-Planck Institute for Experimental Medicine, Göttingen, July 15, 2002, HEILBRONNER, U.: Alpha<sub>2B</sub>adrenoceptor expression in the tree shrew (*Tupaia belangeri*) thalamus: co-localization with GABA and glutamate-like immunoreactivity.

Clinic for Neurological Medicine, Univ. Göttingen, Göttingen, July 22, 2002, FUCHS, E.: Struktur und Funktion der Myelinscheide.  
FUCHS, E.: Chronische psychische Belastung und strukturelle Veränderungen im Gehirn.

Ear/Nose/Throat seminar of the Soros Foundations, Salzburg, A, August 25-31, 2002,  
SIMONYAN, K.: Traumatic dysphonia.  
SIMONYAN, K.: Efferent projections from the laryngeal motorcortex in the rhesus monkey.

St. Vincenz-Hospital, Paderborn, September 18, 2002, FLÜGGE, G.: Auswirkungen von chronischem Stress.

Heidelberg Neurobiology Lectures, Heidelberg, September 25, 2002, FUCHS, E.: Stressful experiences: their effects on brain structure and function.

Zoological Institute, Univ. Amsterdam, NL, September 27, 2002, KOLE, M.: A functional analysis of stress-induced changes at the CA3 neuron.

Karolinska Institute, Stockholm, S, November 22, 2002,  
FUCHS, E.: Animal models of stress research.  
FUCHS, E.: Social conflict: effects on brain function and behavior.

Psychiatric Clinic of the University of Basel, Basel, CH, December 05, 2002,  
FUCHS, E.: Soziale Umwelt, Stress und Veränderungen im Gehirn.

DPZ-Colloquium, Göttingen, December 10, 2002, FUCHS, E.: Stress, Gehirn und Verhalten.

## **List of Publications**

### **Chapters in collected editions**

FLÜGGE, G., VAN KAMPEN, M., FUCHS, E.: Dynamic brain receptor changes in the victims of aggression. In: MARTINEZ, M. (ed.): Prevention and control of aggression and the impact on its victims. Kluwer Academic/Plenum Publishers, New York (2001): 395-400.

FUCHS, E., KRAMER, M., FLÜGGE, G.: What are the neurobiological consequences of stress? In: BROOM, D.M. (ed.): Coping with challenge: Welfare in animals including humans. Dahlem University Press, Berlin (2001): 289-300.

HÄUSLER, U.: Artikulatorische Kiefer- und Lippenbewegungen beim Totenkopffaffen. In GROSS, M., KRUSE, E. (eds.): Aktuelle phoniatriisch-pädaudiologische Aspekte 2000/2001. Band 8. Median-Verlag, Heidelberg (2001): 137-139.

JÜRGENS, U., HÄUSLER, U., DÜSTERHÖFT, F.: Zur Rolle des zentralen Höhlengraus im Mittelhirn bei der Stimmgebung – eine tierexperimentelle Untersuchung. In: GROSS, M., KRUSE, E. (eds.): Aktuelle phoniatriisch-pädaudiologische Aspekte 2000/2001. Band 8. Median-Verlag, Heidelberg (2001): 26-30.

JÜRGENS, U., FICHTEL, C., HAMMERSCHMIDT, K.: On the vocal expression of aversion: A multi-parametric acoustical analysis in a non-human primate. In: CAVÉ, C., GUAITELLA, I., SANTI, S. (eds.): Oralité et gestualité. Interactions et comportements multimodaux dans la communication. L'Harmattan, Paris (2001): 87-91.

KEUKER, J.I.H., MICHAELIS, T., DE BIURRUN, G., LUITEN, P.G.M., WITTER, M.P., FUCHS, E.: Methodological considerations when studying the aging process in

the nonhuman primate brain. In: ERWIN, J. M., HOF, P.R. (eds.): Interdisciplinary topics in gerontology, Vol.31. Aging in nonhuman primates. Karger, Basel (2002): 76-101.

KIRCHHOF, J., HAMMERSCHMIDT, K., FUCHS, E.: Aggression and dominance in tree shrews (*Tupaia belangeri*). Agonistic pattern is reflected in vocal patterns. In: MARTINEZ, M. (ed.): Prevention and control of aggression and the impact on its victims. Kluwer Academic/Plenum Publishers, New York (2001): 409-414.

MORMEDE, P., DALLMAN, M.F., FUCHS, E., HEIJNEN, J.J., HEIM, C., HELLHAMMER, D.H., IRWIN, M.R., PAYKEL, E.S., VON HOLST, D., VON HÖRSTEN, S.: Pathological consequences of stress. Dahlem Conferences. In: BROOM, D.M. (ed.): Coping with challenge: Welfare in animals including humans. Dahlem University Press, Berlin (2001): 337-355.

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## Neurobiology

<b>Publications</b>	<b>2002</b>	<b>2001</b>	<b>2000</b>
1. Books	0	0	0
2. Publication of collected editions	0	0	0
3. Chapters in collected editions	3	8	4
4. Reviewed papers	24	25	19
5. Non-reviewed papers	1	0	0
<b>Total 1 - 5</b>	<b>28</b>	<b>33</b>	<b>23</b>
6. Editorials	0	0	0
7. Electronic publications	1	0	0
8. Abstracts	18	28	19
<b>Publications altogether</b>	<b>47</b>	<b>61</b>	<b>42</b>

### Other scientific activities

#### U. Jürgens

- Co-editor of the "Journal of Medical Primatology"
- Peer reviews for the journals "Behavioral and Brain Sciences", "Cells Tissues Organs", "Experimental Brain Research", "Journal of Comparative Neurology", "Journal of Comparative Physiology A", "Neuroscience" and for the Deutsche Forschungsgemeinschaft
- Member of the Graduate Program "Perspectives of Primatology: Integration of genetic, neurobiological and ethological approaches"
- Member of the "International Neurosciences Study Program", Göttingen
- Member of the "Zentrum für Neurobiologie des Verhaltens", Göttingen

#### E. Fuchs

- Member of the Editorial Board of Neuropsychopharmacology, the official Journal of the American College of Neuropsychopharmacology (ACNP).
- Peer reviewer for the following journals: "Behavioral Brain Research", "Behavioral and Brain Sciences", "European Journal of Neuroscience", "Hormones & Behavior", "Journal of Neuroendocrinology", "Journal of Neuroscience". "Journal of Psychiatric Research", "Neuroscience", "Pharmacology, Biochemistry & Behavior", "Physiology & Behavior", "Progress in Neuro-Psychopharmacology & Biological Psychiatry", "Psychoneuroendocrinology", the Deutsche Forschungsgemeinschaft (DFG), the Israel Science Foundation, the Medical Research Council, the Netherlands Organisation of Scientific Research (NWO), the Italian Ministry for University and Research, and the Universities of Amsterdam, Groningen and Leiden.
- Member of the DFG-Graduate School "Perspektiven der Primatologie: Integration genetischer, neurobiologischer und ethologischer Forschungsansätze".
- Member of the international Graduate School "Neuroplasticity: From molecules to systems".

- Member of the DFG-Research Center Molecular Physiology of the Brain (CMPB).
- Member of the Institute for Multiple Sclerosis Research (IMSF), Göttingen.
- Member of the European Neuroscience Institute Göttingen.
- Member of the MSc/PhD/MD\_PhD Program Neuroscience, Göttingen.
- Member of the "Zentrum für Neurobiologie des Verhaltens, Göttingen.
- Member of the research network "Gepulste Magnetstimulation des Gehirns in der Therapie neuropsychologischer Erkrankungen".
- Member of the research network "Dopamin-produzierende Zellen in experimentellen Modellen der Parkinsonschen Erkrankung".
- Co-ordinator of the EC project EUPEAH (Glucocorticoid hormone programming in early life and its impact on adult health).
- Affiliated Scientist Wisconsin Regional Primate Research Center, Madison, Wisconsin, USA.

### **G. Flügge**

- Peer reviewer for the following journals: "Science", "Neuroscience", "Brain Research", "Journal of Medical Primatology", "Pharmacology, Biochemistry & Behavior", and for the Science Foundation Ireland.
- Member of the SFB 406 "Synaptische Interaktionen in neuronalen Zellverbänden".
- Member of the international Graduate School "Neuroplasticity: From molecules to systems".
- Member of the DFG-Research Center Molecular Physiology of the Brain (CMPB).
- Member of the international MSc/PhD/MD-PhD Program Neuroscience, Göttingen.
- Member of the "Zentrum für Neurobiologie des Verhaltens", Göttingen.
- Member of the research network "Dopamin-produzierende Zellen in experimentellen Modellen der Parkinsonschen Erkrankung".
- Member of the EC project HARSE (Hypertension and Alpha2-Adrenoceptor Subtype Expression).
- Affiliated Scientist Wisconsin Regional Primate Research Center, Madison, Wisconsin, USA.

### **Important activities and functions**

**E. Fuchs** is a member of the managing boards of

- the DFG-Research Center Molecular Physiology of the Brain (CMPB),
- the Institute of Multiple Sclerosis Research (IMSF),
- the European Graduate School "Neuroplasticity: From molecules to systems",
- the Graduate School "Perspektiven der Primatologie: Integration genetischer, neurobiologischer und ethologischer Forschungsansätze",
- the international MSc/PhD/MD.PhD Program Neuroscience Göttingen, and
- the Section Neuroendocrinology of the German Endocrine Society.

- **G. Flügge** is a member of the managing board of the SFB 406 and a member of the supervisory board of the DPZ.

#### **Awards**

- **E. Fuchs** was offered a professorship for Functional Neuroanatomy at the University of Trier and a professorship for Neurobiology at the Medical School, University of Göttingen. He is the first awardee of the prize "Gesellschaft braucht Wissenschaft" donated by the Stifterverband für die Deutsche Wissenschaft and the WGL for his longstanding and successful research on therapy of depressive and neurodegenerative disorders.
- **G. Flügge** received the *venia legendi* in Experimental Neurosciences from the Medical School University of Göttingen.
- **C. Fichtel** received the 2001 award of the DPZ-Förderverein for her work on the vocal expression of emotional states in primates.

**DEPARTMENT OF VIROLOGY AND IMMUNOLOGY**

**Head of Department:** Prof. Gerhard Hunsmann

**General research objectives**

The research focus has shifted during the last two years due to the transfer of personnel from our research group, "Vaccine Development", to a private company and the reintegration of the working group immunogenetics from the working group primate genetics. As in earlier years, however, most of the work within the department was supported by external grant money.

Our efforts aiming to develop an **HIV vaccine** have been intensified. The relevance of our results was greatly improved through additional examination of the MHC typing of the animals used in our studies but also through an improvement of the determination of the cellular immune responses by the ELISPOT technique. This work was conducted exclusively through national and international co-operations and funded by grant money obtained from the BMBF, the EU, and the University of Pohang, Republic of Korea. Moreover, we obtained a grant from the Society for AIDS Research. Despite the fact that vaccines developed by employing the recently developed techniques in molecular genetics have not yet been licensed for immunoprevention and therapy of human infectious diseases, there is ample reason to develop such vaccines. Such vaccines are relatively easy to produce since pathogenic organisms are not being handled. Moreover, production costs of genetic vaccines could be relatively moderate and the technology would allow targeting specific arms of the immune response for stimulation. We and other laboratories have concentrated on such types of vaccines during recent years. For vaccination of rhesus monkeys we have employed cloned SIV structural and non-structural proteins either as bacterial plasmids or integrated into viral vectors such as those derived from Semliki Forest virus and replication-defective Modified Vaccinia virus Ankara (MVA) into different vaccination schedules. Such constructs given in the right application could suppress SIV virus replication under our experimental conditions and improve the immune response after challenge infection. Most of the vaccinated animals did not show any sign of AIDS during the observation period of about 1 ½ years while control animals not vaccinated or receiving sham vaccines died of AIDS within 18 months of challenge. These trials have produced impressive protection in most animals; however, the failure of such a protective response in some of the animals cannot yet be well explained. Further trials have to clarify this point before clinical tests in humans can be recommended. Our work aiming to develop a diagnostic test and perhaps a vaccine for Herpesvirus simiae (B-virus) for rhesus monkeys is progressing slowly. This virus infects the animals of our breeding colony to about 100 %. From a gene bank containing various sequences of the virus we could identify parts of the viral D and B genes but not of the C genes, as yet. We will intensify our efforts in the future in order to improve the diagnosis of this important infection in rhesus monkeys.

Our work on **immunogenetics of macaques** was continued and several new alleles of the MHC classes I and II were identified. New hitherto unknown alleles were sequenced. In the framework of an EU study, MHC typing of *Macaca fascicularis* monkeys was initiated. Since it is very difficult to obtain rhesus monkeys of the required quality in sufficient numbers on the market and our breeding colony is much too small to supply all the animals which we require for our studies, we will focus on the use of cynomolgus monkeys in the future. Work on the immunogenetic projects was financed by the EU, the Society for AIDS Research, and from the graduate training programme "Perspectives in Primatology". This graduate training programme was sponsored by the DFG for another three years.

Our working group **prion research** has intensified its efforts to improve the diagnostics of transmissible spongiform encephalopathies (TSE). For this purpose, phage antibodies were generated which effectively bind to prion proteins. However, until now neither antibodies prepared through phage display nor monoclonal antibodies of PrP<sup>0/0</sup> mice were able to exclusively react with normal or pathogenic folding isomers of the prion molecule thereby discriminating between the pathogenic and non-pathogenic form. Such reagents would be of great value for the diagnostics of material obtained from autopsy but also for the development of an assay identifying infected living animals and humans. The licensing fee obtained through a co-operation with CEA will be used preferentially to improve these projects. In co-operation with other European institutes, we have received a larger grant to assess the risk of transmissibility of TSE from bovine material to humans through the food chain and blood products. This money was granted for five years. To make sure that the animals used are not heterogeneous in their PRNP gene, we have sequenced over 80 cynomolgus macaques in this locus. A comparison of these sequences showed that this gene of the animals employed is 100 % conserved. This is an important prerequisite for the comparison of the results obtained in the co-operating European centres. We expect to have some results to present in our next bi-annual report.

### Structure of the department

By the end of December 2002 the staff of the department comprised the department head, 6 graduate scientists, 2 doctoral students, 6 technicians, 2 disinfection assistants, 5 animal keepers as well as a secretary. Dr. C. Stahl-Hennig headed the working group "animal models" in which another graduated veterinary scientist and 3 technicians were working. The working group "molecular genetics" headed by Dr. K.D. Jentsch was supported by a technician. The working group "prion research" was headed by Dr. A.W. Stuke. One student each was working on his doctoral and diploma thesis respectively. This working group is totally supported by external funds. From January 2002 Dr. U. Sauermann headed the working group "immunogenetics" within the department of Virology and Immunology. She was supported by two technicians.

During the reporting period the tasks of the working group "vaccine development" were transferred into the working group "animal models". This was necessary since PD Dr. Lüke and Dr. Petry had been "adopted" by the company Jenapharm.

The colleagues of this group were working in the department of Virology and Immunology since adequate laboratories were not available in Jena. Within the framework of this co-operation, research on vector systems based on the use of virus-like particles patented by the DPZ was continued. By the end of 2002 the working group consisting of 4 scientists and 1 technician joined Messrs. Berlex in Richmond, CA, USA. Like Jenapharm, also Berlex was taken over by the Schering AG, Berlin. Negotiations on the transfer of the DPZ patent to Schering are under way.

Dr. Zischler, head of the working group primate genetics at the DPZ, moved to the University of Mainz and, therefore, a new head of this group will have to be appointed and restructuring was necessary. Since the immunogenetic research performed by Dr. Sauermann is of particular importance for our department, she is now working within the department of Virology and Immunology.

#### Scientists

Dr. Oliver Ast (-31.10.02)  
Dr. Claudia Goldmann (-31.10.02)  
Dr. Klaus Dieter Jentsch  
PD Dr. Wolfgang Lüke (-31.07.01)  
Dr. Harald Petry (-28.02.01)  
Dr. Ulrike Sauermann (01.01.02-)  
Dr. Michael Spring (-28.02.01)  
Dr. Christiane Stahl-Hennig  
Dr. Nicole Stolte  
Dr. Andreas Stuke  
Dr. You-Suk Suh (01.08.02-)  
Dr. Ying Zhang (-31.12.01)

#### Secretary

Karin Peinemann

#### Technicians

Corinna Boike  
Jacqueline Denti (01.07.02-)  
Karin Giller (-31.07.01)  
Jutta Gloth (-30.09.01)  
Judith Hampe (28.06.01-)  
Ellen Heinemann (-31.08.01)  
Heike Knecht (01.05.-31.10.02)  
Nicole Leuchte (01.07.02-)

Heidi Matthes (01.12.01-15.03.02)  
Heidi Meyer (16.09.02-)  
Anna-Sophie Moldenhauer (-17.07.01)  
Kerstin Petry (15.08.01-31.08.02)  
Sina Plümer (-14.04.02)  
Zeljka Sisic (-14.03.01)  
Anja Wachtel (-30.04.01)

#### PhD Students

Irantzu Allegria Dallo (-30.06.01)  
Gisela Feldmann (-01.04.02)  
Kai Lieder  
Evelyn Meyer  
Thorsten Mühl (01.01.-30.11.02)  
Alexander Strom

#### Undergraduate students

Nadine Dammeier (01.08.01-23.05.02)  
Henrik Müller (01.12.01-30.11.02)

#### Animal keepers

Thorsten Eggers  
Gabriele Marschhausen  
Henning Mascher  
Peter Müller  
Norbert Schwandt

### **Progress during the year**

The following projects were performed by the working groups (WG) vaccine development, animal models, molecular genetics, prion research and immunogenetics (from January 2002) within the reporting period 2001/2002:

**WG Vaccine Development (Head: PD Dr. W. LÜKE)**

Due to the co-operation with the company Jenapharm, the field of activity of the former group "vaccine development" changed significantly. Research focussed on the improvement of a universal **transporter system for gene therapy on the basis of JC virus-like particles (JC-VLP)**. In search of suitable carrier systems for the development of vaccines and for the improvement of gene therapeutical approaches, virus-like particles (VLP) are being used more and more. These particles avoid such disadvantages as recombination and replication as well as immunogenicity. During the reporting period, the production and the packaging of DNA into these VLP was improved. Furthermore, the cell tropism of these particles was investigated in more detail. JC-VLP have a specific activity to cells of the brain and kidney. Bi-specific antibodies were developed for the targeting of other cells in order to extend the natural tropism of these VLP. Ongoing immunogenicity studies have shown that both rabbits and rhesus monkeys do not react immunologically neither to the cellular nor the humoral system. Studies on VLP as gene carrier systems are now being continued at Berlex Inc. in California. The German Primate Centre is no longer involved in these studies. We hope that licensing negotiations with Schering AG, Berlin, with regard to the VLP technique developed in the department and patented by the DPZ will soon be concluded.

**WG Animal Models (Head: Dr. C. STAHL-HENNIG)**

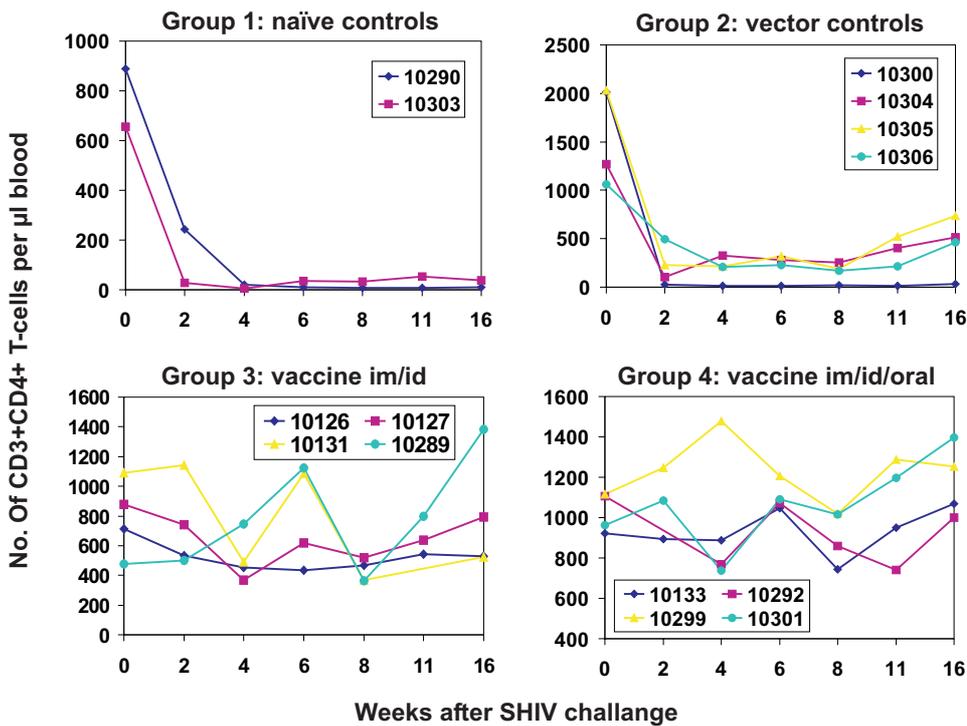
Again the work of this group concentrated on studies on the prophylaxis, pathogenesis and therapy of AIDS using the SIV/SHIV-macaque model. Studies on vaccine development dominated. As before subadult rhesus monkeys served as test animals.

Experiments using different vector combinations for the **development of a vaccine against AIDS** were intensified. According to current knowledge such combinations appear to be safer compared to inactivated whole virus or live-attenuated vaccines.

In collaboration with scientists from the Pohang University in the Republic of Korea, rhesus monkeys were immunised five times with DNA vectors via the intramuscular (i.m.) route over 44 weeks. The DNA vectors expressed different SIV genes. Group 1 comprising 3 monkeys was immunised with DNA plasmids expressing SIVgag-env and -pol. Group 2 comprising 4 monkeys additionally received two further plasmids expressing SIVvif-nef and SIVtat-vpu. Group 3 (3 monkeys) was immunised identically to group 2, but, in addition, received a plasmid expressing mutated human IL-12. The latter was supposed to strengthen the virus-specific cellular immune responses. Four weeks after the final immunisation animals were challenged intravenously with pathogenic SIV. At this time point all vaccinees had low numbers of SIVgag-specific IFN $\gamma$ -secreting lymphocytes in their blood as determined by the ELISPOT assay. This type of secreting cells is generally considered to be a cytotoxic T-cell and its number was slightly higher in group 3 compared to the other vaccinees. No SIV-specific antibodies were detected in any of the vaccinees at the time of challenge. Following challenge virus exposure all vaccinees became in-

fect. However, the group 3 animals had clearly lower viral loads at peak viraemia and in the chronic phase of infection, their viral loads were 10-100fold lower than those of the control group. The latter also applied for group 2. The most marked anamnestic cellular immune responses were observed in group 3 which underlines the supportive effect of IL-12. In summary, partial protection indicated by reduced viral load was observed after application of a multi-component SIV DNA expressing structural and regulatory viral genes. This effect could even be enhanced by co-injection of immunostimulating IL-2 DNA.

