

UNIVERSITÄT BERN

DEPARTMENT OF CLINICAL RESEARCH

www.dkf.unibe.ch

# Jahresbericht 2011 Annual Report 2011

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#### Cover:

Cultured HUVEC cells with F-actin (red) and von Willebrand factor in Weibel-Palade bodies and strings (green). Nuclei are stained with DAPI (blue). Weibel-Palade bodies were described for the first time 50 years ago, in 1962, by Prof. E. Weibel at the University of Bern. *Image: Jakob Zbären* 

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# The DCR at a Glance

# Das DKF auf einen Blick

The Department of Clinical Research (DCR) is a research department of the Faculty of Medicine at the University of Bern.

Founded in 1994, its mission is to provide the best possible environment and infrastructure to researchers at the Inselspital, Bern University Hospital and at the Faculty of Medicine. In 2011, 50 independent research groups, covering almost all fields of biomedical research, were affiliated with the DCR.

The main goal of the DCR is to establish a bridge between laboratory-based biomedical and patientoriented clinical research. This is achieved by offering scientific support to its groups and by operating stateof-the-art Technology Core Facilities and specialised Animal Core Facilities. Das Departement Klinische Forschung (DKF) ist ein Forschungsdepartement der Medizinischen Fakultät der Universität Bern.

Es wurde 1994 mit dem Auftrag gegründet, Forschenden vom Inselspital, Universitätsspital Bern und von der Medizinischen Fakultät eine optimale Infrastruktur zur Verfügung zu stellen. 2011 waren 50 unabhängige Forschungsgruppen dem DKF angeschlossen, die zusammen fast alle Bereiche der biomedizinischen Forschung abdecken.

Das DKF hat sich zum Ziel gesetzt, Brücken zu schlagen zwischen laborbasierter biomedizinischer und patientenorientierter klinischer Forschung. Dieses wird erreicht durch die wissenschaftliche Unterstützung der Forschungsgruppen, sowie den Betrieb von, dem neusten Stand der Technik entsprechenden, Technologie Core Facilities und spezialisierten Tier Core Facilities.



# Foreword – Director's Report

Dear readers and colleagues,

You have in front of you the 2011 Annual Report of the Department of Clinical Research (DCR) at the University of Bern. This is the second report of this kind. Based on the positive feedback on the 2010 edition, I am convinced that you will again find useful information about the activities of our department.

2011 was another busy year for the DCR, with many positive developments. We are still in a growing phase, which is clearly a very good sign! This year, two additional groups became affiliated with the DCR: one from the University Clinic for Cardiology, headed by Prof. Dr. Yves Allemann and Prof. Dr. Urs Scherrer, and another from the University Clinic for Nuclear Medicine, headed by Prof. Dr. Thomas Krause and PD Dr. Martin A. Walter. We warmly welcome them to the DCR and wish them success in their research.

During 2011, eight DCR groups moved to the new Murtenstrasse 50 (Mu50) building, built by the Inselspital Stiftung. These groups are located on two floors, while the other two floors are home to the ARTORG groups. We are glad to see that collaborations between the groups in Mu50 are increasing, and we strongly support further initiatives in this direction. It is clear that these new laboratories have brought some relief to the chronic issue of limited space at the DCR.

Very positive is also the first full year of operation of the Clean Mouse Facility (CMF). The CMF has already delivered hundreds of mice to researchers at the University of Bern and external users, permitting publications in *Science* and *Nature*! In addition, the CMF has been a key asset in the award of prestigious ERC starting grants and SNSF grants. It is clear that the benefit to our faculty is outstanding. The University of Bern has in the CMF a unique facility and it is our aim to run it in a sustainable way for the years to come.

With regard to animal facilities, it is also worth mentioning that our breeding and experimental facilities, the Central Animal Facilities, have now reached excellent hygiene status. However, they face severe space limitations and many of the users of these facilities have to strongly limit their usage. Unfortunately, we have thus far no other realistic option than to wait for the building of new facilities.

Another significant development was the creation of a Genomics Core Facility (www.gcf.dkf.unibe.ch) in July 2011, headed by Prof. Rolf Jaggi. The main task of this facility is to support the planning, preparation of samples and analysis of data of "next generation sequencing" (NGS) projects within the Faculty of Medicine. Thanks to a R'Equip grant from the SNSF, and the collaboration between the Vetsuisse and Phil.-nat. Faculties and the Faculty of Medicine, a NGS platform was created at the University of Bern (www.ngs. unibe.ch). The DCR Genomics Core Facility is there to give you scientific and technical support for your projects of this kind.

Another DCR Core Facility was very successful in 2011. The Mass Spectrometry and Proteomics Laboratory (www.pmscf.dkf.unibe.ch) headed by PD Dr. Manfred Heller provided outstanding services for researchers at the University of Bern. It is also noteworthy that the SNSF has again granted a R'Equip proposal for the acquisition of new equipment, which will allow the facility to be even more efficient and provide results with higher information content.

On another note, we also introduced new statutes in 2011, allowing a



clearer description of the tasks of the DCR and its collaboration with its Board (Kuratorium). This has worked very well! Prof. Dr. Willy Hofstetter was nominated as the DCR Deputy Director and is mainly responsible for facility management and finances.

Before concluding, I would like to remind you that for many years now, on the first Monday of the month, the DCR has held well-attended Research Conferences with outstanding speakers. We have just celebrated the 50th Research Conference. Another less well-known role of the DCR is to promote the career of young scientists. In 2011, 23 students obtained their doctoral degrees in DCR groups; an important achievement for us. For more information about graduations and awards, please see page 46.

Finally, I would like to sincerely thank all the DCR employees and all of you for your constructive spirit and outstanding work for the Department and the research community at the University of Bern.

Prof. Dr. Hugues Abriel, MD PhD

# Vorwort – Bericht des Direktors

Liebe Leserinnen und Leser Liebe Kolleginnen und Kollegen

Der vor Ihnen liegende Jahresbericht 2011 des Departements Klinische Forschung (DKF) der Universität Bern, präsentiert sich bereits zum zweiten Mal in dieser Aufmachung. Aufgrund der positiven Rückmeldungen zum Bericht 2010 bin ich überzeugt, dass Sie darin auch dieses Jahr wieder viele Informationen zu den Forschungsaktivitäten in unserem Departement finden werden.

2011 war für das DKF wieder ein geschäftiges Jahr, mit vielen positiven Entwicklungen. Wir sind immer noch in einer Wachstumsphase, dies ist eindeutig ein sehr gutes Zeichen! In diesem Jahr wurden dem DKF zwei weitere Forschungsgruppen angegliedert: eine aus der Universitätsklinik für Kardiologie unter der Leitung von Prof. Dr. Yves Allemann und Prof. Dr. Urs Scherrer, die andere aus der Universitätsklinik für Nuklearmedizin unter der Leitung von Prof. Dr. Thomas Krause und PD Dr. Martin A. Walter. Wir heissen alle herzlich im DKF willkommen und wünschen eine erfolgreiche Forschungstätigkeit!

Acht Forschungsgruppen des DKF sind im 2011 in das neue, unter der Bauherrschaft der Inselspital Stiftung entstandene Gebäude, an der Murtenstrasse 50 (Mu50) umgezogen. Diese Gruppen sind auf zwei Stockwerken untergebracht und die ARTORG Gruppen auf zwei weiteren Stockwerken beheimatet. Wir freuen uns, dass die Zusammenarbeit zwischen den Gruppen in der Mu50 ständig wächst und unterstützen Schritte in dieser Richtung mit Nachdruck. Es ist offenkundig, dass diese zusätzlichen Raumflächen zu einer gewissen Entspannung des chronischen Platzmangels im DKF geführt haben.

Das erste ganze Betriebsjahr der Clean Mouse Facility (CMF) ist sehr positiv ausgefallen. Die CMF hat bereits Hunderte von Mäusen an Forschende der Universität Bern und externe Kunden geliefert und Publikationen in *Science* und *Nature* ermöglicht! Zusätzlich hat die CMF eine wichtige Rolle bei der Vergabe von renommierten ERC Starting Grants und SNF Grants gespielt. Zweifelsohne ist der Nutzen für unsere Fakultät hervorragend. Die Universität Bern hat mit der CMF eine einzigartige Einrichtung, und es ist unser Ziel, diese in den kommenden Jahren nachhaltig zu führen.

In Bezug auf die Tierhaltung möchte ich erwähnen, dass unsere Einrichtung für Zucht und Forschung, die Zentralen Tierställe, einen ausgezeichneten Hygiene-Status erreicht hat. Jedoch gibt es ernsthafte Kapazitätsprobleme, was von vielen Benutzern eine starke Einschränkung in der Nutzung erfordert. Leider haben wir bis jetzt keine andere, realistische Wahl, als auf den Bau neuer Einheiten zu warten.

Eine weitere wichtige Entwicklung war die Schaffung einer Genomics Core Facility im Juli 2011, geleitet von Prof. Dr. Rolf Jaggi (www.gcf. dkf.unibe.ch). Die Hauptaufgabe dieser Einrichtung besteht darin, die Planung und Vorbereitung von Proben sowie die Analyse von Daten von "Next Generation Sequencing" (NGS) von Projekten innerhalb der Medizinischen Fakultät zu unterstützen. Dank einem R'Equip Grant des SNF und der Zusammenarbeit zwischen der Vetsuisse, Phil.- nat. und Medizinischen Fakultät, konnte an der Universität Bern eine NGS Plattform geschaffen werden (www. ngs.unibe.ch). Die DKF Genomics Core Facility bietet Ihnen wissenschaftliche und technische Unterstützung für Projekte dieser Art.

Eine weitere Core Facility des DKF kann auf ein erfolgreiches 2011 zurückblicken. Das Massenspektrometrie- und Proteomics-Labor (www.pmscf.dkf.unibe.ch), unter der Leitung von PD Dr. Manfred Heller, stellte seine hervorragenden Dienste den Forschenden der Universität Bern zur Verfügung. Erwähnenswert ist, dass der SNF erneut ein R'Equip Gesuch für den Erwerb neuer Geräte bewilligt hat. Dies erlaubt der Einrichtung noch effizienter zu arbeiten und präzisere Resultate zu liefern.

Des Weiteren führten wir neue Statuten ein, mit einem genauen Beschrieb der Aufgaben des DKF und dessen Zusammenarbeit mit dem Kuratorium DKF. Das hat sehr gut geklappt! Prof. Dr. Willy Hofstetter wurde zum stellvertretenden Direktor DKF ernannt. Er ist hauptsächlich verantwortlich für das Facility Management und die Finanzen.

Bevor ich schliesse, möchte ich Sie daran erinnern, dass das DKF seit vielen Jahren, jeweils am ersten Montag des Monats, eine gut besuchte DKF Research Conference mit ausgezeichneten Referenten organisiert. Wir durften kürzlich die 50. DKF Research Conference feiern. Eine andere, weniger bekannte Aufgabe des DKF, ist die Karriereförderung von jungen Wissenschaftlern. Im 2011 wurde an 23 Studenten in DKF Forschungsgruppen der Doktortitel verliehen, eine wichtige Leistung für uns. Mehr Informationen zu den Graduierungen und Auszeichnungen auf Seite 46.

Abschliessend möchte ich allen DKF Mitarbeitenden und Ihnen allen herzlich danken für den Konstruktiven Geist sowie die hervorragende Arbeit, die Sie fürs DKF und die Forschergemeinschaft an der Universität Bern leisten.

Prof. Dr. Hugues Abriel, MD PhD

# Organisation

The role of the DCR is to provide optimal infrastructure and scientific support to its research groups, of which there were 50 at the end of 2011. The vast majority (41) of these groups are from clinics of the Inselspital, Bern University Hospital. The remainder (9) are internal DCR groups, involved in the scientific support and coordination of equipment and infrastructure on a daily basis. The 50 groups are divided into 6 Research Divisions. Equally important, the DCR is responsible for operating Technology and Animal Core Facilities. Furthermore, the groups of the department are supported by central services responsible for administration, informatics and technical support. In 2011, the DCR revised its organisation and statutes, and new departmental rules and regulations (Departementsreglement) are now in force. In the new organisational structure, the core activities are more clearly defined. The DCR Directorate now comprises the Director and a Deputy Director. Another important change was to clarify the responsibilities of the Board of Trustees (Kuratorium). In addition to its role in overseeing DCR strategy, it is now involved in the decision-making process for resource distribution to the DCR groups.

This year, the Board of Trustees also appointed four members to the new External Advisory Board (see below), whose task will be to evaluate the overall strategies and operation of the DCR.

# **External Advisory Board**



#### Prof. Dr. Gisou van der Goot

Professor and Co-Founder, Global Health Institute, Swiss Federal Institute of Technology Lausanne since 2006.

Background: Trained in Engineering at the Ecole Centrale Paris, France; PhD in molecular biophysics at the French Nuclear Research Center, degree from Paris VI University;

postdoc in the European Molecular Biology Laboratory, Heidelberg, Germany; independent group at the Department of Biochemistry, University of Geneva; Associate Professor at University of Geneva Medical School in 2001.

*Research interests*: Interaction of bacterial toxins with host cells, molecular mechanisms of a rare genetic disease due to mutations in anthrax toxin receptor 2.



#### Prof. Dr. Karl Schaller

Professor and Chair, Department of Neurosurgery, Geneva University Medical Center and Faculty of Medicine since 2007; Chair, Membership Committee of the European Association of Neurosurgical Associations.

Background: Trained at the University of Tübingen, Germany; post-

graduate work in academic neurosurgery in Duisburg and Bonn, Germany; funding for the development of intraoperative imaging technology, co-registration of complementary imaging modalities, and clinical neurovascular research.

Surgical and basic research interests: Neurovascular surgery, treatment of epilepsy, surgery of brain tumours.



#### Prof. Dr. Paul Klenerman

Wellcome Trust Research Fellow at the University of Oxford, UK since 1992.

Background: Trained in medicine at the Universities of Cambridge and Oxford, UK; PhD on HIV and T cell escape with Andrew McMichael and Rodney Phillips, Oxford University; postdoc on LCMV T cell

responses under the supervision of Rolf Zinkernagel and Hans Hengartner, University of Zurich; returned to Oxford to work on HCV and persistent viruses.

*Clinical and basic research interests*: Infectious diseases and virology, HCV pathogenesis and vaccines, other persistent viruses such as HIV and CMV.



#### Prof. Dr. Radek Skoda

Professor of Molecular Medicine and Head, Department of Biomedicine, University of Basel since 2002.

Background: Studied medicine at the University of Zurich; trained in internal medicine and haematology at University Hospital Basel; postdoc at the Biozentrum, University of Basel; moved to Department of

Genetics, Harvard Medical School, USA; SNF SCORE Fellow and Head, Molecular Hematology-Oncology Department, German Cancer Research Center, Heidelberg, Germany.

*Research interests*: Molecular pathogenesis of chronic leukaemias, genetic analysis of familial myeloproliferative disorders.





M.E. Müller-Haus Murtenstrasse 35

4



Pavillon 52 Freiburgstrasse 3



Sahli-Haus 2 Freiburgstrasse 14



Murtenstrasse 50

5

8



Kinderklinik Freiburgstrasse 15



Augenklinik Freiburgstrasse 8



Pathologie Murtenstrasse 31

6



Sahli-Haus 1 Freiburgstrasse 14a



Tiefenau Tiefenaustrasse 120c



# **Key People**

# DCR Board of Trustees



Prof. Dr. Christoph Müller Chair

# Directorate



**Prof. Dr. Hugues Abriel** Director



Members

Prof. Dr. Daniel Candinas

Prof. Dr. Sabina Gallati

Prof. Dr. Christian Hess

Prof. Dr. Lutz-Peter Nolte

Prof. Dr. Hans-Uwe Simon

Prof. Dr. Matthias Egger (until Aug.)

Prof. Dr. Peter Jüni (since Sep.)

**Prof. Dr. Willy Hofstetter** Deputy Director

# Directorate Staff and Administration



Bernhard Grossniklaus Management Support and Facility Manager



Verena Frazao Secretary of Director



Véronique Kretschmer Administrator

#### Ex Officio

Prof. Dr. Hugues Abriel Prof. Dr. Marcel Egger Prof. Dr. Peter Eggli Prof. Dr. Matthias Gugger Prof. Dr. Adrian Lussi (until Aug.) Prof. Dr. Anton Sculean (since Sep.) Prof. Dr. Andreas Stuck Marianne Thormann

# Coordinators of Research Divisions



Prof. Dr. Anne-Catherine Andres Tiefenau



**Prof. Dr. Chris Boesch** Pavillon 52



**PD Dr. Manfred Heller** Kinderklinik



Prof. Dr. Willy Hofstetter M.E. Müller-Haus



**Prof. Dr. Rolf Jaggi** Pathologie, Sahli-Haus 1+2



Prof. Dr. Robert Rieben Murtenstrasse 50, Augenklinik

# Heads of Technology Core Facilities



**PD Dr. Manfred Heller** Mass Spectrometry and Proteomics Laboratory



Prof. Dr. Rolf Jaggi Genomics



Dr. Stefan Müller Cytometry Laboratory



**Prof. Dr. Shida Yousefi** Confocal Microscopy

# Cytometry Laboratory www.facslab.unibe.ch

# Achievements 2011

We had a very successful first year with the new state-of-the-art highspeed BD FACS ARIA III cell sorter. Furthermore, the sort form available from our homepage proved very useful for our operators and, to our knowledge, was well received by our users. By the end of 2011, Claudio Vallan had also thoroughly tested the new server-login-system, which he installed for all FACS analysers (except the FACScan). Besides facilitating and "harmonising" billing processes and statistical usage evaluations, this will eventually allow us to provide easier access to the facility out of hours.

We again offered a FACS course this year. In the interest of longer-term planning of the FACS core facility, we organised two seminars with companies providing cytometers and add-on equipment. There is great potential to improve cytometric analyses with regard to methodological versatility, as well as cost and time efficiency.

### **Performance Report**

In 2011, the newer FACS analysers (LSR II SORP and FACS Array) were more heavily used (+42% and +30.5%, respectively) compared to 2010. Sorting increased by 15%, which could be handled thanks to the availability of two cell sorters. In summary, the FACS core facility experienced an increase in total instrument hours of almost 20%.

### Finances

The revenue generated by user fees increased by 14% for quarter (Q) 4 2010 through Q3 2011, compared to the same period the previous year. In addition, equipment maintenance costs were markedly lower in 2011 compared to 2010. However, the FlowJo software site license for 2011, and retroactively also for 2010, has now been charged to our account. Therefore, the net balance for 2011 was negative by almost CHF 7,000.

# Outlook 2012

The server-login-system will be fully introduced as soon as all our staff and users feel comfortable with it. As an indirect consequence, the outof-hours access to the FACS lab will be simplified by providing the necessary keys within the MEM building.

For 2012, we have again planned a FACS course. It is scheduled for April (part 1) and May (part 2). The exact dates can be found on our website, together with a detailed course program and instructions for registration. After successful negotiation with the Graduate School for Cellular and Biomedical Sciences, we can now offer 2 ECTS points to participants of the whole course.

As a core facility, it is our aim to provide top and up-to-date services. Therefore, we hope to purchase a novel kind of cytometer, which would significantly expand our methodological possibilities.



Dr. Stefan Müller stefan.mueller@dkf.unibe.ch

Studies in microbiology at the University of Bern; PhD in 1996. Postdoc in intestinal mucosal immunology at the University of Bristol, UK in 2000/2001; Head, Flow Cytometry Laboratory, School of Cellular and Molecular Medicine in Bristol 2001. Since 2004, Senior Scientist in Gastroenterology at the DCR; Head, Flow Cytometry Core Facility since 2010. Main interests: Immunoreactivity against yeast in Crohn's disease, host-commensal/pathogen interaction at the intestinal mucosa.

