

u^b

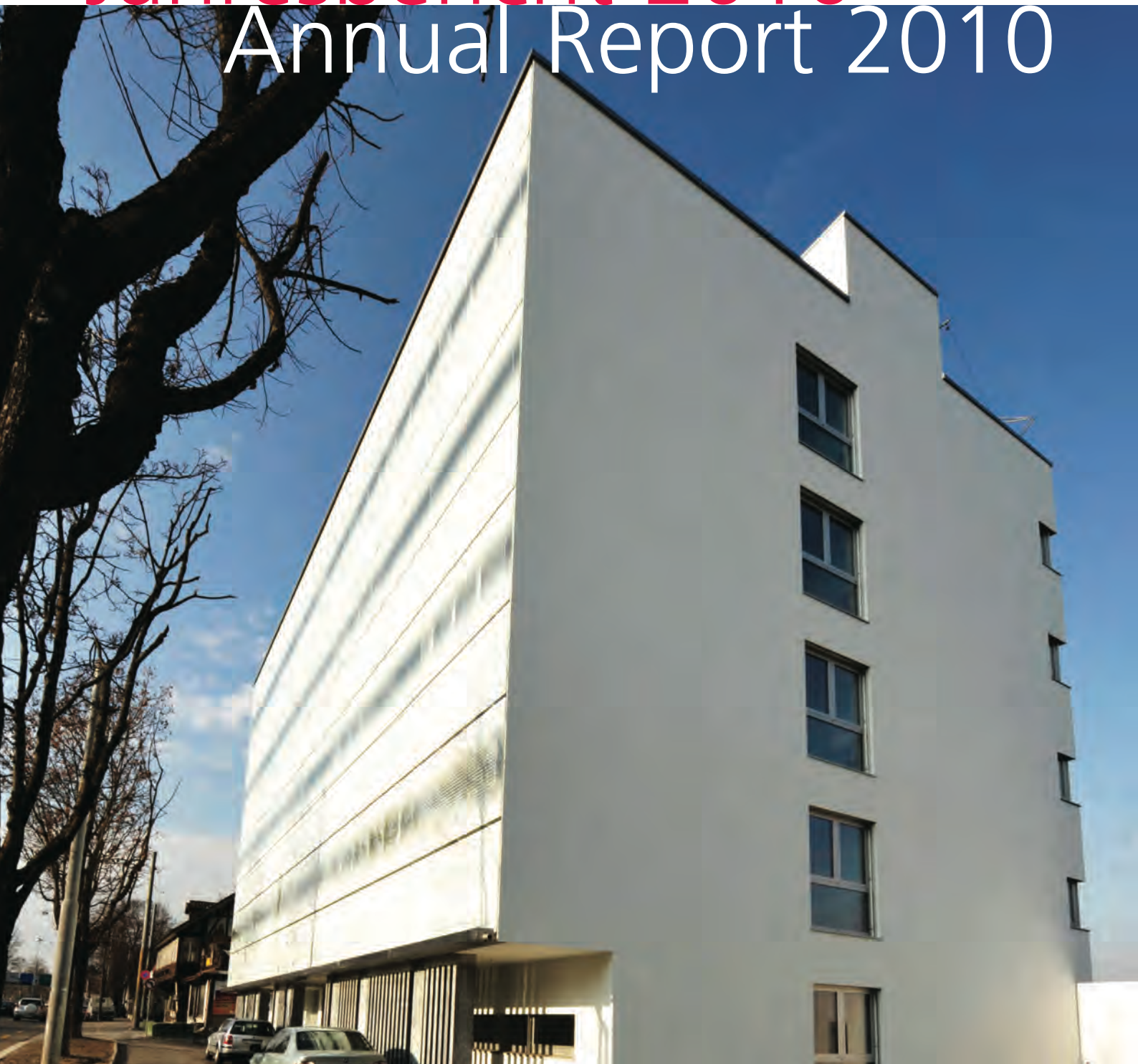
^b
**UNIVERSITÄT
BERN**

DEPARTMENT OF CLINICAL
RESEARCH

www.dkf.unibe.ch

Jahresbericht 2010

Annual Report 2010



Contact:

Véronique Kretschmer
Administrator
Department of Clinical Research
University of Bern
Murtenstrasse 35
3010 Bern
Switzerland

Phone: +41 31 632 3552
Fax: +41 31 632 0946
Email: veronique.kretschmer@dkf.unibe.ch

Members of the University of Bern and Inselspital can obtain a copy of this report online at: www.dkf.unibe.ch

Cover image: The building at Murtenstrasse 50, a new DCR Research Division.

Contents

The DCR at a Glance / Das DKF auf einen Blick	2
Foreword – Director's Report	3
Organisation	4
Organigram	5
Key People	6
DCR Sites	8
Technology Core Facilities	9
DCR Internal Research Groups	12
DCR Research Groups from Clinics of the Inselspital	30
Key Events	34
Personnel Update	35



The DCR at a Glance

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 the researchers of the Inselspital, Bern University Hospital and the Faculty of Medicine. In 2010, 47 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 patient-oriented clinical research, by offering scientific support to its groups and by operating state-of-the-art Technology Core Facilities and specialised Animal Core Facilities.

Das DKF auf einen Blick

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. 2010 waren 47 unabhängige Forschungsgruppen dem DKF angeschlossen, die zusammen fast alle Bereiche der biomedizinischen Forschung abdecken.

Das Ziel vom DKF ist es, durch die wissenschaftliche Unterstützung seiner Forschungsgruppen, sowie den Betrieb von, dem neusten Stand der Technik entsprechenden, Technologie Core Facilities und spezialisierten Tier Core Facilities, Brücken zu schlagen zwischen laborbasierter biomedizinischer und patientenorientierter klinischer Forschung.



Foreword – Director's Report

Dear readers and colleagues,

You have in your hands the 2010 Annual Report of the Department of Clinical Research (DCR) at the University of Bern. I am convinced you will find interesting and useful information about the organisation of the department and our activities.

2010 was my first complete year as the new DCR Director. It was a busy year with many parallel projects, all of which had a common goal – the "raison d'être" of the DCR – to provide the best possible infrastructure and scientific support to our affiliated researchers, so that they can perform high-quality, disease-oriented and translational research.

As in previous years, one of our number one priorities was to provide the DCR research groups with adequate laboratory space. The most visible project was completion of the new research building at Murtenstrasse 50. This project was initiated and concretised by the Inselspital, with the help of a generous endowment from the Heads of the Inselspital clinics. Many of the DCR groups are now located there, with Prof. Dr. Robert Rieben as Coordinator. We are pleased that two floors of the building are being used by most of the groups of the Artificial Organ (ARTORG) Center for Biomedical Engineering Research to start their own research work. We are convinced of the potential for collaboration and synergy, and aim to work closely with these young groups.

In April 2010, we inaugurated four new seminar and meeting rooms on floor H of the M.E. Müller-Haus. Together with the "lounge", they are used daily by DCR members, as well as by many guests. We are very grateful to the Inselspital for this important renovation project.

The new laboratories allowed some of the groups working under non-

optimal conditions to relocate. This is still a work-in-progress. We plan to be finished with the first round of renovations and redistribution by the end of 2011. We are also currently working with the Canton of Bern and the University on "Insel Nord", a new building project in which the DCR will have many new laboratories and an animal house. However, it will take several years before this is completed.

Another positive development in 2010 was the collaboration between the University's three life-science faculties (Vetsuisse, Phil. Nat., and Medicine) to acquire instruments for a "next generation sequencing" platform, to be financed in part by an SNF R'Equip grant. The DCR will invest some of its resources so that the DCR groups have optimal access to this new interfaculty facility. This genomics project is coordinated by Prof. Dr. Rolf Jaggi, Coordinator of the "Pathologie, Sahli-Haus 1+2" Division since October 2010.

Since autumn 2009, the DCR has been operating the Clean Mouse Facility, a new animal facility that allows the breeding and housing of germ-free mice. This facility is now fully functional and has already facilitated the publication of a fascinating study in *Science* (Hapfelmeier et al., 2010) by the DCR's Gastroenterology Group.

The support of young scientists is an important task of the DCR. In 2010, the DCR's Scientific Fund financed three Grants-in-Aid for young Group Leaders of Inselspital clinics and 20 travel grants for PhD students.

As you can see, we had a very dynamic working environment in 2010. This was also evidenced by the many events that were organised, such as the very well-attended monthly DKF Research Conferences, and the key event of the year, the Day of Clinical Research. Moreover, from the begin-



ning of 2011, three new groups will be affiliated with the DCR: Geriatrics and Medicine of Ageing, headed by Prof. Dr. Andreas Stuck; Adult Endocrinology and Diabetology, headed by Prof. Dr. Peter Diem; and Hepatology, headed by Prof. Dr. Jean-François Dufour. We welcome these new scientists to the DCR and wish them every success.

In conclusion, I am convinced that the DCR provides its affiliated scientists and research groups with an excellent environment in which to perform their research in the fast-evolving field of biomedical sciences. The Management and Support staff of the DCR is continuously working on improving its services, despite the increased gap between income and expenses in recent years. I would like you to know that I am always open to your comments and suggestions, and assure you that I will take your concerns seriously.

Finally, let me sincerely thank all the DCR employees and affiliated co-workers for their positive spirit and excellent work.

Prof. Dr. H. Abriel, MD PhD, Director

Organisation

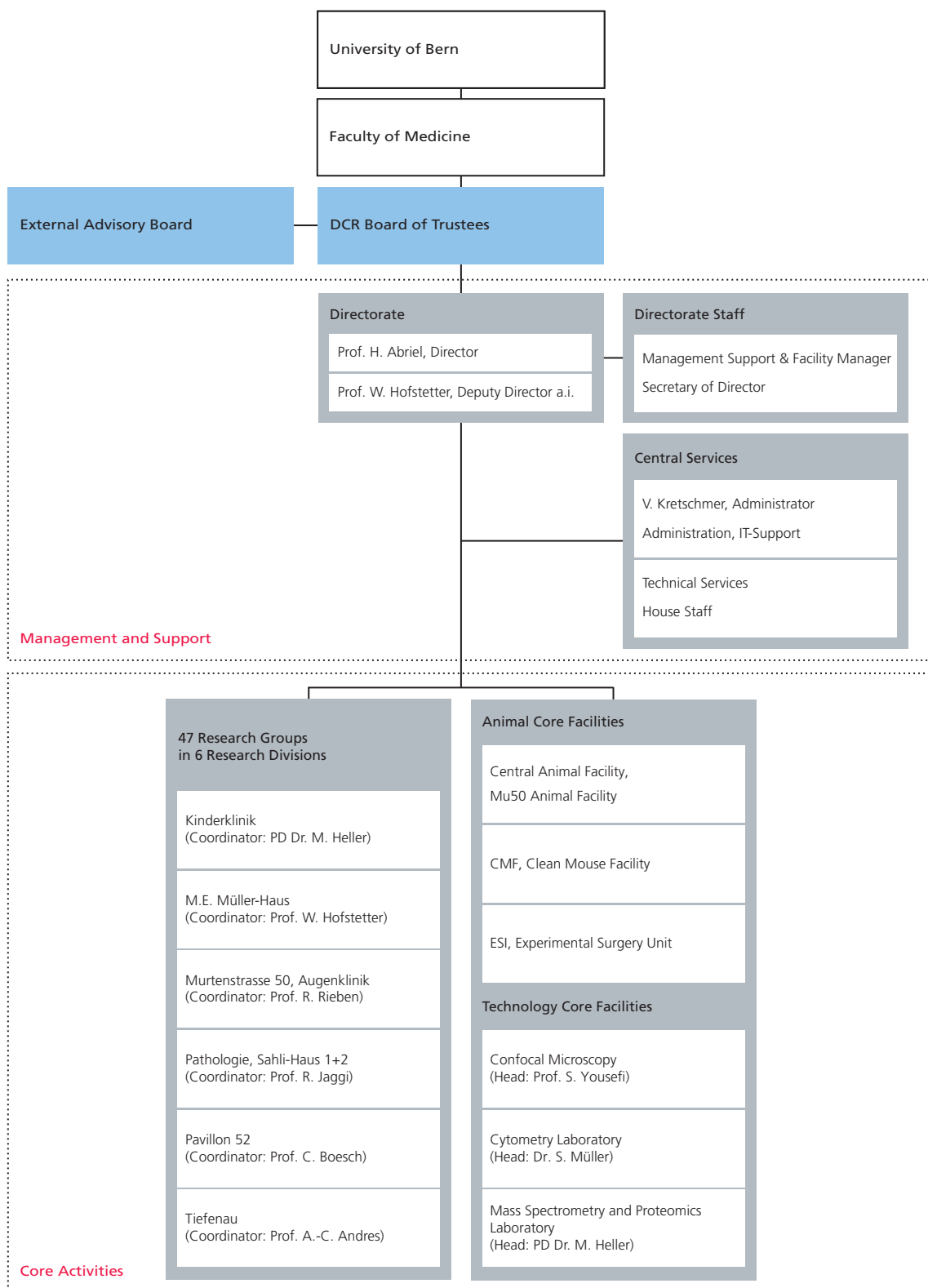
In April 2009, the Directorship of the DCR changed hands. Since then, the DCR has adapted its organisation and statutes, and new departmental rules and regulations (Departementsreglement) will come into force at the beginning of 2011. In the new organisational structure, the core activities are more clearly defined.

The role of the DCR is to provide optimal infrastructure and scientific support to its research groups, of which there were 47 at the end of 2010. The vast majority (38) of these groups are from clinics of the Inselspital, Bern University Hospital, while the remainder (9) are internal DCR groups, involved in the scientific support and coordination of equipment and infrastructure on a daily basis. The 47 groups are divided into 6 Research Divisions. In October 2010, the building at Murtenstrasse 50 became a DCR Division. Equally important, the DCR is responsible for operating Technology and Animal Core Facilities. The groups of the department are supported by central services responsible for admini-

stration, informatics and technical support.

The DCR Directorate, which comprises the Director and Deputy Director, is now supported by a newly created Facility Manager position. Another important change in the new organisation is the clarification of 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. In order to achieve transparency and to clarify the relationship between the groups and the DCR, both the allocated resources and the rights and duties will now be written in time-limited contracts of affiliation. It will be a task of the Board of Trustees to approve these contracts. We will also set up an external Advisory Board, comprising at least three scientists, whose task will be to evaluate the overall strategies and operation of the DCR.





Key People

DCR Board of Trustees



Prof. Dr. Christoph Müller
Chair

Members

Prof. Dr. Daniel Candinas
Prof. Dr. Matthias Egger
Prof. Dr. Sabina Gallati
Prof. Dr. Christian Hess
Prof. Dr. Lutz-Peter Nolte
Prof. Dr. Hans-Uwe Simon

Ex Officio

Prof. Dr. Peter Eggli
Prof. Dr. Andreas Stuck
Prof. Dr. Matthias Gugger
Prof. Dr. Hugues Abriel
Prof. Dr. Adrian Lussi
Prof. Dr. Marcel Egger
Marianne Thormann

Directorate



Prof. Dr. Hugues Abriel
Director



Prof. Dr. Willy Hofstetter
Deputy Director a.i.