To further increase the above-mentioned protective effects another study was initiated in which SIV DNA immunisation was combined with application of replication-incompetent adenovirus (Ad5) recombinant for SIV. Eight monkeys were immunised with a multi-component SIV DNA plus the IL-12 plasmid at weeks 0, 8 and 16. Eight weeks later the animals were injected with Ad5 vectors expressing the same SIV genes as the DNA vectors (SIV-Ad5). All vaccinees received the Ad5 vector mixture i.m., in addition four of them also received it intranasally via spray application. At week 32 all vaccinees plus four other animals which had received the vectors



*Absolute CD4+ cell counts in blood of nonimmunised (group 1 and 2) and DNA/MVA-immunised rhesus monkeys (group 3 and 4) after challenge virus exposure to highly pathogenic SHIV. While in the control animals a dramatic loss of this T-cell population was observed already 2 weeks after the challenge, the vaccinees are protected against this T-cell loss irrespective of the immunisation route (im, intramuscularly; id, intradermally; orally).*

without foreign gene insertions (vector controls) were intrarectally exposed to pathogenic SIV wild type. At the time point of the Ad5 injection only one vaccinee was positive for SIVgag-specific IFN $\gamma$ -secreting lymphocytes. In contrast, all vaccinates presented this kind of reactive cell two weeks later. This reaction was directed against one or even several SIV proteins and was still demonstrable six weeks later at the time of challenge. SIV-specific binding antibodies were hardly detectable after DNA immunisation. However, at the time of challenge all vaccinates had antibodies against SIVenv, 6 out of 8 seemed to be positive for anti-Tat antibodies, but none had anti-SIVgag antibodies. All vaccinates and vector controls were replicating SIV after challenge. Nevertheless, 5 out of the 8 vaccinates had 10-100fold lower peak virus titres compared to the vector controls. Particularly the viral load in the chronic phase of infection was clearly lower in the eight vaccinates. A humoral anamnestic response was observed in the vaccinates against SIVenv, but not against SIVgag. Thus, the chosen immunisation strategy provided clear protective effects as indicated by reduced viral load after mucosal challenge.

Within the framework of a European collaboration involving overall eight centres which are able to perform SIV infection experiments in non-human primates, different vector combinations were checked for their immunogenicity and efficacy. The combinations included SIV-DNA, Semliki-Forest-Virus (SFV) and modified vaccinia virus Ankara (MVA) both recombinant for the same SIV genes already expressed by the DNA. All vectors expressed the structural genes *env* and *gag/pol* and the regulatory genes *rev*, *nef* and *tat*. All groups used identical vaccine batches for immunisation, the immunisation routes for each vector and the immunisation intervals were the same. Furthermore, all used one SIV stock for the rectal challenge virus exposure. Analyses for cell-mediated immunity were performed according to standardised protocols, mucosal and serum antibodies and viral RNA in plasma were determined centrally in specialised laboratories. At DPZ four macaques were immunised at eight-week-intervals once with SIV-DNA intradermally and with SIV-SFV subcutaneously followed by two SIV-MVA immunisations intramuscularly. Another group of four animals received the same order of vaccines with the modification that SIV-SFV and the last SIV-MVA dose were administered oronasally by spray application. Four animals were immunised with the respective empty vectors and served as controls, two untreated monkeys were included as naïve controls. SIV-specific IFN $\gamma$ -secreting T-cells were detectable in one animal from each vaccine group directed against one or more SIV proteins following the final immunisation. However, some vector controls also reacted unspecifically against SIVgag. Virus-specific antibodies were not detectable at the time of challenge. Eight weeks after the final immunisation all test animals were challenged intrarectally with pathogenic SIV wild type. As a consequence all animals became infected. No differences were observed in peak viral loads among any of the groups. However, in contrast to the untreated controls viral loads were reduced in both the vaccinated and the vector control group in the chronic phase of infection. Following challenge, all animals developed SIV-specific IFN $\gamma$ -secreting lymphocytes independent of the test groups they belonged to. There were no differences in the numbers of such reactive cells among the four groups. Only with respect to SIVenv-specific antibodies did we observe differences between vaccinated and controls groups. In the former a clear anamnestic immune response appeared indicating a priming effect by the vaccine application. On the

other hand SIVgag antibodies were primary in nature. In summary, the vector combination tested at DPZ revealed no obvious protective effects.

In collaboration with Dr. Ralf Wagner from the University of Regensburg within the framework of a nationally supported collaboration ("Verbundprojekt") a combination immunisation strategy was tested in the SHIV model involving DNA priming followed by MVA booster immunisation. The synthetic DNA vaccine component consisted of codon-optimised SIVgag-pol and HIV-1 89.6P env. The respective genes were expressed in the MVA system accordingly. Two groups of four monkeys each (group 1 and 2) received the HIV/SIV-DNA vaccine three times in eight-week-intervals both intradermally and intramuscularly. This was followed by an intramuscular injection of recombinant (r) MVA at week 24. After another eight weeks group 1 again was immunised i.m. with rMVA, whereas group 2 received rMVA orally via spray application. This should allow a comparison between systemic and mucosal vaccine application. Another four animals received empty vectors in analogy to the vaccine groups (vector controls), two untreated animals served as naïve controls. Eight weeks after the final immunisation all animals were exposed to the highly pathogenic SHIV 89.6P via the rectal route. To detect virus-specific T-helper cells, lymphocytes were subjected to a proliferation assay using SIVgag for stimulation. Two animals from group 1 and all four animals from group 2 showed a clear proliferative activity shortly before challenge. Following challenge all animals became infected. However, peak viral RNA load was reduced about hundred-fold in one animal from group 1 and three animals from group 2 compared to the naïve control monkeys. RNA load in the chronic phase was clearly decreased in seven out of the eight vaccinates compared to the naïve control group. This, however, also applied for two vector controls. In the SHIV model a dramatic CD4+ T-cell loss is already observed by week 2 after infection. This particular effect was noticed in both control groups. In contrast, all vaccinates were protected from this early loss. Only later on, in one animal from group one, had the CD4+ T-cell subset dropped which coincided with rising viral load. Thus, this investigated vector combination mediated a partial protection after a mucosal SHIV challenge. This was indicated by a reduced viral load in 50 % of the vaccinates in the acute phase of infection, low viral loads in the majority of the vaccinates in the chronic phase of infection and stable CD4+ T-helper cells.

From the comparison of the different tested vector combinations for their immunogenicity and efficacy it is unclear why similar strategies did not confer protection in the SIV model (EU project), whereas in the SHIV model (national cooperation) clear protective effects were observed.

#### **WG Molecular Genetics (Head: Dr. K.-D. JENTSCH)**

Depending on their age, the animals of the rhesus macaque colony of the DPZ are infected with the Herpes virus simiae (B-virus), an alpha Herpesvirus, in the range of 70 to 100%. This virus persists a whole life long in the sensory neurons of the cranial nerves and in the ganglions of the spinal marrow. In most of the cases, an infection is harmless for these monkeys. However, transmission to humans might cause severe encephalopathies which are often fatal. The transmission of this virus is pos-

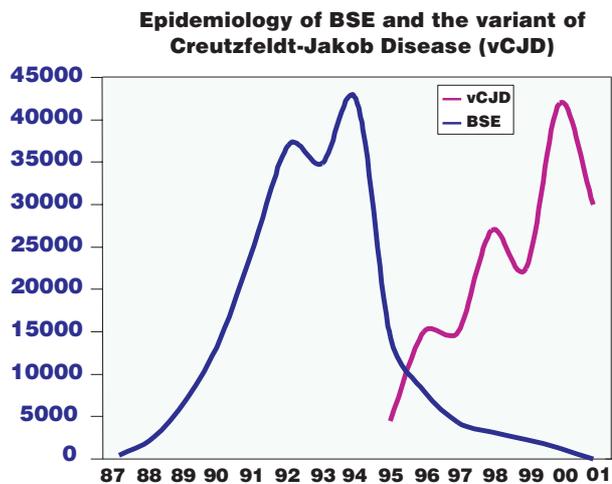
sible through saliva, genital secretion, and through the liquid in the mucosal vesicles of those animals reactivating the B-virus. Especially in the United States of America, several primate centres have established breeding colonies founded on B-virus-negative rhesus monkeys. An important prerequisite is the discrimination of B-virus-infected and noninfected animals by serological or molecular diagnostic techniques. The working group, molecular biology, has optimised several primer pairs for binding of genes coding for B-virus glycoproteins. A library containing fragments of B-virus DNA was provided by Dr. H. Hümer, Institute of Hygiene, University of Innsbruck, Austria. Further samples of cell and culture supernatant from B-virus-infected cells were obtained from Prof. H. Schmitz, Bernhard-Nocht-Institute, Hamburg, Germany. Using the above-mentioned primers, we could amplify sequences from the glycoprotein D and B of the Herpes virus. We are now trying to isolate the complete sequences of these glycoproteins in order to express them *in vitro* to obtain antigens for diagnostics. We also intend to construct Semliki Forest virus vectors containing these Herpes virus glycoproteins in order to use them as vaccines. Before conducting trials in rhesus monkeys we will, however, assay the immunogenicity in mice.

#### **WG Prion Research (Head: Dr. A.W. STUKE)**

BSE (bovine spongiform encephalopathy) is transferable to humans through the consumption of prion-infected beef. In 1995 this new lethal illness was described for the first time in Great Britain and was named variant Creutzfeldt-Jakob disease (vCJD). By the end of 2002 some of 130 cases had been reported ([www.doh.gov.uk/cjd/cjd\\_stat.htm](http://www.doh.gov.uk/cjd/cjd_stat.htm)). The diagnoses were performed by histopathology examinations and by immunodetection methods (detection of proteinase K resistant prion protein (PrPres) with monoclonal antibodies after Western blotting or in ELISA assays). However, both methods are limited to the *post mortem* diagnosis. Furthermore, the diagnosis is possible only in infected animals and humans with progressed illness. In Germany, 240 BSE cows have been reported ([www.verbraucherministerium.de](http://www.verbraucherministerium.de)). Since the infectious prion units, which are necessary to transmit BSE *per os* to humans are unknown, a serious risk assessment is difficult to conduct (see also TSE primate studies of the department of virology). Therefore, we focused our work on the development of molecular tools for the *intra vitam* diagnosis of TSEs (see project **risk assessment in primates of TSE transmission**).

In the project **diagnosis and therapy of TSE diseases by means of evolutive phage antibodies only binding to the pathogenic prion protein form**, a larger number of single chain variable fragment (ScFv) antibodies and peptide phage antibodies were generated and subsequently isolated by biopanning. They all showed signals in enzyme-linked immunosorbent assays (ELISAs) which were reproducibly comparable to the signals of the monoclonal antibodies (mabs) formerly isolated in our department by the DNA immunization protocol. The ScFv antibodies were isolated using the pCANTAB5 vector system from Pharmacia and the peptide phage antibodies using the 12mer random peptide library from NEB. A mixture of synthetic bovine PrP peptides and recombinant bovine PrP was utilized in the

biopanning procedure for the selection of the phages. Fourteen peptide phage antibodies and three corresponding synthetic 12mer peptides were provided to Prof. M. Groschup (Federal Research Institute for Virus Diseases of Animals (BFVA), Insel Riems, Germany). At present, the BFVA is testing their potential anti-prion activity in a cell-based assay. The ability of the recombinant antibodies to discriminate the cellular PrP<sup>c</sup> from the pathogenic PrP<sup>Sc</sup> form is still proceeding in our laboratory. However, experimentally this remains not a simple task to undertake.



The blue curve shows the development of BSE diseases in cattle, the red curve represents the course of vCJD diseases in humans in Great Britain. While the peak level of the BSE epidemic with more than 40,000 cases was reached in 1994, first cases of vCJD were diagnosed one year later. By December 2002, 119 people had died from vCJD.

To characterise the ScFv and peptide phage antibodies, different ELISA and dot blot tests under non-denaturing conditions and Western blot (WB) test after denaturing SDS gel electrophoresis were established. PrP was bound directly onto surfaces or presented by anti-PrP antibodies. As antigens, we used different concentrations of synthetic ovine and bovine PrP peptides, commercially available recombinant bovine PrP<sup>c</sup>, recombinant PrP<sup>c</sup> which was isolated in our laboratory from human cell cultures, and murine PrP<sup>c</sup> and PrP<sup>Sc</sup> which was isolated from infected mouse brains by immobilised metal affinity chromatography (IMAC). Furthermore, BSE material from Great Britain (provided by the Veterinary Laboratory Agency, Weybridge, GB) and Germany (kindly provided by Dr. W. Schulz-Schaeffer, Department of Neuropathology, University Hospital Göttingen) was used as antigen. Additionally, the epitopes of all antibodies were determined in a gridded array ELISA test using 114 overlapping bovine 13mer peptides. Several PrP epitopes of the peptide antibodies from the random peptide library were determined exactly with the tests and antigens described above. Hopefully, this technology will be useful to identify antibodies binding specifically to different PrP forms. However, despite enhanced efforts in recent years to isolate such conformation specific by different laboratories antibodies, they are still missing for a secure TSE diagnosis. Last month, we were using BSE material of different purification levels for the biopanning procedure.

These materials were obtained from the project **isolation of the cellular prion protein (PrP<sup>c</sup>) and the BSE agent (PrP<sup>sc</sup>) from infected cow brains for the characterisation of anti-PrP antibodies** in a diploma thesis (University of Göttingen). In this work the murine and bovine PrP isoforms were separated and enriched by application of the IMAC technique. This work also supplied us with sufficient material for the characterisation of the mAbs and the ScFV and peptide phage antibodies. Thus, the IMAC protocol which uses Cu<sup>2+</sup> chelated to columns was a very successful method especially for the separation of murine, bovine and human PrP isoforms in a presumable nearly native conformation. The distribution of the other cellular proteins in the flow through and eluate of the column was manipulatable by changing of the washing conditions. In combination with subsequent purification procedures (immunoprecipitations and two-dimensional gel electrophoresis) we isolated PrP isoforms with a higher purity compared to previously used protocols. In addition, we will test this method for its ability to enrich the PrP isoforms from larger sample volumes of body fluids (e.g. blood and liquor).

At the end of 2002, initial experiments were conducted in the project **ex vivo replication of the prion protein in a cell culture model**. In this work, we will use the murine 3T3-L1 Tet-Off cell line stably transfected with the human FFI prion protein (PRNP) gene. This cell line was generated in a previous experiment and inducibly over-expresses the prion protein up to 20 times. This enhanced expression should facilitate the *ex vivo* conversion of PrP<sup>c</sup> to PrP<sup>sc</sup> since a larger number of PrP<sup>c</sup> molecules is needed for the intracellular replication reaction. This project has also diagnostic aspects.

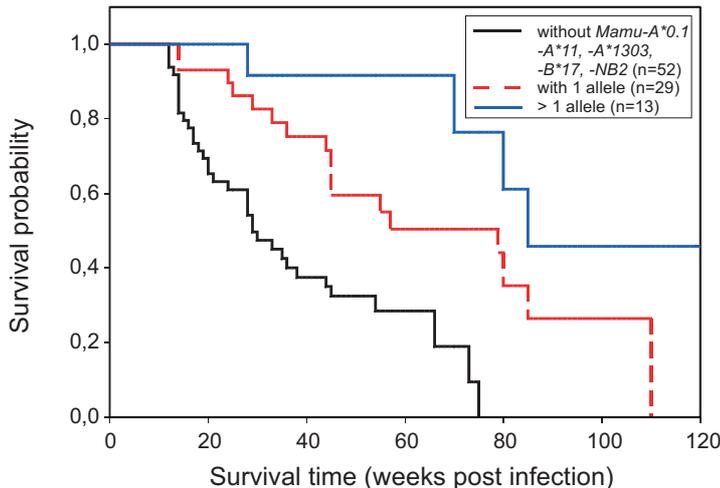
The demand for the mAbs, which had been isolated in the completed EU-funded project **monoclonal antibodies against prion proteins of different species and their characterization**, has not further increased. Two of these mAbs are now included in the BIORAD Platelia<sup>R</sup> BSE test. Mabs 12F10 and 8G8 are also commercially available as immunoreagents from BIORAD.

In the EU-funded project **risk assessment in primates of TSE transmission to humans through food and blood products** we sequenced (in co-operation with Prof. Kaup, Dept. of Veterinary Medicine and Primate Husbandry, DPZ) the DNA of the PRNP gene ORF of *Macaca fascicularis* individuals from the island Mauritius. The sequences showed a complete preservation of the PRNP gene in all animals. A lower number of animals from different geographic regions showed only a few substitution mutations. The PRNP gene of *Macaca mulatta* was also sequenced. Altogether the sequence comparison leads to the conclusion that the PRNP gene is under selection pressure. The reasons are unknown since the biological function of PrP<sup>c</sup> is unclear.

#### **WG Immunogenetics (Head: Dr. U. SAUERMAN, from January 2002)**

The group **immunogenetics** investigates genes encoded on the major histocompatibility complex (MHC) in primate species. The highly polymorphic proteins encoded in the MHC play an important role in triggering adaptive immune responses. The term MHC molecule describes two classes of membrane-anchored glycoproteins which present peptide antigens to T-cells. The recognition of a peptide

bound to a MHC molecule activates both the T-cell and the antigen-presenting cell, triggering an immune response. Since every MHC molecule is only able to present a specific set of peptides, different immune responses can be triggered in different individuals depending on their *Mhc* genes. *Mhc* genes are thus associated with the differential susceptibility to pathogens but also to autoimmune diseases.



*Survival probability of SIV-infected rhesus macaques with not any, one or more "protective" Mhc class I alleles in relation to weeks post infection.*

In recent years we have focussed on the investigation of the **genetic organisation of the rhesus macaque MHC region** and the **development of fast *Mhc*-typing techniques**. The aims are to identify *Mhc* alleles which can be used to prognosticate the disease course in SIV-infected monkeys, and to further validate already known associations, respectively. For many years we have been *Mhc*-typing the experimental animals from several scientific networks, and as a service for external partners. In recent years, priority was given to the typing of the experimental animals of a concerted action within the EU. Within this framework we initiated *Mhc*-typing of cynomolgus macaques (*Macaca fascicularis*).

In addition, we focussed on the *Mhc* class I genes of rhesus macaques (*Macaca mulatta*). During his PhD thesis, Thorsten Mühl developed a technique for separating and sequencing *Mhc* class I cDNAs by a special gel electrophoresis technique. A number of novel *Mhc* class I alleles was identified. To establish fast sequence-based typing techniques, 18 primer pairs were generated. Using these primer pairs, more than 50 different *Mhc* class I alleles were identified. After the typing of more than 90 non-immunised SIV-infected rhesus macaques, 3 alleles were identified which were associated with slower disease progression. *Mhc* class II encoded genotypes associated with rapid disease progression had been identified in our laboratory earlier. By the analysis of *Mhc* class I and class II alleles, the prognosis of disease course has now been substantially improved. Animals for which the disease course can be prognosticated prior to the onset of an experiment are important to investigate immunological and virological parameters influencing disease progression, and to conduct vaccine and therapy trials under standardised conditions.

Rhesus monkeys are not bred in sufficient numbers neither at the DPZ nor within the EU. Furthermore, due to a shortage, it is not possible to obtain rhesus macaques of Indian origin from the USA. Therefore, rhesus monkeys bred in China are imported. These macaques have very different *Mhc* alleles compared to macaques of Indian origin. In these macaques we detected at least 15 novel *Mhc* class II DQB-alleles and about 50 novel DRB-alleles. Furthermore, their disease course differs after infection with SIV. This example shows that it would be of paramount importance to either breed monkeys in sufficient numbers at the DPZ or within the EU or, at least, to obtain only macaques subjected to a defined breeding program. For this reason we also re-initiated the *Mhc* -typing of the rhesus monkeys breeding colony of the DPZ in spite of the lack of reasonable funding.

Within the framework of an EU vaccine study we initiated the development of ***Mhc*-typing techniques for cynomolgus macaques**. The *Mhc*-region of this species is poorly investigated so far. We identified about 30 novel *DRB*-alleles and 6 *Mhc* class I alleles. Those macaques imported from Mauritius show little genetic polymorphism. Since these macaques are frequently used for experimental AIDS research in Great Britain, France and Italy, rapid *Mhc* -typing techniques were developed for them.

In addition, we started to characterise the **DRB-region of toque macaques** (*Macaca sinica*). The investigation of wild, but well investigated toque macaques from the forest of Polonnaruwa, Sri Lanka, will further uncover the role of *Mhc*-polymorphism in the fitness of wild animals.

In co-operation with the department Veterinary Medicine and Primate Husbandry, the characterisation of the **DRB-alleles of lion-tailed macaques** (*Macaca silenus*) was initiated. The study was funded by the post-graduate college "Perspective of Primatology".

Due to the re-integration of the group Immunogenetics into the department Virology and Immunology the tasks will be enlarged by the establishment of viral diagnostic techniques, and by investigations on the role of liver macrophages in experimental SIV infection.

### **Integration into national and international research**

The Department of Virology and Immunology is involved in numerous national and international research projects. Within the framework of the second grant of the graduate training programme "Primatology" (co-ordinator: Prof. Gerhard Hunsmann), a doctoral fellow guided by Dr. Sauermann and Prof. Kaup, Department of Veterinary Medicine and Primate Husbandry was working on her doctoral thesis "Echinokokkosis in wild-living nonhuman primates". Seven institutes from five European countries collaborated in two EU-funded projects co-ordinated by Prof. Hunsmann. (1) "European Network for Vaccine Evaluation in Primates: Combined Vector Immunisation for AIDS Vaccine Development" and (2) Risk Assessment in Primates of TSE Transmission to Humans Through Food and Blood Products". Another project entitled "Genome-wide search for human-specific retrotransposon integrations and their insertion polymorphisms in human populations" funded through the EU INTAS programme, was also co-ordinated by Prof. Hunsmann. Two

Russian and one French research institution collaborated within the framework of this project. A long-lasting co-operation on vaccine development exists with Prof. Sung, Department of Life Science of the Pohang University of Science and Technology, Republic of Korea as well as with a German pharmaceutical company. The table below shows an overview of all co-operations.