### **Staff Members**

Dr. Stefan Müller, Head Dr. Claudio Vallan, Scientific and Educational Support Sabine Schneider, Laboratory Technician Bernadette Wider, Laboratory Technician



# Confocal Microscopy www.pki.unibe.ch/content/confocal\_microscopy

# Achievements 2011

The service team of the Institute of Pharmacology trained more than 50 scientists at the University of Bern on how to apply confocal microscopy and imaging techniques to their specific scientific projects. At least five original articles were published in which the authors used our facility to produce state-of-theart images.

# Performance Report

Thirty-one different research groups from the DCR and/or Inselspital clinics used the confocal microscope "LSM 5 Exciter". The confocal microscope was used for a total of 997 hours.

Again this year, we organised a biannual two-day practical course for PhD and MD students, and technicians. These courses provide beginners with a basic knowledge of fluorescent staining techniques, and of working with confocal microscope and imaging software. Overall, we trained more than 32 scientists in these courses.

Twenty-four different laboratories received support and licences for Imaris software. Dr. Shida Yousefi was responsible for updating and maintaining the floating licences, as well as providing technical support to users.

In terms of personnel resources, Dr. Yousefi was the main person responsible for introducing the confocal microscope and the imaging analysis software (Imaris and Huygens) to new users. Two additional members of Prof. Dr. Hans-Uwe Simon's group, namely Zhaoyue He and Dr. Sébastien Conus, were responsible for training.

# Finances

User fees of CHF 11,442 were collected by the Confocal Microscopy Core Facility. Disbursements included CHF 5,000 for consumables, CHF 1,500 for course expenses and CHF 19,771 for Imaris maintenance. The latter sum includes multiple groups outside the Faculty of Medicine. In addition, the DCR paid a maintenance flat fee of CHF 6,550 and CHF 4,953 for repair of the confocal microscope.

# Outlook 2012

The first part of the biannual practical course mentioned above will take place 17-18 April 2012. In 2012, the DCR plans to relocate the Confocal Microscopy Facility to Murtenstrasse 50. Dr. Fabian Blank will then be responsible for the service.



Prof. Dr. Shida Yousefi shida.yousefi@pki.unibe.ch

PhD at the University of Zurich in 1996. Postdocs at the University of Toronto General Hospital, Canada and Novartis Research Centre, Horsham, UK. Since 2000, Principal Investigator, Institute of Pharmacology, University of Bern. Since 2002, Head, Confocal Microscopy Core Facility, located at the Institute of Pharmacology.

### **Staff Members**

Prof. Dr. Shida Yousefi, Head Dr. Sébastien Conus, Research Associate Evelyne Kozlowski, Laboratory Technician Zhaoyue He, PhD Student



# Genomics (Core Facility) www.gcf.dkf.unibe.ch Molecular Biology (Research Group) www.molbiol.dkf.unibe.ch



# Research Highlights 2011 / Outlook 2012

Our group is interested in estrogen receptor-positive breast cancer and mechanisms of inhibition by antihormone treatment with tamoxifen or letrozol. Unfortunately, more than 20% of these tumours develop a local or distant recurrence despite treatment with either drug. Apparently, some patients treated with tamoxifen might have benefited from letrozol and vice versa.

Although it is well known that a large proportion of receptor-positive breast cancers contain tumour cells that do not express the oestrogen receptor, the role of these receptor-deficient tumour cells is not understood. We plan to separate oestrogen receptor-deficient and receptor-containing cells from individual tumours, characterise their RNA and DNA, and study the impact of both cell types on the outcome of the patient. We will search for criteria that differentiate between patients who need long-term treatment and those who do well without it. Ideally, the results will contribute to a more adequate treatment of patients.

### **Group Members**

Prof. Dr. Rolf Jaggi rolf.jaggi@dkf.unibe.ch

ised medicine.

Prof. Dr. Rolf Jaggi, Group Leader Dr. Stefan Wyder, Bioinformatician Anna Baltzer, Lab Technician (Jan.) Muriel Fragnière, Lab Technician (since July) Isabelle Minder, Lab Technician (until May) Daniel Muellener, Data Manager, Tumorbank Bern Schindler Matthias, MSc Student (since Aug.)

Next generation sequencing is a novel area of research with great promises for clinical applications, e.g., diagnosis and also therapy. Our research group set up a Genomics Core Facility and members of the group will provide experimental and technical support, and bioinformatics assistance to researchers at the Faculty of Medicine.

# Collaborators

Aebi S, Luzerner Kantonsspital, Switzerland Bubendorf L, University of Basel, Switzerland Cathomas R, Kantonspital Graubünden, Switzerland Gautschi O, Luzerner Kantonsspital, Switzerland Kammler R, International Breast Cancer Study Group, Switzerland Kristiansen G, University of Bonn, Germany Krupp G, AmpTech, Germany Pestalozzi B, Zurich, Switzerland Regan M, Dana-Farber Cancer Institute, USA Rothschild S, University of Bern, Switzerland Schäfer S, University of Bern, Switzerland Simeon-Dubach D, Biobank-Suisse, Switzerland

Viale G, European Institute of Oncology, Italy Warth R, Biobank-Suisse, Switzerland

### Grants

Studies in cell biology; PhD in 1982. Postdoc 1984-1986 and Group Leader 1986-1988 at the Ludwig Institute for Cancer Research, Bern. Research Assistant at the Institute of Clinical and Experimental Cancer Research, University of Bern 1988. Research stays and collaboration with Prof. Finian Martin, University College Dublin, Ireland 1989-1992. Since 1998, DCR Group Leader; Head of Genomics Core Facility since 2011. Research interests: Molecular biology of breast and prostate cancer, novel technologies and personal-

#### Amounts allocated for 2011:

Swiss Cancer League: Molecular profiling from archival human breast cancer samples (R. Jaggi) CHF 120,000

Swiss Cancer League: Identification of a clinically applicable prognostic RNA signature of Prostate Cancer (R. Jaggi, G. Kristiansen) CHF 85,600

W.+H. Berger-Janser Foundation: Characterization of ER-negative cancer cells in ER-positive breast cancer (R. Jaggi) CHF 70,000

# **Teaching Activities**

- Matthias Schindler: MSc
- Elective module: Molecular biology
- 1st-year medical students: Problem
- Based Learning
- Omics: Lecture on disease profiling - Selected topics in molecular pathology: Lecture on molecular processes of disease

# Publications

PRO\_10 - A new tissue-based prognostic multigene marker in patients with early estrogen-receptor positive breast cancer. Moor, AE; Guevara, C; Altermatt, HJ; Warth, R; Jaggi, R; Aebi, S (2011) in: Pathobiology 78(3), p. 140-148 (doi: 10.1159/000323809).

Sequence capture and next-generation resequencing of multiple tagged nucleic acid samples for urea cycle disorder mutation screening. Amstutz, U; Andrey-Zürcher, G; Suciu, D; Jaggi, R; Häberle, J; Largiadèr, CR (2011) in: Clin Chem 57(1), p. 102-111.

KPNA2 Expression is an Independent Adverse Predictor of Biochemical Recurrence after Radical Prostatectomy. Mortezavi, A; Hermanns, T; Seifert, HH; Baumgartner, MK; Provenzano, M; Sulser, T; Burger, M; Montani, M; Ikenberg, K; Hofstädter, F; Hartmann, A; Jaggi, R; Moch, H; Kristiansen, G; Wild PJ (2011) in: Clin Cancer Res 17(5), p. 1111-1121.

The homeobox gene HLXB9 is upregulated in a morphological subset of poorly differentiated hepatocellular carcinoma. Wilkens, L; Jaggi, R; Hammer, C; Giger, O; Mueller, D; Inderbitzin, D; von Neuhof, N (2011) in: Virchows Arch 458(6), p. 697-708.



# Mass Spectrometry and Proteomics Laboratory (Core Facility) Protein and Cell Biology (Research Group) www.pmscf.dkf.unibe.ch



### Staff Members

PD Dr. Manfred Heller, Head Dr. Niurka Meneses Moreno, Postdoctoral Fellow Sophie Braga-Lagache, Laboratory Technician (Core Facility) Natasha Buchs Tetkovic, Laboratory Technician (Research Group)

PD Dr. Manfred Heller (manfred.heller@dkf.unibe.ch) PhD in Chemistry/Biochemistry from the University of Bern in 1994. Postdocs abroad with Prof. Dr. Ruedi Aebersold and Prof. Dr. Denis Hochstrasser. Return to Switzerland in 1999. Three years as Senior Scientist at GeneProt Inc., Geneva working on large-scale proteomics projects using LC-MS2, MALDI-MS and robotics. Since 2003, Head, Mass Spectrometry and Proteomics Laboratory, a DCR Core Facility since 2008. Fourteen years' experience in the use of mass spectrometry for protein analytics and bioinformatics.

# Achievements 2011

Our single instrument LC-MS platform was under big demand in 2011. For the first time, we analysed labelled protein samples (SILAC) for accurate relative guantification of proteins from trypanosoma brucei in three different life stages (collaboration with T. Ochsenreiter, Institute of Cell Biology). We installed a new server for automated data processing and backup, as well as new LC-MS/MS interpretation software, in order to cope with the increased workload and the many different data interpretation and validation challenges (e.g., SILAC samples).

We developed a very simple sample preparation protocol for the proteome analysis of conditioned cell media and applied it in a project of T. Geiser's group (Pulmonary Medicine (Adults)), and in differentially shear-stress-activated HUVEC cells (own project). Furthermore, we determined the proteome of microparticles isolated from clinical blood samples of patients treated with external counter pulsation (collaboration with C. Seiler, Cardiology, Inselspital). All these data are under evaluation and will be used to prepare publications. A research article from I. Roditi's group (Institute of Cell Biology), on which we collaborated, was published and several manuscripts are in the pipeline (Roditi and Ochsenreiter groups).

At the start of the year, Dr. Niurka Meneses Moreno, last year's Visiting Scientist, joined our group as a NCCR TransCure Postdoctoral Fellow. She is involved with the characterisation of plasma membrane channel and transport proteins, and has developed protocols for enrichment of plasma membranes and plasma membrane protein complexes. In April, we strengthened our team with the employment of Sophie Braga-Lagache, who is responsible for instrument maintenance and analysis of customer samples.

# Performance Report

Mass Spectrometry and Proteomics Several instances of a damaged autosampler injection valve imposed shutdowns of operation with corresponding delays in sample analyses. We finally resolved a long-standing issue with unstable mass calibration on the orbitrap MS by exchanging the central electrode pulser. In 2011, we performed and billed approx. 440 service jobs.

### Finances

Mass Spectrometry and Proteomics The Faculty of Medicine Resources Committee granted a total of CHF 10,000 to cover the facility's running costs. Despite the necessary repairs, we were able to keep maintenance costs at a lower level than last year. Moreover, revenue for conducted services was almost double in comparison. In summary, we had an extremely busy and successful year that put our facility on a sound financial basis.

# Outlook 2012

In 2012, the floors housing the DCR laboratories in the Children's Hospital will be refurbished. Our laboratory will move to a temporary location within the building in March and back at the beginning of 2013. We will evaluate new LC-MS instrumentation that we intend to purchase in the second half of 2012, made possible due to a successful SNF R'Equip grant application in 2011. The new equipment is urgently needed as backup and to shorten turn-around times for analysis requests.

# Grants

#### Amounts allocated for 2011:

Protein and Cell Biology SNF: NCCR TransCure sub-project: Physiology, pharmacology and pathophysiology of the calciumactivated non-selective cation TRPM4 channel (M. Hediger, H. Abriel, M. Heller) CHF 84,000

### **Teaching Activities**

#### - Ali Al Kaabi: PhD

- 1st-year medical students, block 4&5: Problem Based Learning, Tutor - Proteomics lectures: Tumour biology (Faculty of Medicine, Biomedical Engineering), Omics (Phil. nat. Faculty)



# Bone Biology & Orthopaedic Research www.bonebiology.dkf.unibe.ch



# Research Highlights 2011 / Outlook 2012

Bone Biology & Orthopaedic Research Highlights of our research on bone cell biology, inflammatory diseases and molecular transport systems include:

Inflammatory cytokines like TNF $\alpha$  and IL17 were demonstrated to attenuate osteoclast development through the release of GM-CSF (PhD thesis Elvis Atanga, Deepak Balani).

Within the NCCR "TransCure", we are investigating the roles of TRPV6 and NHA2 in bone metabolism, and the possibility to exploit the glutamate transporter systems as targets for the anabolic regulation of bone (PhD thesis Wenjie Xie).

A bioreactor was developed, allowing an investigation of the effects of complex mechanical loading protocols on constructs of chondrocyte lineage cells and artificial scaffolds (Rainer Egli, PhD thesis, Adel Tekari).

In 2012, a PhD student will commence a project on nanofibrecalcium phosphate composite bone substitute materials within NRP64.

Osteoarthritis Research Highlights of our research on cartilage biology and degeneration, and

# **Group Members**

Bone Biology & Orthopaedic Research Group: Prof. Dr. Willy Hofstetter, Group Leader Dr. Rainer Egli, Senior Scientist Silvia Dolder, Laboratory Technician Mark Siegrist, Laboratory Technician Deepak Balani, PhD Student John Choy, PhD Student (since May) Adel Tekari, PhD Student Wenjie Xie, PhD Student (since May) Osteoarthritis Research Group: PD Dr. Dobrila Nesic, Project Leader Dr. Jose Diaz Romero, Senior Postdoctoral Fellow Dr. Aurélie Quintin, Research Assistant Dr. Michael Schär, Research Assistant Dr. Markus Wilke, Research Assistant

Clinicians with projects in the group: Dr. Christoph Albers, Clinical Research Associate Dr. Frank Klenke, Clinical Research Associate

Prof. Dr. Willy Hofstetter hofstetter@dkf.unibe.ch

MSc in Biochemistry at Swiss Federal Institute of Technology (ETH) Zurich; PhD in Biochemistry (supervisor Prof. N. Herschkowitz) at the Children's Hospital of the Inselspital. Postdoc at the University of Georgia, USA. Joined the Institute of Pathophysiology, University of Bern. Since 1997, Head, Bone Biology & Orthopaedic Research Group, DCR.

imaging techniques to assess osteoarthritic changes include:

A FACS protocol was developed for accurate assessment of \$100 expression in chondrocytes in vitro. In 2012, the biological roles of \$100 proteins in chondrogenesis will be studied.

Combining contrasting agents with microCT, animal models were used to assess osteoarthritic changes in intact knee joints.

The properties of leukocyte- and platelet-rich fibrin are being investigated for eventual use in clinical treatment of tears in the red-white zone of the meniscus.

# Collaborators

Aeberli D, Inselspital, Switzerland Fuster D, Inselspital, Switzerland Imwinkelried T, Synthes, Switzerland

Koller B, Scanco Medical AG, Switzerland

**Loughlin J**, University of Newcastle, UK

Luginbuehl R, RMS Foundation, Switzerland

Müller R, ETH Zurich, Switzerland Schäfer B, Geistlich Pharma AG, Switzerland

Seitz M, Inselspital, Switzerland

Siebenrock KA, Inselspital, Switzerland

Stok K, ETH Zurich, Switzerland Wilkinson M, University of Sheffield, UK

**Zulliger M**, Scanco Medical AG, Switzerland

Zumstein M, Inselspital, Switzerland Zwerina J, Technical University Dresden, Germany

### Grants

#### Amounts allocated for 2011:

Bone Biology & Orthopaedic Research SNF: NCCR TransCure sub-project: Role of ion transporter TRPV6 and other transporters in bone homeostasis (M. Hediger, W. Hofsettter) CHF 70,000

SNF: Osteoclastogenesis and chronic inflammatory rheumatic disorders, (M. Seitz, D. Aeberli, W. Hofstetter) CHF 60,000

SNF: NFP64 – Nanofibres reinforced bone substitute materials: Effect of delayed fibre degradation on cells and tissues (R. Luginbuehl, K. Maniura, W. Hofstetter)

SNF: Biofunctionalization of β-Tricalcium Phosphate Ceramics for the Repair of Osseous Defects (F. Klenke, W. Hofstetter) ITI Foundation: Functionalization of CaP bone substitutes with growth factors (F. Klenke, W. Hofstetter)

RMS: Cartilage Tissue Formation of Cells Seeded on Structured Scaffolds in Physiological Conditions (W. Hofstetter) CHF 60,000

Osteoarthritis Research RMS: The effect of Leukocyte- and Platelet-Rich Fibrin (L-PRF), Leukocyte- and Platelet-Rich Plasma (L-PRP) and blood clot on the migration of fibroblast and endothelial cells: an in vitro study (M. Zumstein, M. Schär, D. Nesic) CHF18,000

KTI 9853.1 PFLS-LS: Comprehensive morphological characterization of arthritis in animal models by microCT – innovative biomarkers for assessment of arthritic cartilage and bone (D. Nesic, R. Mueller, B. Koller) CHF 109,987

# **Teaching Activities**

- Elvis A. Atanga: PhD

- Thomas de Bruyne: MSc Biomedical Engineering
- Masters course in biomedical engineering: Tissue engineering (Nesic), Osteology
- 3rd-year dentistry students: Pathophysiology – bones
- 1st-year medical students: Molecular biology practical courses
- 2nd-year medical students: Kidney block calcium-phosphate metabolism

- 3rd-year biomedicine and cell biology students: Pathology of the musculoskeletal system (Nesic)

# **Publications**

Bone Biology & Orthopaedic Research Association between cam-type deformities and MRI-detected structural damage of the hip: a crosssectional study in young males. Reichenbach, S; Leunig, M; Werlen, S; Nuesch, E; Pfirmann, CW; Bonel, H; Odermatt, A; Hofstetter, W; Ganz, R; Jueni, P (2011) in Arthritis Rheum, 63(12), p. 4023-4030 (doi: 10.1002/art.30589).

Chondrocytes within osteochondral grafts are more resistant than osteoblasts to tissue culture at 37°C. Bastian, JD; Egli, RJ; Ganz, R; Hofstetter, W; Leunig, M (2011) in: J Invest Surg, 24(1), p. 28-34.

TNFa inhibits the development of osteoclasts through osteoblast derived GM-CSF. Atanga, E; Dolder, S; Dauwalder, T; Wetterwald, A; Hofstetter, W (2011) in: Bone, 49(5), p. 1090-1100.

In vitro cytotoxicity of silver nanoparticles on osteoblasts and osteoclasts at antibacterial concentrations. Albers, C; Hofstetter, W; Siebenrock, KA; Landmann, R; Klenke, FM (2011) in: Nanotoxicology, Oct 21.

# Cardiovascular Research www.cvrc.dkf.unibe.ch



### Group Members

Prof. Dr. Robert Rieben, Group Leader Dr. Yara Banz, Research Associate (Pathology)

**Dr. Thusitha Gajanayake**, Postdoctoral Fellow (Hand Surgery)

Dr. Pranitha Kamat, Postdoctoral Fellow Julie Denoyelle, Laboratory Technician Philippe Montavon, Research Fellow, BNF Program (June-Dec.)

Prof. Dr. Robert Rieben robert.rieben@dkf.unibe.ch Anjan Bongoni, PhD Student Claudia Dührkop, PhD Student Shengye Zhang, PhD Student (since Oct.) Linda Kam, MD Student Sabine Müller, MD Student Marie-Christine Franz, BMSc Student (Jan.-June) Sara Cattaneo, Web Designer, BNF Program (Oct.-Dec.)

Studies in biology at the University of Bern; PhD in Immunology in 1992. SNF postdoc in Leiden, The Netherlands 1994-1997 working on xenotransplantation. Involved in several EU research projects since then. Return to Bern in 1997 to establish a research group. Habilitation in 2002; Associate Professor 2007. Since 2005, Group Leader, Cardiovascular Research, DCR. Research interests: Ischemia/reperfusion injury and innate immunity.

# Research Highlights 2011 / Outlook 2012

Vascular endothelial cells and their role in ischemia/reperfusion (I/R) injury as well as in transplant rejection were the focus of our research in 2011, and will continue to be so in 2012. We finalised a study on disaccharide composition of heparan sulfates (HS) during myocardial I/R injury in pigs. We showed that there are differences in 2-O- and N-sulfated HS disaccharides in the plasma of animals before and after experimental myocardial infarction, and that HS-disaccharide species differ depending on ischemia time. The next step will be the development of a multiplex suspension array for rapid characterisation of HS using phage-display antibodies (collaboration with T. van Kuppevelt, Nijmegen).