Directorate Staff and Administration



Bernhard Grossniklaus
Management Support
& Facility Manager



Verena Frazao
Secretary of Director



Véronique Kretschmer
Administrator

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



Dr. Stefan Müller
Cytometry Laboratory



Prof. Dr. Shida Yousefi
Confocal Microscopy

1



M.E. Müller-Haus
Murtenstrasse 35

2



Murtenstrasse 50

3



Pathologie
Murtenstrasse 31

4



Pavillon 52
Freiburgstrasse 3

5



Kinderklinik
Freiburgstrasse 15

6



Sahli-Haus 1
Freiburgstrasse 14a

7



Sahli-Haus 2
Freiburgstrasse 14

8



Augenklinik
Freiburgstrasse 8

9



Tiefenau
Tiefenastrasse 120c



Confocal Microscopy

www.pki.unibe.ch/content/confocal_microscopy

Achievements 2010

In 2010, we trained more than 50 scientists at the University of Bern on how to apply confocal microscopy and imaging techniques to their specific scientific projects. Several original articles were published in which the authors used our facility to produce state-of-the-art images.

Performance Report

During 2010, 30 different research groups from the DCR or clinics of the Inselspital used the confocal microscope "LSM 5 Exciter". The number of hours that the confocal microscope was occupied increased by 47%, from 710 hours in 2009 to 1044 in 2010.

Twice in 2010, we organised a two-day practical course for PhD and MD students, and technicians. These courses provide beginners with a basic knowledge of fluorescent staining techniques, and how to work with confocal microscope and imaging software. Overall, we trained around 30 scientists.

In 2010, the total number of Imaris licenses for new users increased to 27 research laboratories, mainly due to our efforts to train new people during our courses. In addition, we invited a technical expert from Bitplane AG to introduce the newest features of their software and to help with practical training. We also covered the Huygens software that is used to correct any image deficiency during acquisition.

In terms of personnel resources, Shida Yousefi is the main person responsible for introducing the

confocal microscope and the imaging analysis software (Imaris and Huygens) to new users. In her absence, two members of Prof. Dr. Hans-Uwe Simon's group, namely Zhaoyue He and Dr. Sébastien Conus, are responsible for training.

Finances

In 2010, the Confocal Microscopy Core Facility took in CHF 18,365 in user fees. Disbursements included CHF 5,000 for consumables, CHF 3,000 (2 x 1500) for course expenses and CHF 19,961 for Imaris maintenance. The latter sum includes multiple groups outside the Medical Faculty.

Outlook 2011

In 2011, we will continue to provide services to different DCR and Inselspital groups. The biannual practical course mentioned above will also be organised in 2011.

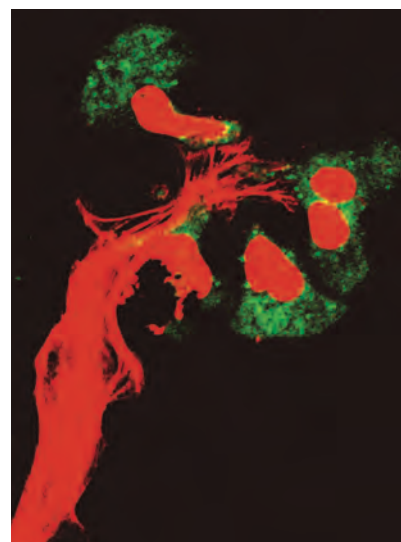
Staff Members

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



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

PhD from the University of Zurich in 1996. First post-doc at University of Toronto General Hospital, Canada, second post-doc at Novartis Research Centre, Horsham, UK. Since 2000, Principal Investigator at the Institute of Pharmacology, University of Bern. Since 2002, Head of the DCR Confocal Microscopy Core Facility, located at the Institute of Pharmacology.



Cytometry Laboratory

www.facslab.unibe.ch

Achievements 2010

Flow Cytometry (also known as fluorescence-activated cell sorting; FACS) became a Core Facility at DCR in 1994. Since then, FACS has become increasingly important and is now indispensable for biomedical research. In the past 15 years, there has been a huge advancement in both the development of equipment and in methodological applications. Over the years, our equipment has been continuously upgraded, with the aim of providing state-of-the-art service to the ever-increasing community of users. In January 2010, Stefan Müller took over as Head from Prof. Dr. Christoph Mueller, who helped establish and successfully run the facility until the end of 2009.

After the retirement of our outdated FACSVantage machine in 2010, we purchased a new, high-speed cell sorter (BD FACS ARIA III), which is equipped with 3 lasers and 11 detectors and is upgradeable. The new machine was installed in the summer and subsequently thoroughly tested by our sort operators. Regular bookings have been possible since September 2010.

We also offered a FACS course, for which participants could register via our newly developed website. The website, mainly administered by Claudio Vallan, is continuously being updated. A hallmark of the website is the link to the new booking form that needs to be completed when a sort is planned with our operators. This form allows the operators to better estimate specific needs and potential issues for a planned sort, and consequently to offer the best possible service to our customers.

Performance Report

The use of our equipment again showed an increase compared to the year before; this time an impressive gain of almost 30%, mostly due to the heavy use of our cell analyser (BD LSR II SORP). Cell sorting also increased by 15%, owing to the availability of the new sorter.

Finances

We did not face exceptional equipment repairs or part replacements in the past financial year (4th quarter 2009 to 3rd quarter 2010). In addition, we observed an increase in revenues from user fees of about 20% compared to the previous period. However, since the 50% FACS Operator position created in late 2009 was charged to our account until the end of 2010, our financial reserve decreased by about 50% compared to 2009.

Outlook 2011

For 2011, we have again scheduled a FACS course. Furthermore, we are planning a seminar and demonstration of a novel type of cytometer, which brings FACS to an as yet unrivalled level by combining it with morphometric analyses.

Staff Members

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



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

Studies in microbiology at the University of Bern; PhD in 2006. Post-doc in intestinal mucosal immunology at the University of Bristol, UK in 2000; Became Head of the Flow Cytometry Laboratory at the School of Cellular and Molecular Medicine there in 2001. Since 2004, Senior Scientist in Gastroenterology at the DCR. Since 2010, Head of the Cytometry Laboratory Core Facility. Main interests: Immunoreactivity against yeast in Crohn's disease, a chronic intestinal inflammatory disorder; Host-commensal/pathogen interaction at the intestinal mucosa.



Mass Spectrometry and Proteomics Laboratory

www.pmscf.dkf.unibe.ch

Achievements 2010

Three research articles on which we collaborated were published. They were concerned with venom composition of a parasitic wasp, identification and analysis of bracovirus particle proteins, and studies on the eukaryotic elongation factor 1A in *Trypanosoma brucei*. Two manuscripts from our own laboratory are under revision for publication.

In May, our group hosted a Biomedical Sciences Masters student for the first time. In addition, from April to July, Niurka Meneses, from the National Autonomous University of Mexico joined our lab as a Visiting Scientist, propelling forward our efforts on the analysis of membrane proteins.

The Mass Spectrometry and Proteomics Laboratory is a founding member of the newly formed Association of Proteomics Core Facilities of Western Switzerland (Repp-So).

Performance Report

Operation of the proteomics mass spectrometer was generally without any significant interruption. Service and maintenance were performed in-house, keeping costs low. Trainees from the Swiss Qualification Program in Biomedicine, Natural Sciences and Research (BNF) helped us to install freely available software for interpretation of mass spectrometry data. In 2010, 204 service jobs were billed.

Finances

The Medical Faculty Resources Committee granted a total of CHF 23,000 to cover the facility's running

costs (CHF 10,000), purchase of new nano-spray source material (CHF 3,000) and for software/hardware improvements (CHF 10,000). A high-voltage power supply board, a new server, nano-spray material and additional consumables, as well as continuing education costs for Natasha Buchs Tetkovic were paid for by this grant. Financing of the replacement of a front-end PC (CHF 8,400) was additionally granted by the Resources Committee in September. The revenue for conducted services was CHF 33,539, from which CHF 897 were paid to the University as overhead. A total of CHF 7,180 were spent for travel and congress fees, software and tech-support, and some additional replacement parts and consumables. In summary, we were able to present an almost balanced budget thanks to the support received from the Faculty.

Outlook 2011

There is increasing interest from many research groups to run liquid chromatography-mass spectrometry-based life-science projects, although the support is not currently available from our side.

Small proteomics events are planned at the University of Geneva, University of Lausanne/EPFL, and University of Bern to inaugurate the Repp-So Association.

Staff Members

PD Dr. Manfred Heller, Head
Natasha Buchs Tetkovic, Laboratory Technician
Ali Al Kaabi, PhD Student



PD Dr. Manfred Heller
manfred.heller@dkf.unibe.ch

Thirteen year's experience in the use of mass spectrometry for protein analytics and bioinformatics. PhD in Chemistry/Biochemistry from the University of Bern in 1994. Post-docs abroad with Prof. Dr. Ruedi Aebersold and Prof. Dr. Denis Hochstrasser. Return to Switzerland in 1999. Three years as Senior Scientist at GeneProt Inc. in Geneva working on large-scale proteomics projects using LC-MS2, MALDI-MS and robotics. Since 2003, Head of the Mass Spectrometry and Proteomics Laboratory, which became a DCR Core Facility in 2008.



Bone Biology & Orthopaedic Research

www.bonebiology.dkf.unibe.ch

Research Highlights 2010 / Outlook 2011

Our research focuses on the areas of bone cell biology, bone and inflammatory diseases, osseointegration of calcium phosphate (CaP) ceramics and metallic implants, and chondrocyte biology. In 2011, a PhD student will start a project on molecular transporters in bone cells. An MSc student from the biomedical engineering program will do a thesis on the modulation of the microenvironment by the surface morphology of implants.

The role of inflammatory cytokines in the development of osteoclasts was investigated, elucidating aspects of the molecular mechanisms of the osteoblast-mediated inhibition of osteoclast formation by tumour necrosis factor alpha (TNF α). It was found that TNF α induces the release of GM-CSF, a member of a group of haematopoietic growth factors, by osteoblasts. GM-CSF in turn attenuates the levels of RANK on haematopoietic precursors, which renders these cells unable to respond to the osteoclastic growth factor RANKL. For the further analysis of the effects mediated by TNF α , growth factor- and receptor-deficient mouse strains were used. Interestingly, the data demonstrate that the effects of TNF α on bone resorption and osteoclastogenesis are not merely stimulatory. By increasing the pool of GM-CSF-dependent progenitor cells, GM-CSF can support the inflammatory response but precursor cells may also be transferred into the bone/bone marrow environment, where they differentiate locally into bone-resorbing osteoclasts.

To assess the potential of bone marrow-derived stromal cells (BMSC) for tissue engineering, we investigated their differentiation capacity and their development into osteoblast-, chondrocyte-, and adipocyte-lineage cells. BMSC were found to preserve a multipotential differentiation capacity. However, an increase in the number of cell doublings decreased their ability to differentiate, the chondrocytic differentiation pathway being the one most severely affected (MSc Doris Weber).

The osseointegration of CaP ceramics was investigated together with F. Klenke and H.J. Sebal (Clinic of Orthopaedic Surgery). Two principle modes of action were applied, either the inhibition of antagonists of bone morphogenic proteins (BMP; collaboration with W. Sebal) or the combination of CaP ceramics and osteogenic and vasculogenic growth factors. Of particular interest was Sebal's finding that a genetically modified BMP2 peptide, maintaining its BMP antagonist-binding property while no longer signalling through the BMP receptors, substantially decreased the quantity of exogenously added growth factor required to stimulate bone growth into a porous CaP ceramic. Osseointegration of resorbable orthopaedic implants was investigated together with T. Imwinkelried by MicroCT and histological analyses.

In collaboration with M. Seitz and D. Aeberli (Clinic of Rheumatology), studies on the development of osteoclast progenitors in peripheral blood of patients with inflammatory bone diseases were extended, and the modulation of their differentiation by inflammatory cytokines was analysed in vitro and in vivo.



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

MSc in Biochemistry at ETH Zurich followed by a PhD in Biochemistry (supervisor Prof. N. Herschkowitz) at the Children's Hospital of the Inselspital. After a post-doc at the University of Georgia, USA, joined the Institute of Pathophysiology, University of Bern (headed by Prof. H. Fleisch). Since 1997, Group Leader of the Bone Biology & Orthopaedic Research Group, DCR.

Group Members

Prof. Dr. Willy Hofstetter, Group Leader

Dr. Rainer Egli, Senior Scientist

Dr. Christoph Albers, Research Associate

Silvia Dolder, Laboratory Technician

Mark Siegrist, Laboratory Technician

Elvis Atanga, PhD Student

Deepak Balani, PhD Student

Adel Tekari, PhD Student (since Sep. 2010)

Doris Weber, MSc Student (until Feb. 2010)

Clinicians with projects in the group:

Dr. Frank Klenke, Clinical Research Associate

Dr. Hand-Joerg Sebal, Clinical Research Associate

Collaborators

Aeberli D, Inselspital, Switzerland

Fuster D, Inselspital, Switzerland

Imwinkelried T, Synthes, Switzerland

Luginbuehl R, RMS Foundation, Switzerland

Sebald W, University of Würzburg, Germany

Seitz M, Inselspital, Switzerland

Siebenrock KA, Inselspital, Switzerland

Wilkinson M, University of Sheffield, UK

Zwerina J, University of Erlangen, Germany

Publications

Influence of defective bone marrow osteogenesis on fracture repair in an experimental model of senile osteoporosis. Egermann, M; Heil, P; Tami, A; Janicki, P; Ito, K; Hofstetter, W; Richards, PJ (2010) in: J Orthop Res, vol. 28, p. 798-804.

Long-term cell-mediated protein release from calcium phosphate ceramics. Wernike, E; Hofstetter, W; Liu, Y; Wu, G; Wismeijer, D; Hunziker, EB; Siebenrock, KA; Klenke, F M (2010) in: J Biomed Mater Res A, vol. 92, p. 463-474.

VEGF incorporated into calcium phosphate ceramics promotes vascularization and bone formation in vivo. Wernike, E; Montjovent, MO; Liu, Y; Wismeijer, D; Hunziker, EB; Siebenrock, KA; Hofstetter, W; Klenke, FM (2010) in: Cells & Materials, vol. 19, p. 30-40.

The influence of PRP on early bone formation in membrane protected defects. A histological and histomorphometric study in the rabbit calvaria. Brogini, N; Hofstetter, W; Hunziker, E; Bosshardt, DD; Bornstein, MM; Seto, I; Weibrich, G; Buser, D (2010) in: Clin Implant Dent Reconstruct, vol. 13, p. 1-12.

Sodium/hydrogen exchanger NHA2 in osteoclasts: subcellular localization and role in vitro and in vivo. Hofstetter, W; Siegrist, M; Simonin, A; Bonny, O; Fuster DG (2010) in: Bone, vol. 47, p. 331-340.

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, vol. 24, p. 28-34.