### Projects and partners in co-operation

(I: interdepartmental projects, E: external co-operation; A: project completed, L: current project)

<b>Projects and Partners of the Department of Virology and Immunology</b>		
<b>Investigations of the cellular and humoral immune response in the course of progressive multifocal leukoencephalopathy (PML)</b> F. WEBER (Dept. of Neurology, Univ. Hospital Göttingen), A. AGUZZI (Univ. Hospital, Zürich, CH), C. SINDIC (Catholic Univ., Brussels, B), T. WEBER (Neurological Hospital, Marienkrankenhaus, Hamburg), P. CINQUE (San Raffaele Hospital, Milano, I), F.-J. KAUP (Dept. of Veterinary Medicine and Primate Husbandry, DPZ), <b>W. LÜKE</b>	E,I	A
<b>Vaccine development against HIV-1</b> <b>H. PETRY, E. MEYER, N. STOLTE, C. STAHL-HENNIG, Y. ZHANG,</b> K. MÄTZ-RENSING, F.-J. KAUP (Dept. of Veterinary Medicine and Primate Husbandry, DPZ), G. HÖHN, S. FISCHER, R. MEYER-PITTROFF (Chair of Energy and Environmental Techniques, Technical Univ. München-Freising), <b>W. LÜKE</b>	E,I	A
<b>JCV-VLP as a universal transporter system for gene therapy</b> <b>C. GOLDMANN, O. AST, E. MEYER, Y. ZHANG,</b> F.-J. KAUP, K. MÄTZ-RENSING (Dept. of Veterinary Medicine and Primate Husbandry, DPZ), J.-D. FAUTECK, W. RÖMER, H. SCHULZ, M. OETTEL (Jenapharm GmbH, Jena), K. LEMKE, J. METZE (IBA, Heiligenstadt), <b>H. PETRY, W. LÜKE</b>	E,I	A
<b>New strategies for stable and safe gene transfer into glia cells</b> L. TENENBAUM (Univ. Brussels, B), U. JÜRGENS (Dept. of Neurobiology, DPZ), <b>H. PETRY, W. LÜKE</b>	E,I	A
<b>Targeting of intracellularly expressed protease inhibitors to the cell membrane and optimisation of packaging into virus particles</b> <b>A. STROM, O. AST, W. LÜKE, K.D. JENTSCH, H. PETRY</b>		A
<b>Development of vectors for membrane-associated HIV-1 protease inhibitors</b> <b>I. ALLEGRIA, O. AST, K.D. JENTSCH, W. LÜKE, H. PETRY</b>		A

<b>Projects and Partners of the Department of Virology and Immunology</b>		
<p><b>Intracellular expression of virus-specific protease inhibitors as a new approach for antiviral gene therapy against HIV infection</b></p> <p><b>O. AST, K. LIEDER, K.D. JENTSCH, W. LÜKE, H. PETRY,</b> M. REBOUD (Inst. Jacques Monod, Paris, F), H.J. SCHRAMM (MPI for Biochemie, Martinsried)</p>	E	A
<p><b>Microbiological and immunological characterisation of Helicobacter infections in rhesus monkeys</b></p> <p>K. MÄTZ-RENSING, E. KUNZ, F.-J. KAUP (Dept. of Veterinary Medicine and Primate Husbandry, DPZ) S. SUERBAUM (Inst. for Hygiene and Microbiology, Univ. Würzburg), B. KNAPP (Chiron-Behring Werke, Marburg), H.J. MONSTEIN (Div. Clinical Microbiology, KMÖ, Linköpping, S), C. KRAFT (Univ. Würzburg), <b>G. FELDMANN</b></p>	E,I	A
<p><b>Development of diagnostic tests for Herpes monkey B virus infections</b></p> <p><b>K.D. JENTSCH,</b> F.-J. KAUP (Dept. of Veterinary Medicine and Primate Husbandry, DPZ), H. SCHMITZ (Bernhard-Nocht-Institute, Hamburg), H. HUEMER (Inst. for Hygiene, Innsbruck, A) C. COULIBALY (Paul-Ehrlich-Institute, Langen), P. LILJESTRÖM (Karolinska Institute, Stockholm, S)</p>	E,I	L
<p><b>Investigations for vaccination of juvenile macaques against Herpes B</b></p> <p><b>K.D. JENTSCH,</b> F.-J. KAUP (Dept. of Veterinary Medicine and Primate Husbandry, DPZ), H. SCHMITZ (Bernhard-Nocht-Institute, Hamburg), P. LILJESTRÖM (Karolinska Institute, Stockholm, S), C. COULIBALY (Paul-Ehrlich-Institute, Langen)</p>	E,I	L
<p><b>SIV infection of rhesus macaques: pathogenesis of intestinal alterations</b></p> <p>F.-J. KAUP, K. MÄTZ-RENSING, K. BINGGER, A. FLOTO (Dept. of Veterinary Medicine and Primate Husbandry, DPZ), M. ZEITZ, T. SCHNEIDER (Univ. Hospital Benjamin Franklin, Berlin), P. RÀCZ, (Bernhard-Nocht-Institute, Hamburg), <b>C. STAHL-HENNIG, N. STOLTE</b></p>	E,I	L
<p><b>The oral cavity as mucosal entry for SIV/SHIV as location for the mucosal application of potential SIV/HIV vaccines and in this context the role of dendritic cells</b></p> <p>K. TENNER-RÀCZ, P. RÀCZ (Bernhard-Nocht-Institute, Hamburg), <b>C. STAHL-HENNIG, N. STOLTE,</b> K. MÄTZ-RENSING, F.-J. KAUP (Dept. of Veterinary Medicine and Primate Husbandry, DPZ), R. STEINMAN (Rockefeller Univ., New York, USA), K. ÜBERLA (Inst. for Molecular and Medical Virology, Univ. Bochum), R. IGNATIUS (Inst. for Infection Medicine, Free Univ. Berlin)</p>	E,I	L

<b>Projects and Partners of the Department of Virology and Immunology</b>		
<p><b>Investigations on the pathogenesis of primary and secondary alterations in different organs of SIV-infected rhesus monkeys</b> F.-J. KAUP, K. MÄTZ-RENSING, P. HOFMANN (Dept. of Veterinary Medicine and Primate Husbandry, DPZ), <b>N. STOLTE, C. STAHL-HENNIG</b></p>	I	A
<p><b>Efficacy studies with replication-defective SIV vectors in rhesus monkeys</b> <b>C. STAHL-HENNIG, N. STOLTE, K. TENNER-RÄCZ, P. RÄCZ</b> (Bernhard-Nocht-Institute, Hamburg), K. ÜBERLA (Inst. for Molecular and Medical Virology, Univ. Bochum)</p>	E	L
<p><b>Immunogenicity and efficacy of DNA vectors expressing structural and accessory genes of SIV and immune-modulating cytokine, with and without combination of SIV-recombinant adeno virus vectors in rhesus monkeys</b> <b>C. STAHL-HENNIG, N. STOLTE, Y.-S. SUH, Y.C. SUNG</b> (Pohang Univ. of Science and Technology, Korea)</p>	E	L
<p><b>Combined immunisation of rhesus monkeys with codon-optimised DNA vectors and recombinant attenuated pox virus vectors expressing the structural proteins Gag-Pol and Env of SIV</b> K. BIEHLER und R. WAGNER (Inst. for Medical Microbiology and Hygiene, Univ. Regensburg), <b>N. STOLTE, C. STAHL-HENNIG</b></p>	E	A
<p><b>SIV-associated leukoencephalopathy: The role of the dopaminergic system on the development of neurodegeneration</b> S. SOPPER, V. TER MEULEN (Inst. for Virology and Immunobiology, Univ. Würzburg), <b>C. STAHL-HENNIG, N. STOLTE</b></p>	E	L
<p><b>Significance of the complement system for SIV/HIV vaccination strategies and the SIV infection in rhesus monkeys</b> C. SPETH, H. STOIBER, M. DIERICH (Inst. for Hygiene, Univ. Innsbruck, A), <b>N. STOLTE, C. STAHL-HENNIG</b></p>	E	L
<p><b>Neopterin in SIV-/SHIV-infected rhesus monkeys</b> <b>C. STAHL-HENNIG, N. STOLTE, D. FUCHS</b> (Inst. for Medical Chemistry and Biochemistry and Ludwig-Boltzmann-Institute for AIDS Research, Univ. Innsbruck, A)</p>	E	L
<p><b>Investigations on the influence of a new protease inhibitor on the chronic SIV infection of rhesus monkeys</b> <b>C. STAHL-HENNIG, N. STOLTE, U. SCHUBERT</b> (Laboratory of Viral Diseases, NIH, USA), N. WEICH (Millenium Pharmaceuticals, Boston, USA)</p>	E	A

<b>Projects and Partners of the Department of Virology and Immunology</b>		
<b>Relevance of co-receptor usage of SIV for viral pathogenesis</b> S. POHLMAN und F. KIRCHHOFF (Inst. for Microbiology, Dept. Virology, Univ. Ulm), N. STOLTE, C. STAHL-HENNIG	E	A
<b>Investigations of the influence of selected Nef functions on the SIV pathogenesis by using SIV Nef mutants</b> F. KIRCHHOFF (Inst. for Microbiology, Dept Virology, Univ. Ulm), N. STOLTE, C. STAHL-HENNIG	E	A
<b>Characterisation of the immune pathogenesis and protective mechanisms in SIV-infected rhesus monkeys</b> M. SPRING, N. STOLTE, C. STAHL-HENNIG, G. FELDMANN, U. SAUERMANN, D. LORENZEN		A
<b>Effects of an early anti-retroviral therapy in combination with therapeutic immunisation to the SIV pathogenesis and immune response</b> M. SPRING, N. STOLTE, C. STAHL-HENNIG, N. BISCHOFBERGER (Gilead Sciences, Inc. CA, USA), Y.C. SUNG (Pohang Univ. of Science and Technology, Korea)	E	A
<b>Effects of an early anti-retroviral therapy in combination with therapeutic DNA immunisation based on autologous SIV <i>env</i> and vector SIV <i>gag</i> to the SIV pathogenesis and immune response</b> C. STAHL-HENNIG, N. STOLTE, N. BISCHOFBERGER (Gilead Sciences, Inc. CA, USA), H. SHIDA (Hokkaido Univ., Sapporo, Japan)	E	L
<b>Combined immunisation of rhesus monkeys with DNA-, Semliki Forest-virus and attenuated pox virus vectors recombinant for the structural SIV proteins Gag-Pol and Env and the SIV regulatory proteins Tat, Rev, and Nef</b> C. STAHL-HENNIG, N. STOLTE, EU-Shared Cost Action "ENVEP" and Programme EVA	E	L
<b>Effects of immune-modulating agents in combination with an anti-retroviral therapy to the early chronic SIV infection</b> C. STAHL-HENNIG, N. STOLTE, Y.-S. SUH, D. PAULSEN, H. RÜBSAMEN-WAIGMANN (Bayer AG, Wuppertal)	E	L
<b>CpGs and colony-stimulating factors (-CSF) as adjuvants for HIV vaccine development</b> C. STAHL-HENNIG, N. STOLTE, R. IGNATIUS (Inst. for Infection Medicine, Free Univ. Berlin), G. HARTMANN (Medical Hospital Innenstadt, München), K. TENNER-RÄCZ, P. RÄCZ (Bernhard-Nocht-Institute, Hamburg)	E	L

<b>Projects and Partners of the Department of Virology and Immunology</b>		
<b>Immunogenicity and efficacy of HIV-1 virus-like particles based on subtype A envelope protein in the SHIV model</b> C. STAHL-HENNIG, F. BUONAGURO (National Inst. of Cancer, Naples, I)	E	L
<b>Role of stress-inducible proteins HSP70 and MIC on the activation of the innate immunity against SIV in rhesus macaques</b> E. GÜNTHER, R. DRESSEL (Dept. of Immunogenetics, Univ. Göttingen), C. STAHL-HENNIG	E	L
<b>Association of MHC genes with the disease development of SIV-infected rhesus monkeys</b> U. SAUERMAN, A.-L. PUAUX (Inst. Pasteur, F)	E	L
<b>Association of MHC genes with the disease development of SIV-infected rhesus monkeys</b> U. SAUERMAN, J. HEENEY (Biomedical Primate Research Centre, Rijswijk, NL)	E	A
<b>Association of MHC genes with the disease development of SIV-infected rhesus monkeys</b> U. SAUERMAN, M. KRAWCZAK (Univ. Kiel)	E	L
<b>Characterisation of MHC genes of lion-tailed macaques</b> A. BLANKENBURG (Dept. of Veterinary Medicine and Primate Husbandry, DPZ), U. SAUERMAN, F.-J. KAUP (Dept. of Veterinary Medicine and Primate Husbandry, DPZ)	I	A
<b>Echinokokkosis in non-human primates</b> A. BLANKENBURG, K. MÄTZ-RENSING, S. RENSING, F.-J. KAUP (Dept. of Veterinary Medicine and Primate Husbandry, DPZ) K. BREHM, M. FROSCH (Inst. for Hygiene and Microbiology, Univ. Würzburg), U. SAUERMAN	E,I	L
<b>Development of a neutralisation test</b> U. SAUERMAN, C. JASSOY (Univ. Leipzig)	E	L
<b>Role of the liver in the course of the SIV infection</b> U. SAUERMAN, T. ARMBRUST, A. AMANZADA, G. RAMADORI (University Hospital Göttingen)	E	L
<b>Characterisation of MHC genes of bonnet monkeys (<i>Macaca radiata</i>)</b> U. SAUERMAN, P. NÜRNBERG (Max-Delbrück-Centrum, Berlin), W. DITTUS (Department of Anthropology, Columbia Univ., New York, USA)	E	L

<b>Projects and Partners of the Department of Virology and Immunology</b>		
<p><b>Central typing of MHC genes of experimental animals within the framework of the ENVEP project</b></p> <p><b>U. SAUERMAN, C. STAHL-HENNIG, F. TITTI</b> (Istituto Superiore di Sanità, Rom, I), <b>M. CRANAGE</b> (Centre for Applied Microbiology and Research, Porton Down, GB), <b>N. ALMOND</b> (National Inst. for Biological Standards and Control, Herts, GB), <b>R. THORSTENSSON</b> (Swedish Inst. for Infectious Disease Control, S), <b>S. NORLEY</b> (Robert-Koch-Institut, Berlin), <b>J. HEENEY</b> (Biomedical Primate Research Centre, Rijswijk, NL), <b>R. Le GRAND</b> (Commissariat à l'Energie Atomique, Fontenay-aux-Roses, F), <b>G. HUNSMANN</b></p>	E,I	L
<p><b>Risk assessment in primates of TSE transmission to humans through food and blood products</b></p> <p><b>A.W. STUKE, F.-J. KAUP</b>, (Dept. of Veterinary Medicine and Primate Husbandry, DPZ), <b>G. HUNSMANN</b></p>	E,I	L
<p><b>Investigations of the risk potential of bovine spongiform encephalopathies</b></p> <p><b>G. HUNSMANN, F.-J. KAUP</b> (Dept. of Veterinary Medicine and Primate Husbandry, DPZ), <b>J. LÖWER</b> (Paul-Ehrlich-Institut, Langen), <b>P. BIERKE</b>, (SIIDC, Stockholm, S), <b>D. DORMONT</b> (CEA, Fontenay-aux-Roses, F), <b>M. POCCHIARI</b> (ISS Rom, I)</p>	E,I	L

**Stays of DPZ scientists in other institutions**

Name/Institute/Duration	Project
Prof. Gerhard Hunsmann Pohang Univ. of Science and Technology (POSTECH), Pohang, Korea 18.-25.05.02	Lectures (Adjunct-Professor)

Visited institution	Duration of stay (2001/2002)		
	< 1 month	1 - 3 months	> 3 months
German universities, research or service institutions	0	0	0
European universities, research or service institutions	0	0	0
Universities, research or service institutions outside Europe	1	0	0
<b>Altogether</b>	<b>1</b>	<b>0</b>	<b>0</b>

## Scientific Contributions

### Doctoral theses

AHMAD-OMAR, O.: Production of monoclonal antibodies and phage antibodies against the bovine prion protein through SFV particle-induced immunisation of PrP<sup>0/0</sup> mice. Department of Mathematics and Sciences, Göttingen University (2001).

MÜHL, T: Characterisation of MHC class I molecules from rhesus macaques (*Macaca mulatta*). Department of Mathematics and Sciences, Rheinische Friedrich-Wilhelms-University, Bonn (2002).

LIEDER, K.: Interface peptides of the viral protease of HIV-1 as antiviral substances for the gene therapy. Department of Mathematics and Sciences, Göttingen University (2002).

### Diploma theses

DAMMEIER, N.: Characterisation of the N-terminal modified major structural protein VP1 of the human polyomavirus JCV. Department of Biology, Göttingen University (2002).

MÜLLER, H.: Isolation of the cellular prion protein (PrP<sup>C</sup>) and the BSE agent (PrP<sup>Sc</sup>) from cattle brain for the characterisation of anti PrP antibodies. Department of Biology, Göttingen University (2002).

### Congress contributions

Annual Meeting of the German Society for Virology, Dresden, Germany, 14.-17.03.01,

MÜNCH, J., STOLTE, N., STAHL-HENNIG, C., SWIGUT, T., SKOWRONSKI, J., KIRCHHOFF, F.: A Mutation in Simian Immunodeficiency Virus Nef which selectively disrupts class I MHC downregulation reverts in infected rhesus macaques.

HILLER, C., TAMGÜNEY, G., STOLTE, N., MÄTZ-RENSING, K., LORENZEN, D., HÖR, S., THURAU, M., WITTMANN, S., SLAVIN, S., FICKENSCHER, H.: The pathogenicity of Herpesvirus Saimiri is strengthened by the thymidin kinase of Herpes Simplex virus.

SCHÄFER, M., WILHELM, T., SCHÄFER, F., LISCHKA, P., STOLTE, N., KAUP, F.-J., SCHNEIDER, T., MÜLLER-LANTZSCH, N., MEYERHANS, A.: Characterisation of the primary infection of the intestine-associated lymphatic tissue with SIV. MEYER, E., HÖHN, G., FISCHER, S., MEYER-PITTROFF, R., PETRY, H., LÜKE, W.: Inactivation of HIV-1 by hydrostatic pressure: A new generation of whole virus vaccines.

MÜNCH, J., ADAM, N., FINZE, N., STOLTE, N., STAHL-HENNIG, C., TEN HAAFT, P., HEENEY, J.L., KIRCHHOFF, F.: Simian immunodeficiency virus without overlapping nef/U3 sequences replicates efficiently in vitro and in infected rhesus macaques.

4<sup>th</sup> Annual Meeting of the American Society of Gene Therapy, Seattle, USA, 30.05.-03.06.01,

GOLDMANN, C., PETRY, H., ZHANG, Y., AST, O., LÜKE, W.: JCV-derived virus-like particles (VLP): A safe, effective and flexible alternative DNA delivery system for gene therapy.

PETRY, H., LORENZEN, D., STOLTE, N., GOLDMANN, C., LÜKE W.: Immunogenicity of VP1-VLP a new DNA delivery vehicle.

6<sup>th</sup> European Conference on Experimental AIDS Research (ECEAR), Edinburgh, GB, 23.-26.06.01,

HUNSMANN, G.: Chair Session "HIV-2 / Microbiocides"

STAHL-HENNIG, C., SPRING, M., STOLTE, N., SUH, Y.S., ZHANG, X., SHIDA, H., HEENEY, J., TEN HAAFT, P., BISCHOFBERGER, N., HUNSMANN, G.: Comparison between clone-derived and tailor-made SIV DNA as therapeutic vaccination of simian immunodeficiency virus (SIV)-infected macaques combined with anti-retroviral treatment.

MEYER, E., HÖHN, G., FISCHER, S., STOLTE, N., HOCKLEY, D., MEYER-PITTROFF, R., PETRY, H., LÜKE, W.: High hydrostatic pressure: an inactivation procedure to produce a whole inactivated virus vaccine against HIV-1 retaining the native envelope glycoprotein complex.

MÜHL, T., STAHL-HENNIG, C., TEN HAAFT, P., HUNSMANN, G., SAUER-MANN, U.: Identification of MHC-class I alleles associated with disease progression in SIV-infected rhesus monkeys.

19<sup>th</sup> Annual Symposium on Nonhuman Primate Models for AIDS Research, San Juan, Puerto Rico, 07.-10.11.01, STAHL-HENNIG, C.: Clone-derived or tailor-made SIV DNA as therapeutic vaccines combined with antiretroviral treatment (ART) in SIV-infected macaques.

Fall Conference of the Korean Society for Immunology, Seoul, Korea, 27.-30.11.01, HUNSMANN, G.: Control of viral replication and prevention of clinical AIDS by DNA vaccination in rhesus monkeys.

Medical and Dental Univ., Dept. of Microbiology, Tokyo, Japan, 01.-03.12.01, HUNSMANN, G.: HIV/AIDS vaccine - evaluations in humans and animal models.

Workshop "International Perspectives: The Future of Nonhuman Primate Resources", National Academy of Sciences, Washington, USA, 17.-19.04.02, HUNSMANN, G.: Nonhuman primates in preclinical research - the European situation.

BIOMED 2, 9th Collaborators Meeting, Lech, A, 20.-23.04.02, STROM, A.: Phage antibodies binding to prion protein antigens.

7<sup>th</sup> European Conference of Experimental AIDS Research (ECEAR), Genua, I, 08.-11.06.02, STAHL-HENNIG, C.: DNA vaccination of rhesus monkeys controls SIV replication and prevents clinical AIDS.

2<sup>nd</sup> Meeting of the National TSE Research Group, Berlin, 27.-28.06.02, STROM, A.: Isolation of PrP-binding sequences from phage peptide libraries.

9<sup>th</sup> International Symposium on the Genetics of Industrial Microorganisms (GIM-2002), Gyeongju, Korea, 01.-05.07.02, HUNSMANN, G.: Retroviral vectors for gene therapy. Chair person Session "Industrial Application of Viruses".