Together with the University Clinic for Plastic and Hand Surgery, we started a project on attenuation of innate immunity and tolerance induction in composite tissue transplantation. In this project, we aim to protect the graft endothelium from I/R injury, thereby attenuating activation of innate immunity. As we have shown earlier in cardiac transplantation models, this strategy should allow for induction of graft-specific tolerance in a clinical setting and, as a final aim, greatly facilitate clinical hand transplantation. In addition, ex vivo and in vitro studies on pigto-human xenotransplantation were performed together with partners from Munich and Geneva.

### Collaborators

Germany

Bovin N, Institute of Bioorganic Chemistry, Russia Gorantla V, University of Pittsburgh Medical Center, USA Hani R, EMPA Dübendorf, Switzerland Heier J, EMPA Dübendorf, Switzerland Jenni HJ, Cardiovascular Surgery, Inselspital Khattab A, Cardiology, Inselspital Klymiuk N, University of Munich, Korchagina E, Institute of Bioorganic Chemistry, Russia Pochechueva T, University Hospital

Zurich, Switzerland

Ruder T, University of Zurich, Switzerland

Seebach J, Geneva University Hospital, Switzerland

**Stringer S**, University of Manchester, UK

Wolf E, University of Munich, Germany

### Grants

#### Amounts allocated for 2011:

SNF: Endothelial cell protection: The role of heparan sulfate proteoglycans and complement in pathophysiology and prevention of ischemia/ reperfusion injury (R. Rieben) CHF 104,000

Biotest Pharma: In vivo and in vitro analysis of complement-scavenging by IgM-enriched intravenous immunoglobulins (R. Rieben) CHF 10,000

CSL Behring: Assessment of the acute (anti-inflammatory) effects of plasma products in a model of acute hind limb ischemia/reperfusion injury in rats (R. Rieben) CHF 55,000

Olga Mayenfisch Foundation: Lokale Immunsuppression zur Induktion der Spender-spezifischen Toleranz bei der "Composite Tissue Allotransplantation" (T. Gajanayake, E. Vögelin, R. Rieben) CHF 20,000

### **Teaching Activities**

- Pranitha Kamat: PhD in Biomedical Sciences

- Marie-Christine Franz: Master in Biomedical Sciences

- Michelle Raess: Master in Medicine - Elective course 5034 for medical students: "Ihr Partner im Labor: Forschung auf den Gebieten Organ-

transplantation, Chirurgie und Herzinfarkt"

- 3rd-year medical students: Problem Based Learning tutorial – "Störungen der Auseinandersetzung zwischen körpereigen und fremd"

- Graduate School for Cellular and Biomedical Sciences PhD students: Immunology tutorial - Four high-school students: Patenschaften für Maturaarbeiten (2-week lab stay each)

### **Publications**

Autotransfusion system or integrated automatic suction device in minimized extracorporeal circulation: influence on coagulation and inflammatory response. Jenni, H; Rheinberger, J; Czerny, M; Gygax, E; Rieben, R; Krähenbühl, E; Carrel, T; Stalder, M (2011) in: Eur J Cardiothorac Surg, 5(39), e139-143.

Multiplex suspension array for human anti-carbohydrate antibody profiling. Pochechueva, T; Chinarev, A; Spengler, M; Korchagina, E; Heinzelmann-Schwarz, V; Bovin, N; Rieben R (2011) in: Analyst, 3(136), p. 560-569.

Preservation of amputated extremities by extracorporeal blood perfusion; a feasibility study in a porcine model. Constantinescu, MA; Knall, E; Xu, X; Kiermeir, DM; Jenni, HJ; Gygax, E; Rieben, R; Banic, A; Vögelin, E (2011) in: J Surg Res, 1(171), p. 291-299.

Role of complement and perspectives for intervention in ischemiareperfusion damage. Banz, Y; Rieben, R (2011) in: Ann Med, Jan 24.

# Center of Regenerative Medicine for Skeletal Tissues



# Research Highlights 2011 / Outlook 2012

Mesenchymal stromal cells (MSCs) are utilised in the engineering of cartilage. Dexamethasone (DEX) is almost invariably applied to potentiate the growth-factor-induced chondrogenesis of MSCs in vitro, although this effect has been experimentally demonstrated only for TGF-β-stimulated bone-marrowderived MSCs. Clinically, systemic glucocorticoid therapy is associated with untoward side effects. Hence, the use of these agents should be avoided or limited. We hypothesise that the influence of DEX on the chondrogenesis of MSCs depends upon their tissue origin and microenvironment (absence or presence of an extracellular matrix), as well as on the nature of the growth factor.

We investigated its effects upon the TGF- $\beta$ 1- and BMP-2-induced chondrogenesis of MSCs as a function of tissue source (bone marrow vs. synovium) and microenvironment (cell aggregates vs. explants). In aggregates of bone-marrow-derived MSCs, DEX enhanced TGF- $\beta$ 1induced chondrogenesis by an up-regulation of cartilaginous genes but had little influence on the BMP-2-induced response. In aggregates

### **Group Members**

Prof. Dr. Ernst B. Hunziker, Group Leader

Dr. Yuelian Liu, Research Assistant Dr. Nahoko Shintani, Research Assistant Dr. Yasukazu Himeda, Postdoctoral Fellow (until July) Dr. Naomi Nishii, Postdoctoral Fellow Fabienne Bourquin, Trainee

Prof. Dr. Ernst B. Hunziker ernst.hunziker@dkf.unibe.ch Walter Hutzli, Support Lab Technician (ad personam) Regina Channi, Secretary Wilbur Helfer, Secretary (since Sep.) Christa Nater, Secretary Corinne Scheiwiller, Secretary (until Aug.) Dr. Ceri England, Text Editor (freelance) Urs Haarmann, Technical Services (freelance)

Fed. dipl. in Medicine and MD degree at the University of Bern; PhD at the Free University of Amsterdam, The Netherlands; Honorary PhD from the University of Kuopio, Finland. Director, M.E. Müller Institute for Biomechanis, University of Bern 1989-2002. Director, ITI Research Institute for Dental and Skeletal Biology, University of Bern 2003-2007. Since 2008, Group Leader, Center of Regenerative Medicine for Skeletal Tissues, DCR.

of synovial MSCs, DEX exerted no remarkable effect on either TGF- $\beta$ 1or BMP-2-induced chondrogenesis. In synovial explants, DEX inhibited BMP-2-induced chondrogenesis almost completely but had little impact on the TGF- $\beta$ 1-induced response. Our data reveal that steroids are not indispensable for the chondrogenesis of MSCs in vitro and that their influence is context dependent. This finding has important implications for MSC-based approaches to cartilage repair.

# Collaborators

Aszodi A, Max Planck Institute for Biochemistry, Germany Boerman O, University of Nijmegen, The Netherlands Grodzinsky A, Massachusetts Institute of Technology, USA Haspl M, University of Zagreb, Croatia Heller M, University of Bern, Switzerland Hofstetter W, University of Bern, Switzerland Jansen J, University of Nijmegen, The Netherlands Lyons K, University of California, Los Angeles, USA Sandell L, Washington University, USA

Siebenrock KA, Inselspital, Switzerland

Vögelin E, Inselspital, Switzerland Wismeijer D, Free University of Amsterdam, The Netherlands

### Grants

#### Amounts allocated for 2011:

NIH/NIAMS USA: Synovium-based articular cartilage tissue engineering (E.B. Hunziker) CHF 89,620

ITI Research Foundation: In vivo degradability and osteoconductivity of calcium phosphate coatings with different crystalline properties (Y. Liu) CHF 19,280

Various sponsors: (E.B. Hunziker) CHF 295,690

# **Teaching Activities**

- MD, DMD, PhD students and Postdoctoral Fellows

# Publications

Differential effects of dexamethasone on the chondrogenesis of mesenchymal stromal cells: Influence of microenvironment, tissue origin and growth factor. Shintani, N; Hunziker, EB (2011) in: Eur Cell Mater, 22, p. 302-320. Functionalization of deproteinized bovine bone with a coating-incorporated depot of BMP-2 renders the material efficiently osteoinductive and suppresses foreign-body reactivity. Wu, G; Hunziker, EB; Zheng, Y; Wismeijer, D; Liu, Y (2011) in: Bone, 49(6), p. 1323-1330.

Stereologic analysis of tibial-plateau cartilage and femoral cancellous bone in guinea pigs with spontaneous osteoarthritis. Wang, SX; Arsenault, L; Hunziker, EB (2011) in: Clin Orthop Relat Res, 469(10), p. 2796-2805.



# Ion Channels and Channelopathies www.ionchannels.dkf.unibe.ch



### **Group Members**

**Prof. Dr. Hugues Abriel**, Group Leader **Dr. Maxime Albesa**, Postdoctoral Fellow (until Mar.)

**Dr. Mohammed Y. Amarouch**, Postdoctoral Fellow (since Sep.)

**Dr. Ludovic Gillet**, Postdoctoral Fellow (since Apr.)

**Dr. Jakob Ogrodnik**, Postdoctoral Fellow (until Apr.)

Prof. Dr. Hugues Abriel hugues.abriel@dkf.unibe.ch Dr. Jean-Sébastien Rougier, Postdoctoral Fellow

Dr. Marc Suter, Postdoctoral Fellow Maria Essers, Laboratory Technician Verena Frazao, Secretary Katarzyna Krystanek, International PhD Student (Feb.-Apr.) Cédric Laedermann, PhD Student Diana A. Shy, PhD Student (since Feb.) Valentin Sottas, PhD Student (since Apr.) Ninda Syam, PhD Student

Training both as a biologist at the Swiss Federal Institute of Technology (ETH) Zurich and physician at the University of Lausanne. After two years at Lausanne University Hospital, a postdoc at Columbia University, USA. In 2002, SNF Professorship and start of independent research studying the role of ion channels in human disorders. Since 2009, Professor of Pathophysiology, University of Bern and DCR Director.

# Research Highlights 2011 / Outlook 2012

Our group investigates the roles played by ion channels in human disorders, so-called "channelopathies", in particular their roles in cardiac arrhythmias. In 2011, we published two studies on the hERG potassium channel, which is very important for long QT syndrome. We showed that hERG is regulated by its ubiquitylation, as we have previously found for other cardiac channels. In another study, we also revealed the structural determinants of hERG responsible for its inhibition by different stereoisomers (part of former PhD student L. Sintra Grilo's thesis). In addition, we demonstrated for the first time that de-ubiguitylating enzymes are also important players in regulating cardiac ion channels (collaboration with T. Jespersen, Denmark).

We also studied the regulation of the calcium channel Cav1.2. In a very fruitful collaboration with cardiologists from Zurich, we demonstrated the first pathogenic mutation in the gene *CACNA2D1*, coding for a subunit of this channel, in a patient with congenital short QT syndrome.

Very positive has also been the launch of an interdisciplinary study financed by the SNF, with the aim of developing a new patch-clamping technique using an atomic force microscopy-based set-up (collaboration with T. Zambelli, ETH Zurich).

# Collaborators

Barò I, French National Agency of Research Networks, CNRS Bezzina C, University of Amsterdam Academic Medical Centre, The Netherlands

**Carrupt P-A**, University of Geneva, Switzerland

**Decosterd I**, University of Lausanne, Switzerland

Fellmann F, University of Lausanne, Switzerland

Hatem SN, French National Agency of Research Networks, INSERM Hediger M, NCCR TransCure, Switzerland Jespersen T, University of Copenhagen, Denmark Lehnart SE, EU Trig Treat FP7 Consortium, University of Göttingen,

Germany Remme CA, University of Amsterdam

Academic Medical Center, The Netherlands

**Staub O**, University of Lausanne, Switzerland

Sychov O, SCOPES SNF Project, Ukraine

Zaklyazminskaya EV, SCOPES SNF Project, Russia

Zambelli T, ETH Zurich, Switzerland

# Grants

#### Amounts allocated for 2011:

SNF: Bonus of excellence – In vivo relevance of the PY and PDZ-domain binding motifs of the cardiac sodium channel Nav1.5 (H. Abriel) CHF 196,616

SNF: Roles of ion channel-interacting proteins in cardiac channelopathies (H. Abriel, E.V. Zaklyazminskaya, O.S. Sychov) CHF 55,500

SNF: NCCR TransCure subproject – Physiology, pharmacology and pathophysiology of the calciumactivated non-selective cation TRPM4 channel (M. Hediger, H. Abriel, M. Heller) CHF 154,000

SNF: Interdisciplinary project – Forcecontrolled patch clamp (pc-FluidFM) (T. Zambelli, H. Abriel) CHF 68,000

European Union: FP7-single stage grant, collaborative project (2009) – EUTrigTreat – Identification and therapeutic targeting of common arrhythmia trigger mechanisms (S. Lehnart, H. Abriel) CHF 190,000

# **Teaching Activities**

Katarzyna Krystanek: PhD (with University of Copenhagen, Denmark)
Coordination of pathophysiology lectures for dentistry students
Dentistry students: Kidney and electrolytes pathophysiology
Master in Biomedical Sciences: Ion

- Master in Biomedical Sciences. Ion channels in cardiac diseases - Bachelor in Life Sciences: Cardiac

ion channels in health and disease

# **Publications**

Block of the hERG channel by bupivacaine: Electrophysiological and modeling insights towards stereochemical optimization. Sintra Grilo, L; Carrupt, PA; Abriel, H; Daina, A (2011) in: Eur J Med Chem, 46(8), p. 3486-3498.

Deubiquitylating enzyme USP2 counteracts Nedd4-2-mediated downregulation of KCNQ1 potassium channels. Krzystanek, K; Borger Rasmussen, H; Grunnet, M; Staub, O; Olesen, SP; Abriel, H; Jespersen, T (2011) in: Heart Rhythm, Oct 22.

Neuronal precursor cell-expressed developmentally down-regulated 4-1 (NEDD4-1) controls the sorting of newly synthesized Ca(V)1.2 calcium channels. Rougier, JS; Albesa, M; Abriel, H; Viard, P (2011) in: J Biol Chem, 286(11), p. 8829-8838.

Patient with syncope and LQTS carrying a mutation in the PAS domain of the hERG1 channel. Sintra Grilo, L; Schläpfer, J; Fellmann, F; Abriel, H (2011) in: Ann Noninvasive Electrocardiol, 16(2), p. 213-218.

Nedd4-2-dependent ubiquitylation and regulation of the cardiac potassium channel hERG1. Albesa, M; Sintra Grilo, L; Gavillet, B; Abriel, H (2011) in: J Mol Cell Cardiol, 51(1), p. 90-98.

Identification of a novel loss-of-function calcium channel gene mutation in short QT syndrome (SQTS6). Templin, C; Ghadri, JR; Rougier, JS; Baumer, A; Kaplan, V; Albesa, M; Sticht, H; Rauch, A; Puleo, C; Hu, D; Barajas-Martinez, H; Antzelevitch, C; Lüscher, TF; Abriel, H; Duru, F (2011) in: Eur Heart J, 32(9), p. 1077-1088.

# Mammary Gland Biology and Carcinogenesis www.dkf.unibe.ch/research-group/2/



# Research Highlights 2011 / Outlook 2012

Eph receptor tyrosine kinases and their membrane-bound ephrin ligands play key roles during morphogenesis. Receptor-ligand interactions result in bi-directional signalling; forward and reverse from the receptor and ligand, respectively. EphB4 and ephrin-B2 are differentially expressed in the mammary gland and their deregulated expression in the mammary epithelium of transgenic mice leads to perturbations in the glandular architecture. Moreover, over-expression of EphB4 and expression of a truncated ephrin-B2 mutant, incapable of reverse signalling, confers a metastatic phenotype on NeuT-initiated mouse mammary tumours.

We have taken advantage of this transgenic model to investigate the role of ephrin-B2 signalling in the control of the mammary stem cell niche and showed that overexpression of the native ephrin-B2 gene leads to an augmentation of the luminal and bi-potent precursor cell fractions. In contrast, mammary glands of truncated ephrin-B2 transgenic mice contained significantly more stem cells and alveolar, ER-positive progenitor cells. Thus,

# **Group Members**

Prof. Dr. Anne-Catherine Andres, Group Leader Dr. Philip Känel, Postdoctoral Fellow

Dr. Robert Strange, Consultant François Achermann, Laboratory Technician

Carlos Wotzkow, Laboratory Technician Stefan Hahnewald, MSc Student (since May)

Prof. Dr. Anne-Catherine Andres anne-catherine.andres@dkf.unibe.ch

Graduated from the Department of Cell Biology, University of Bern. Entered into the field of breast cancer research at the Ludwig Institute, Bern. Established the first oncogene-bearing transgenic mouse strain. Continued the project after 1988 at the Friedrich Miescher-Institute, Basel and subsequently at the CNRS in Strasbourg, France. Since 1991, Group Leader, Mammary Gland Biology Group, DCR; Associate Professor 2002.

ephrin-B2 signalling is involved in the control of the stem cell niche and in the regulation of cell fate decisions.

We now intend to characterise signal transduction pathways involved in the ephrin-B2-induced phenotypes by microarray analyses on RNA from different transgenic mammary epithelial subpopulations. The impact of EphB4 over-expression on the mammary stem cell fate will also be analysed.

# Collaborators

**Djonov V**, University of Bern, Switzerland **Stute P**, University of Bern, Switzerland

### Grants

#### Amounts allocated for 2011:

SNF: The role of EphB4 and ephrin-B2 in the control of the mammary gland stem/progenitor cell population (A.-C. Andres) CHF 64,300

Swiss Cancer League: The role of vascularization and tumor stem cells in the metastatic spread of mammary tumor cells: Studies in a transgenic mouse model (A.-C. Andres) CHF 95,000

Schweizerische Stiftung für Klinisch-Experimentelle Tumorforschung: Transgenic mouse models to study the molecular mechanisms leading to the invasive phenotype of mammary tumors (A.-C. Andres) CHF 50,000

# **Teaching Activities**

 Member, Graduate School Commission Biological Systems
 Member, Commission for the Master Studies Curriculum in Biomedical Sciences

- Bachelor and Master studies in biomedical sciences: Organiser and teacher, tumour biology program

- 1st-year medical students: Organiser and teacher, developmental biology program; transgenic seminar; Lecture on cell death of multicellular organisms

- 1st-year veterinary medicine students: Lecture on transgenic animals

- Graduate School: Molecular biological methods in clinical diagnosis practical course

- Masters in Bioengineering: Molecular biology practical course

- 1st-year medical students elective module: Genetic mutations: cytoand molecular genetics

# Publications

Deregulated ephrin-B2 signaling in mammary epithelial cells alters the stem cell compartment and interferes with the epithelial differentiation pathway. Kaenel, P; Antonijevic, M; Richter, S; Küchler, S; Sutter, N; Wotzkow, C; Strange, R; Andres, AC (2012) in: Int J Oncol, 40(2), p. 357-369.

Preponderance of cells with stem cell characteristics in metastasising mouse mammary tumours induced by deregulated EphB4 and ephrin-B2 expression. Kaenel, P; Schwab, C; Mülchi, K; Wotzkow, C; Andres, AC (2011) in: Int J Oncol, 38(1), p. 151-160.



# Phytopharmacology, Bioanalytics & Pharmacokinetics www.phytopharm.dkf.unibe.ch



### Group Members

#### Prof. Dr. Rudolf Brenneisen, Group

Leader Dr. Christian Lanz, Research Assistant Karin Fürer, PhD Student David Marti, Laboratory Technician, BNF Program (Mar.-Apr.) Dr. Johan Mattsson, Postdoctoral Fellow, BNF Program (June-Nov.)