Prevalence of cam-type deformity on hip magnetic resonance imaging in young males: a cross-sectional study. Reichenbach, S; Jueni, P; Werlen, S; Nuesch, E; Pfirrmann, CW; Trelle, S; Odermatt, A; Hofstetter, W; Ganz, R; Leunig, M (2010) in: Arthritis Care & Research, vol. 62, p. 1319-1327.

Grants

Amounts allocated for 2010:

SNF: NCCR TransCure sub-project: Role of ion transporter TRPV6 and other transporters in bone homeostasis (M. Hediger, W. Hofstetter) CHF 60,000

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

RMS: Cartilage Tissue Formation of Cells Seeded on Structured Scaffolds

in Physiological Conditions (W. Hofstetter) CHF 60,000

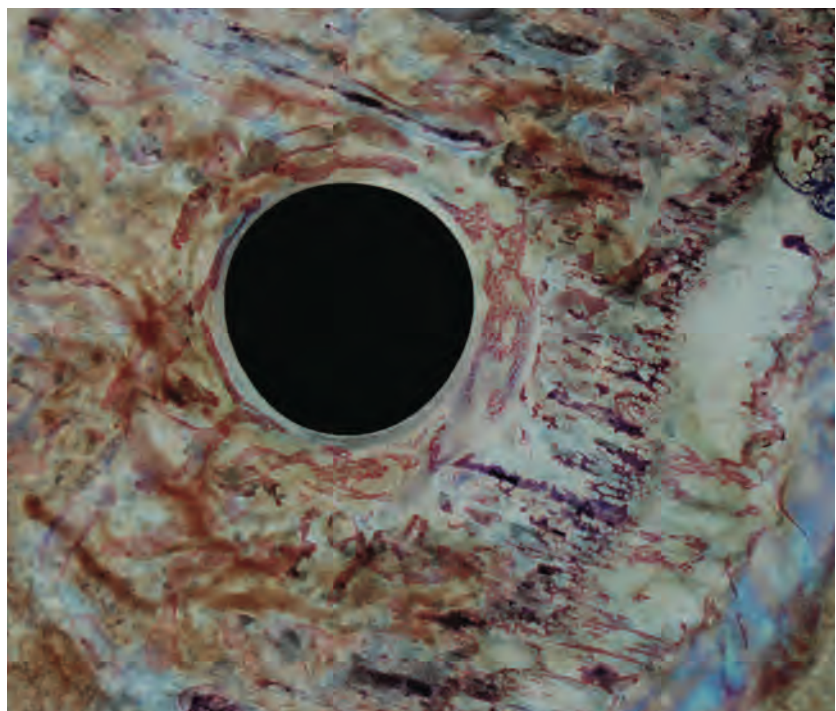
SNF (NFP64): Nanofibres reinforced bone substitute materials: Effect of delayed fibre degradation on cells and tissues (R. Luginbuehl, K. Maniura, W. Hofstetter)

ITI Foundation: Functionalization of CaP bone substitutes with growth factors (F. Klenke, W. Hofstetter)

Synthes: Magnesium implants – osseointegration, degradation (W. Hofstetter)

Teaching Activities

- Doris Weber: MSc Biomedical Engineering
- Masters course in biomedical engineering: Osteology (incl. exams)
- 3rd-year dentistry students: Pathophysiology – Bones
- 1st-year medical students: Molecular Biology: Practical courses (incl. exams)
- 2nd-year medical students: Kidney Block – Calcium-phosphate metabolism



Cardiovascular Research

www.cvrc.dkf.unibe.ch

Research Highlights 2010 / Outlook 2011

Reperfusion of tissue after ischemic events like myocardial infarction, stroke, surgery or transplantation may cause extensive injury. Our group investigated the contribution of the vascular endothelium and pioneered the use of endothelial cell (EC) protectants to attenuate this so-called ischemia / reperfusion (I/R) injury.

Shedding of the endothelial glycocalyx, mainly of heparan sulfate proteoglycans (HSPG), plays an important role in I/R injury. We hypothesised that EC protectants, like low molecular weight dextran sulfate (DXS), may 'functionally replace' shed HSPG. However, in order to understand how 'EC protection' works, we need to know which of the many HSPG species are shed during I/R injury and how this affects, for example, complement and coagulation.

In collaboration with Sally Stringer, we analysed HS disaccharides shed during myocardial I/R injury in pigs. Preliminary data indicate that there are differences in 2- and N-sulfated HS disaccharides in the plasma of animals before and after experimental myocardial infarction, and that HS-disaccharide species also differ depending on ischemia time. We are currently analysing HS-disaccharide species and plan to develop a multiplex suspension array for rapid characterisation of HS using phage-display antibodies, in collaboration with Toin van Kuppevelt.

In vitro experiments in the context of I/R injury were performed to analyse binding of complement factor H and C1-inhibitor to HS and DXS on EC. While binding of C1-inhibitor to EC is seen under these conditions, complement factor H does not bind. These experiments will be continued in 2011. We are working towards an in vitro culture system in which EC are grown under pulsatile flow and adhere to the inner wall of small glass tubes coated by a defined nano-structure, in order to promote optimal growth. The nano-coating is being developed in collaboration with EMPA Dübendorf. The aim of this in vitro system is to have a model for EC activation and protection that allows us to screen potential EC protectants and to reduce animal experiments. Future work on this model will be supported by the 3R Foundation.

Our group hosts the DCR Bio-Plex (Luminex) system, a platform for multiplexed detection of analytes in the fluid phase. For detection of analytes, a sandwich immunoassay is performed on microbeads filled with fluorescent dyes, giving them a unique 'spectral address'. The respective analyte is then detected using fluorescence-labelled antibodies. Analysis kits are commercially available for human, mouse and some rat cytokines but not for porcine antigens. We have therefore been developing assays for porcine inflammation markers. Currently, two assays for 7 and 8 different markers are available, plus a duplex-assay for porcine C3a and C5a. More analytes are continuously being added and the whole set will be made available to both internal and external groups doing experimental work with pigs.



Prof. Dr. Robert Rieben
robert.rieben@dkf.unibe.ch

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

Group Members

Prof. Dr. Robert Rieben, Group Leader

Dr. Yara Banz, Research Associate
Dr. Thusitha Gajanayake, Postdoctoral Fellow (since Apr. 2010)

Julie Denoyelle, Laboratory Technician (since Aug. 2010)

Carmen Fleurkens, Laboratory Technician

Katja Matozan, Laboratory Technician (until Nov. 2010)

Anjan Bongoni, PhD Student

Claudia Dührkop, PhD Student

Pranitha Kamat, PhD Student

Marie-Christine Franz, MSc Student (since July 2010)

Collaborators

Bovin N, Institute of Bioorganic Chemistry, Russia
Hani R, EMPA, Switzerland
Heier J, EMPA, Switzerland
Hess O, Inselspital, Switzerland
Klymiuk N, University of Munich, Germany
Korchagina E, Institute of Bioorganic Chemistry, Russia
Nilsson B, University of Uppsala, Sweden
Pochechueva T, University Hospital Zurich, Switzerland
Seebach J, Geneva University Hospital, Switzerland
Stringer S, University of Manchester, UK
Wolf E, University of Munich, Germany

Publications

Effects of TLR agonists on the hypoxia-regulated transcription factor HIF-1 α and dendritic cell maturation under normoxic conditions. Spirig, R; Djafarzadeh, S; Regueira, T; Shaw, SG; von Garnier, C; Takala, J; Jakob, SM; Rieben, R; Lepper, PM (2010) in: PLoS One, nr. 6, vol. 5, S. e0010983.

Inhibition of direct and indirect TLR-mediated activation of human NK cells by low molecular weight dextran sulfate. Millard, AL; Spirig, R; Mueller, NJ; Seebach, JD; Rieben, R (2010) in: Mol Immunol nr. 14, vol. 14, p. 2349-2358.

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; Gyax, E; Rieben, R; Banic, A; Vögelin, E (2010) in: J Surg Res, DOI 10.1016/j.jss.2010.01.040.

Grants

Amounts allocated for 2010:

SNF: Endothelial cell protection and attenuation of innate immunity in ischemia / reperfusion injury and organ transplantation (R. Rieben) CHF 30,000

EU 6th Research Framework Programme: Reprogramming of the Immune System to Establish Tolerance (RISET) (R. Rieben) CHF 20,000

Biotest Pharma: In vivo and in vitro analysis of complement-scavenging by IgM-enriched intravenous immunoglobulins (R. Rieben) CHF 50,000

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 30,000

CSL Behring: Investigation of acute anti-inflammatory effects of IVIG, sialylated IVIG and rHDL with focus on cardiovascular ischemia/ reperfusion injury (P. Kamat, R. Rieben) CHF 34,000

Miracor Medical Systems: Investigation of the effect of Pressure-controlled Intermittent Coronary Sinus Occlusion (PICSO) on myocardial salvage in a Porcine Myocardial Ischemia-Reperfusion Model (O. Hess, R. Rieben) CHF 60,000

Teaching Activities

- Benedikt Kislinger: MD
- Elective course for medical students: "Ihr Partner im Labor: Forschung auf den Gebieten der Herzchirurgie, Herztransplantation und Herzinfarkt"
- Elective module for Biomedical Sciences Masters students: Endothelial cell protection to prevent ischemia/reperfusion Injury in surgery, transplantation, and myocardial infarction
- 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
- Three high-school students: Patenschaften für Maturaarbeiten (2-week lab stay each)



Center of Regenerative Medicine for Skeletal Tissues

Research Highlights 2010 / Outlook 2011

We investigated the incorporation of the osteoinductive agent BMP-2 into a biomimetically prepared implant coating of calcium phosphate (CaP). The BMP-2 is liberated at a steady rate as the coating undergoes osteoclast-mediated degradation. This mode of delivery promotes bone formation directly (rather than indirectly via an endochondral route) even within a mechanically unstable environment. Under these conditions, the clinical placement of implants would become a safer process in the future.

We evaluated the biomimetic coating of various organic polymers with a protein-functionalised layer of CaP. The chemistry and surface topography of the polymers influence neither the characteristics of the coating nor the mechanisms whereby the protein is incorporated and subsequently released. A broad range of polymeric materials can thus be rendered osteoconductive by coating them with a "universal" layer of CaP, which can be conferred with the property of osteoinductivity by functionalising it with an osteogenic agent such as BMP-2.

In a collaborative project with the Department of Orthopaedics (Inselspital), we are comparing the chondrogenic potential of human synovial tissue that was derived either from young adults with femoral acetabular impingement or from elderly individuals with osteoarthritis. Preliminary findings reveal the chondrogenic potential of human synovial tissue to be impaired neither by age nor by an underlying skeletal pathology.

We are investigating the effects of dexamethasone on the chondrogenic differentiation of synovial cells. Preliminary findings reveal the effects of the agent on this process to be influenced by the nature of the stimulating growth factor and the microenvironment of the cells (artificial matrix or native tissue). The steroid is by no means indispensable to chondrogenesis and can indeed even inhibit it.

We are currently investigating the influence of the mode of OP-1 delivery on osteoinduction at a hostile (osteoporotic) site of implantation. Preliminary data indicate that when this osteogenic agent is co-precipitated with a layer of CaP upon the surface of an implant, the kinetics of its subsequent release are highly conducive to the stimulation and sustentation of bone formation, even within an environment that is characterised by poor bone-healing properties. Furthermore, ossification occurs directly (intramembranously), not indirectly via an endochondral route.



Prof. Dr. Ernst B. Hunziker
ernst.hunziker@dkf.unibe.ch

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

Group Members

Prof. Dr. Ernst B. Hunziker, Group Leader

Dr. Tobias Hägi, Research Assistant

Dr. Yuelian Liu, Research Assistant

Dr. Nahoko Shintani, Research Assistant

Dr. Yasukazu Himeda, Postdoc. Fellow

Dr. Naomi Nishii, Postdoc. Fellow
Linda Gallé, Lab. Technician (until Sept. 2010)

Jeannine Wagner, Lab. Technician (until Mar. 2010)

Fabienne Bourquin, Trainee (since Oct. 2010)

Walter Hutzli, Support Lab. Technician (ad personam)

Regina Channi, Secretary

Christa Nater, Secretary (since June 2010)

Corinne Scheiwiller, Secretary (since Apr. 2010)

Verena Wanner, Secretary (until Apr. 2010)

Dr. Ceri England, Text Editor (freelance)

Urs Haarmann, Technical Services (freelance)

Collaborators

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

Publications

The influence of PRP on early bone formation in membrane protected defects. A histological and histomorphometric study in the rabbit calvaria. Broggini, N; Hofstetter, W; Hunziker, EB; Bosshardt, DD; Bornstein, MM; Seto, I; Weibrich, G; Buser, D (2010) in: *Clinical Implant Dent Relat Res*, vol. 13(1), p. 1-12.

Mechanical insertion properties of calcium-phosphate implant coatings. Hägi, TT; Enggist, L; Michel, D; Ferguson, SJ; Liu, Y; Hunziker, EB (2010) in: *Clin Oral Implants Res*, vol. 21(11), p. 1214-22.

Cell-mediated BMP-2 liberation promotes bone formation in a mechanically unstable implant environment. Hägi, TT; Wu, G; Liu, Y; Hunziker, EB (2010) in: *Bone*, vol. 46(5), p. 1322-7.

The OARSI histopathology initiative – recommendations for histological assessments of osteoarthritis in the rabbit. Laverty, S; Girard, CA; Williams, JM; Hunziker, EB; Pritzker, K P (2010) in: *Osteoarthritis Cartilage*, vol. 18 Suppl. 3, p. S53-65.

Cartilage, bone and synovial histomorphometry in animal models

of osteoarthritis. Pastoureau, PC; Hunziker, EB; Pelletier, JP (2010) in: *Osteoarthritis Cartilage*, vol. 18 Suppl. 3, p. S106-12.

Long-term cell-mediated protein release from calcium phosphate ceramics. Wernike, E; Hofstetter, W; Liu, Y; Wu, G; Sebald, HJ; Wismeijer, D; Hunziker, EB; Siebenrock, KA; Klenke, FM (2010) in: *J Biomed Mater Res A*, vol. 92(2), p. 463-74.

VEGF incorporated into calcium phosphate ceramics promotes vascularisation and bone formation in vivo. Wernike, E; Montjovent, MO; Liu, Y; Wismeijer, D; Hunziker, EB; Siebenrock, KA; Hofstetter, W; Klenke, FM (2010) in: *Eur Cell Mater*, vol. 19, p. 30-40.

The effect of a slow mode of BMP-2 delivery on the inflammatory response provoked by bone-defect-filling polymeric scaffolds. Wu, G; Liu, Y; Iizuka, T; Hunziker, EB (2010) in: *Biomaterials*, vol. 31(29), p. 7485-93.

Biomimetic coating of organic polymers with a protein-functionalized layer of calcium phosphate: the surface properties of the carrier influence neither the coating characteristics nor the incorporation mechanism or release kinetics of the protein. Wu, G; Liu, Y; Iizuka, T;

Hunziker, EB (2010) in: *Tissue Eng Part C Methods*, vol. 16(6), p. 1255-65.