20<sup>th</sup> Annual Symposium on Nonhuman Primate Models for AIDS Research, Monterey, CA, USA, 08.-11.09.02, STAHL-HENNIG, C.: Control of SIV replication and prevention of clinical AIDS in macaques immunised with novel SIV DNA vaccines.

2002 International Meeting of the Institute of Human Virology "Cures for Tomorrow from Research Today", Baltimore, MD, USA, 08.-15.09.02, HUNSMANN, G.: A novel DNA vaccine controls SIV replication and prevents AIDS in immunised macaques.

International Conference on Transmissible Spongiform Encephalopathies, Edinburgh, Scotland, 15.-18.09.02, STROM, A., MÜLLER, H., STUKE, A.: Isolation of prion protein (PrP)-binding peptides by phage display. MÜLLER, H.: Separation of the PrP isoforms by immobilised metal affinity chromatography (IMAC).

EU Conference/Workshop Novel Strategies of Mucosal Immunisation through Exploitation of Mechanisms of Innate Immunity in Pathogen-Host Interaction, Siena, I, 06.-10.11.02, HUNSMANN, G.: Presentation of results obtained in the EU-funded project "European Network for Vaccine Evaluation in Primates: Combined Vector Immunisation for AIDS Vaccine Development" (ENVEP).

### **Seminars**

Journal Club Prion Research, Institute for Neuropathology, Göttingen University, 06.09.01, STUKE, A.: Antibodies inhibit prion propagation and clear cell cultures of prion infectivity. STUKE, A.: Deletion of the alpha (1,3) galactosyltransferase (GGTA1) gene and the prion protein (PrP) gene in sheep.

Parish Hall Nörten-Hardenberg, 06.11.01, HUNSMANN, G.: Our heritable information – decoding, significance and possibilities of interference.

Institute for Virology and Immunobiology, Würzburg University, 09.12.02, STAHL-HENNIG, C.: HIV vaccine development – State of the art.

X-lab, Göttingen, 16.11.02, HUNSMANN, G.: HIV and AIDS – Status quo of the epidemics and research.

## Publications

### Books

HUNSMANN, G., KAUP, F.-J.: The role of non-human primates for the development of an HIV/AIDS vaccine. In: SCHAUER, A.J., SCHREIBER, H.-L., RYN, Z., ANDRES, J. (eds.): Ethics in Medicine. Verlag Vandenhoeck & Ruprecht (2001).

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BENCSIK, A., LEZMI, S., HUNSMANN, G., BARON, T.: Close vicinity of PrP expressing cells (FDC) with noradrenergic fibers in healthy sheep spleen. Dev. Immunol. (2001) 8(3-4): 235-241.

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BUZDIN, A., KHODOSEVICH, K., MAMEDOV, I., VINOGRADOVA, T., LEBEDEV, Y., HUNSMANN, G., SVERDLOV, E.: A technique for genome-wide identification of differences in the interspersed repeats integrations between closely related genomes and its application to detection of human-specific integrations of HERV-K LTRs. Genomics (2002) 79(3): 413-422.

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MÄTZ-RENSING, K., KUNZ, E., KRAFT, C., LORENZEN, D., SUERBAUM, S., KAUP, F.-J.: Experimental *Helicobacter pylori* infection of rhesus macaques (*Macaca mulatta*). Int. J. Med. Microbiol. (2001) 291(1): 33-43.

MAXIMOV, V., MARTYNENKO, A., HUNSMANN, G., TARANTUL, V.: Mitochondrial 16S rRNA gene encodes a functional peptide, a potential drug for Alzheimer's disease and target for cancer therapy. *Medical Hypotheses* (2002) 59(6): 670-673.

MÜHL, T., KRAWCZAK, M., TEN HAAFT, P., HUNSMANN, G., SAUERMAN, U.: MHC class I alleles influence set-point viral load and survival time in simian immunodeficiency virus-infected rhesus monkeys. *J. Immunol.* (2002) 169(6): 3438-3446.

MÜNCH, J., ADAM, N., FINZE, N., STOLTE, N., STAHL-HENNIG, C., FUCHS, D., TEN HAAFT, P., HEENEY, J.L., KIRCHHOFF, F.: Simian immunodeficiency virus in which nef and U3 sequences do not overlap replicates efficiently *in vitro* and *in vivo* in rhesus macaques. *J. Virol.* (2001) 75(17): 8137-8146.

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STAHL-HENNIG, C., STEINMAN, R.M., TEN HAAFT, P., ÜBERLA, K., STOLTE, N., SAELAND, S., TENNER-RÁCZ, K., RÁCZ, P.: The simian immunodeficiency virus *?nef* vaccine, after application to the tonsils of rhesus macaques, replicates primarily within CD4+ T-cells and elicits a local perforin-positive CD8+ T-cell response. *J. Virol.* (2002) 76(2): 688-696.

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<b>Publications</b>	<b>2002</b>	<b>2001</b>	<b>2000</b>
1. Books	0	0	
2. Publication of collected editions	0	0	
3. Chapters in collected editions	0	1	0
4. Reviewed papers	10	17	20
5. Non-reviewed papers	0	0	0
<b>Total 1 - 5</b>	<b>10</b>	<b>18</b>	<b>20</b>
6. Editorials	0	0	0
7. Electronic publications	0	0	0
8. Abstracts	0	0	0
<b>Publications altogether</b>	<b>10</b>	<b>18</b>	<b>20</b>

### **Other scientific activities**

#### **G. Hunsmann**

- Member of the Scientific Advisory Board of the National Centre for Retroviruses (NZR), Zürich, CH.
- Member of the European expert group "Evaluation of Tests for TSE in Bovines".
- Co-ordinator of the EU Concerted Actions "Risk Assessment in Primates of TSE Transmission to Humans Through Food and Blood Products" and "European Network for Vaccine Evaluation in Primates: Combined Vector Immunisation for AIDS Vaccine Development".
- Member of the Programme Management Group, Programme EVA (European Vaccine against AIDS).
- Participation in the following events: XVIIIth Congress of the International Primatological Society, Adelaide, Australia; Meeting of the WHO Working Group on International Reference Materials for Diagnosis and Study of TSEs, WHO, Geneva, CH; TSE-Co-ordinators Meeting, Brussels, B; Symposium "Pathogenicity Mechanisms of Viruses ", Giessen; Hearing "Possibilities and Limits of Research on Stem Cells ", Parliament of Lower Saxony, Hannover; Joint Meeting of the German Association for Combating Virus Diseases (DVV) and the Society for Virology (GfV), Berlin; Round Table Discussion on the occasion of the Bilateral Symposium on behalf of 10 years partnership between Georg August University of Göttingen and Jagiellonian University of Krakow, Göttingen; 7<sup>th</sup> European Conference of Experimental AIDS Research (ECEAR), Genova, I.

### **Important activities and functions**

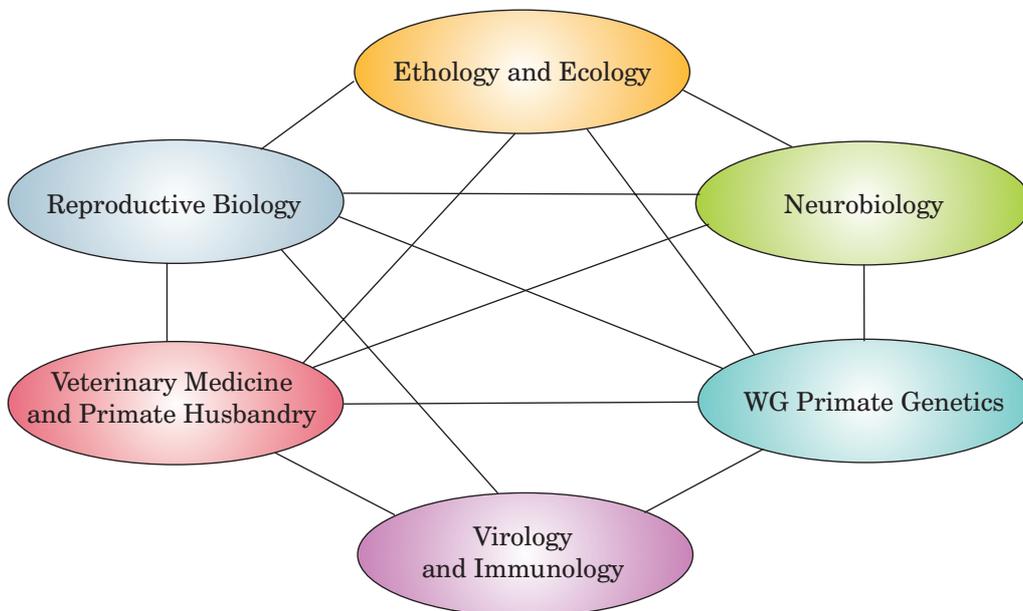
#### **G. Hunsmann**

- Adjunct Professor at the Division of Molecular and Life Science an der Pohang University of Science and Technology (POSTECH), Pohang, Korea.
- Director of the Department of Virology, Georg-August-University Göttingen
- Co-founder and chairman of the board of the Society for AIDS Research.

### **Internal scientific cooperations**

The complexity of primates is reflected by the complexity and the wide spectrum of research topics dealt with at the German Primate Centre (DPZ). Therefore, the departments and working groups of the DPZ concentrate their efforts and resources on manageable areas of the research spectrum and on specific methodological approaches. Thus, they are excellent partners for the essential multidisciplinary collaborations which exist between groups within the DPZ and with national and international groups outside the DPZ. Such cooperations are supported by appropriate funding among others from the DPZ, the EU and the German Research Council. These not only allow an increasing number of scientific problems to be addressed which surpasses the capacity and capabilities of the single departments but optimise the application of the research funds particularly in times of money shortages in public budgets and strongly binds the DPZ into the scientific landscape.

The following graph shows the internal network among the departments and working groups. Details of the various cooperations within the centre can be found in the appropriate project tables. A special mention must be given to the Department of Veterinary Medicine and Primate Husbandry and the Working Group Primate Genetics. On account of special infra-structural duties, the first mentioned cooperates particularly closely, in a variety of ways, within the institute and contributes the most to the service assignments of the DPZ internally and externally. The many



*Internal scientific cooperations*

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cooperations of the Working Group Primate Genetics clearly show that, in the meantime, genetic methods have gained a place in almost all research areas of primatology.

The number of internal and external cooperations of the departments and working groups of the DPZ will probably increase in the next few years. Besides the ever increasing importance of experiments on primates in the field of biomedicine, the structure reform realised at the turn of the year 2002/2003 will help to link together those departments of the DPZ which are thematically similar into sections.

### **The Service of the German Primate Center**

The German Primate Center in Göttingen is unique in Europe and of supra-regional importance. The DPZ understands the entirety of its work including research as a service to science. Our own research is the basis for the competent fulfillment of the service assignment. Mainly interested in the research and services of the DPZ are universities, extra-university and industrial research centers working in related fields as well as nature conservation organizations and government circles.

The DPZ has the special knowledge, experience and both the personnel and structural conditions for import/export, quarantine, breeding and keeping of primates as well as the diagnosis of diseases of these animals and their treatment. Moreover the individual departments and working groups dispose of special knowledge in the fields of behaviour, physiology, genetics, infection and pathology of primates as well as in the realization of biomedical experiments concerned with reproductive biology, neurobiology and infectious diseases.

### **Sales and supplies\* of animals 2001/2002 (total number: 324)**

<b>Species</b>	<b>Number</b>	<b>Recipient</b>
<i>Tupaia belangeri</i>	1	Wilhelma Stuttgart
<i>Callithrix jacchus</i>	46	Covance Laboratories GmbH, Münster
	14	Univ. Göttingen
	3	Zoological Garden, Magdeburg
	2	Serengetipark, Hodenhagen
	1	MorphoSys, Martinsried
	25	Biomedical Primate Research Institute, NL
<i>Saguinus oedipus</i>	1	Odsherreds Dyrepark, DK
	1	Serengetipark, Hodenhagen
	2	Zoological Garden, Osnabrück
	7	Biomedical Primate Research Institute, NL
<i>Saimiri sciureus</i>	4	Zoological Garden, Staßfurt
	4	Odsherreds Dyrepark, DK
	14	Zoological Garden, Jaderberg
	4	Zoological Garden, Aachen
	8	Zoological Garden, Bochum
<i>Macaca silenus</i>	20	Zoological Garden, Cologne (in the scope of the European preservation breeding programme (EEP))

*The Service of the German Primate Center*

<b>Species</b>	<b>Number</b>	<b>Recipient</b>
<i>Macaca fascicularis</i>	4	Univ. Munich, Medical Faculty
	4	Leibniz Institute for Neurobiology, Magdeburg
	1	Ordis Biomed GmbH, Graz, A
	5	Medizinische Hochschule, Hannover
<i>Macaca mulatta</i>	2	Univ. Bremen
	4	Jannssen Pharmaceutica, Cologne
	25	MPI for Biological Cybernetics, Tübingen
	3	Univ. Munich, Medical Faculty
	1	MorphoSys, Martinsried
	5	University Crete, GR
	6*	Lab. of Viral Oncology & AIDS Reference Center, Neapel, I
	3*	NIH, NIAID, Bethesda, USA
	6*	Univ. Leipzig
	16*	Bayer AG, Wuppertal
	19*	Univ. Pohung, Corea
	10*	Hakkaido Univ., Sapporo, Japan
	6*	Univ. Würzburg
37*	Bernhard-Nocht-Institute, Hamburg	
6*	Jenapharm, Jena	
<i>Papio hamadryas</i>	6	Univ. Munich, Medical Faculty

**Keeping of primates for external scientific institutions on 31.12.2001/2002 (total number: 129/121)**

<b>Species</b>	<b>Number</b>	<b>Year</b>	<b>Institution</b>
<i>Saguinus oedipus</i>	2	2001/02	Zoological Garden, Leipzig
<i>Macaca silenus</i>	7/8	2001/02	Zoological Gardens Leipzig, Stuttgart, Erfurt, Cologne (in the scope of the European preservation breeding programme (EEP))
<i>Macaca mulatta</i>	28/23	2001/02	Univ. Pohung, Korea
	7/6	2001/02	Univ. Erlangen
	6/6	2001/02	Univ. Leipzig
	8/4	2001/02	Univ. Würzburg
	14	2001	Univ. Regensburg

*The Service of the German Primate Center*

<b>Species</b>	<b>Number</b>	<b>Year</b>	<b>Institution</b>
<i>Macaca mulatta</i>	6	2002	Jenapharm, Jena
	2/14	2001/02	Bayer AG, Wuppertal
	31/34	2001/02	Bernhard-Nocht-Institute, Hamburg
	6/6	2001/02	Lab. of Viral Oncology & AIDS Reference Center, Neapel, I
	9/8	2001/02	Hakkaido Univ., Sapporo, Japan
	3	2001	NIH, NIAID, Bethesda, USA
	1	2001	Rockefeller Univ., USA
<i>Macaca fascicularis</i>	4	2001/02	Research Center, Jülich
	1	2001	Medizinische Hochschule, Hannover

**Procurement of primates in 2001/2002 (total number: 225)**

<b>Species</b>	<b>Number</b>	<b>Scientific institution</b>
<i>Tupaia belangeri</i>	45	MPI for Brain Research, Frankfurt
	10	Univ. Stuttgart
<i>Callithrix jacchus</i>	22	Univ. Cambridge, GB
	1	Zoological Garden, Bochum
	15	Free Univ., Berlin
<i>Macaca mulatta</i>	92	Hartelust, NL
	4	China
	16	Baxter, Vienna, A
	1	Univ. Tübingen
	9	Aventis, Frankfurt
<i>Macaca fascicularis</i>	9	Hartelust, NL
<i>Papio hamadryas</i>	1	Zoological Garden, Berlin
A confiscated saimiri and a mandrill were taken on. Both animals were passed on to Zoological Gardens.		

An important basic task of the DPZ is the setting up of breeding groups of several primate species. Some of these groups provide animals both for our own investigations and the fulfillment of services. Other breeding groups exclusively serve species preservation and behavioural studies. This breeding also enables us to pass on samples of single animals to external researchers for their work. The center is equipped with special knowledge for the analysis of samples from primates. We carry out a large number of corresponding tests for external scientists. This mainly involves the determination of antibodies against retroviruses, hormonal analyses, bacteriologi-

cal and parasitological investigations and necropsies. Moreover, primates are imported via the DPZ, which are then passed in an optimal health condition to external institutions.

The DPZ looks after the veterinary care of a primate colony of the Institute for Anthropology of the University Göttingen and advises external institutes and zoological gardens on the diagnosis and treatment of primate diseases. Scientists from Germany and from abroad often use the wide scope of methods, the possibility to make field studies in the external stations of the DPZ in Peru and in Madagascar, and the services of the primatology-oriented library also for shorter stays at the DPZ.

The service offers of the DPZ are extended to scientific and technical training and further education in the form of job-related practical training, lectures at universities, the provision of posts and scientific support for graduants and doctoral candidates in the special fields of medicine, veterinary medicine, biology and microbiology as well as chemistry. The DPZ is highly engaged in the support of scientific trainees. The center has built up good relations to the nearby universities in Göttingen and Hannover (Medizinische Hochschule Hannover, Tierärztliche Hochschule Hannover) in the fields of science and research. Moreover, the Chamber of Veterinarians (Tierärztekammer) in Lower Saxony has acknowledged the DPZ as a training center for the specialist veterinarian in pathology and in virology.

The DPZ holds courses for potential users in the form of practical training. We offer a methodical introduction in electron microscopy for trainees, technical assistants and scientists, as well as practical training and further training in the field of animal keeping. In particular, we teach animal keepers and biological laboratory assistants from external institutions the special requirements of primates, and train them to look after these animals. Moreover, the DPZ offers the opportunity to learn histological, bacteriological and parasitological techniques or electron microscopical methods within the scope of the training of biological laboratory assistants and medical technical assistants.

**DEPARTMENT OF VETERINARY MEDICINE AND PRIMATE HUSBANDRY**

**General survey of service supplies**

As central service and infrastructure department of the DPZ the Department of Veterinary Medicine and Primate Husbandry is engaged in extensive work in animal husbandry, animal keeping, veterinary diagnostics and care of the animals. These tasks include, among others, the provision and quarantine of imported primates as well as the sale of animals from our own breeding. Veterinary services comprise veterinary care within the DPZ as well as external, diagnoses and consultations (pathology, microbiology, parasitology, laboratory diagnostics). The veterinary pharmacy of the institute as well as the running of the central food kitchen are part of the department. All animal experiments are supervised and accompanied by veterinarians. Within the scope of these different tasks organ and tissue samples for numerous internal and external groups are taken. The central electron microscopy facilities with a photolaboratory provides personnel and appliances for external and internal users. The head of the department is the official representative for animal protection and for prevention of infectious diseases. Numerous guided tours as well as training and further education in primate husbandry provide practical insight into the keeping of primates and into the work of animal keepers, technical assistants, biologists and veterinarians.

**External services**

In vivo samples are taken for numerous groups by means of minimal invasive and non-invasive techniques. The same applies for organ and tissue samples which are taken during necropsies. The different services during the period 2001-2002 were too numerous to mention all of them, so we only give examples, here.

**Shipment of samples**

<b>Name/Institute</b>	<b>Service</b>
Laboratory for Experimental Immunology, Euroimmun, Lübeck Dr. Müller-Kunert	Several samples of 15 <i>Macaca mulatta</i> , 1 <i>Macaca fascicularis</i> , 2 <i>Macaca fuscata</i> , 40 <i>Callithrix jacchus</i>
Univ.-Hautklinik, Würzburg Dr. Zilliken	Esophagus from 9 nonhuman primates of different species
MPI for Evolutionary Anthropology, Leipzig Dr. Enard	Testicle, CNS, liver samples from 3 <i>Macaca mulatta</i>
Inst. for Biology, Humboldt Univ. Berlin, T. Riede	32 larynx preparations from <i>Macaca mulatta</i>

*Veterinary Medicine and Primate Husbandry*

<b>Name/Institute</b>	<b>Service</b>
Dermatologic Clinic, Munich Dr. Heilmann	Esophagus and/or bladder from 20 animals of different species
Paul-Flechsig-Institut für Hirnforschung, Univ. Leipzig Dr. A. Reichenbach	Eyes from 12 <i>Macaca mulatta</i> , 1 <i>Macaca tibetana</i> , 2 <i>Macaca fuscata</i> , 1 <i>Papio hamadryas</i> , 1 <i>Saimiri sciureus</i>
Univ. Leipzig, R. Ganzer	Urogenital area from 12 <i>Macaca mulatta</i>
Leibniz-Institute for Neurobiology, Magdeburg	Skull preparations from <i>Macaca fascicularis</i>
Anatomisches Institut, LMU Munich Prof. U. Welsch	Different organ samples from various nonhuman primate species
Frauenklinik, Univ. Göttingen, Prof. Dr. H. Jarry	CNS from <i>Callithrix jacchus</i>

### **Diagnostics**

Necropsies with complete histological diagnostics, bacterial and parasitological investigations and documentation

<b>Name/Institute</b>	<b>Service</b>
Allwetterzoo Münster	10 necropsies: <i>Lemur variegatus</i> , <i>Pan</i> sp., 2 <i>Mandrillus</i> sp., <i>Lemur catta</i> , <i>Cebus capucinus</i> , Weißgesichtsseidenaffe, 2 <i>Saguinus oedipus</i> , <i>Leontopithecus chrysomelas</i>
Leibniz-Institute for Neurobiology, Magdeburg	2 necropsies: <i>Macaca fascicularis</i>
Private primate keepers	11 necropsies: <i>Saimiri sciureus</i> , <i>Saguinus</i> sp., <i>Macaca fuscata</i> , <i>Callimico goeldii</i> , 3 <i>Saguinus fuscicollis</i> , 4 <i>Callithrix jacchus</i>
Medizinische Hochschule Hannover	5 necropsies: <i>Macaca fascicularis</i>
Naturpark Kaiserslautern	3 necropsies: 2 <i>Macaca fascicularis</i> , <i>Saimiri sciureus</i>
Tierpark Gettorf	4 necropsies: <i>Callithrix jacchus</i> , <i>Callithrix penicillata</i> , <i>Saguinus</i> sp., <i>Cercopithecus diana</i>
Tierpark Hellabrunn	1 necropsy: <i>Callithrix jacchus</i>
Tierpark Jaderberg	1 necropsy: <i>Callithrix jacchus</i>
Tierpark Thuele	1 necropsy: <i>Lemur catta</i>
Tiergarten Stendal	3 necropsies: <i>Saimiri sciureus</i> , <i>Lemur catta</i> , <i>Saguinus labiatus</i>
Zoo Duisburg	1 necropsy: <i>Pongo</i> sp.