Prof. Dr. Rudolf Brenneisen rudolf.brenneisen@dkf.unibe.ch

Fed. dipl. in Pharmaceutical Sciences and PhD at the University of Bern. Head, Department of Phytochemistry & Pharmacognosy, Institute of Pharmacy, University of Bern 1981. Habilitation and Privatdozent 1988. Vice-Director, Institute of Pharmacy 1990-91; Associate Professor 1993. Since 1997, Group Leader, Phytopharmacology, Bioanalytics and Pharmacokinetics Group, DCR. President, Swiss Academy of Pharmaceutical Sciences; President, Swiss Committee for Drugs of Abuse Testing since 2008.

György Papp, Engineer, BNF Program (Feb.)

Raoul Yankam, MSc, BNF Program (Jan.-Dec.)

**Dr. Bruno Lenta Ndjakou**, Postdoctoral Fellow, SNF International Short Visits Program (Aug.-Oct.)

# Research Highlights 2011 / Outlook 2012

Highlights of our research include:

- Bryophyllum pinnatum showed inhibitory effects on the stimulated or overactive bladder. Flavonoids were identified that are presumed to be active plant constituents. Clinical research is now focussing on sedatory effects, sleep quality and ADHD. - Constituents of plants from Cameroon's ethnomedicine were identified that exhibit antiplasmodial activity against chloroquine-resistant strains of *Plasmodium falciparum*.

- A study on patients suffering from anxiety related to progressive terminal illnesses confirmed that LSD can be an adjunct in difficult-to-treat psychiatric situations.

- In heavy heroin addicts, a new formulation of morphine was superior to methadone in heroin substitution.

- Diacetylmorphine leads to a significant decrease in ACTH and cortisol in heroin-dependent patients (HDP). Stress hormone levels were higher than in healthy controls receiving a placebo, indicating that heroin is being used as a stress protective factor and self-medication by opioidmaintained HDP. MRI, behavioural and biochemical measures showed that HDP exhibit prefrontal structural deficits, whereas acute heroin application leads to an increase in prefrontal activity. This underscores the significance of addicted brain structure for functional activation and drug-taking behaviour in HDP. - Liver samples from patients with alcoholic liver fibrosis (ALF) and hepatic animal cells revealed that the endocannabinoid system plays an important role in liver pathophysiology. Cannabinoid receptor-1 was upregulated in ALF, whereas its inhibition or genetic knockout protects against ALF.

### Collaborators

Berset D, Water & Soil Protection Laboratory Bern, Switzerland Doblin R, Multidisciplinary Association of Psychedelic Studies, USA Freeman D, University of Oxford, UK Gasser P, Solothurn, Switzerland Hamburger M, University of Basel, Switzerland

Liechti M, University Hospital and University of Basel, Switzerland Morrison P, King's College London, UK

Ochen P, Biberist, Switzerland Rieckermann J, EAWAG, Switzerland Schnelle M, Weleda AG, Switzerland Skendaj R, University Hospital Basel, Switzerland

**Stickel F**, University of Bern, Switzerland

**Unfer-Grauwiler S**, Mundipharma Medical, Switzerland

Von Mandach U, University Hospital Zurich, Switzerland

Walter M, University Hospital Basel, Switzerland

Weber M, Kantonsspital St. Gallen, Switzerland

Wüest A, Paracelsus Hospital Richterswil, Switzerland

### Grants

#### Amounts allocated for 2011:

SNF: Effects of diacetylmorphine (heroin) on brain function (M. Walter) CHF 50,000

SNF: Phytochemical and pharmacological study on two plants used in the treatment of malaria in Cameroon (B. Lenta Ndjakou) CHF 12,000

Mundipharma Medical Basel: Analytical monitoring of by-consumption of patients in heroin substitution programs (R. Brenneisen) CHF 16,000

Weleda AG Arlesheim: Clinical efficacy, pharmacology and analytics of Bryophyllum (U. von Mandach) CHF 50,000

Additional funding: Neuropharmacology of iv THC (D. Freeman) CHF 11,400

# **Teaching Activities**

- 1st-year pharmacy students: Introduction to pharmaceutical sciences

# **Publications**

Assessment of total uncertainty in cocaine and benzoylecgonine wastewater load measurements.

Mathieu, C; Rieckermann, J; Berset, J-D; Schürch, S; Brenneisen, R (2011) in: Water Research, 45(20), p. 6650-6660.

Leaf press juice from Bryophyllum pinnatum (Kalanchoe pinnata L.) induces myometrial relaxation. Wächter, R; Brenneisen, R; Hamburger, M; Mennet, M; Schnelle, M; Worel, AM; Simões-Wüst, AP; von Mandach, U (2011) in: Phytomedicine, 19(1), p. 74-82.

Does intravenous delta-9-tetrahydrocannabinol increase dopamine release? A SPET study. Barkus, E; Morrison, PD; Vuletic, D; Dickson, J; Ell, PJ; Pilowsky, LS; Brenneisen, R; Holt, DW; Powell, J; Kapur, S; Murray, RM (2011) in: J Psychopharmacol, 25(11), p. 1462-1468.

Disruption of frontal theta coherence by  $\Delta$ 9-tetrahydrocannabinol is associated with positive psychotic symptoms. Morrison, PD; Nottage, J; Stone, JW; Bhattacharyya, S; Tunstall, N; Brenneisen, R; Holt, D; Wilson, D; Sumich, A; McGuire, P; Murray, RM; Kapur, S; Ffytche, D (2011) in: Neuropsychopharmacology, 36(4), p. 827-836.

Communication breakdown: delta-9-tetrahydrocannabinol effects on pre-speech neural coherence. Stone, JM; Morrison, PD; Brugger, S; Nottage, J; Bhattacharyya, S; Sumich, A; Wilson, D; Tunstall, N; Feilding, A; Brenneisen, R; McGuire, P; Murray, RM; Ffytche, DH (2011) in: Mol Psychiatry, Epub ahead of print (doi: 10.1038/mp.2011.141).

Cannabinoid receptor type I modulates alcohol-induced liver fibrosis. Patsenker, E; Stoll, M; Millonig, G; Agaimy, A; Wissniowski, T; Schneider, V; Mueller, S; Brenneisen, R; Seitz, H; Ocker, M; Stickel, F (2011) in: Mol Med, Epub ahead of print (doi: 10.2119/molmed.2011.00149).

The norepinephrine transporter inhibitor reboxetine reduces stimulant effects of MDMA ("Ecstasy") in humans. Hysek, CM; Simmler, LD; Ineichen, M; Grouzmann, E; Hoener, MC; Brenneisen, R; Huwyler, J; Liechti, ME (2011) in: Clin Pharmacol Ther, 90(2), p. 246-255 (doi: 10.1038/clpt.2011.78).

# Vasoactive Peptide www.dkf.unibe.ch/research-group/22/



# Research Highlights 2011 / Outlook 2012

Our primary research focus is on the physiology and pathology of peptides in cardiovascular disease. Factors contributing to disease include a complex interplay between toll-like receptors, vasoactive peptides and the nitric oxide system. Activation or blockade of specific elements regulating these pathways offer new therapeutic options for modifying damage progression. Modulation can also prevent the loss of insulin-producing beta-cells in the pancreas. Studies of molecular mechanisms regulating vascular cell apoptosis, the innate immune system, dendritic cell activation, cytokine expression and toll-like receptor function are currently in progress. Techniques include proteomics, micro arrays and biochemical analysis, as well as transgenic animal models and cell culture.

Our second research area involves the role of brain glucocorticoids in chronic alcohol abuse. We have on-going clinical trials of glucocorticoid antagonists as therapeutics in the management of withdrawal (funded by the Medical Research Council, UK).

### **Group Members**

Dr. Sidney G. Shaw, Group Leader Jane Shaw, Laboratory Technician Dr. Hemanshu Patel, Visiting Research Fellow (Oct., Nov.) Dr. Janice Tsui, Visiting Research Fellow (Oct., Nov.)

Dr. Sidney G. Shaw shaw@dkf.unibe.ch

MA (Hons) in Biochemistry and PhD in Neuropharmacology at Oxford University, UK. Wellcome Trust Fellow and Lecturer in Pharmacology, Trinity College Oxford 1978-1983. Research Associate, Department of Hypertension, University of Bern 1984-1996. Since 1996, Group Leader, Vasoactive Peptide Group, DCR. Member, Editorial Board of Cardiovasc Med, Vasc Pharmacol and Cardiol Res Pract. Member, Swiss Soc Nephrol, Am Soc Hypertension, European Soc Cardiol and European Assoc Study Diabetes.

In May, the Second International Cardiovascular Diseases Workshop was organized at University College London, UK. This led to the commissioning of a Cardiovascular Research and Practice special issue entitled "Cell Signalling Pathways Leading to Novel Therapeutic Strategies in Cardiovascular Disease", to be published in 2012. Other symposia organised in 2011 included the International Workshop on The Endothelium in Health and Disease, in London, UK and the 12th International Conference on Endothelin-1, in Cambridge, UK.

# Collaborators

Dashwood M, Royal Free Hospital, UK

Jakob S, Inselspital, Switzerland Little H, Kings College London, UK Patel H, Royal Free Hospital, UK Reichen J, University of Bern, Switzerland Rieben R, University of Bern, Switzerland Ruschitzka F, University Hospital Zurich, Switzerland Tsui J, University College London, UK

# Grants

#### Amounts allocated for 2011:

Royal Society: Joint International Research Grant – The role of Toll like receptor signalling in Peripheral Arterial Disease (J. Tsui, S. Shaw) CHF 30,000

Medical Research Council UK: Importance of 11-beta-hydroxysteroid dehydrogenase (HSD-1) in the consequences of chronic alcohol consumption (H. Little, S. Shaw) CHF 80,000

European Foundation for the Study of Diabetes: The role of toll like receptor signalling in diabetes related cardiovascular disease (S. Shaw) CHF 100,000

# **Teaching Activities**

- 3rd-year dental medicine students: Pathology and internal medicine – endocrinology pathophysiology

# **Publications**

Torcetrapib impairs endothelial function in hypertension. Simic, B; Hermann, M; Shaw, SG; Bigler, L; Stalder, U; Dörries, C; Besler, C; Lüscher, TF; Ruschitzka, F (2011) in: Eur Heart J, Sep 14. Additive effect of homocysteine- and cholesterol-lowering therapy on endothelium-dependent vasodilation in patients with cardiovascular disease. Wustmann, K; Klaey, M; Burow, A; Shaw, SG; Hess, OM; Allemann, Y (2011) in: Cardiovasc Ther, Jul 31, Epub ahead of print (doi: 10.1111/j.1755-5922.2011.00272.x).





# DCR Research Groups from Clinics of the Inselspital

Forty-one research groups from clinics of the Inselspital were affiliated with the DCR at the end of 2011. Below is a list of the groups and the names of the Clinic Directors and/or Group Leaders. Eleven of the groups are featured on the following pages. Other groups will be featured in future annual reports.

#### Anaesthesiology

Prof. Dr. Frank Stüber, Astrid Kühr, Dr. Rolf Lauber, PD Dr. Martin Luginbühl

Angiology

Prof. Dr. Iris Baumgartner, PD Dr. Nicolas Diehm

Audiology Prof. Dr. Marco Caversaccio, Prof. Dr. Martin Kompis

#### Cardiology

Prof. Dr. Stephan Windecker, Prof. Dr. Yves Allemann, Prof. Dr. Etienne Delacrétaz, Prof. Dr. Paul Mohacsi, Prof. Dr. Urs Scherrer, Prof. Dr. Christian Seiler, Prof. Dr. Thomas Suter

#### Cardiovascular Surgery

Prof. Dr. Thierry Carrel, Prof. Dr. Hendrik Tevaearai, PD Dr. Marie-Noelle Giraud-Flück, Dr. Sarah Longnus

Cranio-Maxillofacial Surgery Prof. Dr. Tateyuki Iizuka, Dr. Nikola Saulacic

#### Dental Research

Prof. Dr. Anton Sculean, Prof. Dr. Adrian Lussi, PD Dr. Dieter Bosshardt, Prof. Dr. Matthias Chiquet, PD Dr. Sigrun Eick

Dermatology Prof. Dr. Luca Borradori, Dr. Bertrand Favre

Endocrinology of the Breast PD Dr. Petra Stute

Endocrinology/Diabetology (Adults) Prof. Dr. Peter Diem

Endocrinology/Diabetology/ Metabolism (Paediatrics) Prof. Dr. Primus Mullis, Prof. Dr. Christa Flück, Dr. Jean-Marc Nuoffer

# Endometriosis and Reproductive Medicine

Prof Dr. Michel D. Müller, Prof. Dr. Nick A. Bersinger

Endometrium & Ovary Prof. Dr. Michael von Wolff

**Experimental Haematology (Adults)** Prof. Dr. Gabriela Baerlocher, Dr. Elisabeth Oppliger Leibundgut

Gastroenterology (Adults) Prof. Dr. Andrew Macpherson, Prof. Dr. Frank Seibold

Geriatrics/Medicine of Ageing Prof. Dr. Andreas Stuck, PD Dr. Andreas Schoenenberger

Haematology/Oncology (Paediatrics) Prof. Dr. Kurt Leibundgut, PD Dr. Alexandre Arcaro

Hand Surgery PD Dr. Esther Voegelin, Prof. Dr. Robert Rieben

Human Genetics Prof. Dr. Sabina Gallati

Intensive Medicine Prof. Dr. Jukka Takala, Prof. Dr. Stephan Jakob

Internal Medicine Prof. Dr. Beatrice U. Müller

Magnetic Resonance Spectroscopy and Methodology, MRSM Prof. Dr. Chris Boesch

Nephrology and Hypertension Prof. Dr. Felix Frey, Prof. Dr. Brigitte Frey

Neurology Prof. Dr. Christian W. Hess, PD Dr. Alain Kaelin, Prof. Dr. Kai Roesler

Neurosurgery Prof. Dr. Andreas Raabe, Prof. Dr. Michael Reinert

Oncology/Haematology (Adults) Prof. Dr. Martin Fey, PD Dr. Oliver Gautschi, Dr. Urban Novak, Prof. Dr. Thomas Pabst, Prof. Dr. Andreas Tobler, PD Dr. Mario Tschan Ophthalmology

Prof. Dr. Sebastian Wolf, PD Dr. Volker Enzmann, PD Dr. Ute Wolf-Schnurbusch

Orthopaedic Surgery Prof. Dr. Klaus-Arno Siebenrock, Dr. Frank Klenke

#### Perception and Eye Movement

Prof. Dr. Christian W. Hess, PD Dr. Stephan Bohlhalter, Prof. Dr. René Müri, PD Dr. Thomas Nyffeler

#### **Plastic Surgery**

Prof. Dr. Andrej Banic, PD Dr. Mihai Constantinescu, Prof. Dr. Dominique Erni, Prof. Dr. Robert Rieben, Dr. Maziar Shafighi

Prenatal Medicine Prof. Dr. Daniel Surbek

**Psychosomatic Medicine** Prof. Dr. Roland von Känel

Pulmonary Medicine (Adults) Prof. Dr. Thomas Geiser, PD Dr. Christophe von Garnier, PD Dr. Barbara Rothen

**Pulmonary Medicine (Paediatrics)** Prof. Dr. Nicolas Regamey

Radiation Oncology Prof. Dr. Daniel Aebersold, Dr. Yitzhak Zimmer

Rheumatology Prof. Dr. Peter M. Villiger, Dr. Frauke Förger, PD Dr. Daniel Lottaz, Prof. Dr. Michael Seitz, Prof. Dr. Beat Trueb

Thoracic Surgery Prof. Dr. Ralph A. Schmid, PD Dr. Steffen Frese

Triadic Family Functioning Prof. Dr. Daniel Surbek, Dr. Werner Stadlmayr

Tumor-Immunology Prof. Dr. Adrian Ochsenbein

Urology Prof. Dr. George Thalmann, Dr. Marco Cecchini

Visceral and Transplantation Surgery Prof. Dr. Daniel Candinas, PD Dr. Deborah M. Keogh-Stroka

# Audiology

# www.artorg.unibe.ch/content/research\_units/artificial\_hearing\_research

Prof. Dr. Marco Caversaccio marco.caversaccio@insel.ch



MD from the University of Geneva. Research fellowship at Imperial College London, UK. Broad research focus with special interest in technical assistance systems (NCCR CO-ME). Since 2009, Chair and

Director, University Clinic for Ear, Nose and Throat Diseases, Head and Neck Surgery, Inselspital. Since 2010, also Vice-Director, ARTORG Center for Biomedical Engineering, University of Bern.

### **Group Members**

Prof. Dr. Marco Caversaccio, Clinic
Director, Group Leader
Prof. Dr. Martin Kompis, Group Leader
Prof. Dr. Christof Stieger, Group Leader
Jonas Salzmann, Research Assistant
Simona Wiedmer, Research Assistant
Ruth Birrer, MD Student

# Prof. Dr. Martin Kompis martin.kompis@insel.ch



MD from the University of Zurich. PhD in electrical engineering from the Swiss Federal Institute of Technology (ETH) Zurich; MD from the University of Zurich. Postdoc at Purdue University, USA. Since 1997, Head of ent of Otolaryngology,

Audiology, Department of Otolaryngology, Inselspital. Associate Professor of Biomedical Engineering and Acoustics, University of Bern.

Nicolas Gerber, PhD Student (shared with S. Weber, Institute for Surgical Technology & Biomechanics) Jéremie Guignard, PhD Student Anja Kurz, PhD Student Daniel Widmer, MSc Student Prof. Dr. Christof Stieger christof.stieger@artorg.unibe.ch



Studies in electrical engineering, didactics and medical physics at the Swiss Federal Institutes of Technology Lausanne and Zurich, and at the University of Louvain la Neuve, Belgium. PhD from the University of

Neuchâtel. Since 2008, Assistant Professor of Artificial Hearing, University Clinic of Otolaryngology, Head and Neck Surgery, Inselspital.

# Research Highlights 2011 / Outlook 2012

In 2011, research continued in a number of areas, including robots for implantable hearing systems, and implantable and bone-anchored hearing aids. The CTI project "Highprecision robot for implantable hearing systems" won the poster prize at the 2011 CTI Medtech Event. At the same event, a second CTI project "Novel Body Access" was nominated for the 2011 CTI Medtech Award.

In the domain of implantable hearing aids, the novel Direct Acoustic Cochlear Stimulation (DACS) hearing system was successfully implanted within a multicentre study both in Bern and other European centres. The development of the DACS was initialised and driven by our department at the Inselspital, together with Helbling Inc. in Liebefeld, Switzerland. The first hearing and speech recognition results from the new implantees look promising.

A new project in the area of boneanchored hearing aids (baha) started towards the end of 2011. Anja Kurz, a new PhD Student, will look into optimised hearing aid fittings and new technical possibilities of future Baha generations. We hope to know much more in this area within the next few years. In the meantime, we published a book on Baha this year.

### Collaborators

Flynn M, Cochlear Inc, Göteborg, Sweden

Häusler R, Tiefenau Hospital, Spital Netz Bern, Switzerland

### Grants

#### Amounts allocated for 2011:

CTI: Novel Body Access – Project 9952 (C. Stieger) CHF 102,006

CTI: High-precision robot for implantable hearing systems – Project 9957 (M. Caversaccio) CHF 50,529

CTI: Novel Body Access Part 2 – Project 12593 (C. Stieger) CHF 16,375 Cochlear Inc: Baha project (M. Kompis) CHF 18,600

Cochlear Inc: (C. Stieger) CHF 18,280

### Publications

#### Selected publications:

(see page 49 for a complete list)

Benefits of low-frequency attenuation of baha® in single-sided sensorineural deafness. Pfiffner, F; Kompis, M; Flynn, M; Asnes, K; Arnold, A; Stieger, C (2011) in: Ear Hear, 32(1), p. 40-45.

Comparisons of sound processors based on osseointegrated implants in patients with conductive or mixed hearing loss. Pfiffner, F; Caversaccio, M; Kompis, M (2011) in: Otol Neurorotol, 32(5), p. 728-735.