The structure of articular cartilage. Hunziker, EB (2010) in: Archer C, Ralphs J, eds. *Regenerative Medicine and Biomaterials for the Repair of Connective Tissues*. Cambridge, UK: Woodhead Publishing Limited, p. 83-105.

Grants

Amounts allocated for 2010:

SNF: The influence of age and disease on the chondrogenic potential of human synovial stem cells (E.B. Hunziker) CHF 76,170

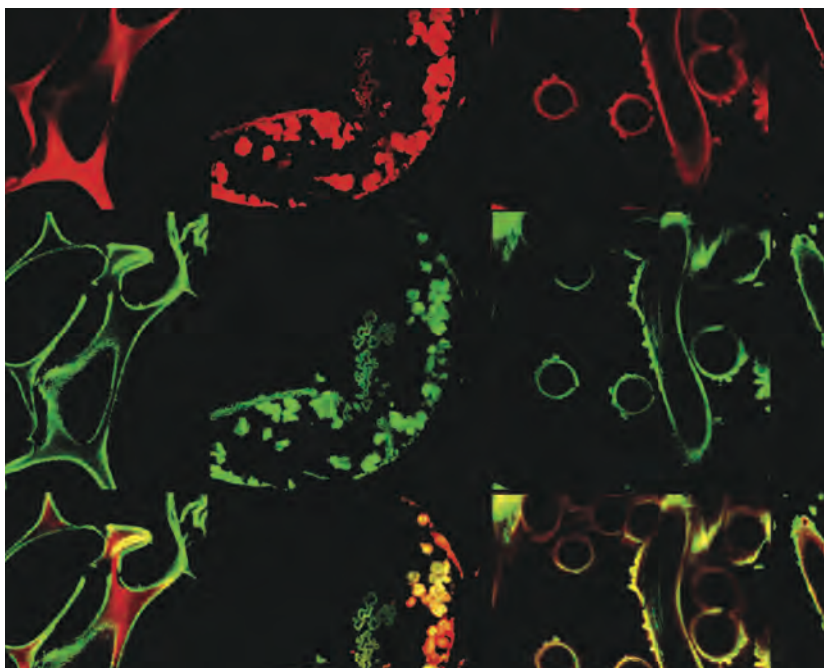
NIH/NIAMS USA: Synovium-based articular cartilage tissue engineering (E.B. Hunziker) CHF 219,260

ITI Research Foundation: In vivo degradability and osteoconductivity of calcium-phosphate coatings with different crystalline properties (Y. Liu) CHF 16,500

Various sponsors: (E.B. Hunziker) CHF 361,700

Teaching Activities

MD, DMD, PhD students and Post-doctoral Fellows



Ion Channels and Channelopathies

www.ionchannels.dkf.unibe.ch

Research Highlights 2010 / Outlook 2011

Our group focuses on the pathophysiological mechanisms underlying human disorders caused by dysfunctional ion channels, so-called "channelopathies". In particular, we are investigating the roles of cardiac ion channels in arrhythmic disorders. In addition, in collaboration with the group of Isabelle Decosterd (University of Lausanne), we are also studying the involvement of sodium channels in chronic pain. The student we co-supervise, Cédric Laedermann, will defend his thesis in summer 2011. 2010 was the first full year at the DCR after our group moved from Lausanne.

We investigated the regulation of the cardiac sodium channel Nav1.5 by interacting proteins. In particular, we demonstrated that at least two populations of Nav1.5 channels are expressed in cardiac cells (Petitprez et al., 2010, Circ Res) using several mouse models, and that this channel may also be regulated by an important muscle protein called utrophin (Albesa et al., 2010, Cardiovasc Res). These projects were performed in collaboration within the EuTrigTreat FP7 consortium (www.eutrigtreat.eu). In 2011, we will continue our studies on two newly generated knock-in mouse models with mutations in the Nav1.5 gene. On the one hand, we will study a mouse line bearing a mutation found in a family with cardiac arrhythmias. We are currently performing a comprehensive cardiovascular phenotyping of these mice. On the other hand, we will investigate a mouse model where the gene of Nav1.5 has a premature stop codon, and hence disrupts the interaction of the channel with important regulatory proteins.

In the framework of an SNF SCOPES project, we started a collaboration aiming to investigate genetic variants in novel candidate genes. For this purpose, Ukrainian and Russian patients with inherited arrhythmic syndromes were enrolled in our study, and genetic analyses will be performed in the human genetic laboratory of Elena Zaklyazminskaya in Moscow.

We also initiated a new project funded as part of the "NCCR TransCure" to study the ion channel TRPM4, which is well expressed in the heart. Recently, three mutations in the gene coding for TRPM4 were found in patients and families with cardiac conduction alterations. The role of this channel in cardiac physiology and the mechanisms underlying the mutation-induced phenotypes are however very poorly understood. In collaboration with cardiologists and geneticists from France, we started to study other genetic variants of this gene. Our goals for the future are to elucidate the molecular and cellular mechanisms underlying the mutation-induced alterations to its function; to find new interacting proteins and study their roles; and to look for chemical compounds that may inhibit or activate this channel.



Prof. Dr. Hugues Abriel
hugues.abriel@dkf.unibe.ch

Training both as a biologist at the ETH Zurich and physician at the University of Lausanne. After two years at Lausanne University Hospital, a post-doc at Columbia University, USA. In 2002, as a Swiss National Science Foundation Professor, start of independent research studying the role of ion channels in human disorders. Since 2009, Professor of Pathophysiology, University of Bern and DCR Director.

Group Members

Prof. Dr. Hugues Abriel, Group Leader

Dr. Konstantin Gusev, Postdoctoral Fellow (until Feb. 2010)

Dr. Jakob Ogrodnik, Postdoctoral Fellow

Dr. Séverine Petitprez, Postdoctoral Fellow

Dr. Jean-Sébastien Rougier, Postdoctoral Fellow

Dr. Marc Suter, Postdoctoral Fellow

Maria Essers, Laboratory Technician

Verena Frazao, Secretary

Maxime Albesa, PhD Student

Cédric Laedermann, PhD Student

Liliana Sintra Grilo, PhD Student

(until Sep. 2010)

Min-Ji Song, PhD Student (Aug.-Oct. 2010)

Ninda Syam, PhD Student

Katja Reinhard, MSc Student (since July 2010)

Collaborators

Barò I, French National Agency of Research Networks, CNRS, France
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, France
Hediger M, NCCR TransCure, Switzerland
Lehnart SE, EuTrigTreat FP7 Consortium, University of Göttingen, Germany
Remme CA, University of Amsterdam Academic Medical Centre, The Netherlands
Staub O, University of Lausanne, Switzerland
Sychov OS, SCOPES SNF Project, Ukraine
Zaklyazminskaya EV, SCOPES SNF Project, Russia
Zambelli T, ETH Zurich, Switzerland

Publications

SAP97 and Dystrophin Macromolecular Complexes Determine Two Pools of Cardiac Sodium Channels Nav1.5 in Cardiomyocytes. Petitprez S; Zmoos AF; Ogrodnik J; Balse E; Raad N; El-Haou S; et al. in: Circ Res, Epub (2010 Dec 16).

Regulation of the cardiac sodium channel Nav1.5 by utrophin in dystrophin-deficient mice. Albesa M; Ogrodnik J; Rougier J-S; Abriel H in: Cardiovasc Res, Epub (2010 Oct 14).

Selective inhibition of persistent sodium current by F 15845 prevents ischaemia-induced arrhythmias. Pignier C; Rougier JS; Vie B; Culie C; Verscheure Y; Vacher B; et al. (2010) in: Br J Pharmacol, vol. 161, p. 79-91.

Variable Na(v)1.5 protein expression from the wild-type allele correlates with the penetrance of cardiac conduction disease in the Scn5a(+/-) mouse model. Leoni AL; Gavillet B; Rougier JS; Marionneau C; Probst

V; Le SS; et al. (2010) in: PLoS One, vol. 5, e9298.

Takotsubo cardiomyopathy and congenital long QT syndrome in a patient with a novel duplication in the Per-Arnt-Sim (PAS) domain of hERG1. Grilo LS; Pruvot E; Grobety M; Castella V; Fellmann F; Abriel H (2010) in: Heart Rhythm, vol. 7, p. 260-5.

Brugada syndrome ECG provoked by the selective serotonin reuptake inhibitor fluvoxamine. Stirnimann G; Petitprez S; Abriel H; Schwick NG (2010) in: Europace, vol. 12, p. 282-3.

Cardiac sodium channel Na(v)1.5 and interacting proteins: Physiology and pathophysiology. Abriel H (2010) in: J Mol Cell Cardiol, vol. 48, p. 2-11.

Ubiquitylation and SUMOylation of cardiac ion channels. Rougier JS; Albesa M; Abriel H (2010) in: J Cardiovasc Pharmacol, vol. 56, p. 22-8.

Grants

Amounts allocated for 2010:

SNF: In vivo relevance of the PY and PDZ-domain binding motifs of the cardiac sodium channel Nav1.5 (H. Abriel) CHF 153,900

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

Sychov) CHF 73,500

SNF: NCCR TransCure sub-project: Physiology, pharmacology and pathophysiology of the calcium-activated non-selective cation TRPM4 channel (M. Hediger, H. Abriel, M.Heller) CHF 175,000

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

Association Française contre les Myopathies: Sodium channel dysregulation in muscle diseases and rescue by proteasome inhibitors (H. Abriel, A. Coulombe) CHF 42,000

Synapsis Foundation: Regulation of voltage-gated sodium channel and neuropathic pain (H. Abriel, I. Decosterd) CHF 50,000

Teaching Activities

- Liliana Sintra Grillo: PhD
- Maxime Albesa: PhD
- Katja Reinhard: MSc Biomedical Sciences
- Coordination of pathophysiology lectures for dentistry students
- Dentistry students: Kidney and electrolytes pathophysiology
- Master in Biomedical Sciences: Ion channels in cardiac diseases
- Bachelor in Life Sciences: Cardiac ion channels in health and disease



Magnetic Resonance Spectroscopy and Methodology

www.amsm.dkf.unibe.ch

Research Highlights 2010 / Outlook 2011

Two in-house and five collaborative SNF projects define the major part of the group's activity. One of our own and two collaborative projects (Endocrinology, Inselspital and Physiology, University of Lausanne) deal with insulin resistance and nutrition-induced changes. In cohort studies, the influences of fat, carbohydrate, and protein intake on insulin resistance, liver lipids, and skeletal muscle are being studied. Non-invasive measurements of ATP synthesis and creatine-kinase activity using phosphorus magnetic resonance spectroscopy have been developed to measure mitochondrial activity. Three PhD students are working on MR spectroscopy of the metabolic syndrome and insulin resistance.

In the second in-house project, specific resonances of exchangeable amid protons are being studied in the brain, partially at ultra-high magnetic field strength (with ETH Zurich). Two-dimensional MR spectroscopy sequences and post-processing methods are being developed to help extract features of the MR spectrum that are otherwise hidden by overlapping resonances. Measurements of the diffusion characteristics in kidney can be used to differentiate pure diffusion from micro-perfusion. These values are correlated with renal function and thus allow for a non-invasive evaluation of transplanted kidneys. So-called "magic angle spinning spectroscopy", which allows studies of intact tissue in high-resolution NMR magnets, was developed in collaboration with the Institute for Organic Chemistry, University of Bern. The unsurpassed spectral resolution of this system can be used to better characterise spectra of in vivo tissue obtained using clinical magnets with lower spectral quality and sensitivity.

From January 2011, our group will be integrated into the Institute of Diagnostic, Interventional and Pediatric Radiology, Inselspital, thus becoming an external DCR research group. This will mean a shift from the Siemens TRIO MR system to the similar but less homogeneous VERIO. Since magnetic field homogeneity is crucial for spectroscopy, we hope that the larger bore will outweigh the lower homogeneity. Our studies on insulin resistance will be extended to organs such as heart and pancreas. To differentiate the effects of aging vs. a sedentary lifestyle on insulin sensitivity, measurement of mitochondrial activity will be carried out in cohorts of liver patients, and in healthy exercise-trained and untrained subjects of different ages. A renewal of the project to support methodological developments in MR spectroscopy of the brain (partially done on a 7 Tesla magnet at the ETH Zurich) has been granted by the SNF, and allows two PhD students to continue to work on this project.



Prof. Dr. Chris Boesch
chris.boesch@insel.ch

Studies in physics 1971-1976 (dipl. sc. nat. 1976), PhD 1979, ETH Zurich. Studies in medicine 1977-1986, (MD 1986) University of Zurich. Research Assistant, University Children's Hospital, Zurich 1986-1990. Professor, University of Bern since 1991. President, European Society for Magnetic Resonance in Medicine and Biology 1997-1998; President, International Society for Magnetic Resonance in Medicine 2001-2002. Visiting Professor, University Claude Bernard Lyon 1 2006. President, Research Commission, University of Bern since 2008.

Group Members

Prof. Dr. Chris Boesch, Group Leader

Prof. Dr. Roland Kreis, Scientific Staff

PD Dr. Peter Vermathen, Scientific Staff

Verena Beutler, Technician

Karin Zwygart-Brügger, Technician

Dr. Charles Mamisch, Research Associate (since Mar. 2010)

Christine Bolliger, PhD Student

Andreas Boss, PhD Student

Vaclav Brandejsky, PhD Student

Tania Buehler, PhD Student

Erin MacMillan, PhD Student

Regula Koenig, Diploma Student

Collaborators

Bösiger P, ETH Zurich, Switzerland
Carlier P, Groupe Hospitalier Pitié-Salpêtrière, France
Decombaz J, Nestlé Research Center, Switzerland
Möller H, Max Planck Institute for Human Cognitive and Brain Sciences, Germany
Schick F, University of Tübingen, Germany
Scheurer E, Ludwig Boltzmann Institute, Austria
Tappy L, University of Lausanne, Switzerland

Publications

In-House:

Comparison of physiological triggering schemes for diffusion-weighted magnetic resonance imaging in kidneys. Binser T; Thoeny HC; Eisenberger U; Stemmer A; Boesch C; Vermathen P (2010) in: J Magn Reson Imaging, 31(5), p. 1144-50.

Standardized protocol for a depletion of intramyocellular lipids (IMCL). Ith M; Huber PM; Egger A; Schmid JP; Kreis R; Christ E; Boesch C (2010) in: NMR Biomed, 23(5), p. 532-8.

Evaluation of renal allograft function early after transplantation with diffusion-weighted MR imaging. Eisenberger U; Thoeny HC; Binser T; Gugger M; Frey FJ; Boesch C; Vermathen P (2010) in: Eur Radiol, 20(6), p. 1374-83.

The Effect of Growth Hormone Replacement Therapy on Different Fat Compartments: A Whole Body Magnetic Resonance Imaging Study. Egger A; Buehler T; Boesch C; Diem; Stettler; Christ ER in: Eur J Endocrinol, epub-ahead-of-print (doi:10.1530/EJE-10-0702).

Estimation of the postmortem interval by means of 1H magnetic resonance spectroscopy of decomposing brain tissue: influence of ambient temperature. Ith M; Scheurer E; Kreis R; Thali M; Dirnhofer R; Boesch C in: NMR Biomed, epub-ahead-of-print (doi:10.1002/nbm.1623).