*Veterinary Medicine and Primate Husbandry*

<b>Name/Institute</b>	<b>Service</b>
Zoo Dortmund	3 necropsies: <i>Saimiri sciureus</i> , 2 <i>Callimico</i> sp.
Zoological Garden Halle	2 necropsies: <i>Saimiri sciureus</i>
Zoo Hannover	1 necropsy: <i>Semnopithecus entellus</i>
Zoo Köln	6 necropsies: <i>Pygathrix nemaeus</i> , 2 <i>Cheirogaleus medius</i> , <i>Callithrix geoffroyi</i> , <i>Varecia variegata</i> , <i>Leontopithecus rosalia chrysomelas</i>
Zoo am Meer, Bremerhaven	1 necropsy: <i>Pan troglodytes</i>
Zoo Magdeburg	3 necropsies: <i>Pongo pygmaeus</i> , <i>Callithrix geoffroyi</i> , <i>Callithrix penicillata</i>
Zoo Rostock	1 necropsy: <i>Erythrocebus patas</i>
Vivarium Darmstadt	2 necropsies: <i>Callithrix penicillata</i> , <i>Cebuella pygmaea</i>
All kinds of institutions	137 bacteriological investigations, 85 parasitological investigations

**Miscellaneous**

<b>Name/Institute</b>	<b>Service</b>
Sartorius AG, Göttingen	Development of a morphological method by means of cryo-sections
Veterinary Institute, Univ. Göttingen	Histological diagnostics in clinical and necropsy material
Schaper & Brümmer GmbH, Salzgitter	Extensive histological investigations on the fertility toxicology of rats
Tropentierhygiene, Univ. Göttingen Dr. Muna	Extensive negative-staining investigations of bacteria
Greendale Vet. Lab. Surrey, GB Dr. Wesche	Veterinary consultations on the pathology of primates
Private primate keeper Fasciani, Söhrewald	Veterinary consultations and care
Janssen Pharmaceutica, Köln Dr. Tegtmeyer	Measurement of cerebral pressure of primates with veterinary care, taking of samples, consultations
Veterinary Pathology, Univ. Zürich, CH Prof. Dr. Ehrensperger	Histological investigations in selected cases of primate pathology
Mssrs. Intervet, Boxmeer, NL Dr. E.-M. Kuhn	Analysis of diverse transmission electron microscopical figures

### **Transfer of knowledge/consultations**

Various organisations, offices, authorities, journalists and colleagues of several institutions often benefit from the diversified expertise in this very special field of veterinary medicine. Numerous guided tours for visitors are regularly organized. In the reporting period we had among others visitors from the working group animal protection of the SPD, Hannover, the managing committee of the CDU Landesverband, several citizens groups from Göttingen, especially within the scope of the 25-year-celebration of the DPZ, student groups from the universities of Göttingen and Würzburg, employees of the Institute of Parasitology from the Veterinary University of Hannover, the official delegation from Göttingen's twin city Thorun (Poland), Mssrs. Ifm Europe GmbH, and a Polish group of doctors. Interviews and information for the press, television etc. were given to representatives of the following media: press office W. Kappler, Spiegel-NTV, HR 1, HR 2, NDR 3, NDR 4, WDR 5, Der Spiegel, Deutsche Welle, ORF, Süddeutsche Zeitung.

More extensive expert opinions and consultations were provided within the reporting period for the Landratsamt Ostalbkreis, Schering AG and the fraction Bündnis 90/Die Grünen in the Bavarian Landtag. We had talks with scientists from various countries on the research possibilities at the DPZ, the realization of projects or our experiences with primate keeping in general, for example, Prof. Dr. Ingrid Redbo (University Uppsala, S), Prof. Sayuti (University Bogor, Indonesia), Dr. Supraptini (Primate Center, Indonesia), Dr. Shalev and colleague (Mssrs. Brains-Gate Ltd., Israel), Prof. Dr. Moges (Ethiopia), Prof. Dr. Vizlo (University Kiev, Ukraine), Prof. Paulus, Prof. Ramadori, Prof. Czerny, Dr. Liebtanz, Dr. Schulz-Schäfer (University Göttingen), Prof. G. Steinhoff (Medizinische Hochschule, University Hannover), Dr. Martin (Leibniz Forschungslaboratorium für Biotechnologie und künstliche Organe, Hannover), Dr. Baskin (Tulane National Primate Research Center, now Charles River Company, USA).

The working group electron-microscopy has been participating for several years in the ring experiments (2001: No. 10, 11; 2002: No. 12, 13) of the Robert-Koch-Institute, Berlin, in order to ensure the quality of the electron-microscopical virus diagnostics and is also integrated into the public network for the diagnostic of EM-agents. The working group prion research is part of the TSE-forum, the SIV research belongs to the network of competence HIV/AIDS.

<b>Institution/collaborator</b>	<b>Subject</b>
Tierärztliche Hochschule, Hannover F.-J. Kaup	Examinations within the scope of veterinary examinations (14 times)
Tierärztliche Hochschule Hannover F.-J. Kaup	Four oral doctoral examinations
Veterinary Chamber Hesse F.-J. Kaup	Two examinations of veterinarian specialists in pathology
Veterinary chamber Lower Saxony F.-J. Kaup	Authorized for further training of veterinarian specialists for pathology. Three examinations for veterinarian specialist for anatomy and for pathology

*Veterinary Medicine and Primate Husbandry*

<b>Institution/collaborator</b>	<b>Subject</b>
Summer School, Eur. Coll. Vet. Pathol. F.-J. Kaup	Training of veterinary pathologists, preparation for the Board Exam Dipl. ECVP
School for VMTA, Tierärztliche Hochschule, Hannover F.-J. Kaup	Lessons in the following fields: histological techniques, pathology, immunohistology; examinations; three school trainees in primate husbandry
Univ. Weihenstephan K. Mätz-Rensing	Training of a colleague in the basics of immunohistological techniques
Tierärztliche Hochschule Hannover F.-J. Kaup, K. Mätz-Rensing	Six trainees for a compulsory six-week-training in veterinary medicine
Free Univ., Berlin F.-J. Kaup, K. Mätz-Rensing	Trainee for a compulsory six-week-training in veterinary medicine
Tierärztliche Hochschule Hannover F.-J. Kaup	Lectures: diseases of wild animals, pathology of primates, infectious viral diseases of primates
Central experimental animal laboratories, Univ. Göttingen F.-J. Kaup	Consultations on pathohistological evaluations in small experimental animals
Employment office Nienburg F.-J. Kaup	Two pupils during a job profile day
Diverse schools U. Schönmann	Two school trainees
MPI for Evolutionary Anthropology, Leipzig F.-J. Kaup, Mätz-Rensing	Training of a veterinarian in Pathological Diagnostics under Outdoor Conditions
Eur. Ass. Zoo Wildl. Vet. F.-J. Kaup	Workshop on primate diseases for a group of students
Tierärztliche Hochschule Hannover Inst. for Pathology F.-J. Kaup	Once a week, necropsy practicals during the winter semester 2001/2002

**Candidates for diploma (D) and doctorate (P)**

<b>University/Name</b>	<b>Subject</b>
Tierärztliche Hochschule Hannover Christiane Kott (P)	Immunohistochemical Her-2 expression in canine mammary carcinomas
Tierärztliche Hochschule Hannover Jarno Marius Schmidt (P)	Immunohistochemical characterization of angiogenesis in neoplastic processes (in cooperation with PD Dr. H. Augustin, Freiburg)

*Veterinary Medicine and Primate Husbandry*

<b>University/Name</b>	<b>Subject</b>
Tierärztliche Hochschule, Hannover Georg Rode (P)	On the pathogenesis of dental calculus in dogs
Tierärztliche Hochschule Hannover Anja Blankenburg (P)	On the echinococcosis in <i>Macaca silenus</i> : pathogenetical investigations including MHC-characterization
Tierärztliche Hochschule, Hannover Karin Binger (P)	Light optical and electronmicroscopical investigations for the evidence of SIV (Simian Immunodeficiency Virus) in the rectum of experimentally infected rhesus monkeys ( <i>Macaca mulatta</i> )
Tierärztliche Hochschule Hannover Andrea Quohs (P)	Investigations on the marmoset wasting syndrome in the colony of common marmosets ( <i>Callithrix jacchus</i> ) at the German Primate Center
Tierärztliche Hochschule Hannover Frank Runge (P)	Immunohistochemical characterization of inflammatory cells in the stomach of rhesus monkeys with a chronic <i>Helicobacter pylori</i> -infection

**Guest researchers from national and international institutions**

<b>Name/Institute/Duration</b>	<b>Project</b>
Prof. Dr. Masangkay Univ. of the Philippines, Los Banos 01.05.-09.08.01	Immunohistological methods for evidence of disease agents in veterinary pathology
Prof. Dr. Roland Estrada, Univ. of the Philippines, Bacnotan 10.-29.05.01	RFFIT-systems in experiments on rabies vaccines

<b>Place of employment of the guest</b>	<b>Duration of stay (2001/2002)</b>		
	<b>&lt; 1 month</b>	<b>1 - 3 months</b>	<b>&gt; 3 months</b>
Africa	0	0	0
America (without USA, Canada)	0	0	0
USA, Canada, Australia	0	0	0
Asia	1	1	0
Germany	0	0	0
EU, remaining Western Europe	0	0	0
Central and Eastern Europe	0	0	0
<b>Altogether</b>	<b>1</b>	<b>1</b>	<b>0</b>

## **Events**

For four years the Department of Veterinary Medicine has been organizing the Göttingen Symposium "Primates in Biomedical Research: Diseases and Pathology" in which interested veterinarians from Europe, occasionally also from the USA, meet in Göttingen in order to exchange ideas. In 2001 the third symposium took place. In 2002 we tried to organize an event at the Paul-Ehrlich-Institute in Langen which was orientated more veterinary-clinically. In 2003 the event is planned as a parallel session to the annual congress of the German primatological society taking place in Leipzig. Meanwhile about 30 veterinarians from different countries use this opportunity to present both their scientific data and exchange experiences in the special field of veterinary medicine. Guest speakers so far have been Prof. Dr. P. Biberfeld, Sweden, Dr. G. Baskin, USA, Prof. Dr. E. Buse, Covance Lab., Münster.

## **DEPARTMENT OF ETHOLOGY AND ECOLOGY**

### **General survey of service supplies**

Members of the department are involved in teaching and training of students of several national and international universities. Our field research stations in Madagascar and Peru offer the opportunity for field courses, internships and research projects for external users. Furthermore, members of the department provide internal and external service information on general aspects of primate biology, taxonomy, behaviour, and ecology.

### **Teaching, transfer of knowledge**

<b>Name/Institute</b>	<b>Service</b>
Univ. Giessen PD Dr. E.W. Heymann	Seminar "Ecology of primates", WT 2000/2001
Univ. Giessen PD Dr. E.W. Heymann	Practical course "Primate ethology", ST 2001
Univ. Giessen PD Dr. E.W. Heymann	Seminar "Primate and tropical ecology", WT 2001/2002, WS 2002/2003
Univ. Nacional de la Amazonía Peruana, Iquitos, Peru PD Dr. E.W. Heymann	Field course "Ecology of New World primates", ST 2001
Univ. Giessen und Univ. Nacional de la Amazonía Peruana, Iquitos, Peru PD Dr. E.W. Heymann	Field course "Primate and tropical ecology", ST 2002
Tierärztliche Hochschule Hannover PD Dr. E.W. Heymann	Lecture "Aspects of diet selection in primates"
Univ. Autónoma Madrid, E PD Dr. E.W. Heymann	Lecture and seminar "Socio-ecology of primates", WT 2000/2001
EUPREN PD Dr. E.W. Heymann	Role of field studies for husbandry and well-being of primates
IGS Bonn-Bad Godesberg PD Dr. E.W. Heymann	Support of a student trainee
Several schools in Göttingen ("Girlsday") PD Dr. E.W. Heymann	Field studies of primates – why and how
Univ. Würzburg PD Dr. P.M. Kappeler	Lecture "Introduction to primate biology", WT 2000/2001
Univ. Würzburg PD Dr. P.M. Kappeler	Practical course "Primate ethology", SS 2001

*Ethology and Ecology*

<b>Name/Institute</b>	<b>Service</b>
Univ. Würzburg PD Dr. P.M. Kappeler with Prof. K.E. Linsenmair, Dr. B. Fiala and Dr. D. Mahsberg (Univ. Würzburg)	Practical course with seminar "Animal ecology II", WT 2000/2001
Univ. Würzburg PD Dr. P.M. Kappeler with Prof. K.E. Linsenmair, Dr. B. Fiala und Dr. D. Mahsberg (Univ. Würzburg)	Practical course with seminar "Animal ecology II", ST 2001
Univ. Würzburg WS 2001/2002 PD Dr. P.M. Kappeler	Lecture "Quantitative behavioural and evolutionary biology"
Univ. Würzburg PD Dr. P.M. Kappeler with Prof. K.E. Linsenmair, Dr. B. Fiala and Dr. D. Mahsberg (Univ. Würzburg)	Practical course with seminar "Animal ecology II", WT 2001/2002
Univ. Würzburg PD Dr. P.M. Kappeler	Practical course with seminar "Human sociobiology", ST 2002
Univ. Würzburg PD Dr. P.M. Kappeler with Prof. K.E. Linsenmair, Dr. B. Fiala and Dr. D. Mahsberg (Univ. Würzburg)	Practical course with seminar "Animal ecology II", ST 2002
Univ. Würzburg PD Dr. P.M. Kappeler with Prof. K.E. Linsenmair, Dr. B. Fiala and Dr. D. Mahsberg (Univ. Würzburg)	Practical course with seminar and excur- sion "Animal ecology II", WT 2002/2003
Univ. Göttingen J. Ostner and O. Schülke	Seminar "Darwin's misjudged theory – sexual selection and human evolution", WS 2001/2002
Vgs Verlagsgesellschaft, Köln Dr. D. Zinner	Scientific advice for the German edition of "Cousins"

**Candidates for diploma (D) and doctorate (P)**

<b>University/Name</b>	<b>Subject</b>
Zoological Institute, Univ. Göttingen Stefanie Brand (D)	Social behaviour and olfactory communi- cation of white-faced sakis
Zoological Institute, Univ. Tübingen Melanie Dammhahn (D)*	Social system of pygmy mouse lemurs ( <i>Microcebus berthae</i> )
Zoological Institute & Museum, Univ. Hamburg Manfred Eberle (P)*	Social system of gray mouse lemurs ( <i>Microcebus murinus</i> )

*Ethology and Ecology*

<b>University/Name</b>	<b>Subject</b>
Inst. for Biology, Univ. of Aarhus, DK Tina Fredsted (P)*	Population genetics of grey mouse lemurs ( <i>Microcebus murinus</i> )
Zoological Institute, Univ. Ulm Roland Hilgartner (P)	Causes and mechanisms of pair-living in <i>Lepilemur ruficaudatus</i>
Faculty of Biology, Univ. Bielefeld Maren Huck (P)*	Socio-endocrinological and genetic analyses of male reproductive strategies in mous- tached tamarins
Faculty of Biology, Univ. Münster Petra Löttker (P)*	Socio-endocrinological and genetic analyses of female reproductive strategies in mous- tached tamarins
Faculteit Wetenschappen, Univ. Antwerpen, B Iris Leinfelder (P)	Social strategies of female hamadryas baboons in captivity
Tierärztliche Hochschule Hannover Britta Müller (P)*	Endoparasites and ecology of three sympatric New World monkeys
Inst. for Animal Ecology and Tropical Biology, Univ. Würzburg Julia Ostner (P)*	Sex-specific reproductive strategies in red-fronted lemurs ( <i>Eulemur fulvus rufus</i> )
Facultad de Biología, Univ. Nacional de la Amazonía Peruana, Iquitos, Peru Marcos Roland Oversluijs Vasquez (D)	Vigilance and social roles in <i>Saguinus mystax</i>
Facultad de Biología, Univ. Nacional de la Amazonía Peruana, Iquitos, Peru Jenni Perez Yamacita (D)	Ecology of <i>Callicebus cupreus</i>
Département de Paléontologie et d'Anthro- pologie Biologique, Univ. d'Antananarivo, Madagascar Veromanitra Raharimanantsoa (D)	Olfactory communication in red-fronted lemurs, <i>Eulemur fulvus rufus</i>
Département de Paléontologie et d'Anthro- pologie Biologique, Univ. d'Antananarivo, Madagascar Odon Rakotonirainy (D)	Competition between nocturnal lemurs
Département de Paléontologie et d'Anthro- pologie Biologique, Univ. d'Antananarivo, Madagascar Emilienne Rasoazanabary (D)	Life history of <i>Microcebus murinus</i>
Département de Paléontologie et d'Anthro- pologie Biologique, Univ. d'Antananarivo, Madagascar David Rasolofoson (D)	Vigilance in red-fronted lemurs, <i>Eulemur fulvus rufus</i>

*Ethology and Ecology*

<b>University/Name</b>	<b>Subject</b>
Inst. für Tierökologie und Tropenbiologie, Univ. Würzburg Oliver Schülke (P)*	Social system of fork-tailed lemurs ( <i>Phaner furcifer</i> )
Inst. de Biologie, Éco-Éthologie, Univ. de Neuchâtel, CH Clemence Dirac (D)	Feeding competition in <i>Propithecus verreauxi verreauxi</i>
Département de Paléontologie et d'Anthro- pologie Biologique, Univ. d'Antananarivo, Madagascar Léonard Razafimanantsoa (P)	Behavioural ecology of <i>Mungotictis decemlineata</i>
* internal co-operations with the Departments of Reproductive Biology, Primate Genetics and Veterinary Medicine and Primate Husbandry	

**Guest researchers from national and international institutions**

<b>Name/Institute/Duration</b>	<b>Project</b>
Dr. Ricardo Mondragón-Ceballos Inst. Nacional de Psiquiatría, Subdirección Neurociencias, Tlalpan, México 15.02.-16.11.01	Reconciliation in cotton-top tamarins
María Suarez Alvarez Departamento de Psicología, Univ. Autónoma de Madrid, Madrid, E 19.10.01-30.04.02	Social organisation and endocrinology of cotton-top tamarins

<b>Place of employment of the guest</b>	<b>Duration of stay (2001/2002)</b>		
	<b>&lt; 1 month</b>	<b>1 - 3 months</b>	<b>&gt; 3 months</b>
Africa	0	0	0
America (without USA, Kanada)	0	0	1
USA, Canada, Australia	0	0	0
Asia	0	0	0
Germany	0	0	0
EU, remaining Western Europe	0	0	1
Central and Eastern Europe	0	0	0
<b>Altogether</b>	<b>0</b>	<b>0</b>	<b>2</b>

**Events**

- 3<sup>rd</sup> Göttinger Freilandtage, 11-14 December 2001
- 5<sup>th</sup> Kirindy Symposium, 23 August 2002

**WORKING GROUP PRIMATE GENETICS**

**General survey of service supplies**

By establishing a phylogenetically broad collection of primate samples including tissue material, cell cultures and DNA which is available to the scientific community, the Primate Genetics Group is trying to support comparative work of other groups. The Primate Genetics Group is part of the cooperative "Gene Bank of Primates"- project and complements this project by establishing its own collection of primate tissue and DNA bank in cooperation with the Department of Veterinary Medicine and Primate Husbandry, and the Department of Reproductive Biology, and external partner/ current status: ca. 400 samples from more than 80 species which represent all deeper splits of the primate infraorders and include all archontan orders. Information on this material can be obtained from

<http://www.dpz.gwdg.de/GENEbank>.

Genomic libraries from *Tupaia belangeri*, *Callithrix jacchus* and *Macaca mulatta* that were constructed in cooperation with the Resource Center of the German Human Genome project (see Annual Report 1999) are listed and can be obtained from <http://www.rzpd.de>.

The Primate Genetics Group is part of the EU-project "INPRIMAT", which, as an infrastructural initiative of the 5<sup>th</sup> Framework, makes primate material available to the scientific community.

**External services**

Activities in this context pertain to the "Gene Bank of Primates"-project, and mainly include provision of samples (DNAs and tissue) for ca. 50 colleagues in Germany and abroad.

Institution/Name	Service
Zoo Romagne, F	Paternity and determination of (sub)species status "Stud book spider monkeys" "Stud book squirrel monkeys"
Zoo Madrid, E	Paternity and determination of (sub)species status "Stud book squirrel monkeys"
Zoo Landau	Paternity and determination of (sub)species status "Stud book spider monkeys"

**Transfer of knowledge, consultations**

Name/Institute	Service
Univ. Göttingen Hans Zischler	Graduiertenkolleg "Perspectives of Primatology", SS 2001

**Candidates for diploma (D) and doctorate (P)**

University/Name	Subject
Faculty of Biology, Univ. Hamburg Andreas Hapke (P)	Population genetics and differentiation of <i>Cheirogaleus medius</i>
Faculty of Biology, Univ. Göttingen Oliver Piskurek (D)	Comparison of the evolution of genes and pseudogenes of the mitochondrial ribosomal genes of primates
Faculty of Biology, TU München Christian Roos (P)	Molecular phylogeny of primates
Faculty of Biology, Univ. Göttingen Jelka Cimermann(D)	Molecular basis of reproductive isolation in primates: sequence evolution of the sperm proteins PH-20 and P47
Faculty of Biology, Univ. Giessen Silke S. Singer (P)	Inter- and intraorganellar DNA-transpositions as molecular cladistic markers in primate phylogeny

**Guest researchers from national and international institutions**

Name/Institute/Duration	Project
Lara Modolo Anthropologie und Museum, Univ. Zürich, CH 15.-29.05.02	<i>Macaca sylvanus</i> population genetics

Place of employment	Duration of stay (2001/2002)		
	< 1 month	1 - 3 months	> 3 months
Africa	0	0	0
America (without USA, Canada)	0	0	1
USA, Canada, Australia	0	0	0
Asia	0	0	0
Germany	0	0	0
EU, remaining Western Europe	1	0	1
Central and eastern Europe	0	0	0
<b>Altogether</b>	<b>1</b>	<b>0</b>	<b>0</b>

**Events**

- Participation in the organisation and realisation of the symposium "Primate Evolution: Phylogenetic, Physiological and Behavioural Aspects", DPZ, 06.02.01.