Design of a semi-implantable hearing device for direct acoustic cochlear stimulation. Bernhard, H; Stieger, C; Perriard, Y (2011) in: IEEE Trans Biomed Eng, 58(2), p. 420-428. Implantable bone conduction hearing aids. Kompis, M; Caversaccio, M; eds. (2011), Karger, Basel, ISBN 978-3-8055-9699-2.

In-the-canal vs. behind-the-ear microphones improve spatial discrimination on the side of the head in bilateral cochlear implant users. Mantokoudis, G; Kompis, M; Vischer, M; Häusler, R; Caversaccio, M; Senn, P (2011) in: Otol Neurotol, 32(1), p. 1-6.



# Cranio-Maxillofacial Surgery www.dkf.unibe.ch/research-group/57/

# Prof. Dr. Tateyuki lizuka tateyuki.iizuka@insel.ch



MD and DDS in Germany; PhD in Medicine 1992. Since 1996, Associate Professor at Helsinki University, Finland. Since 2000, Professor of Cranio-Maxillofacial Surgery at the University of

Bern; Clinic Director since 2006. Lecturer at Helsinki University, External Professor at Osaka Dental University, Japan and National University of Singapore. Director of postgraduate programmes in oral and maxillofacial surgery in Switzerland, Germany, Finland and the European Association for Cranio-Maxillofacial Surgery. Dr. Nikola Saulacic nikola.saulacic@insel.ch



Studies in dental medicine and MSc from the University of Belgrade, Serbia. European PhD in 2005 at the University of Santiago de Compostela, Spain. Research and Teaching Associate at the University of Geneva

2006-2007. Since 2007, Research Associate at the University of Bern. Since 2012, Group Leader, Cranio-Maxillofacial Surgery Group.

### **Group Members**

**Prof. Dr. Tateyuki lizuka**, Clinic Director, Group Leader

Dr. Nikola Saulacic, Group Leader Dr. Erik Hedbom, Senior Scientist (until Dec.)

Dr. Eliane Brolese, Research Assistant Dr. Ken Nakahara, Research Assistant Dr. Benoit Schaller, Research Associate Inga Grigaitiene, Laboratory Technician (until Dec.)

Caroline-Dominique Zürcher, Secretary

# Research Highlights 2011 / Outlook 2012

Our research group focuses on bone regeneration and augmentation. The role of periosteum in bone biology has received renewed attention, particularly in the cranio-facial region, because of the exclusively membranous apposition and lack of growth cartilage. The tensile strains tending to pull the periosteum away from the bone are typically osteogenic. To identify the regulatory mechanism fundamental to periosteal distraction osteogenesis (PDO), we established a unique rodent calvaria model. The relative contribution of periosteum and pristine bone to new bone formation was investigated. The periosteum demonstrated a dominant role in new bone formation when the marrow cavities were not opened. Furthermore, the application of a collagen barrier membrane in PDO was beneficial to bone formation. The mean maximal bone height in the group with membrane outranged the total amount of distraction performed, and was even twice as high as the pristine bone.

Further evaluation of this promising treatment modality includes highly specific therapeutic measures such as application of osteoinductive growth factors at particular locations. Based on the favourable outcome of the present experimentation, the use of a more clinically analogous model is advocated.

Current research activities include the development of an automatic distraction model of rabbit calvaria and an intra-oral model of PDO in dogs.

### Collaborators

Buser D, University of Bern, Switzerland Hofstetter W, University of Bern, Switzerland Juodzbalys G, University of Kaunas, Lithuania Lombardi T, University of Geneva, Switzerland Kurita K, University of Nagoya, Japan Scolozzi P, Geneva University Hospital, Switzerland Wahl G, University of Bonn, Germany

### Grants

#### Amounts allocated for 2011:

Swiss Dental Association: The comparison of continuous and discontinuous automatic periosteal distraction in the calvarium of rabbits (N. Saulacic, T. Iizuka, P. Scolozzi) CHF 52,545

# **Publications**

Analysis of new bone formation induced by periosteal distraction in a rat calvarium model. Saulacic, N; Schaller, B; lizuka, T; Buser, D; Hug, C; Bosshardt, D (2011) in: Clin Implant Dent Relat Res, Epub ahead of print (doi:10.1111/j.1708-8208.2011.00355.x)

Periosteal distraction osteogenesis and barrier membrane application: an experimental study in the rat calvaria. Saulacic, N; Schaller, B; Bosshardt, D; Buser, D; Jaun, P; Haeniwa, H; lizuka, T (2011) in: J Periodontol, Epub ahead of print (doi.10.1902/jop.2011.110418)

Neurolytic effects of ampicillin on the rat infraorbital nerve. Saulacic, N; Lombardi, T; Stojčev-Stajčić, L; lizuka, T; Stajcić, Z (2011) in: J Oral Pathol Med, Epub ahead of print (doi.10.1111/j.1600-0714.2011.01098.x)

Relative contributions of osteogenic tissues to new bone formation in periosteal distraction osteogenesis: histological and histomorphometrical evaluation in a rat calvarium. Saulacic, N; Hug, C; Bosshardt, D; Schaller, B; Buser, D; Haeniwa, H; lizuka, T (2011) in: Clin Implant Dent Relat Res, Epub ahead of print (doi: 10.1111/j.1708-8208.2011.00400.x)

Osteogenic potential of autogenous bone grafts harvested with four different surgical techniques. Miron, R; Hedbom, E; Saulacic, N; Zhang, Y; Sculean, A; Bosshardt, DD; Buser, D (2011) in: J Dent Res, 90(12), p. 1428-1433

Premature osteoblast clustering by enamel matrix proteins induces osteoblast differentiation through up-regulation of connexin 43 and N-cadherin. Miron, RJ; Hedbom, E; Ruggiero, S; Bosshardt, DD; Zhang, Y; Mauth, C; Gemperli, AC; lizuka, T; Buser, D; Sculean, A (2011) in: PLoS One, 6(8), e23375

Adsorption of enamel matrix proteins to a bovine derived bone grafting material and its regulation of cell adhesion, proliferation and differentiation. Miron, RJ; Bosshardt, D; Hedbom, E; Zhang, Y; Haenni, B; Buser, D; Sculean, A (2011) in: J Periodontol, Epub ahead of print (doi: 10.1902/jop.2011.110480)



# Dental Research www.zmk.unibe.ch/content/research

Prof. Dr. Anton Sculean anton.sculean@zmk.unibe.ch



Studied dentistry at Semmelweis University, Hungary. Postgraduate education in Münster, Germany and Aarhus, Denmark. Habilitation in Homburg, Germany. Head, Department of Periodontology, Radboud

University Nijmegen, The Netherlands 2004-2008. Since 2008, Chairman, Department of Periodontology; Head of Research, School of Dental Medicine since 2011.

PD Dr. Dieter Bosshardt dieter.bosshardt@zmk.unibe.ch



Studied biology at the ETH Zurich; PhD in natural sciences. Postdoc at the Faculty of Dental Medicine, University of Montreal, Canada 1994-1997. Research Scientist, Departments of Periodontology and Oral

Surgery, University of Bern 2000-2007; Habilitation in 2006. Since 2008, Head, Robert K. Schenk Laboratory for Oral Histology, Department of Oral Surgery and Stomatology.

### Group Members

Prof. Dr. Anton Sculean, Head of Research, School of Dental Medicine Prof. Dr. Adrian Lussi, Clinic Director,

- Laboratory Head
- Dr. Cathrin Brevik, Research Assistant
- Dr. Simon Flury, Research Assistant Dr. Tamara Koch, Research Assistant
- Dr. Anne Peutzfeld, Research Assistant

Dr. Ekaterina Rakhmatullina, Research Assistant

Dr. Thiago Saads Carvalho, Research Assistant (since Sep.)

Dr. Hermann Stich, Research Assistant

# Research Highlights 2011 / Outlook 2012

The Bosshardt Group has projects on: 1) Bone and soft tissue healing around dental implants of different materials and surface modifications, 2) Bone and periodontal regeneration using autologous bone grafts, substitute materials and barrier membranes, and 3) Bone and peri-

#### Prof. Dr. Adrian Lussi adrian.lussi@zmk.unibe.ch



Studied chemical engineering at the ETH Zurich; Masters degree. Teaching license in chemistry. PhD in dentistry at the University of Bern. Research interests: Erosion, caries diagnosis and minimally invasive

preparation techniques. Since 2006, Head, Department of Preventive, Restorative and Pediatric Dentistry; Executive Chairman, School of Dental Medicine since 2011.

# Prof. Dr. Matthias Chiquet matthias.chiquet@zmk.unibe.ch



ETH Zurich; PhD in cell biology. Postdoc at the Department of Embryology, Carnegie Institution, USA. Junior Group Leader, Biocenter, University of Basel 1986-1995; Habilitation in 1990.

Studied biology at the

Research Group Head, M.E. Müller Institute for Biomechanics and ITI Institute, University of Bern 1995-2006. Since 2009, Head, Laboratory for Oral Molecular Biology, Department of Orthodontics and Dentofacial Orthopedics.

Dr. Cheiab Zeinab, Research Assistant Barbara Beyeler, Laboratory Technician Isabel Hug, Laboratory Technician Brigitte Megert, Laboratory Technician

PD Dr. Dieter Bosshardt, Laboratory Head

Dr. Nikola Saulacic, Research Scientist Monika Aeberhard, Laboratory Technician

Thuy Trang Nguyen, Laboratory Technician

Silvia Owusu, Laboratory Technician David Reist, Laboratory Technician Margrit Rüfenacht, Laboratory Technician

odontal regeneration using growth factors.

The Chiquet Group is working on two projects: 1) Mechanotransduction in fibroblasts, i.e., the mechanism by which cells sense mechanical forces and respond by changes in gene expression, and 2) Aetiology of cleft palate formation in the Bmp7 knockout mouse (collaboration with D. Graf, University of Zurich). PD Dr. Sigrun Eick sigrun.eick@zmk.unibe.ch



Studied dentistry at the University of Jena, Germany; DMD degree. Microbiological diagnostics and research on oral microbiology at the Institute of Medical Microbiology, University Hospital of Jena 1987-

2009; Habilitation in 2001. Research stays at the Jagiellonian University, Poland. Since 2009, Head, Laboratory of Oral Microbiology, Department of Periodontology. University Bern Umhabilitation in 2011.

# **Prof. Dr. Matthias Chiquet**, Laboratory Head

Antonia Colangelo, Auxiliary Technician Susan Blumer, Laboratory Technician Sabrina Ruggiero, Laboratory Technician Neha Gadhari, PhD Student Nikos Gkantidis, DDS Student

PD Dr. Sigrun Eick, Laboratory Head Antonia Colangelo, Auxiliary Technician Regula Hirschi, Laboratory Technician Sabrina Ruggiero, Laboratory Technician Catherine Solioz, Laboratory Technician Marianne Weibel, Laboratory Technician Richard Miron, PhD Student

The Eick Laboratory is: 1) Analysing microorganisms and immuno-markers in clinical trials of about 500 implants, 2) Assessing the efficacy of antimicrobial treatment in vitro, and 3) Determining the importance of bacterial enzymes in periodontitis, also in association with systemic diseases (collaboration with Jagiel-lonian University).

The Lussi Laboratory is involved in three projects: 1) Diagnosis of caries and minimally invasive preparation techniques, 2) Adhesion of dental materials to dental hard tissue, and 3) Diagnosis, prevention and treatment of dental erosion. Another group in the department deals with clinical issues.

### Collaborators

Blom A, Lund University, Sweden Chiquet-Ehrismann R, University of Basel, Switzerland Cochran D. University of Texas

Health Science Center at San Antonio, USA

Ganss C, Schlueter N, University of Giessen, Germany

Graf D, University of Zurich, Switzerland

Hellwig E, University of Freiburg, Germany

**lizuka T**, Inselspital, Switzerland **Jentsch H**, University Hospital of Leipzig, Germany

Kantyka T, Jagiellonian University, Poland

Koch M, University of Cologne, Germany

Meier C, Bossen A, Bern University of Applied Sciences, Biel, Switzerland Meier W, University of Basel, Switzerland

Möller B, Inselspital, Switzerland Moses O, Tel Aviv University, Israel

Pfister W, Guentsch A, Jena University Hospital, Germany

Potempa J, Jagiellonian University, Poland

Sharma PK, University Medical Center Groningen, The Netherlands Shellis P, University of Bristol, UK Sroka A, Jagiellonian University, Poland

**Taubert A**, University of Potsdam, Germany

### Grants

#### Amounts allocated for 2011:

SNF: Engineering the microenvironment: mechanosensation and asymmetric stem cell division in physiologically relevant cell niches (J. Brugger, M. Lutolf, M. Textor, M. Chiquet) CHF 57,000 CMS Dental ApS: Effect of photoactivated disinfection using a lightemitting diode in the red spectrum (S. Eick, A. Sculean) CHF 19,425

Deppeler: In vitro evaluation of surface roughness and adhesion of bacteria and cells following root instrumentation with "Intensiv/ Deppeler" diamond curettes (S. Eick, A. Sculean, A. Lussi) CHF 8,000

DFS-Diamon: Efficacy of Osteora® on host cells (S. Eick, A. Sculean) CHF 26,500

EMS: Effectiveness of a new erythritol powder air-polishing in supportive periodontal therapy. An examiner-masked, controlled clinical study (A. Sculean) CHF 6,000

GABA: Interaction of stannous ions with dental hard tissues (E. Rakhmatullina, A. Lussi) CHF 10,500

GABA: Initial erosion-inhibiting effect of stannous and fluoridecontaining mouthrinse (E. Rakhmatullina, A. Lussi) CHF 23,000

Institute Straumann: Influence of human blood on the adsorption of enamel matrix proteins to root surfaces and human PDL cell attachment (A. Sculean, R. Miron, D. Bosshardt) CHF 7,400

Institute Straumann: Periodontal regeneration with Emdogain in diabetic rats (E. Hedbom, N. Saulacic, R. Miron, D. Bosshardt, D. Buser) CHF 18,275

ITI: Comparative histologic and histomorphometric study of osseointegration of titanium, titanium-zirconium and titanium-aluminum-vanadium dental implants in a minipig maxilla model (D. Buser) CHF 52,728

ITI: Examination of the osteogenic potential of autogenous bone graft particles in vitro and in vivo (E. Hedbom, N. Saulacic, R. Miron, D. Bosshardt, D. Buser) CHF 62,470

ITI: Long-term retrospective evaluation of survival and complication rates of implants and implantsupported reconstructions in partially edentulous patients (G. Salvi) CHF 15,000

Kerr Corporation: Vickers Hardness, Elastic Modulus, and Depth of Cure

of a New Resin Composite (A. Peutzfeld, A. Lussi) CHF 3,700

Swiss Association for Preventive and Restorative Dentistry SVPR: Prevention of erosion (A. Lussi) CHF 6,200

Swiss Society of Odontology: Noncontact diagnostic tool for quantification of dental erosion (A. Lussi, E. Rakhmatullina) CHF 11,000

### **Publications**

#### Selected publications:

(see page 49 for a complete list)

The role of bone debris in early healing adjacent to hydrophilic and hydrophobic implant surfaces in man. Bosshardt, DD; Salvi, GE; Huynh-Ba, G; Ivanovski, S; Donos, N; Lang, NP (2011) in: Clin Oral Implants Res, 22(4), p. 357-364.

Premature osteoblast clustering by enamel matrix proteins induces osteoblast differentiation through up-regulation of connexin 43 and N-cadherin. Miron, RJ; Hedbom, E; Ruggiero, S; Bosshardt, DD; Zhang, Y; Mauth, C; Graf, A; Iizuka, T; Buser, D; Sculean A (2011) in: PLoS One, 6(8) e23375.

Nano-stenciled gold pattern that inhibit focal contact formation induce lamellipodia formation in fibroblasts. Lutz, R; Pataky, K; Gadhari, N; Marelli, M; Brugger, J; Chiquet, M (2011) in: PLoS One, 6(9), e25459.

Comparison of real-time polymerase chain reaction and DNA-strip technology in microbiological evaluation of periodontitis treatment. Eick, S; Straube, A; Guentsch, A; Pfister, W; Jentsch, H (2011) in: Diagn Microbiol Infect Dis, 69(1), p. 12-20.

Application of the specular and diffuse reflection analysis for in vitro diagnostics of dental erosion: correlation with enamel softening, roughness, and calcium release. Rakhmatullina, E; Bossen, A; Höschele, C; Wang, X; Beyeler, B; Meier, C; Lussi, A (2011) in: J Biomed Opt, 16(10), p. 107002.

# Experimental Haematology (Adults) www.dkf.unibe.ch/research-group/68/

Prof. Dr. Gabriela M. Baerlocher gabriela.baerlocher@insel.ch



MD from the University of Bern. Postgraduate course in experimental medicine at the University of Zurich. Clinical training in internal medicine (FMH) and haematology (FMH/FAMH) in Chur and Bern. Postdoc suthere Califactic

at the University of Southern California, Los Angeles, USA and Terry Fox Laboratory, Vancouver, Canada. Since 2002, physician at the Department of Hematology, Inselspital and DCR Group Leader. Since 2005, Head, Stem Cell Laboratory. Assistant Professor 2006; Associate Professor 2010. Dr. Elisabeth Oppliger Leibundgut elisabeth.oppliger@insel.ch



Studies in pharmacy at the University of Bern. PhD in molecular genetics, postdoc at the DCR establishing molecular diagnostics in haematological neoplasia. Since 1999, Head, Molecular Diagnostics Laboratory

of Hematology, Inselspital, and DCR Group Leader. FAMH in Medical Genetics 2004. Research interests: Molecular biomarkers in haematological neoplasia and pathophysiology of myeloproliferative neoplasms.

# **Group Members**

Prof. Dr. Gabriela M. Baerlocher, Group Leader Dr. Elisabeth Oppliger Leibundgut, Group Leader Dr. Meike Dahlhaus, Postdoctoral Fellow (since Sep.) Dr. Alexandre Theocharides, Postdoctoral Fellow (since Sep.) Dr. Thomas von Känel, Postdoctoral Fellow (until Aug.) Ingrid Helsen, Laboratory Technician Anna Pham, PhD Student (since May) Claudio Brunold, MSc Student Patricia Darlington, MD Student Claudia Kobel, MD Student (until July) Daniela Rogenmoser-Dissler, MD Student (until Oct.)

# Research Highlights 2011 / Outlook 2012

In the framework of our research on the pathophysiology of haematopoesis, we established molecular analyses for all relevant molecules involved in hereditary defects of telomere pathways, and identified several new patients and family members with known or new mutations. A particular highlight was the identification of mutations in a new telomere-associated molecule in Coats' plus syndrome that will be published in collaboration with a group in the UK in *Nature Genetics*.

Myeloproliferative neoplasms (MPN) are stem cell disorders characterised by unlimited cellular proliferation and thromboembolic events. We discovered that not only telomerase is inhibited by a telomerase inhibitor in stem and progenitor cells of patients with MPN but that the unlimited cellular proliferation can be suppressed. These findings form the basis of a clinical study and were presented at the American Society of Hematology annual meeting. The precise mechanism leading to the often life-threatening thrombotic events in MPN is still unclear. By gene expression profiling of cultured endothelial cells of MPN patients, we found a massive overexpression of adhesion molecules, suggesting the involvement of activated endothelial cells in thrombosis formation.

Alexandre Theocharides received the Research Prize at the 2011 DCR Day of Clinical Research for his project: The haematopoietic hierarchy in myeloproliferative neoplasms.