Brain Metabolite Composition in Relation to Cognitive Functioning and Dystrophin Mutations in Boys

with Duchenne Muscular Dystrophy. Kreis R; Wingeier K; Vermathen P; Giger E; Kaufmann F; Joncourt F; Zwygart K; Boesch C; Steinlin M in: NMR Biomed, epub-ahead-of-print (doi:10.1002/nbm.1582).

Non-invasive assessment of exercise-related intramyocellular acetylcarnitine in eu- and hyperglycemia in type 1 diabetic subjects using 1H-magnetic resonance spectroscopy. Boss A; Kreis R; Jenni S; Ith M; Nuoffer JM; Christ E; Boesch C; Stettler C. in: Diabetes Care, epub-ahead-of-print (doi:10.2337/dc10-1534).

Collaborations:

A plasma global metabolic profiling approach applied to an exercise study monitoring the effects of glucose, galactose and fructose drinks during post-exercise recovery. Bruce SJ; et al. (2010) in: J Chromatogr B Analyt Technol Biomed Life Sci, 878, p. 3015-3023.

Topographic electrophysiological signatures of FMRI Resting State Networks. Jann K; et al. (2010) in: PLoS One, 5(9), e12945.

Structural analysis of Heschl's gyrus in schizophrenia patients with auditory hallucinations. Hubl D; et al. (2010) in: Neuropsychobiology, 61(1), p. 1-9.

pH-dependent distribution of chlorin e6 derivatives across phospholipid bilayers probed by NMR spectroscopy. Vermathen M; et al. (2010) in: Langmuir, 26, p. 11085-11064.

Association of individual resting state EEG alpha frequency and cerebral blood flow. Jann K, et al. (2010) in: Neuroimage, 51(1), p. 365-72.

Effects of a short-term overfeeding with fructose or glucose in healthy young males. Ngo Sock ET; et al (2010) in: BR J Nutr, 103(7), p. 939-43.

Effects of short-term overfeeding with fructose, fat and fructose plus fat on plasma and hepatic lipids in healthy men. Sobrecases H; et al. (2010) in: Diabetes Metab, 36(3), p. 244-6.

Effects of a whey protein supplementation on intra-hepatocellular lipids in obese female patients. Bortolotti M; et al. in: Clin Nutr

epub-ahead-of-print (doi:10.1016/j.clnu.2011.01.006).

Neuropsychological impairments and the impact of dystrophin mutations on general cognitive functioning of patients with Duchenne muscular dystrophy. Wingeier K; et al. in: J Clin Neurosci epub-ahead-of-print (doi:10.1016/j.jocn.2010.07.118).

Grants

Amounts allocated for 2010:

SNF: Multi-nuclear magnetic resonance spectroscopy and imaging on a clinical whole-body MR-system: integration and application of the MR-toolbox for studies on insulin resistance (C. Bösch, R. Kreis, L. Tappy, E. Christ) CHF 104,978

SNF: Magnetic Resonance Techniques to Investigate Human Brain Physiology: Novel Acquisition and Processing Methods to Extend the Scope and Robustness of Clinical Spectroscopy at High Magnetic Fields (R. Kreis, C. Boesch, P. Bösiger) CHF 98,342

SNF: Multi-nuclear magnetic resonance spectroscopy and imaging on a clinical whole-body MR-system: insulin resistance, ageing, and physical activity (C. Bösch, L. Tappy, E. Christ, J.-F. Dufour, R. Kreis) CHF 12,858

Multiple third party funding: (C. Boesch) CHF 258,508

Teaching Activities

- Tobias Binser: PhD
- Philipp Markus Huber: MD
- Problem Based Learning (Boesch, Kreis, Vermathen)
- Elective module for 3rd-year medical students: "Forschung in der Magnetresonanz-Spektroskopie (Kernspinresonanz)" (Boesch)
- Human medicine, Bioengineering and Chemistry lectures (Boesch, Vermathen)

Mammary Gland Biology and Carcinogenesis

Research Highlights 2010 / Outlook 2011

Ephrin receptor tyrosine kinases and their membrane-bound ephrin ligands play key roles during morphogenesis and adult tissue homeostasis. Receptor-ligand interactions result in forward and reverse signalling from the receptor and ligand, respectively. We have previously shown that EphB4 and ephrin-B2 are differentially expressed in the mammary gland and that their deregulated expression in the mammary epithelium of transgenic mice leads to perturbations of the mammary parenchyma and vasculature. In addition, over-expression of EphB4 and expression of a truncated ephrin-B2 mutant, capable of receptor stimulation but incapable of reverse signalling, confers a metastasising phenotype on NeuT-initiated mouse mammary tumours.

We have taken advantage of this transgenic tumour model to compare stem cell characteristics between the non-metastasising and metastasising mammary tumours. Analysis of the expression of markers for progenitor cells exhibiting a decreasing differentiation grade revealed that the metastasising tumour phenotype coincides with the appearance of stem and early progenitor cells. Thus, the deregulated expression of EphB4 and ephrin-B2 may interfere with the homeostasis of the stem/progenitor cell pool before tumour formation is initiated. This change in the tumour origin may have led to the acquisition of the metastatic tumour phenotype.

To investigate the role of ephrin-B2 signalling in the control of the mammary stem cell niche, we analysed the mammary stem and progenitor cell population in transgenic mice over-expressing the truncated ephrin-B2 mutant. We showed that mammary glands of truncated ephrin-B2 transgenic mice indeed contain significantly more cells in the stem cell-enriched fraction. In addition, the bi-potent progenitor- and the alveolar, estrogen receptor-positive cell fractions were increased. Thus, truncated ephrin-B2 expression leads to an accumulation of stem cells and to a shift of the differentiation pathway towards the alveolar and estrogen-positive cell fate. This indicates that intact ephrin-B2 signalling is necessary for the control of the stem cell niche and the regulation of the differentiation pathway.

In view of the suspected role of Eph and ephrin molecules in the control of stem cell compartments and the hypothesis of cancer stem cells as the origin of metastatic growth, we intend to deepen investigation of the mammary stem/progenitor cell population in our transgenic model systems. Firstly, the impact of EphB4 over-expression, also inducing metastatic tumour growth, on the mammary stem cell fate will be analysed by FACS-based quantification and functional analyses. Secondly, microarray analyses on RNA gained from the different transgenic mammary epithelial subpopulations are envisaged to characterise the signal transduction pathways involved in the EphB4-ephrin-B2 induced phenotypes.



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 CNRS in Strasbourg, the European centre for transgenic technology. Since 1991, Group Leader of the Mammary Gland Biology and Carcinogenesis Group, DCR; first as Junior Group Leader, since 2002 as Associate Professor.

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

Milica Antonijevic, Msc Student
(from Sep. 2010)

Collaborators

Djonov V, University of Bern, Switzerland

Stute P, Bern University Women's Hospital, Switzerland

Publications

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, A-C (2011) in: *Int J Oncol*, vol. 38, p. 151-160.

The mammary vasculature revisited. Andres, A-C; Djonov, V (2010) in: *J Mammary Gland Biol Neoplasia*, vol. 15, p. 319-328.

In vitro investigation into the potential of a mistletoe extract to alleviate adverse effects of cyclophosphamide. Burkhart, J; Wälchli, C; Heusser, P; Weissenstein, U; Baumgartner, S; Andres, A-C (2010) in: *Alt Therapies*, vol. 16, p. 40-48.

- Member, Commission for the Master Studies Curriculum in Biomedical Sciences
- Bachelor and Masters in Biomedical Sciences: Organiser and Teacher, Tumour Biology program
- 1st-year medical students: Organiser and Teacher, Developmental Biology program
- 1st-year medical students: "Cell death of multicellular organisms" lecture
- 1st-year medical students: Transgenic Seminar
- 1st-year veterinary medicine students: "Transgenic animals" lecture
- Graduate School: "Molecular biological methods in clinical diagnosis" practical course
- Masters in Bioengineering: "Molecular Biology" practical course
- Elective module for 1st-year medical students: "Genetic mutations: cyto- and molecular genetics"

Grants

Amounts allocated for 2010:

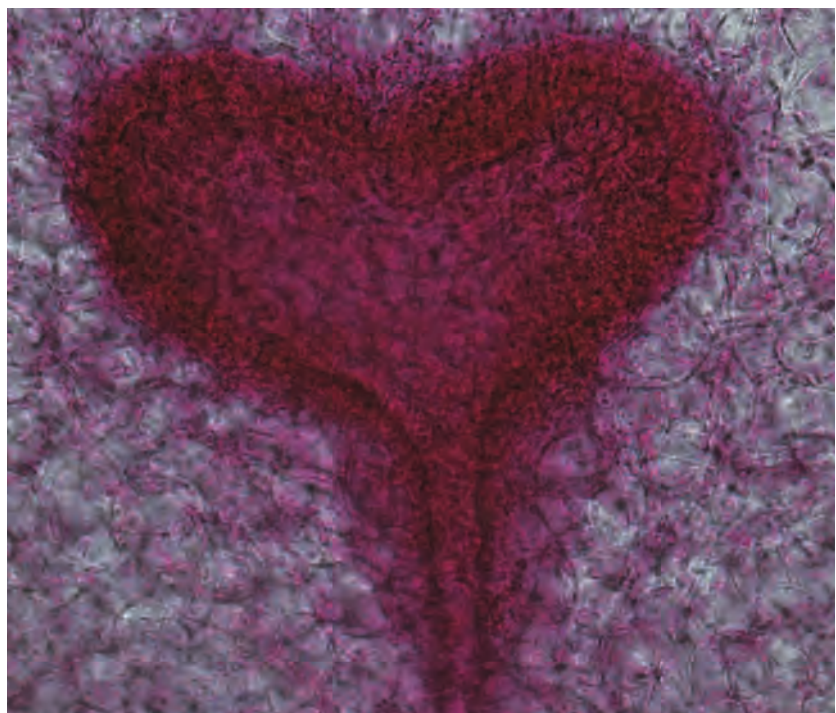
SNF: The role of EphB4 and ephrin-B2 in the control of the mammary gland stem/progenitor cell population (A.-C. Andres) CHF 64,300

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 52,600

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

- Philip Känel: PhD
- Caroline Schwab: MD
- Kathrin Mülchi: MD
- Member, Graduate School Commission "Biological Systems"



Molecular Biology

www.molbiol.dkf.unibe.ch

Research Highlights 2010 / Outlook 2011

Gene expression measurement of individual genes became possible around 30 years ago. Within about ten years, methods were developed to simultaneously measure expression of thousands of genes on miniaturised platforms (DNA chips or microarrays) to which specific oligonucleotides for each gene of interest were bound. Since then, thousands of tumour specimens have been analysed, resulting in new classifications and prognostic and predictive profiles. However, such studies depend on intact RNA, which can only be isolated from fresh or fresh-frozen tumour material, not available on a regular basis. Sample collection is laborious and must be set up for each project separately. It would be highly preferable if the same material collected for histological assessment could also be processed for gene expression studies. Unfortunately, diagnostic material is routinely fixed with formalin and embedded in paraffin, resulting in partial degradation and cross-linking of RNA to other cellular structures.

Until recently, it seemed impossible to isolate usable RNA from fixed material. It took us several years to develop reliable and reproducible protocols to allow quantitative gene expression measurements from such tissue (e.g., by real-time PCR). We validated our protocols on several independent breast cancer cohorts and also tested them on other archival material (normal prostate, prostate cancer, lung cancer, bladder cancer). Finally, we filed a patent in Munich in 2009 to protect our protocol and reagents. AmpTec, a company located in Hamburg, now sells a kit for RNA isolation from archival material based on our procedure (RNA ready FFPE). The kit is available in most European countries, in Canada and the United States, in Taiwan and Japan. We plan to apply the method and further develop its potential in the context of several prospective and retrospective clinical studies.

Massive improvements in DNA sequencing procedures have become available in the last few years. So-called "Next Generation Sequencing" (NGS) allows researchers to sequence large DNA regions or entire genomes in single experiments. However, NGS is still a complex and costly technology. DCR plans to establish a "Genomics Core Facility", offering support (experimental design, sample preparation, sequencing runs) to researchers of the Medical Faculty planning NGS experiments. NGS experiments will generate enormous amounts of data, requiring specialised equipment and tools for data processing and analysis. A bioinformatics infrastructure is planned in order to support researchers during data processing and analysis. This will be facilitated through direct support of collaborations with experts at Vital-IT in Lausanne.

Tissue banking is an important and essential pre-requisite for many clinically oriented research projects. Access to histologically well-defined, high-quality material enables researchers to perform their own projects or to significantly contribute to larger, high-impact projects. Our group will continue to support tumour banking at the Medical Faculty. The Tumorbank Bern has recently moved to the Institute of Pathology, where sample collection and quality controls will be further optimised.



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

Studies in Bern; PhD in Cell Biology 1982. Postdoc 1984-1986 and Group Leader 1986-1988 at the Ludwig Institute for Cancer Research, Bern. Moved to the Institute of Clinical and Experimental Cancer Research, University of Bern 1988. Research stays in Dublin collaborating with Prof. Finian Martin, University College 1989-1992. DCR Group Leader since 1998. Research interests: molecular biology of breast cancer; improvement of diagnosis, prognosis and treatment of breast cancer through personalised medicine.