**DEPARTMENT OF REPRODUCTIVE BIOLOGY**

**General survey of service supplies**

- Reproductive diagnostics: Hormone analyses, ultrasound investigations, sperm analyses
- Supply of organ and sample material
- Testing of antisera
- Immunohistological and -chemical investigations
- Advice on aspects of reproductive biology and physiology in primates
- Training and education of diploma and doctoral students and technicians

**External services**

Institution/Name	Service
Anthropological Institute, Univ. Göttingen Prof. H. Rothe	Faecal progestogen analyses for cycle monitoring in the marmoset monkey
Zoological Garden Stuttgart Dr. W. Rietschel	Faecal hormone analyses for fertility control in a female gorilla
Inst. of Animal Breeding and Animal Genetics, Univ. Göttingen Prof. W. Holtz	Advice on the development of ELISA's
Zoological Garden Krefeld Dr. W. Dreßen	Faecal progestogen analyses for cycle monitoring in <i>Leontopithecus chrysopygus</i>
Zoological Garden Osnabrück Dr. U. Magiera	Advice on faecal glucocorticoid measurements for assessing stress levels in African wild dogs
Zoological Garden Duisburg Dr. G. Hartmann	Faecal hormone analyses for fertility control in a female gorilla
Univ. Hospital Eppendorf, Hamburg Dr. A. Haemisch	Advice on urinary and faecal glucocorticoid measurements in mice
IBL, Hamburg Dr. Strauss	Advice on oestradiol analyses in long-tailed macaques
Roehampton Institute, London, UK Dr. D. Curtis	Advice on HPLC techniques and the establishment of a hormone laboratory
Roehampton Institute, London, UK Dr. J. Setchell	Advice on faecal steroid analyses in orang utans
School of Veterinary Medicine, Hannover T. Wagemann	Advice on non-invasive hormone measurements in tigers
Bristol Zoo, UK Dr. B. Carroll	Faecal hormone analyses for fertility control in female gorillas

*Reproductive Biology*

<b>Institution/Name</b>	<b>Service</b>
Laboratory of Pharmacology & Toxicology, Hamburg Dr. Leuschner	Semen collection and analyses in 18 long-tailed macaques
Serengetipark Hodenhagen Dr. M. Boer	Semen collection and analyses for fertility control in the bengal tiger
Zoological Garden Krefeld Dr. W. Dreßen	Semen collection and fertility control in a male <i>Leontopithecus chrysopygus</i>
Zoological Garden Rostock Dr. Linke	Semen collection and fertility control in lion-tailed macaques
Several zoos	Hormone analyses for monitoring ovarian function and pregnancy in Asian and African elephants
Mini-Tüb, Tiefenbach Dr. Müller-Schlösser	Toxicological tests of embryo-culture-plates
Several institutes	Advice in applications and developments of reproduction technologies

**Transfer of knowledge, consultations**

<b>Name/Institute</b>	<b>Service</b>
Univ. Mexico, Mexico P. Nayudu	Training of external PhD students from Mexico
Senckenberg-Museum, Frankfurt M. Heistermann, J.K. Hodges	Practical course on "Hormone analyses in faeces" part of the event "Week of Biodiversity"
School of Veterinary Medicine, Hannover A. Schrod	Lecture and practical demonstration on semen collection and analysis in non-human primates
Felix-Klein-Gymnasium, Göttingen M. Heistermann	Training in endocrine techniques as part of a practical course for school children
University Extension Göttingen A. Einspanier, M. Heistermann, P. Nayudu	Training for technicians in biology
School of Veterinary Medicine, Hannover A. Einspanier	Practical course on steroid receptor analyses in the uterus of silver, blue and red foxes, zebra, tiger and lion
Centre for Life Sciences Study, Bogor Agricultural Univ., Indonesia A. Schrod	Workshop for Indonesian veterinarians on "Computer assisted semen evaluation"
Inst. of Cell Biology and Animal Ecology School of Veterinary Medicine, Hannover B. Husen	Practical course in "Hormonal signal transduction in mammals"; Practical course in Biology for teachers

*Reproductive Biology*

<b>Name/Institute</b>	<b>Service</b>
Institut Pertanian, Bogor Agricultural Univ., Indonesia J.K. Hodges	Establishment of a Memorandum of Understanding on education, technology transfer and scientific cooperation for the promotion of research and conservation of Indonesian Wild Life
School of Veterinary Medicine, Hannover A. Einspanier	Lectures for students of Veterinary Medicine on Primatology and Reproductive Biology
Centre for Life Sciences Study, Bogor Agricultural Univ., Indonesia M. Heistermann	Training in non-invasive methodologies of hormone analyses and establishment of a hormone laboratory

**Candidates for diploma (D) and doctorate (P)**

<b>University/Name</b>	<b>Subject</b>
Faculty of Biology, Univ. Cologne Christelle Ademmer (D)	Reproduction and stress in Douc langurs ( <i>Pygathrix nemaeus</i> ): non-invasive assessment of endocrine status
Faculty of Biology, Univ. Hamburg Ulrike Möhle (P)	Metabolism and excretion of testosterone in male non-human primates and its significance for the development of non-invasive methods for assessing male gonadal activity
Faculty of Biology, Univ. Giessen Thomas Ziegler (P)	Socio-endocrine studies on reproductive strategies of female Hanuman langurs ( <i>Semnopithecus entellus</i> ) in Nepal
Faculty of Reproductive Medicine, School of Veterinary Medicine, Hannover Ingo Schwabe (P)	Significance of estradiol synthesis by 17 $\beta$ -hydroxysteroid dehydrogenase type1 and type7 in the ovary and placenta of the marmoset monkey
Faculty of Reproductive Medicine, School of Veterinary Medicine, Hannover Annette Schrod (P)	Comparative analyses on sperm motility, morphology and morphometry in non-human primates with different mating systems
Faculty of Biology, Univ. Bayreuth Karin Reichert (P)	Socio-endocrine studies on the regulation and functional significance of perineal swelling in the bonobo ( <i>Pan paniscus</i> )
Faculty of Biology, Univ. Münster André Ganswindt (P)	Endocrine and behavioural correlates of musth in captive African elephants
Faculty of Veterinary Medicine, Univ. Giessen Alexander Schneiders (P)	Comparative studies on sperm characteristics in callitrichid primates

*Reproductive Biology*

<b>University/Name</b>	<b>Subject</b>
Faculty of Biology, Univ. Leipzig Tobias Deschner (P)	Socio-endocrine investigations on the functional significance of sexual swellings in free-ranging chimpanzees of the Tai National Park, Ivory Coast
Faculty of Biology, School of Veterinary Medicine, Hannover Ekaterina Vorobieva (P)	Endocrine correlates of dominance and mating success in chimpanzees and bonobos
School of Veterinary Medicine, Hannover Nicola Wolff (P)	Behavioural and endocrine measures of stress and gonadal status in male gorillas living in all male groups
Faculty of Biology, Univ. Berlin Antje Engelhardt (P)	Endocrinological, behavioural and genetical studies of male and female reproductive strategies in free-ranging long-tailed macaques
Faculty of Biology, Univ. Würzburg Julia Ostner (P)*	Socio-endocrinology and social system of red-fronted lemurs.
Faculty of Biology, Univ. Bielefeld Maren Huck (P)*	Socio-endocrine and genetic analyses of reproductive strategies in male moustached tamarins in Peru
Faculty of Biology, Univ. Münster Petra Löttker (P)*	Socio-endocrine and genetic analyses of reproductive strategies in female moustached tamarins in Peru
Faculty of Reproductive Medicine, School of Veterinary Medicine, Hannover Ellen Preußing (P)	Embryo flushing in the marmoset monkey ( <i>Callithrix jacchus</i> ) - establishment of non-invasive methods of embryo retrieval
Faculty of Medicine, Univ. Göttingen Svenja Verhagen (P)	Examination of factors influencing relaxin secretion in luteal tissue of the common marmoset monkey
Faculty of Reproductive Medicine, School of Veterinary Medicine, Hannover Nicola Beindorff (P)	Examination of the aging corpus luteum in the marmoset monkey
Faculty of Reproductive Medicine, School of Veterinary Medicine, Hannover Frauke Hegermann (P)	Effect of oxytocin on ovulation and luteinization in the common marmoset monkey
Faculty of Medicine, Univ. Göttingen Iris-Nadine Tillmann (P)	The role of IGFI and relaxin on the theca cells of the marmoset monkey
Faculty of Medicine, Univ. Göttingen Hanan Kennich (P)	Renin-angiotensin-system in the theca cells of the common marmoset monkey
Faculty of Medicine, Univ. Göttingen Jan Stumper (P)	Effect of relaxin and IGFI on the regulation of matrix components

*Reproductive Biology*

<b>University/Name</b>	<b>Subject</b>
Faculty of Biology, National Univ. Mexico City, Mexico Jorgelina Barrios de Tomasi (P)	Investigation of the effects of different molecular variants of FSH on follicle growth and cell proliferation <i>in vivo</i> and <i>in vitro</i>
Faculty of Reproductive Medicine, School of Veterinary Medicine, Hannover Alessandra Quaggio Augusto	Effect of growth factors on follicle development in the marmoset monkey
Faculty of Medicine, Univ. Giessen Katja Bogner (P), Stefan Kuhnert (P)	Investigation of the development of the marmoset zona pellucida
National Univ. Mexico City, Mexico Leonor Hernandez (P)	Development of reproductive technologies in New World monkeys
Physiological Chemical Institute Veterinary Medical Faculty, Univ. Leipzig Christina Simon (P)	Studies on local factors influencing cervical ripening in <i>Callithrix jacchus</i>
Faculty of Reproductive Medicine, School of Veterinary Medicine, Hannover Angela Brüns (P)	Estradiol synthesising enzyme cytochrom-P450-aromatase and its significance for female reproductive physiology in the primate model, <i>Callithrix jacchus</i>
* Internal co-operations of the Departments of Reproductive Biology and of Ethology and Ecology and the Working Group Primate Genetics.	

**Guest researchers from national and international institutions**

<b>Name/Institute/Duration</b>	<b>Project</b>
Leonor Hernandez Univ. Mexico, Mexico 06.02.-30.11.01	Development of reproductive technologies in New World monkeys
Matthias Schulz Dept. Internal Medicine, Univ. Göttingen 01.04.01-30.09.02	Studies on tumor markers
Muhammad Agil Bogor Agricultural Univ., Bogor, Indonesia 25.05-19.08.01	Hormone analyses in the urine and faeces of the male and female Sumatran rhinoceros
Birgen Meulemann Univ. Antwerp, B 05.-19.07.01	Urinary glucocorticoid measurements in bonobos
Dr. Christophe Abegg Univ. Strasbourg, F 17.-30.07.01; 27.01.-05.02.02	Evolution, behaviour and <i>in situ</i> conservation of the Mentawai islands macaques

*Reproductive Biology*

<b>Name/Institute/Duration</b>	<b>Project</b>
Dr. Ross Bathgate Howard Florey Institute, Australia 11.-20.08.01	Species differences in relaxin
Andrew Siebel Howard Florey Institute, Australia 20.-30.08.01	The role of oxytocin in the process of parturition
Yvonne Ponke IHF, Hamburg 09.-17.09.01	Genetic analyses of tissue samples
Maria Suarez Univ. Madrid, E 15.10.01-30.03.02	Glucocorticoid measurements in the faeces of cotton-top tamarins
Dr. Ann McLarnon Univ. Roehampton, UK 19.11.-08.12.01; 28.01.-03.02.02	Training in the establishment and management of a hormone laboratory
Susanne Ulbrich Inst. of Physiology, München 17.-25.02.02	Factors affecting oocyte maturation
Hera Maheshwari Center for Life Sciences Study, Bogor Agricultural Univ., Indonesia 23.07.02-24.01.03	Training in non-isotopic hormone assays and other laboratory techniques
Petra Kretzschmar Univ. Erlangen 26.11.02-28.02.03	Glucocorticoid measurements in the faeces of free-ranging white rhinoceros

<b>Place of employment of the guest</b>	<b>Duration of stay (2001/2002)</b>		
	<b>&lt; 1 month</b>	<b>1 - 3 months</b>	<b>&gt; 3 months</b>
Africa	0	0	0
America (without USA, Kanada)	0	0	1
USA, Canada, Australia	2	0	0
Asia	0	1	1
Germany	2	0	2
EU, remaining Western Europe	5	0	1
Central and Eastern Europe	0	0	0
<b>Altogether</b>	<b>9</b>	<b>1</b>	<b>5</b>

**Events**

- The Department and its staff were involved in the organisation and realization of the symposium "Primate Evolution: Phylogenetic, Physiological and Behavioural Aspects" (Co-organizer: Prof. Hodges), which was held at the DPZ in 2001 as part of the Graduiertenkolleg "Perspectives in Primatology".
- Prof. Einspanier organized a primatological workshop at the Hannover School of Veterinary Medicine in the winter semesters 2000/2001 and 2001/2002.
- In addition, Dr. Heistermann and Prof. Hodges participated in the event "The Tree of Life" as part of the "Week of Biodiversity" in the Senckenberg Museum, Frankfurt, from 27.11.-02.12.01.
- During the last two years, the Department has invited several significant scientists for lectures, e.g. Prof. Joanne Fortune, Cornell University, NY, USA, Dr. Ross Bathgate, Howard Florey Institute, Melbourne, Australia, Dr. Willie Smits, Balikpapan Orang Utan Reintroduction Project, Indonesia.

## **COGNITIVE NEUROSCIENCE LABORATORY**

### **General survey of service supplies**

Because the Cognitive Neuroscience Laboratory (CNL) was in the process of being established during the period covered by this report, service was focussed on lecturing and consulting. Additionally, the guests of the CNL provided an expansion to the number of talks given at the DPZ.

### **Transfer of knowledge, consultations**

<b>Institution/Name</b>	<b>Service</b>
Int. MSc/PhD-Program Neurosciences, Univ. of Göttingen S. Treue, S. Katzner, F. Pieper	Courses in methods and lab. training SS 2002 and WS 2002/03
Univ. of Würzburg, Faculty of Psychology S. Treue, S. Katzner, F. Pieper, T. Womelsdorf	Seminar and lab. demonstrations on visual perception for students and lecturers
Univ. of Göttingen S. Treue	Lectures in Biopsychology for psychology students in WS 2002/03
Cold Spring Harbor Laboratories, New York, USA S. Treue	Lectures in Summer Course "Computa- tional Neuroscience: Vision"
Demonstrations and seminars for visitors S. Treue, S. Katzner, F. Pieper, T. Womelsdorf	Open house on the occasion of the 25 <sup>th</sup> anniversary of the DPZ
Students und scientific staff of the Univ. of Göttingen S. Treue	Journal club "Visual Cortex"
Journalists und media representatives S. Treue	Scientific consulting

### **Candidates for diploma (D) and doctorate (P)**

<b>University/Name</b>	<b>Subject</b>
Int. MSc/PhD-Program Neurosciences, Univ. of Göttingen (P) Pinar Boyraz	The perception of visual motion in man and monkey
Faculty of Biology, Univ. of Göttingen Laura Busse (P)	Attentional modulation of visual motion processing

*Cognitive Neuroscience Laboratory*

<b>University/Name</b>	<b>Subject</b>
Faculty of Biology, Univ. of Göttingen Steffen Katzner (P)	Attentional modulation on visual motion processing
Faculty of Biology, Univ. of Göttingen Florian Pieper (P)	Visual information processing in the temporal lobe of macaque monkeys
Faculty of Biology, Univ. of Göttingen Thilo Womelsdorf (P)	Neuronal correlation of selective attention within macaque area MT/V5

**Guest researchers from national and international institutions**

<b>Name/Institute/Duration</b>	<b>Project</b>
Eugene Simine Center for Vision Research, York Univ., Toronto, CDN 06.-16.02.02, 27.03.-07.04.02	Localisation of cortical processing of visual motion in man using functional imaging
Dr. Dr. Julio Martinez-Trujillo Centre for Vision Research, York Univ., Toronto, CDN 02.-31.07.02	Attentional influence on visual information processing

<b>Place of employment of the guest</b>	<b>Duration of stay (2001/2002)</b>		
	<b>&lt; 1 month</b>	<b>1 - 3 months</b>	<b>&gt; 3 months</b>
Africa	0	0	0
America (without USA, Canada)	0	0	0
USA, Canada, Australia	2	0	0
Asia	0	0	0
Germany	0	0	0
EU, remaining Western Europe	0	0	0
Central- und Eastern Europe	0	0	0
<b>Altogether</b>	<b>2</b>	<b>0</b>	<b>0</b>

**Events**

The Cognitive Neuroscience Laboratory hosted numerous scientific seminars held by guests from Europe, USA and Canada, as listed below.

- Dr. Pascal Fries, Donders Centre for Cognitive Neuroimaging, Univ. Nijmegen, NL, 15.03.02: The functional role of neuronal coherence for attentional stimulus selection.

- Ansgar R. Koene, Helmholtz Inst., Univ. Utrecht, NL, 19.04.02: Modelling curvature polarity in multi-stable 3D structure-from-motion.
- Dr. Fred Hamker, California Institute of Technology (Caltech), Pasadena, USA, 14.06.02: A computational systems approach toward understanding the temporal dynamics of perception and object recognition.
- Dr. Mark van Rossum, Dept. of Biology and Center for Complex Systems, Brandeis Univ., Massachusetts, USA, 17.06.02: Fast propagation and computation in layered feed-forward networks.
- Dr. Alexander Thiele, Henry Wellcome Building for Neuroecology, University of Newcastle Upon Tyne, UK, 24.07.02: Attention reduces inferential processes in vision.
- Prof. Rüdiger van der Heydt, Dept. of Neuroscience, Johns Hopkins Univ., Baltimore, Maryland, USA, 23.08.02: Figure-ground representation in the visual cortex: Global structure in local feature maps.
- Dr. Chris Tinsley, School of Psychology, Nottingham Univ., UK, 27.09.02: Neural responses to moving 2-D images in the primary visual cortex.
- Dr. Jose Raul Naranjo Muradas, Cognitive Neuroscience Sector of the International School for Advanced Studies, Trieste, I, 18.10.02: Dynamics of the frontoparietal network for reaching movements in humans: an EEG approach.
- Prof. Dr. John Tsotsos, Center for Vision Research, York Univ., Toronto, CDN, 13.11.02: Selective Tuning Model for Visual Attention: Computational Foundations and Relationship to Human/Primate Vision.
- Dr. Thorsten Schormann, Inst. für Neuroanatomie und C. und O. Vogt Inst. für Hirnforschung, Univ. of Düsseldorf, 09.12.02: Ein Beitrag der Physik zur Evolutionsanalyse: Vom Affen- zum menschlichen Gehirn.

**DEPARTMENT OF NEUROBIOLOGY**

**General survey of service supplies**

- Provision of tree shrews (*Tupaia belangeri*)
- Provision of diverse primate organs
- Stereotactic brain operations
- Neurohistological methods
- Tests of psychopharmacological compounds in stress experiments
- Neuroendocrinological investigations
- Digital acoustic analyses

**Transfer of knowledge, consultations**

<b>Name/Institute</b>	<b>Service</b>
Univ. Göttingen U. Jürgens	Lecture "Das Säugergehirn" WS 2000/2001, 2001/2002, 2002/2003
Univ. Göttingen U. Jürgens	Lecture "Lernphysiologie" SS 2001, 2002,
Univ. Göttingen Jürgens	Lectures within the Int. Neurosciences Study Program WS 2001/2002, WS 2003/2003
Univ. Göttingen U. Jürgens	Diploma examination
Free Univ. Berlin U. Jürgens	External doctoral examination
Technical School, Braunschweig U. Jürgens	External doctoral examination
FB Biologie and Bereich Human Medicine, Univ. Göttingen E. Fuchs	Introduction to animal experimentation – course and seminar WS 2000/2001, SS 2001, WS 2001/ 2002, SS 2002, WS 2002/2003
Int. MSc/PhD Program Neuroscience, Univ. Göttingen E. Fuchs	Lectures, courses and tutorials in neuroanatomy, neuropharmacology and behavioral biology 2000/2001, 2001/2002, 2002/2003
Int. MSc/PhD Program Neuroscience, Univ. Göttingen E. Fuchs	Entrance examinations and interviews; final examinations
Bezirksregierung Braunschweig E. Fuchs	Member of the commission for § 15 TierschG

*Neurobiology*

<b>Name/Institute</b>	<b>Service</b>
Univ. Leiden, NL E. Fuchs	Expert opinion on doctoral examinations
Cornell Univ., Ithaca, USA G. Flügge	Expert opinion on the appointment of an associate professor
Bereich Humanmedizin, Univ. Göttingen G. Flügge	Psychopharmacology WS 2000/2001, SS 2001, WS 2001/2002, SS 2002, WS 2002/2003
Int. MSc/PhD Program Neuroscience, Univ. Göttingen G. Flügge	Lectures, tutorials, seminars, courses in neuroanatomy and neuropharmacology 2000/2001, 2001/2002, 2002/2003
Int. MSc/PhD Program Neuroscience, Univ. Göttingen B. Czeh und J. Keuker	Seminar und course: Hippocampus 2000/ 2001, 2001/2002, 2002/2003

**Candidates for diploma (D) and doctorate (P)**

<b>University/Name</b>	<b>Service</b>
Faculty of Biology, Univ. Göttingen Silvana Siebert (D)	The role of periaqueductal grey for the elicitation of vocalization from the squirrel monkey brainstem
Faculty of Biology, Univ. Göttingen Florian Pieper (D)	Neuronal activity in the pericentral colliculus inferior during vocalization
Faculty of Biology, Univ. Göttingen Monika Palchaudhuri (P)	Serotonin 1A-receptors in the brain of tree shrews
Faculty of Biology, Univ. Bielefeld Gesa-Vollmann Honsdorf (P)	Adrenal steroid hormones as modulators of structural features of neural cells
Univ. Leiden, NL Marja van Kampen (P)	Effect of antidepressants on behaviour and central nervous functions in socially stressed tree shrews
Graduate School Behavioral and Cognitive Neurosciences, Univ. Groningen, NL Jeanine Keuker (P)	Neurobiological substrates of ageing in non-human primate brains
Graduate School Behavioral and Cognitive Neurosciences, Univ. Groningen, NL Maarten Kole (P)	Stress and adrenal steroid hormones as modulators of electrophysiological features of hippocampal neurones
School of Veterinary Medicine, Hannover Frank Dusterhöft (P)	Vocalization-correlated neuronal activity in the periaqueductal grey of squirrel monkeys
School of Veterinary Medicine, Hannover Kristina Simonyan (P)	Anterograde connections of the cortical larynx area in the rhesus monkey