# Collaborators

Alter B, National Cancer Institute, Washington, DC, USA Ansari M, University Hospital Geneva, Switzerland Cross N, University of Southampton, UK Crow Y, University of Manchester, UK Grimwade D, King's College London, UK Hehlmann R, University of Mannheim, Germany Hermouet S, University of Nantes, France Hochhaus A, University of Jena, Germany Lansdorp P, Terry Fox Laboratory of Hematology/Oncology Vancouver, Canada and University of Groningen, The Netherlands Müller M, University Hospital Mannheim, Germany

Pallisgaard N, Vejle Hospital, Denmark
Röth A, University Hospital of Essen, Germany
Rovo A, University Hospital of Basel, Switzerland
Tichelli A, University Hospital of Basel, Switzerland

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### Grants

#### Amounts allocated for 2011:

Research Prize (funded by Faculty of Medicine, University of Bern): The hematopoietic hierarchy in myeloproliferative neoplasms (A. Theocharides) CHF 30,000

Geron Corporation Scientific Grant: Pre-clinical studies to evaluate antitumor efficacy of GRN163L in samples from patients with lymphoproliferative disorders (G.M. Baerlocher) CHF 42,000

Geron Corporation Scientific Grant: Pre-clinical study to evaluate the effect of imetelstat on megakaryocyte-CFU growth in essential thrombocythemia (ET) samples (G.M. Baerlocher) CHF 51,000

Geron Corporation Clinical Grant: Phase II trial to evaluate the activity of imetelstat in patients with essential thrombocythemia who require cytoreduction and have failed or are intolerant to previous therapy, or who refuse standard therapy (G.M. Baerlocher) CHF 50,000

Geron Corporation Scientific Grant: Pharmacodynamic assays for patients with essential thrombocythemia in the clinical imetelstat study (G.M. Baerlocher, E. Oppliger Leibundgut) CHF 380,000

Bernische Krebsliga: Characterization of endothelial cells, correlation with the JAK2 V617F mutation and possible contribution to thrombosis formation in polycythemia vera (E. Oppliger Leibundgut) CHF 55,000

Novartis Educational Grant: Molecular monitoring of the BCR-ABL transcripts and standardization of complete molecular response in patients with CML (E. Oppliger Leibundgut and G.M. Baerlocher) CHF 19,000

Novartis: Swiss wide standardization of the molecular monitoring of the BCR-ABL transcripts in CML patients in the frame of the European project EUTOS for CML (E. Oppliger Leibundgut) CHF 34,000

### Publications

Telomere length is associated with disease severity and declines with age in dyskeratosis congenita. Alter, BP; Rosenberg, PS; Giri, N; Baerlocher, GM; Lansdorp, PM; Savage, SA; (2011) in: Haematologica, Epub head of print (PMID 22058220).

Impact of additional cytogenetic aberrations at diagnosis on prognosis of CML: long-term observation of 1151 patients from the randomized CML Study IV. Fabarius, A; Leitner, A; Hochhaus, A; Müller, MC; Hanfstein, B; Haferlach, C; et al. (2011) in: Blood, 118(26) p. 6760-6768.

Deregulated expression of Kruppellike factors in acute myeloid leukemia. Humbert, M; Halter, V; Shan, D; Laedrach, J; Oppliger Leibundgut, E; Baerlocher, GM; et al. (2011) in: Leuk Res, 35(7), p. 909-913.

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Telomeres and prognosis in patients with chronic lymphocytic leukaemia. Sellmann, L; de Beer, D; Bartels, M; Opalka, B; Nückel, H; Dührsen, U; et al. (2011) in: Int J Hematol, 93(1), p. 74-82.

Nabelschnurblut-Stammzellspende: Wie ist der heutige Stand? Wagner, AM; Troeger, C; Nicoloso, G; Bart, T; Schwabe, R; Castelli, D; et al. (2011); in Schweiz Med Forum, 11(39), p. 676-680.

CML – eine Auswahl an Highlights vom ASH-Meeting 2010. Baerlocher, GM in: Leading Opinions Hämatologie-Onkologie, May 2011.

Recruitment of platelets, white blood cells, and hematopoietic progenitor cells during high-yield plateletpheresis. Fontana, S; Rados, L; Schmid, P; Oppliger Leibundgut, E; Mansouri Taleghani; B (2011) in: Transfusion, 51(9) p. 2034-2043 (doi: 10.1111/j.1537-2995.2011.03117.x.).

# Neurology www.neuro-bern.ch/cms/index.php?id=139

Prof. Dr. Christian W. Hess christian.hess@insel.ch



MD at the University of Zurich in 1973. Research Fellow in experimental neurophysiology at the Physiological Institute, Zurich in 1974; specialist in Neurology in 1981. Visiting Scientist at the Institute of Neurology,

University of London, UK 1986. Habilitation at the University of Bern in 1987. Since 1990, Chair of Neurology, University of Bern and Clinic Director, University Clinic for Neurology, Inselspital.

# Group Members

Prof. Dr. Christian W. Hess, Clinic Director PD Dr. Kaelin Alain, Group Leader

PD Dr. Kaelin Alain, Group Leader Prof. Dr. Kai Roesler, Group Leader PD Dr. Alain Kaelin alain.kaelin@dkf.unibe.ch



Bern in 1991; specialised in neurology. Fellowship in movement disorder and neurophysiological research at the National Institute of Neurological Disorders and Stroke, Bethesda, USA 1999-

MD at the University of

2001. Since 2002, Head, Movement Disorders Center, University Clinic for Neurology, Inselspital. Conducting a clinical and basic research program in movement disorders.

Prof. Dr. Jean-Marc Burgunder, Research Associate Dr. Oliver Findling, Research Associate Dr. Christine Capper-Loup, Research Associate Prof. Dr. Kai Rösler kai-michael.roesler@insel.ch



MD at the University of Bern in 1982. After 4 years research on skeletal muscle at the Institute of Anatomy, University of Bern and the University of Southern California, Los Angeles, USA, soecialisation in neurol-

ogy in Bern. Since 2002, Head, Muscle Center, University Clinic for Neurology, Inselspital. Responsible for neuromuscular biopsies in the Neuromorphology Laboratory and a research program in clinical neurophysiology.

Theres Lauterburg, Laboratory Technician Ursula Walker, Laboratory Technician Daniel Brechbühl, MD Student Caroline Frey, MD Student Dominik Rebell, MD Student

# Research Highlights 2011 / Outlook 2012

Our research projects aim at a better understanding of the neurophysiology of Parkinson's Disease (PD). In clinical research, we are mainly interested in the pathophysiological sensorimotor mechanisms occurring in PD. For example, we investigated the impact of the disease on motor learning and on the perception of rhythms. Our main priority has changed, however, to the pathophysiology of levodopa-induced dyskinesia. These disabling involuntary movements occurring in PD patients treated with levodopa are both a clinical and a research challenge. In our most important publication in 2011, we described the predictive factors for this dyskinesia.

In basic research, 2011 was a transition period. We finished the analysis of several projects using the 6-hydroxydopamine rat model of PD. All these projects used the standardised "Ethovision" open-field analysis system. Also in animal research, we now want to focus our research on levodopa-induced dyskinesia. We were successful in obtaining two grants, which will allow us to start the first project investigating the role of the enkephalinergic system in this form of dyskinesia.

### Collaborators

Bloch J, University of Lausanne, Switzerland Brunet JF, University of Lausanne,

Switzerland

Luft A, University of Zurich, Switzerland

**Geiser E**, Massachusetts Institute of Technology, USA

### Grants

#### Amounts allocated for 2011:

Swiss Parkinson Association: Histological impact of autologous brain cell transplantation in a monkey MPTP model of Parkinson's disease (A. Kaelin-Lang, J. Bloch) CHF 50,000 Swiss Parkinson Association: Cortical plasticity in Parkinsonian rats with levodopa induced dyskinesia (A. Kaelin-Lang) CHF 35,000

Baasch-Medicus Award 2011: Cortical plasticity in Parkinsonian rats with levodopa induced dyskinesia (A. Kaelin-Lang, A. Luft) CHF 50,000

# **Publications**

Motor sequence learning performance in Parkinson's disease patients depends on the stage of disease. Stephan, MA; Meier, B; Zaugg, SW; Kaelin-Lang, A (2011) in: Brain Cogn, 75(2), p. 135-140.

Schlaglichter 2010: Neurologie. Kaelin-Lang, A; Schuepbach, WM (2011) in: Schweiz Med Forum, 11(3), p. 40-41.

Parkinson's disease and the bones. Gnädinger, M; Mellinghoff, HU; Kaelin-Lang, A (2011) in Swiss Med Wkly, 16(141), w13154, Review (doi: 10.4414/smw.2011.13154).

The function of dopaminergic neural signal transmission in auditory pulse perception: Evidence from dopaminergic treatment in Parkinson's patients. Geiser, E; Kaelin-Lang, A (2011) in: Behav Brain Res, 225(1), p. 270-275.

Monoclonal gammopathy missed by capillary zone electrophoresis. Schild, C; Egger, F; Kaelin-Lang, A; Nuoffer, JM (2011) in: Clin Chem Lab Med, 49(7), p. 1217-1219.

Resting Tremor in Parkinson's Disease is a Negative Predictor of Levodopa-Induced Dyskinesia. Kipfer, S; Stephan, MA; Schuepbach, WM; Ballinari, P; Kaelin-Lang, A (2011) in: Arch Neurol, 68(8), p. 1037-1039.

Deep brain stimulation of the globus pallidus internal improves symptoms of chorea-acanthocytosis. Li, P; Huang, R; Song, W; Ji, J; Burgunder, JM; Wang, X; Zhong, Q; Kaelin-Lang, A; Wang, W; Shang, HF (2011) in: Neurol Sci, Aug 24.

Frühdiagnose des Morbus Parkinson: Nicht-motorische Symptome geben wichtige Hinweise. Kaelin-Lang, A (2011) in: Info Neurologie & Psychiatrie, 9(2).

Pilot study on a fast postoperative programming approach to subthalamic nucleus stimulation in Parkinson's disease. Li, P; Mao, B; Shang, H; Kaelin-Lang, A; Wang, W (2011) in: Neurol India, 59(5), p. 669-673.



# Neurosurgery

# www.neurochirurgie.insel.ch/de/lehre-und-forschung/forschungslabor

Prof. Dr. Andreas Raabe andreas.raabe@insel.ch



Trained in Chemnitz, Leipzig and Frankfurt, Germany, with visits as a clinical observer to Cambridge, UK, Munich, Germany and Phoenix, USA. Since 2008, Clinic Director, University Clinic for Neurosurgery,

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Inselspital. Expertise: Vascular neurosurgery, tumour surgery and spinal microsurgery. Research focus: Use of intraoperative technologies during vascular and tumour surgery, such as image guidance, fMRI and tractography, intraoperative imaging, fluorescence diagnostics and advanced intraoperative electrophysiological monitoring and mapping.

#### Prof. Dr. Michael Reinert mmv.reinert@insel.ch



MD at the University of Basel. Residencies in surgery, internal medicine and neurosurgery in Basel, Aarau and Bern. Clinical research neurotrauma fellowship in Richmond, USA 1998-99. Board certification in

neurosurgery 2002. SNF grant on laser tissue soldering 2003-2005. Habilitation in 2007. Specialization in neurovascular surgery. Since 2008, Vice-Chairman, Department of Neurosurgery. Associate Professor of Neurosurgery in 2011. Secretary, Swiss Society of Neurosurgery.

### **Group Members**

Prof. Dr. Andraes Raabe, Clinic Director Prof. Dr. Michael Reinert, Group Leader Dr. Lukas Andereggen, Junior Doctor Dr. Serge Bogni, Postdoctoral Fellow Eva Schlachter, MD Student Daniel Schöni, MD Student

# Research Highlights 2011 / Outlook 2012

Our group focuses on the development of minimal invasive surgical techniques, especially tissue fusion. The integration of nanotechnology leads to a precise, predictable tissue fusion. We have developed a new multilayer indocyanine-greencontaining polycoated nanoparticle suitable for implantation into a polymer for laser tissue fusion. The longterm effects of nanoparticle-containing polymer are being investigated.

Our research focuses on three different aspects:

1) Development of sutureless tissue fusion for vascular anastomosis.

2) Transport of nanoparticles in a biodegradable implant.

3) Tissue soldering for endoscopic techniques.

Each of these aspects is covered by a research grant and is being addressed together with the collaborators listed hereafter.

A further research topic is to establish the role of perfluorocarbon, an artificial oxygen carrier, as a neuroprotector in severe head injury and in subarachnoid haemorrhage. Prof. Dr. Michael Reinert is the Global Principal Investigator for the multicentre "Safety and Tolerability of Oxycyte in Patients With Traumatic Brain Injury" (STOP-TBI) study.

### Collaborators

Constantinescu M, Inselspital, Switzerland

Frenz M, University of Bern, Switzerland

Mevissen M, University of Bern, Switzerland

**Pieles U**, University of Applied Sciences Northwestern Switzerland **Schönbächler A**, University of Applied Sciences Northwestern Switzerland

Widmer HR, University of Bern, Switzerland

### Grants

#### Amounts allocated for 2011:

SNF: Sutureless endoluminal and transluminal microvscular laser anastomosis (M. Constantinescu, M. Reinert, M. Frenz) CHF 100,000

KTI: Tissue soldering with nanoparticle scaffold (M. Frenz, M. Reinert) CHF 510,000

SNF: Transport of nanoparticles after release from a biodegradable implant (M. Frenz, M. Mevissen, M. Reinert, U. Pieles) CHF 130,000

### **Publications**

Glue enhanced excimer laser-assisted nonocclusive anastomosis: a laboratory investigation. Alfieri, A; Reinert, M (2011) in: Eur Surg Res, 46(1), p. 32-37.

Metabolic pathway and distribution of superparamagnetic iron oxide nanopartciles: in-vivo study. Schlachter, E; Widmer, HR; Bregy, A; Lörnnfors, T; Vajtai, I; Corazza, N; Bernau, V; Weitzel, T; Mordasini, P; Slotboom, J; Herrmann, G; Bogni, S; Hofmann, H; Frenz, M; Reinert, M (2011) in: Int J Nanomedicine, 6, p.1793-1800.

Nanoshell assisted laser soldering of vascular tissue. Schöni, DS; Bogni, S; Bregy, A; Wirth, A; Raabe, A; Vajtai, I; Pieles, U; Reinert, M; Frenz, M (2011) in: Lasers Surg Med, 43(10), p. 975-983.

Restenosis after microsurgical nonpatch carotid endarterectomy in 586 patients. Reinert, M; Mono, ML; Kuhlen, D; Mariani, L; Barth, A; Beck, J; Andres, RH; Gralla, J; Wymann, R; Schmidt, J; Kauert, C; Schroth, G; Arnold, M; Mattle, HP; Raabe, A; Fischer, U (2011) in: Acta Neurochir (Wien), Nov.

Tissue fusion, a new opportunity for sutureless bypass surgery. Bogni, S; Schöni, D; Constantinescu, M;

Wirth, A; Vajtai, I; Bregy, A; Raabe, A; Pieles, U; Frenz, M; Reinert, M (2011) in: Acta Neurochir Suppl, 112, p. 45-53, Review.



# Orthopaedic Surgery www.dkf.unibe.ch/research-group/31/

Prof. Dr. Klaus-Arno Siebenrock klaus.siebenrock@insel.ch



Graduated from University of Tübingen Medical School, Germany in 1986. Training as an Orthopaedic Surgeon at the University of Munich, Germany and Inselspital, Bern. Orthopaedic fellowships at the Mayo

Clinic and University of California, Los Angeles, USA. Board certified orthopaedic surgeon since 1997. Venia docendi for orthopaedic surgery at the Inselspital, Bern in 2002. Since 2005, Director and Chairman, University Clinic for Orthopaedic Surgery, Inselspital.

Our research group is embedded in the Bone Biology & Orthopaedic Research Group led by Prof. Dr. Willy Hofstetter. He co-supervises our projects and we share his laboratory technicians (Silvia Dolder, Mark Siegrist).

# Dr. Frank M. Klenke frank.klenke@insel.ch



Graduated from University of Heidelberg Medical School, Germany in 2001. MD at the University of Heidelberg in 2002. Training as an Orthopaedic Surgeon at the University of Heidelberg, Germany

and Inselspital, Bern. Research Assistant at the DCR 2005-2007. PhD at the Free University of Amsterdam, The Netherlands in 2010. Since 2010, Consultant Surgeon at the University Clinic for Orthopaedic Surgery, Inselspital.

### **Group Members**

Prof. Dr. Klaus-Arno Siebenrock, Clinic Director Dr. Frank M. Klenke, Project Leader Dr. Christoph Albers, Postdoctoral Fellow

Dr. Hans-Jörg Sebald, Postdoctoral Fellow

John Choy, PhD Student

# Research Highlights 2011 / Outlook 2012

Our research focuses on the development of composites of  $\beta$ -tricalcium phosphate ( $\beta$ -TCP) ceramics and bioactive proteins for the repair of osseous defects. In particular, our aim is to biofunctionalise  $\beta$ -TCP ceramics using a sustained co-delivery system of L51P, an inhibitor of bone morphogenetic protein (BMP) antagonists, the angiogenic growth factor VEGF, and the osteoclast differentiation and activation factor RANKL. We hope to promote bone formation, biomaterial vascularisation and osteoclastmediated material resorption.

A coating technique achieving a sustained release of growth factors from ceramic biomaterials was developed (collaboration with E.B. Hunziker and Y. Liu). This technique enables us to couple the release of bioactive proteins from ceramic bone substitutes to the resorptive activity of osteoclast and to improve the efficacy of growth factor delivery for bone repair. More recently, the mechanisms underlying the osteoinductive activity of a molecularly engineered variant of bone morphogenetic protein 2 (BMP-2), called L51P, were analysed. L51P was successfully applied to increase the efficacy of BMP-2 in rat femoral defect healing.

In 2012, we will focus on the promotion of osteoclastic biomaterial resorption with RANKL and initiate the first in vivo trial with RANKLloaded biomaterials. Furthermore, multiple proteins will be loaded on the biomaterials to stimulate bone formation and material resorption simultaneously.

# Collaborators

Bohner M, Robert Mathys Foundation, Switzerland Hunziker EB, University of Bern, Switzerland Liu Y, Academic Center for Dentistry Amsterdam, The Netherlands Sebald W, University of Würzburg, Germany

### Grants

#### Amounts allocated for 2011:

SNF: Biofunctionalization of  $\beta$ -TCP ceramics for the repair of osseous defects (F.M. Klenke, W. Hofstetter) CHF 68,192

ITI Foundation: Biofunctionalization of calcium phosphate ceramics for the repair of osseous jaw defects (F.M. Klenke, W. Hofstetter) CHF 53,061

Amgen Extramural Research, USA: Biofunctionalization of CaP ceramics for osseous defect repair. Promotion of biomaterial resorption with a sustained delivery system of RANKL (F.M. Klenke)

### **Publications**

# **Selected publications:** (see page 50 for a complete list)

In vitro cytotoxicity of silver nanoparticles on osteoblasts and osteoclasts at antibacterial concentrations. Albers, CE; Hofstetter, W; Siebenrock, KA; Landmann, R; Klenke, FM (2011) in: Nanotoxicology, Oct 21. The cam-type deformity of the proximal femur arises in childhood in response to vigorous sporting activity. Siebenrock, KA; Ferner, F; Noble, PC; Santore, RF; Werlen, S; Mamisch, TC (2011) in: Clin Orthop Relat Res, 469(11), p. 3229-3240.

Delayed gadolinium-enhanced magnetic resonance imaging of cartilage (dGEMRIC) in Femoacetabular impingement. Mamisch, TC; Kain, MS; Bittersohl, B; Apprich, S; Werlen, S; Beck, M; Siebenrock, KA (2011) in: J Orthop Res, 29(9), p. 1305-1311.

Giant Cell Tumor of Bone: Risk Factors for Recurrence. Klenke, FM; Wenger, DE; Inwards, CY; Rose, PS; Sim, FH (2011) in: Clin Orthop Relat Res; 469(2), p. 591-599.

Synovial sarcomas usually metastasize after >5 years: a multicenter retrospective analysis with minimum follow-up of 10 years for survivors. Krieg, AH; Hefti, F; Speth, BM; Jundt, G; Guillou, L; Exner, UG; von Hochstetter, AR; Cserhati, MD; Fuchs, B; Mouhsine, E; Kaelin, A; Klenke, FM; Siebenrock, KA (2011) in: Ann Oncol, 22(2), p. 458-467.