Group Members

Prof. Dr. Rolf Jaggi, Group Leader
Prof. Dr. Stefan Aebi, Oncologist
Anna Baltzer, Lab Technician (since Sep. 2010)

Isabelle Minder, Lab Technician
Andrea Oberli, Lab Technician (until June 2010)

Daniel Muellener, Data Manager, Tumorbank Bern

Andreas Moor, Student (until May 2010)

Collaborators

Aebi S, Canton Hospital Lucerne, Switzerland
Altermatt HJ, Pathology Länggasse, Switzerland
Amstutz U, University of Bern, Switzerland
Ditzel H, University of Southern Denmark
Gautschi O, Canton Hospital Lucerne, Switzerland
Günthert A, Women's Hospital Bern, Switzerland
Kammler R, International Breast Cancer Study Group, Switzerland
Kristiansen G, University of Zurich, Switzerland
Krupp G, AmpTech, Germany
Largiader C, University of Bern, Switzerland
Leyland-Jones B, Winship Cancer Institute, USA
Pestalozzi B, University of Zurich, Switzerland
Regan M, Dana-Farber Cancer Institute, USA
Rothschild S, University of Bern, Switzerland
Viale G, European Institute of Oncology, Italy

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

Stiftung für Krebsbekämpfung: Vergleich von Gewebeproben aus verschiedenen Biobanken der Schweiz: Analyse der Genexpression mit RNA aus gefrorenen und aus fixierten Mammakarzinom-Gewebeproben (R. Jaggi, S. Simeon-Dubach) CHF 73,000

Teaching Activities

- Ursula Amstutz: PhD (PI: C. Largiader)
- Andreas Moor: MD (Co-PI: S. Aebi)
- 1st-year students: Problem Based Learning

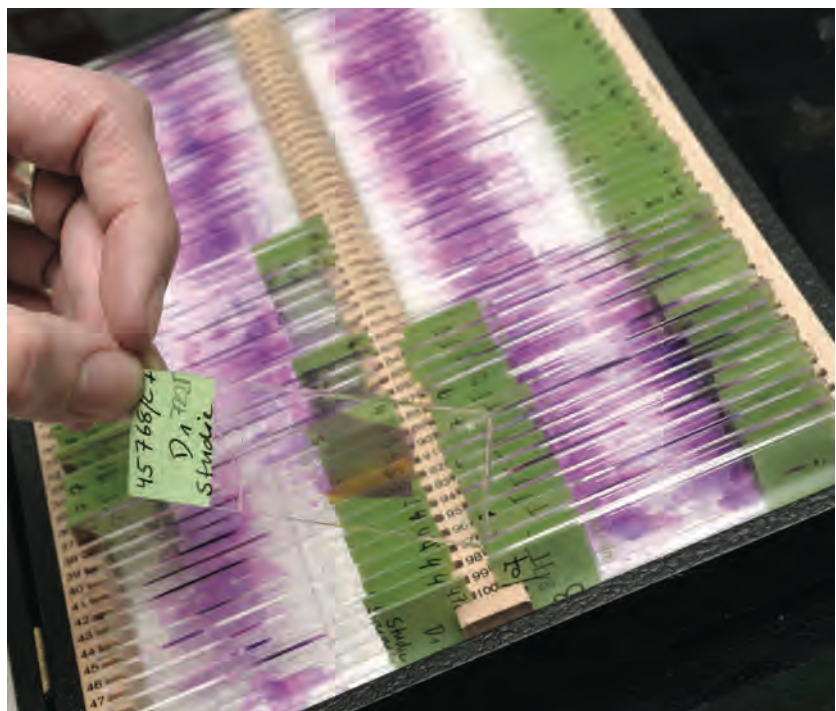
Publications

Hepatic gene expression profile in mice perorally infected with *Echinococcus multilocularis* eggs. Gottstein B; Wittwer M; Schild M; Merli M; Leib SL; Muller N; Muller J; Jaggi R (2010) in: PLoS One 5(4), e9779.

Molecular risk assessment of BIG 1-98 participants by expression profiling using RNA from archival tissue. Antonov J; Popovici V; Delorenzi M; Wirapati P; Baltzer A; Oberli A; Thurlimann B; Giobbie-Hurder A; Viale G; Altermatt HJ; Aebi S; Jaggi R (2010) in: BMC Cancer 10:37 (doi:10.1186/1471-2407-10-37).

Grants

Amounts allocated for 2010:
 Swiss Cancer League: Molecular profiling from archival human breast cancer samples (R. Jaggi) CHF 120,000



Phytopharmacology, Bioanalytics and Pharmacokinetics

www.phytopharm.dkf.unibe.ch

Research Highlights 2010 / Outlook 2011

In vitro (muscle strips of human myometrium after caesarean section) and clinical studies with *Bryophyllum pinnatum* (Weleda preparation) showed the tocolytic effects of its press juice and isolated fractions (mainly flavonoids). Experiments on human myometrium cells showed an inhibitory effect on the oxytocin-induced increase of the intracellular calcium concentration. We plan to isolate the active constituents of *Bryophyllum* and determine their structure and pharmacology. We will also evaluate clinical indications other than tocolysis, such as sedation and effect on bladder function, using animal models and in clinical studies on pregnant women.

Another study assessed the pharmacodynamic and pharmacokinetic interactive effects of the selective norepinephrine transporter inhibitor reboxetine and 3,4-methylenedioxymethamphetamine (MDMA, "Ecstasy") in 16 healthy subjects. Reboxetine reduced MDMA-effects, including elevations in plasma norepinephrine, increases in blood pressure and heart rate, as well as subjective drug high, stimulation and emotional excitation, despite an increase in plasma concentrations of MDMA and of its active metabolite 3,4-methylenedioxyamphetamine (MDA). The results demonstrate a critical role for transporter-mediated norepinephrine release in the cardiovascular and stimulant-like effects of MDMA in humans.

A double-blind, placebo-controlled phase-II study was conducted on patients suffering from anxiety related to progressive terminal illness. It was shown that lysergic acid diethylamide (LSD) is an adjunct option in such difficult-to-treat psychiatric situations.

The development of a highly sensitive GC/MS method allowed us to observe street heroin by-consumption of heavy heroin addicts participating in a substitution program with methadone and morphine. It was shown that the urine monitoring of acetylcodeine, a specific street-heroin marker, is a reliable tool to estimate the efficiency of and to validate such substitution programs. In another project, the neuropharmacology of heroin was studied by brain-imaging after intravenous administration of pharmaceutical heroin and PK/PD data analysis based on plasma profiles of heroin and major metabolites.

GC/MS and LC-MS/MS analyses allowed us to monitor xenobiotics (therapeutic drugs and abused substances) in influx and efflux samples collected in major Swiss sewage treatment plants. It was concluded that the cleaning efficiency of the plants is not always sufficient to fully eliminate these substances. For Bern, the cocaine consumption was back-calculated based on long-term measurements and after elimination of uncertainty parameters by computer-modelling.

We plan to establish a GC/MS and/or LC-MS/MS method to allow the determination of endocannabinoids (e.g., the CB-1 receptor agonist anandamide) in a biological matrix (plasma, liver, etc.), in order to study, for example, the role of the endocannabinoid system in liver diseases.



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

Fed. dipl. in Pharmaceutical Sciences, University of Bern 1975; PhD in Phytochemistry and Pharmacognosy 1979. Head of Department of Phytochemistry and Pharmacognosy, University of Bern 1981. Habilitation and Privatdozent 1988. Vice-Director, Institute of Pharmacy, University of Bern 1990-91; Associate Professor 1993. Since 1997, Group Leader of the Phytopharmacology, Bioanalytics and Pharmacokinetics Group, DCR. Since 2008, President, Swiss Academy of Pharmaceutical Sciences; President, Swiss Committee for Drugs of Abuse Testing.

Group Members

Prof. Dr. Rudolf Brenneisen, Group Leader

Dr. Sandrine Gouinguéné, Postdoctoral Fellow (until Dec. 2010)

Dr. Christian Lanz, Postdoctoral Fellow

Karin Fürer, PhD student (since Dec. 2010)

Jelena Hasanova, MSc, BNF program (since Sep. 2010)

Raoul Yankam, Chemist, BNF program (since Dec. 2010)

Collaborators

Berset D, Water & Soil Protection Laboratory Bern, Switzerland
Doblin R, Multidisciplinary Association of Psychedelic Studies, USA
Gasser P, Solothurn, Switzerland
Gertsch J, University of Bern, Switzerland
Greif R, Inselspital, Switzerland
Hamburger M, University of Basel, Switzerland
Honey G, University of Cambridge, UK
Liechti M, University Hospital and University of Basel, Switzerland
Morrison P, King's College London, UK
Oehen P, Biberist, Switzerland
Rieckermann J, EAWAG, Switzerland
Schnelle M, Weleda AG, Switzerland
Skendaj R, University Hospital Basel, Switzerland
Stickel F, University of Bern, Switzerland
Theiler L, Inselspital, Switzerland
von Mandach U, University Hospital Zurich, Switzerland
Walter M, University Hospital Basel, Switzerland
Weber M, Cantonal Hospital St. Gallen, Switzerland
Wüest A, Paracelsus Hospital Richterswil, Switzerland

concentration in human myometrial cells. Simões-Wüst, AP; Grãos, M; Duarte, CB; Brenneisen, R; Hamburger, M; Mennet, M; Ramos, F; Schnelle, M; Wächter, R; Worel, AM; von Mandach, U (2010) in: *Phytomedicine* vol. 17, p. 980-86.

Grants

Amounts allocated for 2010:

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

SNF: Pharmacological interaction between reboxetine and 3,4-methylenedioxymethamphetamine (Ecstasy): pharmacological effects and pharmacokinetics (M. Liechti) CHF 50,000

Mundipharma Medical Basel: Analytical monitoring of by-consumption of patients in heroin substitution programs (R. Brenneisen) CHF 150,000

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

Additional funding: Neuropharmacology of iv THC (P. Morrison) CHF 10,000

Teaching Activities

2nd-semester pharmacy students: Introduction to Pharmaceutical Sciences

Publications

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 in: *Neuropsychopharmacology*, Epub (2010 Dec 8).

Analysis of illicit and illicit drugs in waste, surface and lake water samples using large volume direct injection high performance liquid chromatography – Electrospray tandem mass spectrometry (HPLC-MS/MS). Berset, J-D; Brenneisen, R; Mathieu, C (2010) in: *Chemosphere* vol. 81, p. 859-66.

Juice of *Bryophyllum pinnatum* (Lam.) inhibits oxytocin-induced increase of the intracellular calcium



Vasoactive Peptide

Research Highlights 2010 / Outlook 2011

A primary research interest of our group is the physiological and pathological role and interactions of peptides in cardiovascular disease related to diabetes and the progression of associated vascular damage. Contributing factors involve a complex interplay between several vasoactive peptides, including endothelin-1, angiotensin II, vascular endothelial growth factor, adrenomedullin and the nitric oxide system. We have recently shown that blocking effects of some of these mediators may offer new therapeutic options for modifying the course of disease and preventing the onset and progression of diabetic retinopathy. Additional studies have identified peptides intrinsically involved in the autoimmune-mediated onset of type-1 diabetes and progression of atherosclerosis. Modulation of their activity can prevent the loss of insulin producing beta-cells in the pancreas and preserve endothelial function. Islet cell auto-antibodies (those involved in T-cell activation) are present long before beta-cell destruction occurs. Current studies are investigating the molecular mechanisms underlying effects of protective peptides and antagonists that regulate or control apoptosis, the innate immune system, dendritic cell activation, cytokine expression and toll-like receptor function. The approach is multidisciplinary and involves the use of proteomics, micro arrays and biochemical techniques, as well as transgenic animal models and cell culture.

In May, the 2nd International Cardiovascular Diseases Workshop was organised in collaboration with Dr. Janice Tsui at University College and the Royal Free Hospital, London, UK. This elicited the commissioning, as Principle Guest Editor, of a *Cardiol Res Pract* special issue "Cell Signalling Pathways Leading to Novel Therapeutic Strategies in Cardiovascular Disease", recently posted on the journal website (www.sage-hindawi.com/journals/crp/osi/).

A secondary area of research in our group is centred on the mechanisms and role of glucocorticoids in the consequences of withdrawal from chronic alcohol consumption. This initiated the organisation of the 2010 symposium "The importance of glucocorticoids and alcohol dependence and neurotoxicity" (Rose et al., 2010, *Alcohol Clin Exp Res*), and lead to the establishment of on-going international multicentre clinical trials on the potential benefits of glucocorticoid antagonists in the management of withdrawal from chronic alcohol abuse, funded by the MRC UK.

Sidney Shaw has been invited to speak at the April 2011 Research Society on Alcoholism Symposium on "Glucocorticoids" with Prof. Hilary Little in Volterra, Italy. Together with Dr. Tsui, he is organising the 3rd University College London and Royal Free International Symposium on "Advances in Cardiovascular Disease", to be held in London on 20 May 2011. He is also co-organising the International Workshop on "The Endothelium in Health and Disease" in London on 17 June 2011. In addition, Sidney Shaw is a member of the Organising Committee for the "12th International Conference on Endothelin-1", to be held in Cambridge UK in September 2011.



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

MA (Hons) in Biochemistry, Oxford University 1974; Dr. phil. nat. in Neuropharmacology 1978. Wellcome Trust Fellow, Lecturer in Pharmacology, Trinity College Oxford, UK 1980-1983. Research Associate, Department of Hypertension, University of Bern 1984-1996. Editorial Board *Cardiovasc Med* 1996-2010; Since 2008, *Vasc Pharmacol*; Since 2008, *Cardiol Res Pract*. Member, Swiss Society for Nephrology; American Society of Hypertension; German Society for Nephrology; European Society of Cardiology; European Association for the Study of Diabetes. Since 1996, Group Leader of the Vasoactive Peptide Group, DCR.

Group Members

Dr. Sidney G. Shaw, Group Leader
Jane Shaw, Laboratory Technician
Dr. Hemanshu Patel, Visiting Research Fellow (April, May 2010)
Dr. Janice Tsui, Visiting Research Fellow (April, May 2010)

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, Inselspital, Switzerland
Ruschitzka F, University Hospital Zurich, Switzerland
Tsui J, University College London, UK

Publications

Effects of TLR agonists on the hypoxia-regulated transcription factor HIF-1 α and dendritic cell maturation under normoxic conditions. Spirig R; Djafarzadeh S; Regueira T; Shaw SG; von Garnier C; Takala J; Jakob SM; Ribben R; Lepper PM (2010) in PLoS One, 5(6), e0010983.

The importance of glucocorticoids and alcohol dependence and neurotoxicity. Rose A; Shaw SG; Prendergast MA; Little HJ (2010) in: Alcohol Clin Exp Res 2011-2018.

Grants

Amounts allocated for 2010:

Royal Society Joint International Research Grant: The role of Toll like receptor signaling 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 100,000

Teaching Activities

- Leila Isidrova: PhD (Co-PI: J. Reichen)
- 3rd-year dental medicine students: Pathology and Internal medicine – Endocrinology Pathophysiology



DCR Research Groups from Clinics of the Inselspital

Thirty-eight research groups from clinics of the Inselspital are affiliated with the DCR. Below is a list of the groups and the names of the Clinic Directors and/or Group Leaders. On the following pages is a selection of research highlights from some of the groups.