*Neurobiology*

<b>University/Name</b>	<b>Service</b>
Faculty of Biology, Free Univ. Berlin Claudia Fichtel (P)	Parametric characteristics of emotional correlates in the vocalization of squirrel monkeys
Faculty of Biology, Technische Univ. Braunschweig Lutz Lütke (P)	Electrophysiological investigations in vocalization of squirrel monkeys
Faculty of Biology, Free Univ. Berlin Elisabeth Scheiner (P)	Comparative studies of non-verbal vocalizations in hearing and hearing-impaired human infants
Faculty of Medicine, Univ. Göttingen Lisa Kotthaus (P)	NMDA-receptors in the brain of a genetically modified mouse
School of Veterinary Medicine, Hannover Stefanie Hannig (P)	Anterograde projections of the ventral paralemniscal zone in the squirrel monkey
School of Veterinary Medicine, Hannover Eva Dujardin (P)	Afferent connections of the periaqueductal vocalization area in the squirrel monkey
Faculty of Biology, Free Univ. Berlin Janna Kirchof (P)	Predator avoidance of tamarins in the Amazonian rain forest of Peru: Function of alarm calls and their use in interspecific associations
Univ. Pamplona, E Gabriel de Biurrun (P)	Modulation of cognition by stress, age and gender
Faculty of Medicine, Univ. Göttingen Anja Fischer (P)	Neurobiological basis of neurogenesis in the adult CNS
Faculty of Biology, Univ. Ulm Steffen Hage (P)	Neuronal activity in the ventrolateral pons during audio-vocal interaction
Univ. Barcelona, E Nuria Estape-Cot (P)	Establishment of behavioural and cognitive tests for marmoset monkeys
Int. MSc/PhD Program Neuroscience, Univ. Göttingen Urs Heilbronner (P)	Alpha2B-adrenoceptor expression in the tree shrew thalamus
Int. MSc/PhD Program Neuroscience, Univ. Göttingen Nashat Abumaria (P)	Transcriptional effects of antidepressant drugs
Int. MSc/PhD Program Neuroscience, Univ. Göttingen Keneoue Thinyane (P)	Functional integration of modified embryonic stem cells in an experimental model for Parkinson's disease
Graduate School Behavioral and Cognitive Neurosciences, Univ. Groningen, NL Marieke van der Hart (P)	Behavioural characterisation of new potential antidepressive drugs

**Guest researchers from national and international institutions**

<b>Name/Institute/Duration</b>	<b>Project</b>
Julieta Alfonso Univ. Nacional de General San Martin, San Martin, Argentina February 05-April 15, 2002 and September 17-October 15, 2002	Molecular biological experiments on the effect of stress and cortisol treatment in tree shrews
Alessandro Bartolomucci Univ. Parma, I October 18, 1999-March 31, 2001	Learning strategies in tree shrews
Gabriel De Biurrun Univ. Pamplona, E June 01, 1999-December 31, 2002	Modulation of cognition by stress, age and gender
Tanja Costoli Univ. Parma, I September 12, 2001-December 31, 2002	Quantification of the central nervous receptor systems of rats with high and low aggressiveness
Dr. Susanne Fauser Univ. Göttingen September 26, 2000-October 31, 2001	Functional neuroanatomical studies on the effect of rTMS
Dr. Eleonora Isovich Univ. Buenos Aires, Argentina October 01, 1998-March 31, 2002	Dopaminergic system and stress
Anna Perez Univ. Valencia, E October 04-December 15, 2001	rTMS and its impact on neurogenesis
Katrin Pietz Univ. Würzburg September 02-October 12, 2002	Behavioural testing of marmosets monkeys
Davide Ponzi Univ. Parma, I October 08, 2002-April 01, 2003	Introduction to quantitative <i>in vitro</i> receptor autoradiography
Olga Pudovkina Solvay, Weesp, NL August 05, 2002-August 15, 2003	Behavioral analysis of tree shrews
Mirjana Ruhleder Univ. Würzburg February 11, 2002-March 22, 2002	Cognitive tests in marmosets monkeys

*Neurobiology*

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Place of employment of the guest	Duration of stay (2001/2002)		
	< 1 month	1 - 3 months	> 3 months
Africa	0	0	0
America (without USA, Canada)	0	1	1
USA, Canada, Australia	0	0	0
Asia	0	0	0
Germany	0	2	1
EU, remaining Western Europe	0	1	5
Central and Eastern Europe	0	0	0
<b>Altogether</b>	<b>1</b>	<b>4</b>	<b>7</b>

**Events**

- Prof. Fuchs acted as a member of the organization committee of the 5<sup>th</sup> Annual Meeting of the Neuroendocrinology section of the German Society for Endocrinology in Marburg (2001) and organized the 46<sup>th</sup> Annual Meeting of the German Society for Endocrinology in Göttingen (2002). As the coordinator of the EU research project EUPEAH, he organized the first meeting of the project leaders which took place at the DPZ in December 2002.

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**DEPARTMENT OF VIROLOGY AND IMMUNOLOGY**

**General survey of service supplies**

The Department of Virology and Immunology provides facilities for keeping experimental animals under S2 and S3 safety conditions. Furthermore, a safety laboratory for performing gene technical work under S3 safety conditions is available for the colleagues of the DPZ as well as for external scientists. In addition, blood and tissue samples from rhesus monkeys as well as monoclonal antibodies against the human and bovine prion protein are available.

**External services**

<b>Name/Institute</b>	<b>Service</b>
Research Co-operative "SIV Model in Rhesus Macaques: Studies on Pathogenesis and Vaccination"	Provision and quarantine of 21 rhesus monkeys and keeping of 87 rhesus monkeys as well as substantial services for these projects
EU-Shared Cost Action "DETEC", Co-ordinator: Prof. P. Ràcz, Bernhard-Nocht-Institute, Hamburg,	Provision and quarantine of 35 rhesus monkeys and keeping of 57 rhesus monkeys as well as substantial services for these projects
Bayer Forschungszentrum, Wuppertal, Dr. D. Paulsen	Provision (7x) of citrated blood from experimentally naïve and SIV-infected rhesus monkeys
Robert-Koch-Institute, Berlin, Erik Seibold	Provision (8x) of citrated blood from experimentally naïve and SIV-infected rhesus monkeys
Impfstoffwerk Dessau-Tornau, Dr. K. Meißner	Provision (26x 9 ml each) of citrated blood in "Alseverscher" solution from experimentally naïve rhesus monkeys
Vet Diagnostics Ltd., Small Dole, West Sussex, GB Dr. C. King	Provision (6x) of a total of 25 ELISA plates
Clinical Pharmacology, Medical Hospital Innenstadt, München, Dr. G. Hartmann	Provision of citrated blood from experimentally naïve rhesus monkeys
Inst. for Microbiology, Dept. of Virology, Ulm Univ. Prof. F. Kirchhoff	Provision of citrated blood from experimentally naïve rhesus monkeys

**Transfer of knowledge, consultations**

<b>Name/Institute</b>	<b>Service</b>
Dept. of Biology, Göttingen Univ.  C. Stahl-Hennig A. Stuke U. Saueremann K.D. Jentsch	Practical training "Animal Virology" (14 days) within the framework of Microbiological Practical Training for Advanced Students II, Dept. of Biology of Göttingen University, winter term 2001/02: Infection and pathogenesis Detection of prions Immunogenicity of infectious diseases Determination of promotor activity with the help of the CAT test
Göttingen Univ. G. Hunsmann, C. Stahl-Hennig, U. Saueremann, A. Stuke, T. Mühl, K.D. Jentsch	Lecture and seminar "Animal Virology" Subjects "Viruses", "Viral Diseases", "Immune Response", "Prevention and Therapy", summer term 2001
Medical School Hannover G. Hunsmann	Lecture on the topic "Retrovirology" during the summer terms 2001 and 2002

**Candidates for diploma (D) and doctorate (P)**

<b>University/Name</b>	<b>Subject</b>
Dept. of Biology, Göttingen Univ. Gisela Feldmann (P)	Rhadino-viral transformation of autologous T-cells for adoptive cell transfer in the rhesus monkey model
Dept. of Biology, Göttingen Univ. Evelyn Meyer (P)	Characterisation of V1/V2 env HIV-1 mutants
Dept. of Biology, Göttingen Univ. Alexander Strom (P)	Investigation of cellular and pathogenic prion proteins with phage-display techniques
Dept. of Mathematics and Sciences, Göttingen Univ. Kai Lieder (P)	Interface peptides of the viral protease of HIV-1 used as gene-therapeutic, antiviral substances
Dept. of Biology, Hannover Univ. Irantzu Alegria (P)	Identification and characterisation of surface antigens from peripheral blood monocytes for a VP1-VLP-mediated DNA transport by means of receptors
Dept. of Mathematics and Sciences, Göttingen Univ. Omar Ahmad-Omar (P)	Production of monoclonal antibodies and phage antibodies against the bovine prion protein by SFV particle-induced immunisation of PrP <sup>0/0</sup> mice

*Virology and Immunology*

<b>University/Name</b>	<b>Subject</b>
Dept. of Mathematics and Sciences, Bonn Univ. Thorsten Mühl (P)	Characterisation of MHC class I molecules from rhesus monkeys ( <i>Macaca mulatta</i> )
Dept. of Biology, Göttingen Univ. Nadine Dammeier (D)	Characterisation of the N-terminal modified major structural protein VP1 of the human polyomavirus JCV
Dept. of Biology, Göttingen Univ. Henrik Müller (D)	Isolation of the cellular prion protein (PrPC) and the BSE virus (PrPSC) from cattle brains for the characterisation of anti-PrP-antibodies

**Guest researchers from national and international institutions**

<b>Name/Institute/Duration</b>	<b>Project</b>
Dr. Wolfgang Bergter Medical School Hannover, D 09.12.99-31.12.01	Radio immunotherapy of HIV infection
Dr. You-Suk Suh POSTECH Univ., Pohang, Korea 19.02.-31.07.01	Collaborative prophylactic and therapeutic vaccine trials in the SIV macaque model for AIDS research (within the framework of a collaboration with Prof. Y.-C. Sung)
Dr. Xianfeng Zhang Hokkaido Univ. Sapporo, Japan 20.02.-30.05.01	Prevention of onset of AIDS by library vaccine (in the framework of a collaboration with Prof. Shida)
Dr. Jörg Bäsecke University Hospital Göttingen, D Dept. of Hematology 01.03.-31.08.02	The leukemia gene AML1/ETO in the NOD/SCID model

<b>Place of employment of the guest</b>	<b>Duration of stay (2001/2002)</b>		
	<b>&lt; 1 month</b>	<b>1-3 months</b>	<b>&gt; 3 months</b>
Africa	0	0	0
America (without USA, Kanada)	0	0	0
USA, Canada, Australia	0	0	0
Asia	0	0	2
Germany	0	0	2
EU, remaining Western Europe	0	0	0
Central and Eastern Europe	0	0	0
<b>Altogether</b>	<b>0</b>	<b>0</b>	<b>4</b>

## **Events**

During the reporting period, the Department of Virology and Immunology invited the following guests to give a seminar at the DPZ:

- Dr. Marie-Laure Yaspo, MPI for Molecular Genetics, Berlin, D, 25.04.01: Functional genomics and evolution of human chromosome 21 genes: impact for molecular medicine
- Dr. Hansruedi Bueler, Institute of Molecular Biology, Zurich Univ, CH, 13.08.01: Gene transfer and therapy in the nervous system with adeno-associated viral vectors (within the framework of the graduate training programme "Perspectives of Primatology").
- PD Dr. Ulf Dittmer, Institute for Virology and Immunology, Würzburg Univ., D, 24.10.01: The Friend virus mouse model: A model for the development of vaccines and immune therapies against retroviruses
- Prof. Dr. Eugene Sverdlov, Institute of Molecular Genetics, Russian Academy of Science, Moscow, RUS, 25.02.02: The comparative analysis of distributions of retroelements in closely related genomes.
- Dr. Yuri B. Lebedev, Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, Moscow, RUS, 17.10.02: Human-specific retroelements: identification, genome distribution and possible impact on human speciation.
- Dr. Thomas Friedrich, Wisconsin Regional Primate Research Center, Madison, WI, USA, 31.10.02: What mad pursuit? What struggle to escape? The functional significance of AIDS virus escape from CTL responses.
- Prof. Ralph M. Steinman, The Rockefeller University, New York, USA, 17.12.02: Dendritic cells and the control of immunity and tolerance.

## Internal Services

All departments of the DPZ have manifold internal cooperations. Most of the services were provided by the **Department of Veterinary Services and Primate Husbandry**.

In the sector of services, the Department of Veterinary Services and Primate Husbandry cooperates with all departments of the DPZ. Some examples are veterinary care for the experimental animals of the Department of Neurobiology and the Department of Reproductive Biology, the purchase, quarantine, and sale of animals or the provision of animal keepers. All scientific investigations with operations on animals are accompanied by a veterinarian. The veterinary pharmacy of the DPZ supplies the medicines required for veterinary care. Moreover, the service for the departments comprises necropsies, microbiological and parasitological investigations as well as diagnostic laboratory tests. In addition to diagnostic activities during necropsies, biological samples (organs, tissue, blood, urine, liquor liquids) are taken for further scientific investigations. The Working Group Primate Genetics, which does not have experimental animals of its own, is, for example, supplied with samples of diverse species for studies on evolution genetics. By means of minimally invasive and non-invasive techniques, *in vivo* samples are taken for several scientific employees of the institute.

The breeding colonies of the DPZ are extensively looked after by the Department of Veterinary Services and Primate Husbandry. This includes the breeding choice, keeping and veterinary care for the animals and the related regular checkup of the colonies as well as controlling measures. The central histological laboratory and the central electron microscopy unit with photo laboratory are also used for their own preparations by almost all departments. This includes, for example, routine paraffin embedding, use of the microtomes, raster electron microscopical preparation of sperm or negative staining of virus preparations. Moreover, the task of the DPZ representative for animal protection with the processing of more than 30 planned animal experiments and the legally prescribed tasks connected with it belong to the internal service. The Head of the Department is also the representative of the German Primate Center for the prevention of infections.

Apart from the necropsies for external facilities, a further 336 animals were necropsied in the years 2001-02. 119 animals from our own breeding colonies were investigated for diagnostic reasons. A total of 125 rhesus monkeys were necropsied for the Department of Virology and Immunology. In addition to the perfusion fixation of six rhesus monkeys, 55 squirrel monkeys and 33 tree-shrews from the Department of Neurobiology and 21 common marmosets from the Department of Reproductive Biology were investigated morphologically. During the necropsies, several biological samples (organs, tissue, blood, urine, liquor liquids) were taken in the scientific interest and, in addition, diagnostics for continuing scientific investigations performed.

During the reporting period a total of 1783 bacteriological, 1462 parasitological and 31 mycological investigations were carried out for internal purposes. In addition

to diagnostic examinations within the scope of the population checkup, necropsy diagnostics and quarantine examinations, 267 bacteriological and 50 parasitological examinations were carried out in experimental animals of the Department of Virology and Immunology and 583 bacteriological and 80 parasitological examinations on animals of the Department of Neurobiology. 197 faeces samples were bacteriologically and 43 parasitologically analyzed for the Department of Reproductive Biology.

Internal services of the **Department of Neurobiology** were the handing over of organs of squirrel monkeys and tree shrews which had to be euthanized within the scope of neurobiological experiments. Male and female sexual organs were given to the Department of Reproductive Biology and epididymides to the Working Group Genetics.

Members of the **Department of Ethology and Ecology** advise other departments and working groups of the DPZ on biology and taxonomy of primates, use of geographical information systems and statistics.

Members of the **Working Group Primate Genetics** also advise the employees of the DPZ on problems concerned with biology and taxonomy. Moreover, the use of molecular techniques, phylogenetic tree reconstructions and microsatellite analyses is arranged.

Employees of the **Department of Reproductive Biology** support the Department of Veterinary Services and Primate Husbandry in several aspects of breeding hygiene. This includes, for example, the cryoconservation of sperm, assessment of the sperm quality and advice as to the breeding suitability of the animals. Also in pathomorphological examinations of sexual organs the Department of Veterinary Services and Primate Husbandry uses the methodological competence of the Department of Reproductive Biology, for example, for a better immunohistological classification of testicle and ovary tumors. Moreover, endocrinological analyses are made for both the Department of Veterinary Services and Primate Husbandry and the Department of Neurobiology (Working Group Fuchs).

The **Department of Virology and Immunology** carries out virological examinations and procedures especially for the Department of Veterinary Services and Primate Husbandry. This applies, for example, for the determination of CD4/CD8 cells of Facs-analyses, SIV-infection with virus cultivations and determination of the viremia. The laboratories and the equipment are used by employees of the Department of Veterinary Services and Primate Husbandry for molecular biological methods. The leading veterinarian of the Department of Virology and Immunology is one of two representatives for the protection of animals, an employee of the Department of Virology and Immunology is safety adviser according to the genetic engineering law.

Apart from the Department of Veterinary Services and Primate Husbandry the **Functional Unit Digital Information Processing and Communication** is a central service and infrastructure facility of the DPZ which closely cooperates with

### *Internal Services*

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all departments of the DPZ. The manifold tasks with internal services comprise, for example, the fields of EDP with procurement, installation and maintaining of hard- and software including the operation of the DPZ intranet, the continuous running of the library or the cultivation of internal communication via the publication of "DPZ-aktuell", and advice to employees as to statistical questions. The central photo laboratory is available for all questions concerning photo-documentation and the production of posters. The unit closely cooperates with all departments in the field of animal documentation including administrative tasks concerned with purchase and sale of animals and tissue samples.

**DIGITAL INFORMATION PROCESSING AND COMMUNICATION  
(DIP/COMM.)**

**Head:** Dr. Dr. Michael Schwibbe

Library

Horst Gervenat (-31.03.02)

Dr. Stefanie Heiduck (15.03.02-)

Photolaboratory

Margrit Hampe

Animal Documentation

Heike Klensang

Hard- und Software

Thomas Schmelzer

**General Information**

The main functions of the working group are to be found in services related to digital information processing, library, photo-laboratory and animal documentation as well as an internal and external exchange of information.

Long-term plans for digital information processing have to be realized, kept in step with technological advances and adapted to the specific needs of the users. Moreover, the scientific staff is advised on experimental designs and on mathematical and statistical analyses of their data. Specific programs for ongoing problems which cannot be solved by standard software are developed and instruction in the use of software and hardware is provided.

The library holds, in cooperation with a counseling committee, the responsibility for taking all decisions related to long-term subscriptions to series, journals and database literature to serve the interests of a primatological institute.

For computerized animal documentation, inputs from technicians from the various animal holding facilities are checked and tested for plausibility. The database is analyzed for scientific and administrative requests. Our group is responsible for the organisation of import and export as well as for the transport of animals and tissue samples for the center and other institutes. Various national and international laws concerned with animal keeping, animal protection, epidemics, transportation and customs have to be taken into consideration as well as house internal regulations. Correspondingly, these processes are quite time-consuming and require a current knowledge of the law. The know-how of the DPZ gained over more than 15 years has been used intensively by other institutes and even by governmental authorities.

Regarding external communication duties, the group keeps in contact with national and international press agencies to supply them with information material on outstanding efforts and events of the center. The group organizes visits to the DPZ for interested individuals and groups and establishes contacts between visitors with specific questions, including the press and the corresponding specialists in the research groups.

Quarterly, the journal "DPZ-aktuell" is published. This provides information on the latest developments in the DPZ, reports from the management, from the works committee and from the departments. Moreover, it provides details of lectures, official trips and new projects. Since 1998, together with Prof. Ganzhorn of the University of Hamburg, the DPZ publishes the "Lemur News". As the DPZ is the editor of the journal "Primate Report", which is published three times a year and includes the "Scientific Report" of the DPZ, the working group compiles the papers and prepares them for printing by DTP.

## **The Information Technology (IT)**

The person in charge of the DIP/COMM field developed a framework IT-concept in 2000. It describes the basal parameters of the IT equipment, discusses procedures for data safety and data security, and considers future developments and personnel requirements. The concept can be easily adapted to any new specific conditions in the IT sector and to the users' requirements. The general IT-concept of the Primate Center is archived under <http://www.dpz.gwdg.de/infra/it.pdf>.

### Wireless local area network (WLAN)

In 2001 the GWDG (German Scientific Society for Data Processing) expanded the WLAN from central Göttingen to the external areas, in particular to the northern parts of the university. The DPZ supported this initiative: Three relay antennas, as access points were set up on the roof of the Center. Thus, users from the student hostel and the nearby institutes of the University can be connected themselves via the DPZ to the Internet. In the main lecture hall of the Center also a wireless access to the LAN has been configured.

Thus the DPZ has taken a further step towards physical and scientific cross-linking with the university and offers an additional service to the *Alma mater*.

### Network

An expert's assessment of the GWDG pointed out solutions for the further development of the DPZ, which will be arranged in order to network the new external facilities, currently under construction. At the end of the year 2001 the net lines of the Center were switched to the containers of the Department of Cognitive Neurosciences.

The integrated mail- and internet-server of the DPZ has been running on a Windows system, that is particularly sensitive, as is well known, to all forms of attacks from outside (Hacking, IP spoofing etc.). Therefore, we decided to run both functions on separate Linux servers. On June 2001 the Internet server, which was based on Windows 2000, was shut down. All incoming mails were directed by the GWDG to the new Linux server, so that no mails were lost. The new system offers the possibility to assign pseudonyms, it has a vacation function, permits the creation of mailing lists and an automatic forwarding to other mail addresses. The mail server is accessible from everywhere via Webmail. The old Web server was replaced by a new computer with a time delay of two seconds.

At the end of 2002 the number of computers in the Center amounted to 161. In addition, there were 12 laptops and 4 decentralized computers with specific scientific applications. At present, the net is operated via 8 servers, 5 on NT -, 2 on Linux -, 1 on Novell basis. In the working group of Primate Genetics an additional decentralized Sun station is in use.