# Perception and Eye Movement

www.eyelab.dkf.unibe.ch

# Prof. Dr. Christian W. Hess christan.hess@insel.ch



MD at the University of Zurich in 1973. Research Fellow in experimental neurophysiology at the Physiological Institute, Zurich in 1974; specialist in Neurology in 1981. Visiting Scientist at the Institute of Neurology,

University of London, UK 1986. Habilitation at the University of Bern in 1987. Since 1990, Chair of Neurology, University of Bern and Clinic Director, University Clinic for Neurology, Inselspital.

# PD Dr. Stephan Bohlhalter stephan.bohlhalter@luks.ch



MD degree at the University of Zurich in 1994. Chief, Division for Restorative and Behavioral Neurology, Luzerner Kantonsspital and Lecturer (PD) in neurology at the University of Bern. President, Swiss

Parkinson Association Research Committee and Advisory Panel. Research interests: Higherorder motor disorders in stroke and Parkinson's Disease using functional MRI and repetitive transcranial magnetic stimulation.

# Research Highlights 2011 / Outlook 2012

In 2011, we were active in clinical research into the regulation of hemispheric imbalance after focal brain lesion using transcranial magnetic stimulation (TMS). We were successful in showing that TMS is able to improve neurological deficits such as neglect or aphasia by interfering with the intact, hyperactive hemisphere. The effect was long-standing and enduring, and therefore therapeutically useful.

Another topic of research concentrated on praxia, gesture and language. To study the perceptive aspects of these high-level cognitive processes, we used eye movement analysis, and TMS to interfere with behaviour production. These projects are multi-year studies.

# **Group Members**

Prof. Dr. Christian W. Hess, Clinic Director, Group Leader PD Dr. Stephan Bohlhalter, Group

Leader Prof. Dr. René Müri, Group Leader

**PD Dr. Thomas Nyffeler**, Group Leader **Dr. Manuel Bertschi**, Postdoctoral Fellow

**Dr. Sebastian von Arx**, Postdoctoral Fellow

#### Prof. Dr. René Müri rene.mueri@dkf.unibe.ch



MD at the University of Bern in 1984. Clinical formation in Bern and Basel; FMH certification in Neurology 1991. Postdoc at INSERM U 289, Hôpital de la Salpêtrière, Paris, France 1993-1995. Venia Docendi for

Neurology in 1997. Since 2004, Head, Unit of Cognitive and Restorative Neurology, Inselspital. Titular Professor in 2005; Associate Professor of Neurology in 2008.

For 2012, our research will be intensified in the fields of both SNF projects that started in 2011, and the group will have a closer collaboration to the Gerontechnology and Rehabilitation Group.

# Collaborators

Annoni JM, University of Fribourg, Switzerland

Mosimann UP, University of Bern, Switzerland

Nef T, University of Bern, Switzerland

### Grants

#### Amounts allocated for 2011:

SNF: Neural basis of praxis production: From higher-order processing to fine motor control (S. Bohlhalter) CHF 110,000

SNF: Aphasia and co-speech gestures (R. Müri) CHF 146,000

Tobia Brusa, Dipl. Ing. Silvia Chaves, PhD Student Simone Hopfner, PhD Student Mathias Lüthi, PhD Student Rahel Schumacher, PhD Student Tim Vanbellingen, PhD Student

PD Dr. Thomas Nyffeler thomas.nyffeler@insel.ch



MD at the University of Bern in 1995. Neurology residency training in Geneva, Zurich and Bern, and in Paris, France. Lecturer in neurology (PD) at the University of Bern in 2009; joined the Perception and Eye

Movement Laboratory in 2002. Research interests: Physiological and pathophysiological aspects of visual perception of space. Since 2007, Senior Consultant, Division for Cognitive and Restorative Neurology, Inselspital.

SNF: Bilingualism (R. Müri/T. Nyffeler) CHF 100,000

Göhner Stiftung: Transcranial Magnetic Stimulation in Neurorehabilitation (R. Müri, T. Nyffeler) CHF 80,000

# Publications

The link between visual exploration and neuronal activity: A multi-modal study combining eye tracking, functional magnetic resonance imaging and transcranial magnetic stimulation. Chaves, S; Vannini, P; Jann, K; Wurtz, P; Federspiel, A; Nyffeler, T; Luethi, M; Hubl, D; Wiest, R; Dierks, T; Müri, RM (2011) in: Neuroimage, Nov, Epub ahead of print (PMID: 22079455).

Short and valid assessment of apraxia in Parkinson's disease. Parkinsonism Relat Disord. Vanbellingen, T; Lungu, C; Lopez, G; Baronti, F; Müri, RM; Hallett, M; Bohlhalter, S (2011) in: Parkinsonism Relat Disord, Dec, Epub ahead of print (PMID: 22177625).

Bilateral neglect after bihemispheric strokes. Cazzoli, D; Schumacher, R; Baas, U; Müri, RM; Wiest, R; Bohlhalter, S; Hess, CW; Nyffeler, T (2011) in: Cortex, Sep, Epub ahead of print (PMID: 21995967).

Impaired finger dexterity in Parkinson's disease is associated with praxis function. Vanbellingen, T; Kersten, B; Bellion, M; Temperli, P; Baronti, F; Müri, RM; Bohlhalter, S (2011) in: Brain Cogn, 77(1), p. 48-52.

Vertical bias in neglect: A question of time? Cazzoli, D; Nyffeler, T; Hess, CW; Müri, RM (2011) in: Neuropsychologia, 49(9), p. 2369-2374.

A new bedside test of gestures in stroke: The Apraxia Screen of TULIA (AST). Vanbellingen, T; Kersten, B; Van de Winckel, A; Bellion, M; Baronti, F; Müri, RM; Bohlhalter, S (2011) in: J Neurol Neurosurg Psychiatry, 82(4), p. 389-392.

Spontaneous recovery of visuallytriggered saccades after focal lesions of the frontal and parietal eye fields: A combined longitudinal oculomotor and fMRI study. Nyffeler, T; Hubl, D; Wurtz, P; Wiest, R; Hess, CW; Müri, RM (2011) in: Clin Neurophysiol, 122(6), p. 1203-1210.

Interference with gesture production by Theta Burst Stimulation over left inferior frontal cortex. Bohlhalter, S; Bertschi, M; Vanbellingen, T; Wurtz, P; Cazzoli, D; Nyffeler, T; Hess, CW; Müri, RM (2011) in: Clin Neurophysiol, 122(6), p. 1197-1202.

Cognition and driving in older persons. Wagner, JT; Müri, RM; Nef, T; Mosimann, UP (2011) in: Wiss Med Wkly, Jan, p. 140



# **Psychosomatic Medicine**

# inneremedizin.insel.ch/de/ueberuns1/innere-psychosomatik

Prof. Dr. Roland von Känel roland.vonkaenel@insel.ch



Training in biobehavioural research at the University of California, San Diego, USA and the Swiss Federal Institute of Technology (ETH) Zurich. Since 2004, Head, Psychosomatic Division, Inselspital and Senior

Lecturer in somato-psychosocial medicine, University of Bern. Internist and psychiatrist with research interests in the psychobiological pathways linking psychosocial stress with somatic diseases.

# Group Members

Prof. Dr. Roland von Känel, Head and Group Leader PD Dr. Stefan Begré, Research Associate Dr. Niklaus Egloff, Research Associate Dr. Marie-Louise Gander Ferrari, Research Associate Dr. Alexander Hänsel, Research Associate Stefanie Stauber, PhD Student

# Research Highlights 2011 / Outlook 2012

We showed that patients who perceive increased fear of dying, helplessness and pain during myocardial infarction (MI) have a greater risk of hospital readmissions due to a cardiovascular event in the following 3 years. Those with greater levels of post-traumatic stress triggered by the traumatic experience of MI also have an increased rehospitalisation risk.

In a series of partly prospective studies, we further pinpointed psychobiological mechanisms relevant to the increased cardiovascular disease risk in dementia caregivers, including chronic low-grade inflammation and subclinical atherosclerosis.

In patients with Crohn's disease (CD), who were followed for 18 months, we identified poor quality of life, post-traumatic stress triggered by CD and perceived distress as predictors of a poor disease course, including flares, complications and non-response to therapy.

If validated against an electronic pressure algometer, a calibrated clothes peg yielded clinically meaningful information on pain sensitivity, suggesting that it is an easy-toadminister and low-cost method of measuring pain sensitivity in clinical routine. We further showed that seeing and identifying with a virtual body can decrease pain perception. This finding may inform novel therapeutic interventions for chronic pain patients.

Research in 2012 will focus on the biological stress reactivity in hypertensive individuals and those with inflammatory bowel disease.

### Collaborators

Barth J, Cámara RJ, University of Bern, Switzerland Cohort Lausanne (CoLaus) Study Group: www.colaus.ch Curatolo M, Inselspital, Switzerland Demarmels Biasiutti F, Inselspital, Switzerland Fischer JE, University of Heidelberg, Germany Grant I, Dimsdale JE, Mills PJ, University of California, San Diego, USA Kudielka BM, University of Regensburg, Germany Ladwig K-H, Helmholtz Zentrum Munich, Germany Malan L, North-West University, Potchefstroom, South Africa Saner H, Schmid J-P, Inselspital, Switzerland Schnyder U, University Hospital Zurich, Switzerland Steptoe A, University College London, UK Swiss Inflammatory Bowel Disease Cohort Study (SIBDCS) Group: www.ibdcohort.ch Thurston RC, University of Pittsburgh, USA Wirtz PH, University of Bern, Switzerland Znoj H, Messerli-Bürgy N, University of Bern, Switzerland

# **Publications**

#### Selected publications:

(see page 50 for a complete list)

Effect of Alzheimer Caregiving on Circulating Levels of C-Reactive Protein and Other Biomarkers Relevant to Cardiovascular Disease Risk: A Longitudinal Study. von Känel, R; Mills, PJ; Mausbach, BT; Dimsdale, JE; Patterson, TL; Ziegler, MG; Ancoli-Israel, S; Allison, M; Chattillion, EA; Grant, I (2011) in: Gerontology, Epub ahead of print (PMID 22133914).

Algometry with a clothes peg compared to an electronic pressure algometer: a randomized crosssectional study in pain patients. Egloff, N; Klingler, N; von Känel, R; Cámara, RJ; Curatolo, M; Wegmann, B; Marti, E; Gander Ferrari, ML (2011) in: BMC Musculoskelet Disord, 12, p. 174.

Distress related to myocardial infarction and cardiovascular outcome: a retrospective observational study. von Känel, R; Hari, R; Schmid, JP; Saner, H; Begré, S (2011) in: BMC Psychiatry, p. 98.

Posttraumatic stress in Crohn's Disease and its association with disease activity. Cámara, RJ; Gander, ML; Begré, S; von Känel, R; Swiss Inflammatory Bowel Disease Cohort Study Group (2011) in: Frontline Gatroenterol, p. 2-9 (doi:10.1136/ fg.2010.002733).

Mood and nonmood components of perceived stress and exacerbation of Crohn's disease. Cámara, RJ; Schoepfer, AM; Pittet, V; Begré, S; von Känel, R; Swiss Inflammatory Bowel Disease Cohort Study Group (2011) in: Inflamm Bowel Dis, 17(11), p. 2358-2365 (doi: 1002/ ibd.21623).



# Rheumatology www.ria.insel.ch

Prof. Dr. Peter M. Villiger peter.villiger@insel.ch



# Prof. Dr. Michael Seitz michael.seitz@insel.ch



MD at the University of Heidelberg, Germany. Training in immunology and postgraduate work in internal medicine and rheumatology. Since 1992, Deputy Head, University Clinic of Rheumatology, Clinical Immu-

nology and Allergology, Inselspital. Associate Professor of Rheumatology 1995. Held SNF research grants in cytokine research and osteoimmunology. Research focus: Osteoclastogenesis in chronic rheumatic inflammation.

### **Group Members**

**Prof. Dr. Peter M. Villiger**, Clinic Director, Group Leader

Dr. Frauke Förger, Group Leader Manuela Tham, PhD Student Janine Weix, PhD Student Gabriele Schlör, MD Student (until May) Janine Vetsch, Master Student (since Aug.)

# Research Highlights 2011 / Outlook 2012

The Villiger and Förger Group investigated mechanisms of pregnancyrelated immunoregulation that have an impact on disease amelioration in autoimmune rheumatic diseases. In this context, the role of soluble factors such as adipocytokines, as well as cellular factors such as gammadelta T cells were studied.

The Lottaz Group studied the role of host mucosal proteases in inflammatory bowel disease (IBD). In collaboration with the Institute of Social and Preventive Medicine, University Dr. Frauke Förger frauke.foerger@insel.ch



MD at the Ludwig Maximilian University of Munich, Germany in 1995. Postdoc at the Inselspital investigating immunoregulatory cytokines and T cell subtypes in pregnancyinduced remission of ince 2006. Senior Rheu-

rheumatic diseases. Since 2006, Senior Rheumatologist and Head, Outpatient Clinic for pregnant women with rheumatic diseases.

#### Prof. Dr. Beat Trueb beat.trueb@dkf.unibe.ch



Studied biochemistry at the ETH Zurich; PhD on extracellular matrix proteins. Postdoc at the University of Washington, Seattle, USA. Independent Group Leader with SNF START Fellowship at the ETH Zurich. Head, Divi-M.E. Müller Institute for

sion of Biochemistry, M.E. Müller Institute for Biomechanics, University of Bern 1995. Associate Professor 2001. Since 2008, Group Leader, University Clinic of Rheumatology, Clinical Immunology and Allergology, Inselspital.

**PD Dr. Daniel Lottaz**, Group Leader (until Oct.)

Dr. Camila Mendes, Postdotoral Fellow (until Apr.)

**Dr. Stefan Wyder**, Postdoctoral Fellow (until Apr.)

Gesine Kaiser, Student (until Feb.) Prof. Dr. Michael Seitz, Group Leader Dr. Daniel Aeberli, Clinical Research Associate

of Bern, the group developed a new method to identify novel genes involved in IBD, based on a systematic analysis of all types of genetic studies ever published.

The Seitz Group examined the role of TNF $\alpha$  on osteoclastogenesis in chronic rheumatic disorders, and the differential role of TNF $\alpha$  and IL-17 in mouse osteoclastogenesis. Next, the group will study the effect of anti-TNF $\alpha$  treatment on the trafficking of osteoclast precursor cells in a TNF $\alpha$  transgenic mouse model of arthritis.

The Trueb Group investigated a novel FGF receptor called FGFRL1. Fgfrl1 knock-out mice die at birth

PD Dr. Daniel Lottaz daniel.lottaz@insel.ch



MD at the University of Bern in 1992; clinical internships 1992-1994; MD PhD in 1998. Postdoc in Switzerland and abroad 1998-2007. Venia docendi in Molecular Medicine 2011. Coordinator, EC-FP7 IBDase

project on the aetiology and pathogenesis of inflammatory bowel disease 2008-2011. Since 2007, Head, Rheumatology Laboratory.

Deepak Balani, PhD Student Richard Kamgang, Research Assistant Prof. Dr. Beat Trueb, Group Leader Dr. Simon Gerber, Postdoctoral Fellow (until Mar.) Ruth Amann, PhD Student Ralph Bessey, PhD Student (until July) Xiaochen Yang, PhD Student (since Aug.) Lei Zhuang, PhD Student

and lack both metanephric kidneys. The group found that the novel receptor is involved in cell-cell fusion. When transfected into CHO cells, FGFRL1 induces fusion into large syncytia comprising several hundred nuclei.

### Collaborators

Bond JS, Penn State University, Hershey, USA Engelhardt B, Stein J, University of Bern, Switzerland Fernig D, School of Biological Sciences, Liverpool, UK Häupl T, Charité - Universitätsmedizin Berlin, Germany Hofstetter W, University of Bern, Switzerland Jameson S, Duke University, USA

Mohammadi M, New York University School of Medicine, USA Overall CM, University of British Columbia, Canada

Slavotinek A, University of California, San Francisco, USA *IBDase Research Consortium*: Artieda M, Progenika, Spain

**Becker-Pauly C**, University of Mainz, Germany **Darfeuille-Michaud A**, University of Clermont-Ferrand, France

Hansson G, University of Gothenburg, Sweden Monteleone G, University of Rome

"Tor Vergata", Italy Pender S, University of Southamp-

ton, UK Rescigno M, European Institute of

Oncology Foundation, Italy Vermeire S, University of Leuven, Belgium

#### Grants

#### Amounts allocated for 2011:

SNF: Osteoclastogenesis in chronic arthritis (M. Seitz, W. Hofsetter, D. Aeberli) CHF 47,000 SNF: Role of the novel growth factor receptor FGFRL1 in health and disease (B. Trueb) CHF 115,850

EC-FP7 grant: IBDase, Proteases and their inhibitors in inflammatory bowel disease: From etiopathogenetic insight to innovative therapy (D. Lottaz) CHF 100,000

Abbott Grant: The role of gammadelta T cells in pregnancy induced remission of rheumatic diseases (F. Förger) CHF 16,600

Muscle Foundation: Role of the novel receptor FGFRL1 in myoblast fusion (B. Trueb) CHF 49,000

Olga Mayenfisch Stiftung: The role of gammadelta T cells in pregnancy induced remission of rheumatic diseases (F. Förger) CHF 13,000

### **Publications**

#### Selected publications:

(see page 51 for a complete list)

Enhanced activity of meprin-α, a pro-migratory and pro-angiogenic protease, in colorectal cancer. Lottaz, D; Maurer, CA; Noël, A; Blacher, S; Huguenin, M; Nievergelt, A; Niggli, V; Kern, A; Müller, SJ; Seibold, F;

Friess, H; Becker-Pauly, C; Stöcker, W; Sterchi, EE (2011) in: PLoS One, 6(11), e26450.

Biology of FGFRL1, the fifth fibroblast growth factor receptor. Trueb, B (2011) in: Cell Mol Life Sci, 68(6), p. 951-964.

Interaction of the receptor FGFRL1 with the negative regulator Spred1. Zhuang, L; Villiger, P; Trueb, B (2011) in: Cell Signal, 23(9), 1496-1504.

Treatment with biologics of pregnant patients with rheumatic diseases. Ostensen, M; Förger, F (2001) in: Curr Opin Rheumatol, 23(3), p. 293-298.

Protective effect of A/H1N1 vaccination in immune-mediated disease--a prospectively controlled vaccination study. Adler, S; Krivine, A; Weix, J; Rozenberg, F; Launay, O; Huesler, J; Guillevin, L; Villiger, PM (2011) in: Rheumatology, Dec 14, Epub ahead of print (PMID: 22171015).

# Tumor Immunology www.ochsenbeinlab.ch

Prof. Dr. Adrian Ochsenbein adrian.ochsenbein@insel.ch



Øinsel.ch
MD at the University of Bern in 1992. Postgraduate education in internal medicine and medical oncology in Solothurn and Bern. Research Fellow, Institute for Experimental Immunology, University of Zurich

1996-1999. Postdoc at the Fred Hutchinson Cancer Research Center, Seattle, USA 2001-2002. Independent Group Leader with SNF Professorship at the DCR 2003. Since 2011, Chief Physician at the University Clinic for Medical Oncology, Inselspital.

### Group Members

Prof. Dr. Adrian Ochsenbein, Group Leader

Dr. Carsten Riether, Postdoctoral Fellow Dr. Christian Schürch, Postdoctoral Fellow

Mohamad Al Sayed, PhD Student (since Feb.)

Tamara Hilmenyuk, PhD Student

Anne-Laure Huguenin, Laboratory Technician Paranetharran Pushpanathan, Laboratory Technician Sarah Gabriel, BMSc Student (since Aug.) Carla Ruckstuhl, BMSc Student (since Aug.) Michael Amrein, MD Student Elias Bührer, MD Student

# Research Highlights 2011 / Outlook 2012

Our lab analyses the immunosurveillance of cancer in solid tumours and, more recently, of lymphomas and leukaemias. In addition to the tumour-protective role of the immune system, there is growing evidence that the immune system can also increase tumour growth and progression. We are focusing on the role of the adaptive immune system, mainly cytotoxic T cells, in this process. Understanding these pathways could open new therapeutic strategies to treat cancer.