Anaesthesiology

Prof. Dr. Frank Stüber, Dr. Rolf Lauber

Angiology

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

Audiology

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

Cardiology

Prof. Dr. Otto Hess, Prof. Dr. Etienne Delacrétaz, Prof. Dr. Paul Mohacsi, 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. Erik Hedbom

Dermatology

Prof. Dr. Luca Borradori, Dr. Bertrand Favre

Endocrinology of the Breast

PD Dr. Petra Stute

Endocrinology/Diabetology/Metabolism (Paediatrics)

Prof. Dr. Primus Mullis, 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

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

Nephrology and Hypertension

Prof. Dr. Felix Frey, Prof. Dr. Brigitte Frey

Neurology

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

Neurosurgery

Prof. Dr. Andreas Raabe, PD Dr. Michael Reinert, Prof. Dr. Hans-Rudolf Widmer

Oncology/Haematology (Adults)

Prof. Dr. Martin Fey, 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, Dr. Ute Wolf-Schnurbusch

Oral Microbiology

PD Dr. Dieter Bosshardt, Prof. Dr. Matthias Chiquet, PD Dr. Sigrun Eick, Dr. Erik Hedbom

Orthopaedic Surgery

Prof. Dr. Klaus-Arno Siebenrock

Perception and Eye Movement

Prof. Dr. Christian Hess, Prof. Dr. René Müri

Plastic Surgery

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

Prenatal Medicine

Prof. Dr. Daniel Surbek

Psychosomatic Medicine

Prof. Dr. Roland von Känel

Pulmonary Medicine (Adults)

Prof. Dr. Thomas Geiser, Dr. Christophe von Garnier

Pulmonary Medicine (Paediatrics)

Prof. Dr. Nicolas Regamey

Radiation Oncology

Prof. Dr. Daniel Aebersold, Dr. Yitzhak Zimmer

Rheumatology

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

Thoracic Surgery

Prof. Dr. Ralph A. Schmid, Dr. Steffen Frese

Triadic Family Functioning

Prof. Dr. Daniel Surbek, Dr. Werner Stadlmayr

Tumor-Immunology

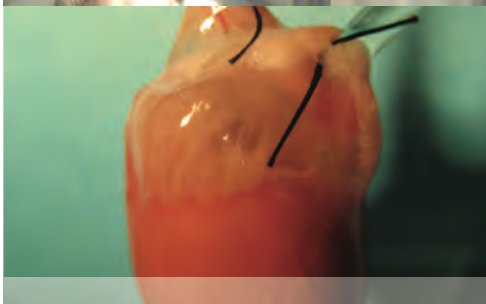
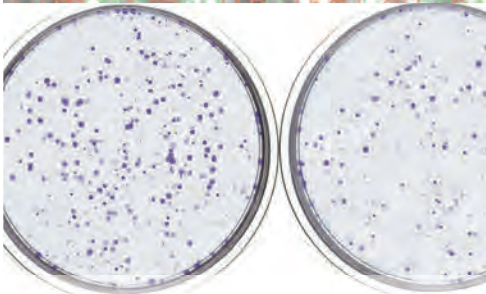
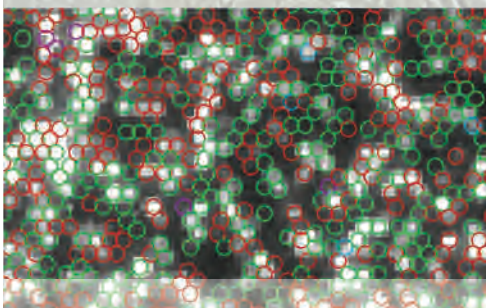
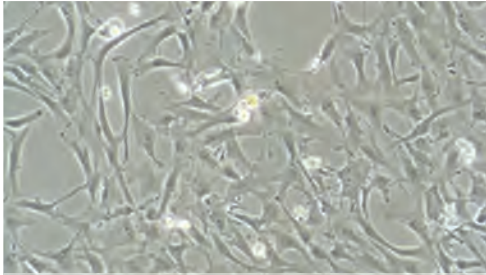
Prof. Dr. Adrian Ochsenbein

Urology

Prof. Dr. George Thalmann, Dr. Marco Cecchini

Visceral and Transplantation Surgery

Prof. Dr. Daniel Candinas, Dr. Deborah Stroka



Thoracic Surgery

Lung emphysema is a major health problem with no curative therapy. Stem cell-based therapeutic approaches are promising, although limited by the lack of an appropriate stem cell source. We have identified and are currently investigating human lung mesenchymal stem cells with the ability to engraft, differentiate into multiple cell lineages, express survival factors and repair damaged lung cells.

Human Genetics

Next generation sequencing (NGS) has revolutionised medical and biological research. The purchase of an NGS system has given DCR groups access to this research tool. Our projects focus on targeted resequencing to characterise pathogenic and modifying gene variants of the mitochondrial and cystic fibrosis transmembrane conductance regulator (CFTR) interactomes (protein interaction networks). We hope to translate our findings into new diagnostic and therapeutic strategies.

Radiation Oncology

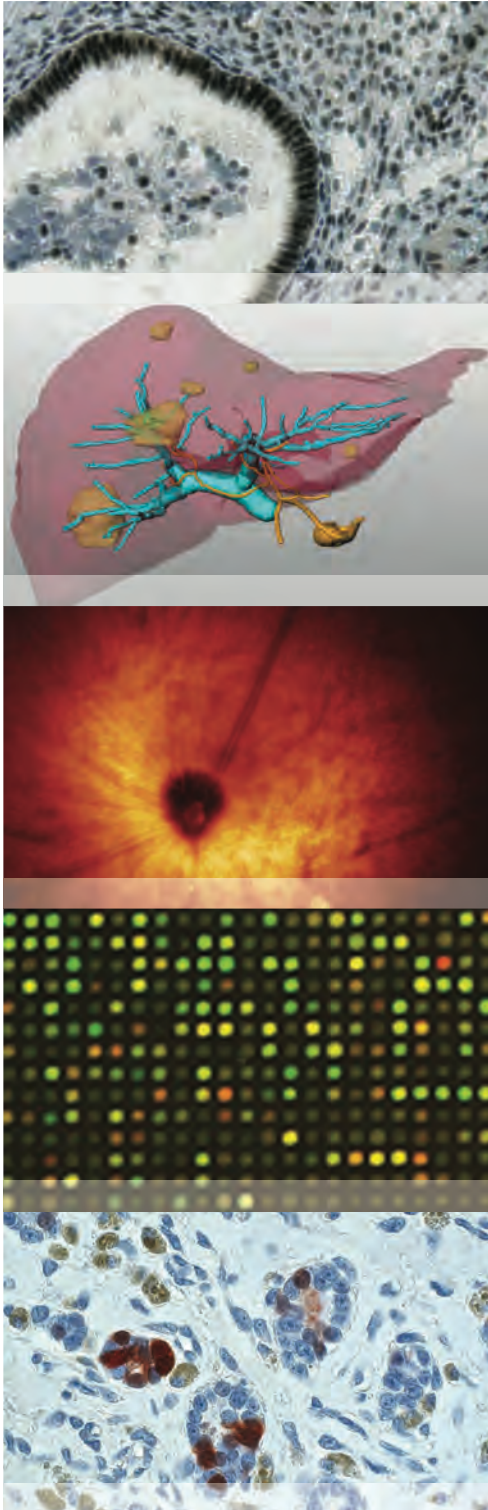
Increasing tumour cytotoxicity by combining ionising radiation with molecular targeted therapy is a novel and rapidly developing modality in radiation oncology. Our group focuses on establishing experimental combination protocols using inhibitors of the MET receptor tyrosine kinase together with ionising radiation, as well as on understanding the signalling crosstalk between the MET system and the DNA damage response.

Plastic Surgery and Hand Surgery

Survival of tissues or amputated limbs after prolonged periods of ischemia is crucial for the success of replantation, as well as for composite tissue allotransplantation. Our research teams are developing methods to preserve amputated limbs by perfusion with oxygenated whole blood. In addition, a project on tolerance induction in composite tissue allotransplantation is about to start.

Cardiovascular Surgery

We combine complementary strategies to address the multiple pathogenic mechanisms of heart failure, with the overall objective of improving treatment options. Recent innovative findings: ex vivo-produced tissue constructs prevent contractile deterioration (Tissue Engineering Group); effective in vivo myocardial transfection with electroporation (Gene Therapy Group); enhanced β -adrenergic signalling reverses atrophy in unloaded hearts (Reverse Remodeling Group); and novel reperfusion strategies reduce ischemic injury (Ischemia-Reperfusion Group).



Endometriosis and Reproductive Medicine

Endometriosis affects up to 20% of women during their reproductive years, often resulting in severe pain and otherwise unexplained infertility. The pathophysiology of endometriosis and how it causes pain is still unclear. Our projects focus on the inflammatory response accompanying endometriosis. We recently identified links between cytokine production/regulation with endometriotic lesion growth and the pain experienced.

Visceral and Transplantation Surgery

Complex surgical procedures are often chosen as a curative treatment option for diseases affecting visceral organs, in particular diseases and malignancies of the liver and pancreas. By focusing on the process of liver regeneration, pathology of ischemia reperfusion injury and complexity of liver and pancreatic tumours, our research aims to improve surgical outcomes and treatments for these organs.

Ophthalmology

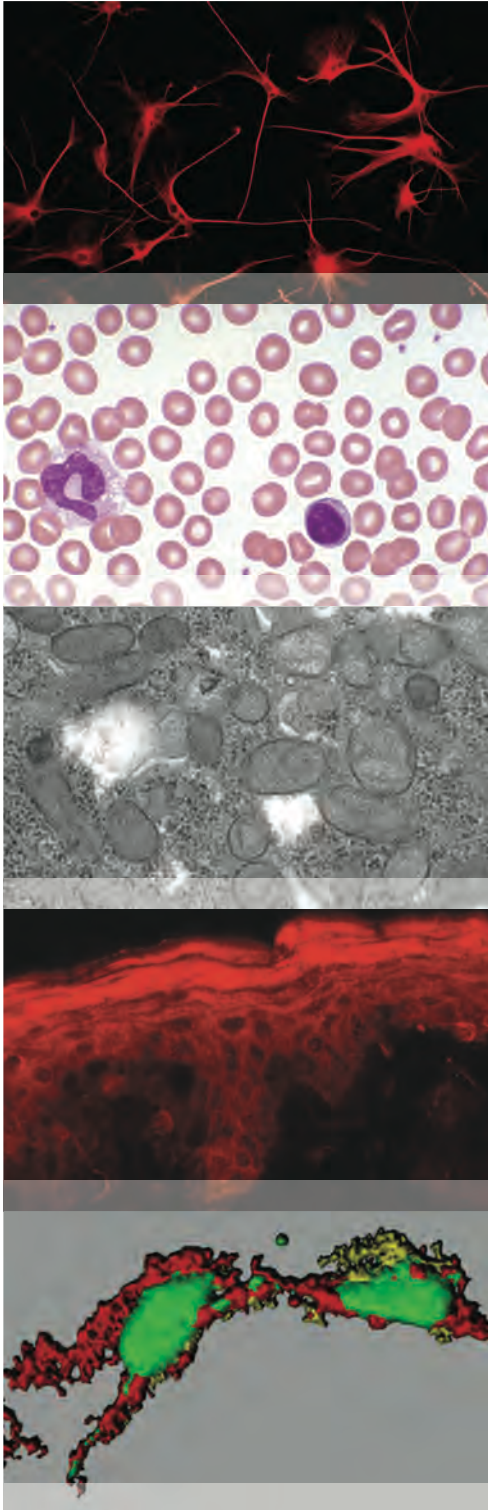
Retinal degeneration is the leading cause of blindness in the industrialised world. Animal models are crucial for the development of new therapies. In our current project, optical coherence tomography is being used to visualise retinal degeneration in mice. This novel technique allows us to follow the efficacy and time course of neuroprotective or stem cell-based regenerative treatments.

Haematology/Oncology (Paediatrics)

Cancer is the second leading cause of death in children. Novel therapies are urgently needed for patients with a poor prognosis. We aim to identify new drug targets for childhood cancers by combining different approaches: (a) RNA interference screening in established cellular models of childhood cancers, (b) pharmacological inhibitor screening, and (c) expression profiling of primary tumour samples.

Urology

Prostate cancer is the malignancy most commonly affecting males in the industrialised world. The cancer stem cell hypothesis postulates that tumour growth is sustained by rare, stem/progenitor-like cancer cells. We have characterised these cells in animal models and in clinical specimens of prostate cancer. Their isolation from blood will be useful for the identification of patients at risk for metastasis.



Prenatal Medicine

Pre-term birth often leads to brain damage with long-term neurodevelopmental sequelae. Perinatal transplantation of stem cells may improve neuroregeneration. We use a perinatal rodent model of inflammatory and hypoxic brain damage followed by stereotactic intraventricular transplantation of embryonic or placenta-derived stem cells. This model allows us to assess the effects of stem cell grafts on functional outcome.

Haematology/Oncology (Adults)

Autophagy (literally "self-eating") is a bulk degradation mechanism associated with cellular fitness and genome integrity. Its role in cancer is controversial since it has both tumour suppressor functions, by preventing accumulation of defective proteins/organelles, as well as oncogenic functions, by promoting tumour cell survival upon anti-cancer therapy. We identified a novel role for autophagy in the pathogenesis of acute myeloid leukemia.

Intensive Medicine

Severe infections accompanied by organ dysfunction are major causes of death of patients in intensive care units. In 2010, we evaluated the effects of infection, its treatment, and endogenous vasoregulating substances on mitochondrial function in clinically relevant models of severe sepsis. We were able to describe abnormalities in mitochondrial performance that were dependent on time of treatment initiation and that varied between organs.

Dermatology

Paraneoplastic pemphigus is a devastating autoimmune disease with multi-organ involvement, associated with certain types of cancer. Patients produce several auto-antibodies predominantly targeting structural antigens important for tissue cohesion, resulting in severe skin and mucosa blistering. We recently identified a previously unknown antigen recognised by PNP auto-antibodies as the broad-range protease inhibitor alpha-2-macroglobulin-like 1. This discovery opens new paths of research.

Pulmonary Medicine (Adults and Paediatrics)

Our research focuses on lung injury, inflammation, repair and regeneration. In particular, we are studying the effects of inhaled nanoparticles on lung epithelial and dendritic cells using advanced 3D cell culture models. We look at the mechanisms of nanoparticle-lung cell interactions by microscopic, immunological and biomolecular techniques. Moreover, we are investigating virus-lung epithelial cell interactions, focusing on mechanisms of innate immunity to viral infections in patients with cystic fibrosis. Finally, we are developing novel therapeutic approaches using growth factors and stem cells to support repair and regeneration in lung fibrosis.

Key Events

Day of Clinical Research 2010

02.-03.11.

A large and interested audience followed the presentations of **Dr. Markus Stöckli** (Novartis Institutes for Biomedical Research, Basel, Switzerland) entitled "About biological tissues, label-free molecular imaging and mass spectrometry" and **Prof. Michel D. Ferrari** (Leiden Centre for Translational Neuroscience, Department of Neurology, Leiden University Medical Centre, Leiden, The Netherlands) entitled "Migraine – the quest for prophylactic treatment".

One hundred and eighty-seven abstracts were submitted for poster prizes. Thirteen candidates applied for the Research Prize (funded by the University of Bern Faculty of Medicine and the DCR Scientific Fund). The winner was **Dr. Stephan von Gunten** from the Institute of Pharmacology, University of Bern.

The next Day of Clinical Research will be held on 1-2 November 2011.

01.03.

Prof. Andreas Reichenbach, Paul-Flechsig-Institute for Brain Research, Leipzig, Germany: *Neuroglia – the eminence grise of the brain.*

12.04.

Prof. Dr. med. Rüdiger von Kries, Head, Division of Epidemiology, Ludwig-Maximilians-University, Institute of Social Paediatrics and Adolescent Medicine, Munich, Germany: *Long term effects of breastfeeding on cardiovascular risk factors.*

07.06.

Prof. Dr. Erwin Wagner, Director Cancer Cell Biology Programme, Spanish National Cancer Research Centre, Madrid, Spain: *Novel functions of Fos/AP-1 proteins in bone physiology and disease.*

06.09.

Prof. Dr. Oliver Eickelberg, Director, Comprehensive Pneumology Center and Institute of Lung Biology and Disease, Helmholtz Zentrum München, Germany: *Mechanisms of epithelial-mesenchymal transition in chronic lung disease.*

04.10.