## New devices

### *Storage system*

To compensate for a weakness in the central availability of disk space, an 80 gigabyte Snap-server has been integrated into the net. This server has the advantage of being accessible to different operating systems (Windows 9x, NTx, 2000, Unix, OS2, Linux, MacOS). In the long run, this system, which will continuously be improved, will replace the older Novell server.

### *Projector*

In the central lecture hall of the DPZ an LCD projector which only supports a simple VGA mode is permanently installed. Consequently, no high-resolution graphics can be projected. In 2001, an efficient and portable projector with an XGA standard which can also be used in the decentral seminar rooms was acquired. These days, powerpoint presentations are standard techniques for scientific lectures. In order to enable the staff to prepare their presentations decentralized and allow them to be flexible on lecture trips, an additional small projector was purchased, which is available to all staff members. One of the two portable projectors must always be available at the Center.

### *Multimedia station*

A central multimedia station including the appropriate hardware was set up in the reporting period. Several programs are installed on this computer, which allow analog video films to be digitalized, video sequences that were recorded with digital video camera to be cut and to be archived on a server. It is connected to a high resolution slide scanner.

### *Laptop*

The centrally provided hardware for all staff members was supplemented by a second laptop. This became necessary because the number of lectures held with visual support by programs like powerpoint has increased rapidly. Thus, now two devices are available for in-house use and for business trips, whereby one laptop must always remain in the Center.

### *Digital camera*

The hardware available for decentralized use was supplemented by a digital Nikon camera (Coolpix 995). Beside the adapters for tele- and wide-angle objectives as well as an adaptive system for slide digitalisation, this system provides many more features for image processing than the system used so far.

## **DIP working group of the Leibniz Community**

The 2001/2002 meetings of the Leibniz Community's IT working group took place at the Institute for Low-temperature Plasma Physics in Greifswald (INP), at the Hamburger World Economy Archives (HWWA), at the Institute for Troposphere Research in Leipzig (IFT) and at the Scientific Community Gottfried Wilhelm Leibniz (WGL) in Bonn. The following topics were discussed: Central purchase of software by the WGL, characteristic numbers for IT personnel, framework IT concepts, evaluation of IT concepts and equipment by the senate committee of the WGL. The Internet site of the group is available on the www-server of the DPZ (<http://www.dpz.gwdg.de/wbledv/wbledv.htm>). Minutes of the meetings can be downloaded with links and documents for appropriate background information.

## **Library and News services**

In the reporting period, a framework concept for a "Special Library Primatology" was written according to the requirements of a modern library management, which was recommended by the German Research Council (DFG), the supraordinate Scientific Advising Committee of the Federal Republic of Germany (Wissenschaftsrat, WR), the Max-Planck Society (MPG) and the University Rectors' Conference (HRK).

### Library

The organization of the library, the number of its publications and the activities of the library committee were explicitly praised in the assessment of the WR. A petition from the committee was to open the library to the public via internet connection. This has been realized. The library system which had been operated so far by the program "Reference manager" and in Internet by "Web poster Reference" migrated to the program "Bibliotheca 2000" of the Bond Company.

Extensive preliminary work and clearing of the data base were carried out by the new librarian Dr. Stefanie Heiduck, so that the data from the old system could be converted without any problems. New acquisitions are now running directly into a Web OPAC (on-line public access catalogue).

Thus, with the new system, we are in the "state of the art" and have achieved more comfort. Already existing entries in the data base are still being systematized and standardized. With this system, we have also followed the recommendations of the DFG, the WR, and the scientific advisory board of the DPZ to keep the "Special Library Primatology" of the Center available online. The library stock now consists of more than 4200 monographs and series, 71 journals and scientific magazines are subscribed to.

### On-line access

In the reporting period several accesses to on-line journals were subscribed to and an updated collection of links to e-print-servers was provided, see:

<http://www.dpz.gwdg.de/bib/bib/new-access.html>. Under the address:

<http://www.dpz.gwdg.de/bib/bib/journals.htm> a collection of approx. 600 journals is presented, which allow on-line access. These entries are classified as full text, abstracts only etc., with information on their availability as print medium in the vicinity of the

Campus (State and University Library of Lower Saxony Göttingen, Max-Planck-Institute for Experimental Medicine and for Biophysical Chemistry). Each staff member can create his individual portfolio from this collection according to his scientific interests.

The efforts to provide the Center with videos for all aspects of primatological research were taken up again. The stock will be soon made accessible to the public on the library server under the program "Bibliotheca 2000". Over 120 videos are now available in the library for check-out, which inform about research methods, primate species and TV-reports with participation of the DPZ.

#### Use of external news services

DIP/COMM is registered with the discussion forums of "Alloprimates" and "Primate Science (PIC, Seattle)", with the news servers of the "Information Service Science (IDW)", with the German Research Council (DFG), the Federal Ministry for Education and Research (BMBF) and the information service of "Picture of Science (BDW)". The news considered as relevant for the research and for the service of the Center are transmitted to the staff members of the Center via email. In the reporting period, over 250 messages concerned with biology, ecology, medicine, research promotion and research policy were sent out, also to external scientists, who requested subscription to the mailing list.

#### Electronic publications

Documents of the Center, which may be of interest for external users, are available as electronic publications in the Internet. They include the editions of DPZ-aktuell starting from the first edition in 1989, the English version of the annual scientific reports starting from 1997, the information brochures on the departments of the Center, the strategic papers for the development of the DPZ, abstracts of DPZ symposia and the editions of the Lemur News as well as of the Primate Report starting from 2000 (<http://www.dpz.gwdg.de/epub.htm>). With this, we follow a recommendation of the library commission of the DFG (in: "Electronic publications in the literature and information offer of scientific libraries. Library committee. Bonn, June 1995).

Since the middle of 2000, DIP/COMM has been offering the service of placing posters of staff members in pdf-format in the net. In so doing, we wish to appreciate the work invested in poster preparation of scientific results that are usually only published in an abstract volume. Colleagues have long been demanding and do appreciate this service. These posters can be downloaded at

<http://www.dpz.gwdg.de/poster.htm>, classified according to departments and work groups.

### **Internal and external communication**

The scientific advising committee recommended publicizing the DPZ nationally and internationally as a research institute with service function. For this purpose, a long-term concept was developed in 1993, whose individual components have now been completed. In 2001 the framework "internal and external communication" was

completed revised and adapted to the new recommendations of the University Rectors' Conference (HRK), the MPG, the WR and the DFG. Special attention was paid to the recommendation of "opening science to a broad public". On this basis, the concept was supplemented by several further activities within the reporting period.

#### Visits and lectures

In the years 2001/2002, 1600 individuals and 22 groups visited the DPZ with an average of 10 participants per group. Their range of interests is widely spread: Excursions of commercial companies, private groups of seniors and of teachers, various groups from the university, members of parliament of Lower Saxony, working groups of the local town administration, members of groups fighting for animal rights, participants in biomedical congresses at the university, officials of political parties. For all the groups, DIP/COMM organized visits to the Center, lectures and contacts to the scientists.

#### The new scientific generation

For the Göttinger initiative XLAB, whose intention is to introduce experimental scientific research to young pupils, the DPZ has arranged a series of offers, which allows these pupils to become familiar with the methodology of Primatology. As in every year, the DPZ took part in the Göttinger Weeks "Science and Youth". Several school classes from the town and the region visited the DPZ and were informed about our work and research results. Thus, the DPZ contributed to the anchoring of the university town Göttingen in the consciousness of future students. Last but not least, the DPZ is engaged in the initiative "Girls day", which is trying to open up the classic male dominated professions and careers in the realms of physical and natural sciences to our new female generation.

#### Seminars and colloquia

In the years 2001/2002, 34/43 scientists - 26/36 of them were external - presented their current research projects, their final data and their special know-how at DPZ colloquia, seminars and Graduate Colleges. The colloquia primarily serve internal information exchange between the departments and working groups. Additionally, they are publicly announced and find huge interest at the university. Four scientists from Germany and the USA presented their research within a series of lectures on the "Progress of the Primatology" on the occasion of the 25<sup>th</sup> anniversary of the DPZ.

#### The Internet presentation

Since the end of 1995 the DPZ is present in the Internet (<http://www.dpz.gwdg.de>). The homepage provides information about the departments and working groups as well as about the administration and infrastructure, it informs about research activities of the departments and working groups, about the interdisciplinary goals, about projects, and the library and publications etc. Information on how the DPZ is organized and which primate species are held in the center is presented. In order to make the service that the DPZ offers for its external users, and the know-how of the Center more transparent and public pages with the appropriate specifications are provided.

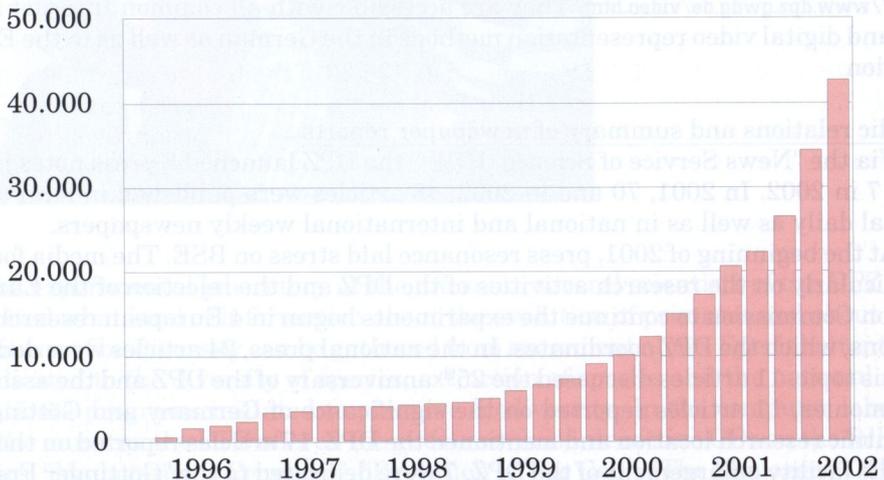
*The reorganization*

In the reporting period a reorganization of the Internet presentation was carried out. The layout of the general pages with frames was abandoned, the main menu was reduced to 11 links relevant for the external representation of the DPZ. The central presentation of the departments was unified to allow resenting of department and work group-specific details in submenus. Participants of an internal discussion forum agreed on a basic standard with a left frame and a right information page, as already realized in the pages of the Departments of Ethology and Ecology as well as Cognitive Neurosciences. In order to explain the structure of such a design to the staff members, DIP/ COMM organized a course, which encountered a high resonance.

*The statistics*

The program "Websuxess" for the evaluation of internet visits provides statistics about the number of virtual visitors and retrieved pages, about time courses sorted by years, months, days and time, about the visits of departmental pages sorted into subdirectories and about the keywords, which led the search engines to the DPZ server. It is possible to identify the virtual visitors, to determine how much importance they focus on which department or working group and - mostly - in which country the visitors are located. From these results the international attention drawn to the DPZ can be derived. These Web statistics of the DPZ are public and can be obtained at <http://www.dpz.gwdg.de/access/index.html>. Herewith, we wish to contribute to the transparency of the international interest aimed at the research and services of the Center.

**Number of visitors to the DPZ-homepage  
(quarterly)**



*The number of virtual visitors to the DPZ's internet pages has exponentially grown from 1995 to now. On average, by the end of 2002 there were 45,150 visitors quarterly. The main interest focussed on the pages of the Department of Ethology and Ecology, followed by the Department of Virology and Immunology.*

The DPZ's internet pages enjoy great popularity. At the end of 2002 more than 17,000 virtual visitors per month were registered. The pages of the Department of Ethology and Ecology are in the top of the charts, followed by the Department of Virology and Immunology, and the Department of Reproductive Biology. The majority of the visitors are from Germany, followed by Great Britain and the USA.

#### *External service*

In accordance with the central role of the DPZ within the European primate breeding and primatological research facilities, the internet pages of EUPREN (European Primate Resources network) were further maintained and updated. The DPZ also presents the pages of the EMRG (European Marmoset Research Group) and complies thereby with its function as reference center. A survey of the primate species and their number held in European zoos and research institutes broken down into males, females and offspring can be obtained under: <http://www.dpz.gwdg.de/infra/census.htm>

#### The DPZ film

The film on the DPZ is now five years old and needs urgent updating in accordance with the recent development of the Center and its research fields. In the reporting period, we began to videotape research work from the Departments of Neurobiology, Ethology and Ecology, Primate Genetics, Reproductive Biology and Virology and Immunology. These sequences will serve as modules for a new video edition.

Within the reorganization of the DPZ's web pages, the presentation of video sequences was also realized: The video "About the DPZ" was cut into sequences and digitised broken down to the specificities of the departments, working groups and functional units. These sequences are accessible in the formats AVI, RM and ASF at <http://www.dpz.gwdg.de/video.htm>. They are accessible with all common Internet browsers and digital video representation methods in the German as well as in the English version.

#### Public relations and summary of newspaper reports

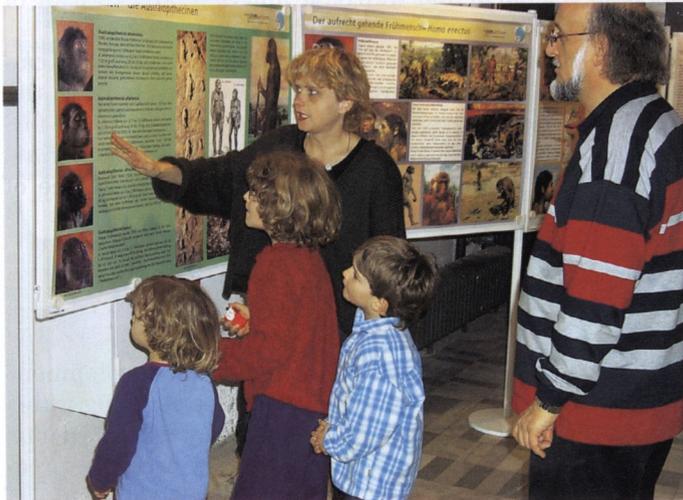
Via the "News Service of Science (IDW)" the DPZ launched 8 press notes in 2001 and 7 in 2002. In 2001, 70 and in 2002, 48 articles were published in local and regional daily as well as in national and international weekly newspapers.

At the beginning of 2001, press resonance laid stress on BSE. The media focussed particularly on the research activities of the DPZ and the rejection of the European Union Commission to continue the experiments begun in 4 European research institutions, which the DPZ coordinates. In the national press, 24 articles were dedicated to this topic. 11 articles discussed the 25<sup>th</sup> anniversary of the DPZ and the associated ceremonies, 11 articles reported on the significance of Germany and Göttingen as scientific research location and mentioned the DPZ. 17 articles reported on the plans for the facility enlargement of the DPZ, 7 were dedicated to the "Göttinger Freiländertag" and 7 to Professor Treue's appointment as new director of the DPZ. However, the summary presented here can only be understood as an incomplete overview. A professional monitoring of all the reports on the DPZ in the press is at present not considered for financial reasons.

In order to document the activities of DIP/COMM. in public relations and their impact on the media, an internet page ([www.dpz.gwdg.de/foerder/zeitung/zeitung.htm](http://www.dpz.gwdg.de/foerder/zeitung/zeitung.htm)) is maintained. On this web page all national and international articles concerning the DPZ which have been published since 1999 can be downloaded in pdf format.

### Exhibition "The Tree of Life"

In 2001, the DPZ together with the Institute for Zoo and Wild Animal Research (IZW), Berlin, organized the action day "The Tree of Life" as part of the series "Life means diversity" at the Senckenbergmuseum (SNG), Frankfurt/Main. The program was organized by Dr. Dr. Michael Schwibbe. The evolution and the biodiversity of mammals, particularly the Primates, was presented in a poster exhibition and several lectures. With the aid of Senckenberg exhibits, graphic and 3-dimensional reconstructions elucidated the evolution of the pre- and early human beings and the evolution of the Neanderthals up to contemporary human beings.



*The visitors to the exhibition at the Senckenbergmuseum became familiar with the topic "The Tree Of Life" by a poster demonstration, a series of lectures, a powerpoint presentation and interactive computer games.*

In the experimental laboratory at the museum, several scientists of the DPZ demonstrated what kind of information about the evolution of primates and about the mechanisms of biodiversity can be gathered from excrement alone. Special attention was dedicated to the diversity of species, extinction of species and the national and international programs initiated to preserve biodiversity. In the computer laboratory of the museum the DPZ offered the guests several interactive CDs on the following topics: "Madagascar's Primates", "Evolution", "The Cell", "The Phylogeny Of Humans". Schwibbe contributed a paper to the "kleine Senckenbergreihe", which covered the topics of the presentations. In addition, a powerpoint presentation was designed, which combines the most relevant items of the evolution of primates with standardised photographs of the skulls of the early human primates.

For the DPZ's 25<sup>th</sup> anniversary, the exhibition was presented in Göttingen in September 2002. On the occasion of "The Year of Geosciences", the exhibition was presented under the theme "Planet Earth" in October in Munich and in November in Dresden. Already for the celebration of 25<sup>th</sup> anniversary of the DPZ the posters were updated and extended by additional themes: "Methods in Palaeoanthropology", "Intermediate Stages of Humans and Animal", "Charles Darwin" and "Missing Links". The exhibition was enriched by reconstructions of hominid skulls from the Anthropological Institute of the University of Göttingen, and for Dresden and Munich from the company SOMSO.

The exhibition in Frankfurt was visited by approx. 10,000 people, that in the Technical University of Munich by approx. 25,000, that at the German Primate Center by approx. 1,000 and that at the World-Trade Center in Dresden by approx. 12,000 people.

Exhibitions are temporally limited events at a certain place. The visitors can talk with each other and discuss the themes with the scientists present only for a restricted time. A new way to present the research to the public is provided by the Internet. It offers a permanent availability of information, allows the visitor to determine the amount of time spent at the particular web page and to repeat viewing of the information as often as necessary.

The posters, the powerpoint presentations and the accompanying documents can be downloaded at <http://www.dpz.gwdg.de/hominiden/start.htm>. Two lectures held at the exhibition in the Senckenbergmuseum are provided on this page in audio/video format. An additional page offers international links on human evolution. All materials provided in the internet, are also available on a CD-ROM, which is sent free of charge to all interested customers.

## **Anniversary "25 years DPZ"**

The KulturKontor Göttingen was asked to summarize the historical development of the Center since the 60ies by studying archive documents and performing interviews with time witnesses. The resulting paper was supplemented by texts from our staff and now represents a comprehensive report of the DPZ's history up to the present day. The manuscript was edited by a working group under the leadership of Heike Klensang, consisting of Professor Treue, the KulturKontor, Karin Peinemann and Ulrike Walbaum, who all corrected and commented on the manuscript. External experts developed a professional layout for the chronicle.

DIP/COMM arranged the program for the anniversary week, in which the DPZ presented itself to the public with experiments, lectures and guided tours. More than 1,000 visitors, 12 school classes and groups took advantage of the offers. Several guests participated in the meetings several times and the second time brought their children and grandchildren, as well as colleagues. We are grateful to Uwe Schönmann for organizing the visits and the flow of the visitors in the experimental stations, which were conducted by the Departments of Neurobiology, Cognitive Neurosciences and Reproductive Biology.



The 25<sup>th</sup> anniversary celebration was mainly held for to the colleagues of the center, but the people of Göttingen interested in the work of the DPZ were more than welcome as well. Numerous people from the scientific community, representatives of Lower Saxony and of the Federal State Government congratulated and praised the achievements of the DPZ in national and international science as well as for the town of Göttingen as a research location: Prof. Hans-Jürg Kuhn as the founding director of the DPZ, Prof. Horst Kern as the president of the University, MinRat Christian Börger as a representative of the Ministry of Science in Hanover (MWK), MinDirig Reinhard Junker from the Federal Ministry for Education and Research (BMBF), Prof. Ulrich Welsch as the chairman of the DPZ's Scientific Advisory Board, Prof. Hans-Olaf Henkel as the president of the Scientific Society Gottfried Wilhelm Leibniz (WGL) and as speaker of the European Primate Resources Network (EUPREN), Dr. Ronald Bontrop from the Netherlands Primate Center. Dr. Reinhard Grunwald brought greetings from the DFG (German Research Council), the largest German research organization, and from his time as an administrative managing director he could report some amusing details from the institute's early history.

The musical entertainment was provided by the well-known Göttinger jazz band "The New Orleans Syncopaters", for the culinary enjoyment a barbecue station was set up in front of the party tent, inside of which the past and the future of the DPZ was discussed until well into the night. The director switched off the light.

## **Publications**

### **Editorials**

GANZHORN, J.U., RAKOTOSAMIMANANA, B., SCHWIBBE, M.H (eds.): The Newsletter of the Madagascar Section of the I.U.C.N./S.S.C. Primate Specialist Group. Lemur News (2001) 6.

GANZHORN, J.U., RAKOTOSAMIMANANA, B., SCHWIBBE, M.H (eds.): The Newsletter of the Madagascar Section of the I.U.C.N./S.S.C. Primate Specialist Group. Lemur News (2002) 7.

KAPPELER, P.M., KNOGGE, C., SCHWIBBE, M. (eds.): 3. Göttinger Freilandtage: Sexual Selection in Primates: Causes, Mechanisms, Consequences. Primate Report (2001) 60-1.

SCHWIBBE, M.H. (ed.): Wissenschaftlicher Jahresbericht 2000. Aus dem Deutschen Primatenzentrum (2001).

SCHWIBBE, M.H. (ed.): Annual Scientific Report 2000 of the German Primate Center. Primate Report (2000) 60.

SCHWIBBE, M.H. (ed.): Infectious Diseases and Animal Models in Primates. Primate Report (2002) 62.

SCHWIBBE, M.H. (ed.): Div. Articles. Primate Report (2002) 63.

SCHWIBBE, M.H., JONES, C.B. (eds.): Sampling Neotropical Primates: Implications for Conservation and Socioecology (2001) 61.

SCHWIBBE, M., SINGH, M., KAUMANN, W., KNOGGE, C. (eds.): Proceedings of the Fifth International Symposium on Lion-tailed Macaque, Mysore, India (Part 2). Primate Report (2001) 59.

SCHWIBBE, M.H., ZIEGLER, T. (eds.): Mixed Species Exhibits in German Zoological Gardens (Part 1). Special References on Primates. Primate Report (2002) 64.

### **DPZ Chronicle**

SCHWIBBE, M.H. (ed.): 25 Jahre DPZ: Deutsches Primatenzentrum 1977-2002. Aus dem Deutschen Primatenzentrum (2002).