The main focus is on the interaction of the immune system with leukaemia stem cells (LSCs). In order to cure leukaemia, LSCs need to be targeted, however, these cells are selectively resistant to cytostatic drugs and irradiation. We documented that BCR/ABL+ leukaemia stem and progenitor cells express the TNF receptor family member CD27. CD27 ligation on LSCs increased the expression of Wnt target genes and increased proliferation and differentiation of LSCs. Blocking CD27 signalling delayed disease progression and prolonged survival. Furthermore, CD27 signalling promoted growth of BCR/ABL+ human leukaemia cells by activating the Wnt pathway. Therefore, targeting CD27 on LSCs may represent an attractive therapeutic approach to block the Wnt/ $\beta$ -catenin pathway in leukaemia.

We plan to extend our analysis to acute myeloid leukaemia and to other members of the TNF receptor family. In addition, we will validate our results in human AML stem cells in vitro and in xeno-transplantation.

### Collaborators

Macpherson A, McCoy K, Balmer ML, University of Bern, Switzerland Matter MS, Tzankov A, University Hospital Basel, Switzerland Merkler D, University of Geneva, Switzerland Pinschewer DD, University of Geneva, Switzerland Schwaller J, University of Basel, Switzerland Tschan MP, University of Bern, Switzerland

### Grants

#### Amounts allocated for 2011:

SNF: Bonus of excellence – Molecular mechanisms of the adaptive immune system involved in cancer progression (A. Ochsenbein) CHF 178,000

Swiss Cancer League: Immunogenicity of chronic myeloid leukemia stem cells (A. Ochsenbein) CHF 104,141

Swiss Cancer League: Wenner Prize (A. Ochsenbein) CHF 50,000

Bernese Cancer League: (A. Ochsenbein, C. Schürch, C. Rither) CHF 32,500

Berger Janser Stiftung: (A. Ochsenbein) CHF 114,000

Gertrud Hagmann Stiftung: (C. Schürch) CHF 161,215

Swiss Life Jubiläumsstiftung: (C. Schürch) CHF 20,000

Ehmann Stiftung Savognin: (C. Schürch, C. Riether) CHF 25,000

Olga Mayenfisch Stiftung: (C. Schürch, C. Riether) CHF 20,000

Foundation for Research on Transfusion and Transplantations: (C. Schürch, C. Riether) CHF 50,000 SAKK/AMGEN: (A. Ochsenbein) CHF 25,000

# **Publications**

Destruction of lymphoid organ architecture and hepatitis caused by CD4+ T cells. Matter, MS; Hilmenyuk, T; Claus, C; Marone, R; Schurch, C; Tinguely, M; Terracciano, L; Luther, SA; Ochsenbein, AF (2011) in: PLoS One 6 (9): e24772.

First-line temozolomide combined with bevacizumab in metastatic melanoma: a multicentre phase II trial (SAKK 50/07). von Moos, R; Seifert, B; Simcock, M; Goldinger, SM; Gillessen, S; Ochsenbein, A; Michielin, O; Cathomas, R; Schlappi, M; Moch, H et al (2011) in: Ann Oncol 23(2), p. 531-536.

Clinical outcome with bevacizumab in patients with recurrent highgrade glioma treated outside clinical trials. Hofer, S; Elandt, K; Greil, R; Hottinger, AF; Huber, U; Lemke, D; Marosi, C; Ochsenbein, A; Pichler, J; Roelcke, U et al (2011) in: Acta Oncol 50(5), p. 630-635.

CD27 signaling on chronic myelogenous leukemia stem cells activates Wnt target genes and promotes disease progression. Schurch, C; Riether, C; Matter, MS; Tzankov, A; Ochsenbein, AF in: J Clin Invest (in press).

Quantitative analysis of O6-methylguanine DNA methyltransferase (MGMT) promoter methylation in patients with low-grade gliomas. Ochsenbein, AF; Schubert, AD; Vassella, E; Mariani, L (2011) in: J Neurooncol 103(2), p. 343-351.



# **Key Events**

# Day of Clinical

#### Research 2011

#### 1-2 Nov. 2011

A large and interested audience followed the presentations of **Prof. Dr. Stefan Schneeberger** (Department of Visceral, Transplant and Thoracic Surgery, Innsbruck Medical University, Austria) entitled "Hand and composite tissue allotransplantation: current state and promises for the future" and **Prof. Dr. Stefan Mundlos** (Max Planck Institute for Molecular Genetics/Charité-Universitätsmedizin Berlin, Germany) entitled "HOX genes sculpture our bones".

Ten candidates applied for the Research Prize (funded by the Faculty of Medicine, University of Bern) and 184 abstracts were submitted for DKF Poster Prizes and the Alumni MedBern Prize. The winners were (left to right in photo below): Best project by a medical student - Lukas Zürcher (Theodor Kocher Institute); best patientoriented project – Florian Singer (Pulmonary Medicine (Paediatrics), DCR); Research Prize - Dr. Alexandre Theocharides (Experimental Haematology (Adults), DCR and University Clinic of Haematology, Inselspital); best laboratory-oriented project - Dr. Robert H. Andres (University Clinic for Neurosurgery, Inselspital); Alumni MedBern Prize - Dr. Michaela Medovà (Radiation Oncology, DCR) represented by Dr. Y. Zimmer.

The next Day of Clinical Research will be held 13-14 November 2012.

# DKF Research Conferences 2011

With an average of 60 visitors each month, the DKF Research Conferences continue to be very successful. In 2011, we were pleased to present the following speakers:

#### 7 Feb. – Prof. Dr. Ron M.A. Heeren

Institute for Atomic and Molecular Physics, Foundation for Fundamental Research on Matter, Amsterdam, The Netherlands Label-free biomolecular imaging in clinical research with mass spectrometry based microscopy.

**7 Mar.** – Prof. Dr. Burkhard Becher Institute of Experimental Immunology, University of Zurich, Switzerland The role of IL-12 as a tumour suppressor and its impact on innate and adaptive immunity.

**4 Apr.** – **Prof. Dr. Oliver Fackler** Department of Infectious Diseases, Virology, University Hospital, Heidelberg, Germany

Manipulations of host cell actin remodelling and trafficking by the HIV-1 pathogenesis factor Nef.

**2 May** – **Prof. Dr. Peter Vaupel** Department of Radiooncology and Radiotherapy, University Medical Center, Mainz, Germany *Tumour hypoxia and malignant progres-*

sion: A vicious circle.

#### **6 June – Dr. Markus Rudin** Institute for Biomedical Engineering, University and ETH Zurich, Switzerland Imaging hypoxia, hypoxia signalling and angiogenesis in experimental tumour models.

# **4 July** – Prof. Dr. Scott R. Whittemore

Department of Neurological Surgery, School of Medicine, University of Louisville, Kentucky, USA Are current experimental models and treatments of spinal cord injury clinically relevant?

#### **5 Sep.** – Prof. Dr. Srini V. Kavery Cordelier Research Center, Pierre and

Cordeller Research Center, Pierre and Marie Curie University, Paris, France Human IgG as a biological immune response modifier: The tale of IVIg.

#### 3 Oct. – Dr. Isabelle Cleynen

Department of Pathophysiology, Translational Research Center for Gastrointestinal Disorders, KU Leuven, Belgium Genes and what they tell us: Lessons learned from genome wide association studies on inflammatory bowel disease.

#### 7 Nov. – Prof. Dr. Sven Bergmann

Department of Medical Genetics, University of Lausanne, Switzerland Give me your DNA and I tell you where you come from – and maybe more!

#### **5 Dec.** – Prof. Dr. Isabelle Maridonneau-Parini

Institute of Pharmacology and Structural Biology, Toulouse University III, France Mechanisms of macrophage migration in 3D environments, role of podosomes.

In 2012, DKF Research Conferences will take place as usual every first Monday of the month from 5-6 pm, followed by an apéro.



# Personnel Update

### Academic Degrees

The following academic degrees were awarded to DCR group members:

Full Professor Prof. Dr. Jean-François Dufour Hepatology

Full Professor (Extraordinarius) Prof. Dr. Adrian Ochsenbein Tumor Immunology

#### **Associate Professor**

Prof. Dr. Martin Czerny Cardiovascular Surgery

Prof. Dr. Robert E. Hunger Dermatology

**Prof. Dr. Alexander Kadner** Cardiovascular Surgery

Prof. Dr. Nils Kucher Angiology

Prof. Dr. Michael Reinert Neurosurgery

**Prof. Dr. Hans Ulrich Rothen** Intensive Medicine

Prof. Dr. Dagmar Simon Dermatology

Titular Professor Prof. Dr. Stefanos Demertzis Cardiovascular Surgery

**Prof. Dr. Javier Fandino** Intensive Medicine

#### Lecturer (Privatdozentln)

PD Dr. Stefan Begré Psychosomatic Medicine

PD Dr. Florian Dick Cardiovascular Surgery

PD Dr. Sigrun Eick Dental Research

PD Dr. Steffen Frese Thoracic Surgery PD Dr. Daniel G. Fuster Nephrology and Hypertension

PD Dr. Oliver Gautschi Oncology/Haematology (Adults)

**PD Dr. Deborah M. Keogh-Stroka** Visceral and Transplantation Surgery

**PD Dr. Daniel Lottaz** Rheumatology

PD Dr. Amit V. Pandey Endocrinology/Diabetology/ Metabolism (Paediatrics)

**PD Dr. Christophe von Ganier** Pulmonary Medicine (Adults)

PD Dr. Ute Wolf-Schnurbusch Ophthalmology

PhD (supervisors in brackets) Ali Al Kaabi (PD Dr. Manfred Heller) The role of endothelial cells in human coronary collateral growth

#### Elvis A. Atanga (Prof. Dr. Willy Hofstetter) Characterization of tumor necrosis factor-alpha dependent inhibition of osteoclast development

Matthias Bachtler (Prof. Dr. Brigitte Frey, Dr. Andreas Pasch) Role of enteroviruses in mesangial renal disease

#### Manuel Chiusa (Dr. Christian Zuppinger)

The role of growth and survival factors in the myocardium challenged by cardiotoxic cancer therapy

### Dario Cazzoli

(Prof. Dr. René Müri) Mechanisms directing visuospatial attention: what theta burst stimulation and eye movement analysis can tell us Daniel Guo Quae Chong

(Prof Dr. Roland Kreis) Two-dimensional linear-combination model fitting: Tools and applications for in-vivo magnetic resonance spectra

#### Markus Germann

(Prof. Dr. George Thalmann) The cellular basis of prostate cancer progression to castration resistance

#### Andrea Hirsch

(Prof. Dr. Christa E. Flück) Beyond human adrenal androgen biosynthesis

#### Pranitha Jayadev Kamat

(Prof. Dr. Robert Rieben) Ischemia reperfusion injury: The role of immune response and the endothelium during myocardial infarction

#### Meret Ann Lauterburg

(Prof. Dr. Felix Frey) Uninephrectomy reduces 11βhydroxysteroid dehydrogenase type 1 and type 2 concomitantly with an increase in blood pressure in rats

#### **Catherine Nicolo**

(PD Dr. Amit V. Pandey) Pharmacogenomics of human P450 oxidoreductase

#### Alexandre Simonin

(Prof. Dr. Matthias Hediger, PD Dr. Daniel Fuster) Regulation of Na+/H+ exchanger 1 (NHE1) plasma membrane abundance

#### **Emilie Stauffer**

(Dr. Stefan Farese, Prof. Dr. Brigitte Frey) Sodium thiosulfate in uremia induced vascular calcification

#### Georgette Stern

(Prof. Dr. Urs Frey) Environmental influences on autonomic regulatory processes and airway function

#### Lei Zhuang

(Prof. Dr. Beat Trueb) Functional domains of the receptor FGFRL1

#### MD (supervisors in brackets) Claudia Kobel

(Prof. Dr. Gabriela Baerlocher, Dr. Elisabeth Oppliger Leibundgut) Assesment of TET2 mutations in myeloproliferative neoplasms and their correlation to clinical parameters

#### Emrush Rexhaj

(Prof. Dr. Urs Scherrer) Fetal programming of vascular dysfunction in mice: role of epigenetic mechanisms (University of Lausanne)

#### Daniela Rogenmoser-Dissler

(Prof. Dr. Gabriela Baerlocher, Dr. Elisabeth Oppliger Leibundgut) The CLLU1 expression distinguishes chronic lymphocytic leukemia from other B-cell neoplasms

#### Eva Schlachter

(Prof. Dr. Michael Reinert) Metabolic pathway and distribution of superparamagnetic iron oxide nanoparticules: in vivo study

#### MD PhD (supervisors in brackets) Simon Andreas Häfliger

(Prof. Dr. Thomas Pabst) Protein disulfide isomerase blocks CEBPA translation and is up-regulated during the unfolded protein response in acute myeloid leukemia

#### Sacha Rothschild

(PD Dr. Oliver Gautschi) Posttranscriptional regulation by microRNAs and autophagy – two new mechanisms involved in the Src-ID1 signaling pathway in lung cancer

**DVM PhD** (supervisors in brackets) **Carine Gennari-Moser** (Prof. Dr. Markus Mohaupt) Aldosterone in normal and preeclamptic pregnancy

#### **Christine Göpfert**

(Prof. Dr. Brigitte Frey) Effect of electroporation-mediated diphtheria toxin A expression on human prostate xenograft tumors in SCID mice

#### Awards

The following DCR group members received awards in 2011:

#### Prof. Dr. Chris Boesch

Magnetic Resonance Spectroscopy and Methodology Radiology Editor's Recognition Award – Radiology

#### Monika Dornbierer

Cardiovascular Surgery ESC-Award for best oral presentation – 22nd European Students' Conference "Perspectives and Challenges in Regenerative Medicine"

#### Géraldine Guex

Cardiovascular Surgery Best Poster Award – 7th Swiss Experimental Surgery Symposium; Daily Winner Award for best oral presentation of the day – 22nd European Students' Conference "Perspectives and Challenges in Regenerative Medicine"

### PD Dr. Alain Kaelin Neurology

Baasch-Medicus Preis

Dr. Frank Klenke, Dr. Christoph Albers, Dr. Hans-Jörg Sebald, Prof. Dr. Klaus-Arno Siebenrock, Prof. Dr. Willy Hofstetter Bone Biology & Orthopaedic Research and Orthopaedic Surgery Wilhelm Roux Prize 2011 – German Association for Orthopaedics and Orthopaedic Surgery

#### Prof. Dr. Roland Kreis

Magnetic Resonance Spectroscopy and Methodology Appointed "Fellow of the Society" at the Annual Meeting of the International Society of Magnetic Resonance in Medicine

#### Cédric Laedermann

Ion Channels and Channelopathies Best abstract prize for oral presentation – Euroanaesthesia 2011: European Society of Anaesthesiology

#### Dr. Johannes Lemke

Human Genetics Forschungsförderungspreis – Swiss League Against Epilepsy

#### Dr. Andreas Eduard Moor

Molecular Biology 1. Fakultätspreis für die beste Dissertation des Jahres – Faculty of Medicine, University of Bern

#### PD Dr. Thomas Nyffeler

Perception and Eye Movement Eberhard Ketz Prize – Gönnervereinigung Neurorehabilitation pro humanis

#### Prof. Dr. Adrian Ochsenbein

Tumor-Immunology Robert Wenner Prize 2011

#### Simone Portmann

Visceral and Transplantation Surgery Research Award for best oral presentation – 98th annual meeting of the Swiss Surgical Society

#### Dr. Emrush Rexhaj

Cardiology

AstraZeneca Scholarship – The Swiss Society of Hypertension; Respiration Section Award – Experimental Biology 2011 Meeting: American Physiological Society

#### Dr. Nikola Saulacic

Cranio-Maxillofacial Surgery André Schroeder Research Prize – International Team for Implantology

#### Dr. Isabelle Schepens

Dermatology Outstanding paper award 2011 – Bern Immunology Club

#### Prof. Dr. Christian Seiler

Cardiology Teacher of the Year 2011 – Human Medicine, University of Bern

#### Dr. Florian Singer

Pulmonary Medicine (Paediatrics) DKF Poster Prize for best patientoriented project

#### PD Dr. Deborah M. Keogh-Stroka

Visceral and Transplantation Surgery Research Award for best poster presentation – 98th annual meeting of the Swiss Surgical Society Caroline tum Suden/Frances A. Hellebrandt (Dr. Stefano Rimoldi) Cardiology

Professional Opportunity Award – Experimental Biology 2011 Meeting: American Physiological Society

Prof. Dr. Daniel Surbek, Dr. Martin Müller, Ursula Reinhart, Ruth Sager, Dr. Andreina Schoeberlein Prenatal Medicine Research Excellence Award – Society for Maternal-Fetal Medicine

**Prof. Dr. Hendrik Tevaearai** Cardiovascular Surgery 5th Ypsomed-Innovationspreis – 1st prize

**Dr. Alexandre Theocharides** Experimental Haematology (Adults) *Research Prize 2011* 

**Dr. Thomas von Känel** Experimental Haematology (Adults) *Viollier Prize 2011* 

### Staff Changes

New Staff Steven Balestra IT-Support (30%), Administration (since Oct.)

Larissa Bettler Laboratory Technician (30%), Osteoporosis Densitometry DOPH (since Oct.)

#### Michele Cibien IT-Support (60%), Administration (since July)

**Muriel Fragnière** Laboratory Technician (100%), Molecular Biology & Genomics (sinc

Molecular Biology & Genomics (since July)

Véronique Kretschmer DCR Administrator (95%), Administration (since Jan.)

**Dr. Hai Li** PhD (100%), Gastroenterology (Adults) (since Aug.)

Yvonne Roschi House Staff (75%), Mu50 (since Feb.) Valentin Sottas Doctoral Student (100%), Ion Channels and Channelopathies (since Apr.)

Jan Stohler IT-Support (40%), Administration (since July)

Dr. Stefan Wyder PhD (72%), Molecular Biology & Genomics (since July)

Resignations Mario Aeby IT-Support (20%), Administration (until July)

Dr. Stefano Di Santo Research Assistant (100%), Neurosurgery (until Dec.)

**Dr. Siegfried Hapfelmeier** Research Assistant (100%), Gastroenterology (Adults) (until Feb.)

Guy Marchon IT-Support (80%), Administration (until July)

Isabelle Minder Laboratory Technician (100%), Molecular Biology & Genomics (until May)

Daniel Muellener Laboratory Technician (43%), Urology (until Dec.)

Isolde Okere Laboratory Technician (30%), Osteoporosis Densitometry DOPH (until Oct.)

Paranetharran Pushpanathan Laboratory Technician (20%), Tumor-Immunology (until Dec.)

Dr. Emma Slack Research Assistant (36%), Gastroenterology (Adults) (until Oct.)

Short Employment (<12 months) Dr. Maxime Albesa

PhD (100%), Ion Channels and Channelopathies (Jan.-March)

Dr. Mohamed Yassine Amarouch

PhD (70%), Ion Channels and Channelopathies (Sep.-Oct.) Julia Cahenzli Doctoral Student (100%), Gastroenterology (Adults) (Oct.)

Begonia Fudrini Doctoral Student (100%), Gastroenterology (Adults) (Sep.)

Mathias Grieder Doctoral Student (86%), Perception and Eye Movement (Jan.-Dec.)

Christopher Jackson Doctoral Student (100%), Human Genetics (Jan.)

Melissa Lawson Doctoral Student (100%), Gastroenterology (Adults) (Sep.-Dec.)

Diana Amy Shy Doctoral Student (100%), Ion Channels and Channelopathies (Aug.-Dec.)

# **Additional Publications**

# Audiology (p. 28)

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Editing and Layout: Leah Witton Coordination: Verena Frazao DCR Director: Prof. Dr. Hugues Abriel Photos: DCR; Susi Bürki, Inselspital Print: Rub Graf-Lehmann AG, 3001 Bern; PrintServices, Inselspital

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