Prof. Dr. Peter Lichter, Division of Molecular Genetics, German Cancer Research Center (DKFZ), Heidelberg, Germany: *Analysis of pathomechanisms in brain tumors by integrated molecular profiling.*

01.11.

Dr. Andreas Caduff, Chief Technology Officer, Solianis Monitoring AG, Zurich Switzerland: *Non invasive glucose monitoring and the challenges involved.*

06.12.

Prof. Dr. Bart M. ter Haar Romeny, Department of Biomedical Engineering, Biomedical Image Analysis, Eindhoven University of Technology, Eindhoven, The Netherlands: *Bio-mimicking the Brain for Biomedical Image Analysis.*

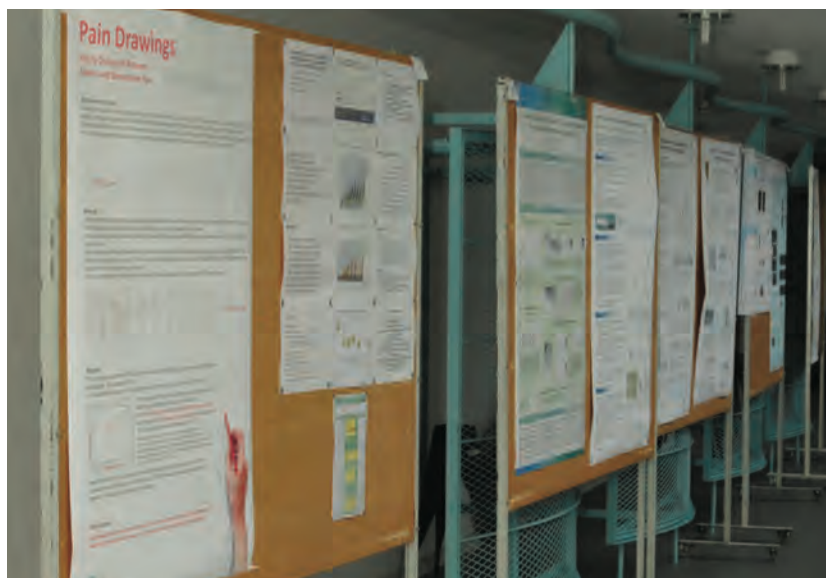
In 2011, the DKF Research Conference will take place as usual from 5-6 pm every first Monday of the month, and will be followed by an apéro.

DKF Research Conferences 2010

With an average of 65 visitors each month, the DKF Research Conferences continue to be very successful. In 2010, we were pleased to present the following speakers:

01.02.

Prize winners "Fonds für Preisarbeiten auf dem Gebiet der Diagnostik und Therapie": **Dr. Stefan Farese** and **Dr. Andreas Pasch**, Department of Nephrology and Hypertension, and **Prof. Dr. Lorenzo Alberio**, Department of Hematology and Central Hematology Laboratory, Inselspital.



Personnel Update

Academic Degrees

The following academic degrees were awarded to DCR group members:

Full Professor

Prof. Dr. George Thalmann, Urology

Full Professor (Extraordinarius)

Prof. Dr. Christian Seiler, Cardiology

Associate Professor

Prof. Dr. Gabriela M. Baerlocher, Experimental Haematology (Adults)
 Prof. Dr. Nick A. Bersinger, Endometriosis and Reproductive Medicine
 Prof. Dr. Christa E. Flück, Endocrinology/Diabetology/Metabolism (Paediatrics)
 Prof. Dr. Burkhard Möller, Rheumatology
 Prof. Dr. Beatrice U. Müller, Internal Medicine
 Prof. Dr. Thomas Pabst, Oncology/Haematology (Adults)
 Prof. Dr. Thomas Suter, Cardiology
 Prof. Dr. Michael von Wolff, Endometrium & Ovary

Lecturer (PrivatdozentIn)

PD Dr. Alexandre Arcaro, Haematology/Oncology (Paediatrics)
 PD Dr. Mihai Adrian Constantinescu, Plastic Surgery
 PD Dr. Nicolas Alexander Diehm, Angiology
 PD Dr. Ute Eisenberger, Nephrology and Hypertension
 PD Dr. Volker Enzmann, Ophthalmology
 PD Dr. Geneviève Escher, Nephrology and Hypertension
 PD Dr. Marie-Noëlle Giraud-Flück, Cardiovascular Surgery

PhD (Supervisors in brackets)

Maxime Albesa (Prof. Dr. Hugues Abriel)
 Post-translational regulation of cardiac ion channel expression

Jasmin Batliner (PD Dr. Mario Tschan)
 Identification and characterization of MicroRNAs and Novel PU.1 targets involved in the pathogenesis of acute myeloid leukemias

Michael Beyeler (Prof. Dr. Beat Trueb)
 Identification of a fibronectin interaction site in the extracellular matrix protein ameloblastin

Tobias Binser (PD Dr. Peter Vermathen, Prof. Dr. Chris Boesch)
 Evaluation of kidney function by multi-modal magnetic resonance imaging and spectroscopy in renal transplantation

Amadé Bregy (PD Dr. Michael Reinert)
 Neuroprotection by Sutureless Vascular

Tissue Fusion and Artificial Oxygen Carriers

Christina Claus (Prof. Dr. Adrian Ochsenbein)
 Treating chronic viral infections and solid tumors by blocking CD27 signaling

Marianne Eyholzer (Prof. Dr. Thomas Pabst)
 miR-223 and -29b trigger granulocyte differentiation & are regulated by the myeloid key transcription factor CEBPA – an interplay disrupted in human AML

Simon Gerber (Prof. Dr. Beat Trueb)
 Role of fibroblast growth factor receptor like-1 in mouse kidney development

Leila Idrissova (Prof. Dr. Jürg Reichen, Dr. Sidney Shaw)
 Liver fibrosis: Targeting mTOR, ras and different G-proteins in man and rat

Philip Känel (Prof. Dr. Anne-Catherine Andres)
 The role of EphB4 and ephrin-B2 in the regulation of the mammary epithelial cell fate

Thomas von Känel (Prof. Dr. Sabina Gallati)
 Characterization of genetic factors affecting disease outcome in cystic fibrosis

Alexander Lämmle (Dr. Deborah Stroka)
 Interplay between Hypoxia-Inducible Factor-1 α and SIRT1 protein deacetylase in hypoxic cancer cells

Didier Lochmatter (Prof. Dr. Primus Mullis)
 Autosomal dominant forms of isolated growth hormone deficiency and its therapeutic approach by RNA interference

Michaela Medova (Dr. Yitzhak Zimmer)
 Evaluation of anti-MET small molecules in inhibition of tumor-associated angiogenesis and in sensitization of tumor cells to DNA damaging agents

Flurin Pfiffner (Prof. Dr. Martin Kompis)
 Optimizing the benefit of bone anchored hearing aids

Tomas Regueira (Prof. Dr. Stephan Jakob)
 Mitochondrial function in sepsis, regulation and impact of common interventions

Chiara Secondini (Prof. Dr. George Thalmann)
 Osteolytic bone metastasis: it is not all about bone resorption

Raschid Setoud (Prof. Dr. Brigitte Frey)
 Evaluation of steroidal and non-steroidal derivatives for androgen receptor-mediated gene delivery

Liliana Sintra Grilo (Prof. Dr. Hugues Abriel)
 The cardiac hERG channel: a multiple approach for a better understanding of the long QT syndrome

Florian Steinberg (Prof. Dr. Beat Trueb)
 A functional study of the FGFR1 receptor in cell fusion and FGF signaling

Angela Suana (Prof. Dr. Hans-Peter Marti)
 Therapeutic application of immunoliposomes in experimental mesangial proliferative glomerulonephritis

Isabelle Vögeli (PD Dr. Genevieve Escher)
 Effect of CYP27A1 on steroid metabolism and reverse cholesterol transport

Monika Wnuk (Prof. Dr. Uyen Huynh-Do)
 Glomerular capillary repair in Thy1.1 nephritis: identification of underlying mechanisms and molecular players

Pascal Wurtz (Prof. Dr. René Muri)
 From basic aspects to everyday behaviour: insights from eye movement analysis

Zijang Yang (Dr. Christoph Kalka)
 The role of endothelial progenitor cells in therapeutic neovascularisation

Rahel Zulliger (PD Dr. Volker Enzmann)
 Cellular and molecular changes in animal models of retinal degeneration

MD (Supervisors in brackets)
 Philipp Huber (Dr. M. Ith, Prof. Dr. Chris Boesch)
 Standardized protocol for a depletion of intramyocellular lipids (IMCL)

Benedikt Kislinger (Prof. Dr. Robert Rieben)
 Comparison of minimal versus standard extracorporeal circulation in a pig model

Kathrin Mülchi (Prof. Dr. Anne-Catherine Andres)
 Stammzellen und Metastasierung beim Mammakarzinom: Der Einfluss der p21^{Waf} Expression auf die Tumormalignität

Julian Schardt (Prof. Dr. Thomas Pabst)
 The role of the unfolded protein response in the pathogenesis of acute myeloid leukaemia and its clinical implication

Caroline Schwab (Prof. Dr. Anne-Catherine Andres)
Erhöhte Häufigkeit von Tumorzellen mit Stammzellcharakteristika in malignen metastasierenden Brustkarzinomen im Vergleich zu benignen Karzinomen der NeuT Mutation

Awards

The following DCR group members received awards in 2010:

Dr. Eliane Angst, Visceral and Transplantation Surgery
Best oral presentation – Swiss Surgical Society Annual Meeting 2010

Dr. Stefano Di Santo, Angiology
Shared Pfizer Research Prize (Cardiovascular, Urology, Nephrology Research)

Dr. Sylvie Eigeldinger, Cardiovascular Surgery
Best poster prize – Congress of the European Society for Surgical Research

Dr. René Fahrner, Visceral and Transplantation Surgery
Best poster prize – Swiss Surgical Society Annual Meeting 2010

Dr. Steffen Frese, Thoracic Surgery
Jahrespreis der Schweizerischen Gesellschaft für Thoraxchirurgie

Anne Géraldine Guex, Cardiovascular Surgery
Young Investigator's Award for best oral presentation – 2nd EACTS Meeting on Cardiac and Pulmonary Regeneration

Tamara Hilmenyuk, Tumor-Immunology
Förderpreis DKF für die beste Arbeit in der präklinischen Forschung

Dr. Elisabeth Kieninger, Pulmonary Medicine (Paediatrics)
Young Investigator Award – International Conference on Paediatric Pulmonology 2010; Förderpreis DKF für die beste Arbeit in der klinischen Forschung

Dr. Didier Lochmatter, Endocrinology/Diabetology/Metabolism (Paediatrics)
Travel Grant, Research Grant – European Society for Paediatric Endocrinology

Dr. Michaela Medova, Radiation Oncology
Best Presentation Award – 14th Annual SASRO (Scientific Association of Swiss Radiation Oncology)

PD Dr. Thomas Nyffeler, Perception and Eye Movement
Robert Bing Prize

Berna Oezdemir, Urology
First prize for best abstract – 25th Anniversary Meeting of the European Association for Urology; Travel Award – 10th International Conference Cancer-Induced

Bone Disease, Sheffield, UK; Travel Award – 19th Meeting of the EAU Section of Urological Research, Barcelona

Prof. Dr. Thomas Pabst, Oncology/Haematology (adults)
Bristol-Myers Squibb Switzerland Hematological Malignancies Award 2010

Dr. Flurin Pfiffner, Audiology
Medical Cluster Award 2010 for best doctoral thesis in biomedical engineering at the University of Bern; Best poster award – International Conference on Cochlear Implants and Other Auditory Implantable Technologies 2010

PD Dr. Andreas Schoenenberger, Geriatrics/Medicine of Ageing
Research prize – Swiss Society of Hypertension

Dr. Christian Schürch, Tumor-Immunology
ICI 2010 Travel Scholarship – EFIS European Federation of Immunological Societies

Chiara Secondini, Urology
Travel Award – 10th International Conference Cancer-Induced Bone Disease, Sheffield, UK

Dr. Emma Slack, Gastroenterology (Adults)
Bern Immunology Award – Beste wissenschaftliche Arbeit; Junior IBD prize – Schweizerische Gesellschaft für Gastroenterologie

Mathieu Stadelmann, Cardiovascular Surgery
Best oral presentation – EACTS Young Investigator's Award 2010 of the European Association for Cardio-Thoracic Surgery

Dr. Peter Studer, Visceral and Transplantation Surgery
Poster prize – American Transplant Congress 2010; Best presentation – Centre for Vascular Biology Research, Boston

Zijang Yang, Angiology
Shared Pfizer Research Prize (Cardiovascular, Urology, Nephrology Research)

Staff Changes

New Staff

Dr. Christine Capper Loup, Research Assistant (15%), Neurology (since Apr. 2010)

Franziska Gisler, Doctoral Student (50%), Human Genetics (since Dec. 2010)

Mathias Grieder, Doctoral Student (43%), Perception and Eye Movement (since Sep. 2010)

Dr. Christian Lanz, Research Assistant (50%), Phytopharmacology, Bioanalytics & Pharmacokinetics (since Aug. 2010)

Isabelle Minder, Lab Technician (100%), Molecular Biology (since Aug. 2010)

Daniel Muellener, Lab Technician (43%), Urology (since Jan. 2010)

Dr. Stefan Müller, Head (30%), Cytometry Laboratory (since Jan. 2010)

José Schranz, Secretary (80%), Administration (since Feb. 2010)

Resignations

Regula Käch, DCR Administrator (100%), Administration (until Jan. 2010)

Dr. Thomas von Känel, PhD (50%), Human Genetics (until Oct. 2010)

Dr. Brett McKinnon, Research Assistant (100%), Endometriosis and Reproductive Medicine (until June 2010)

Dr. Pascale Meyer, Research Assistant (50%), Phytopharmacology, Bioanalytics & Pharmacokinetics (until May 2010)

Isabelle Minder, Apprentice (100%), Molecular Biology (until July 2010)

Andrea Oberli, Lab Technician (90%), Molecular Biology (until July 2010)

Dr. Séverine Petitprez, Research Assistant (100%), Ion Channels and Channelopathies (until May 2010)

Dr. Pascal Wurtz, PhD (25%), Perception and Eye Movement (until June 2010)

Short Employment (<12 months)

Dr. Sandrine Gouinguéné, Research Assistant (37%), Phytopharmacology, Bioanalytics & Pharmacokinetics (July-Aug. 2010)

Christopher Jackson, Doctoral Student (50%), Human Genetics (Dec. 2010)

Dr. Robert Kalicki, MD (50%), Nephrology (Aug.-Oct. 2010)

Anita Portner, DCR Administrator (100%), Administration (Feb.-Aug. 2010)

Dr. Aurélie Sansonnens, MD (42%), Nephrology, May-Aug. (Sep.-Nov. 2010; illness replacement)

Dr. Martina Schobesberger, Research Assistant (12%), Molecular Biology (Jan.-May 2010)

Design concept, Editing: Leah Witton
Graphics, Layout: Patrizia Catucci
Coordination: Verena Frazao
DCR Director: Prof. Hugues Abriel
Photos: Susi Bürki, Inselspital
Print: PrintServices Inselspital

