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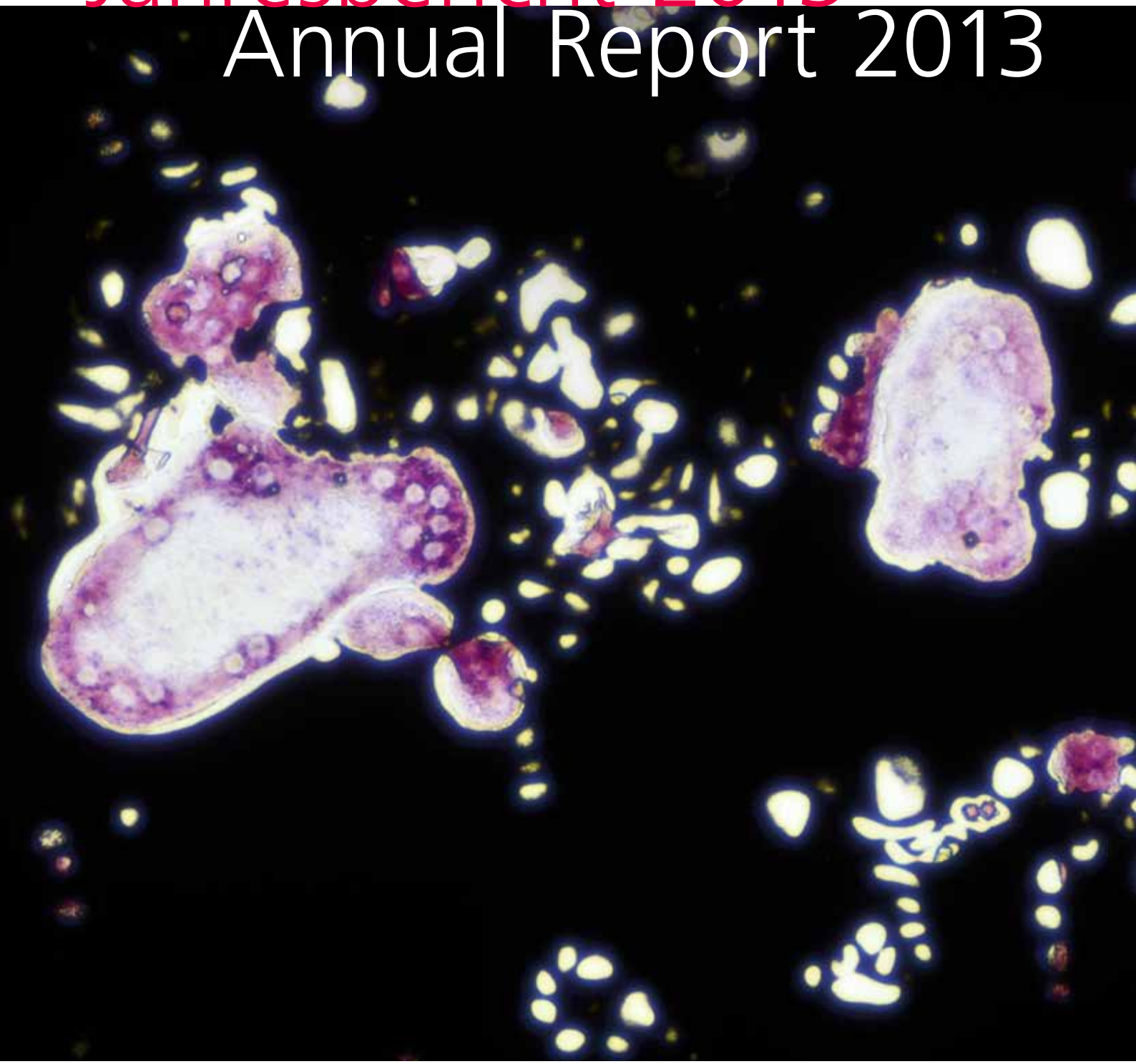
Jahresbericht 2013
Annual Report 2013



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

Cover:
Mouse osteoclasts were generated from bone marrow progenitors. The differentiated cells were seeded onto a calcium phosphate layer and were cultured for 24 hours. The resorption lacunae are visible as white areas in the black calcium phosphate layer (von Kossa staining). Osteoclasts are visualised by staining for the marker enzyme tartrate resistant acid phosphatase (TRAP).
Image: Silvia Dolder (Bone Biology & Orthopaedic Research)

Contents

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.

It was founded in 1994 with the mission to provide the best possible environment and infrastructure to researchers at the Inselspital, Bern University Hospital and at the Faculty of Medicine. In 2013, 47 independent research groups, covering almost all fields of biomedical research, were affiliated with the DCR.

The DCR aims to bridge laboratory-based biomedical and patient-oriented clinical research through the scientific support of its groups and by operating state-of-the-art Technology Core Facilities and specialised Animal Core Facilities. It also hosts the Clinical Trials Unit (CTU) Bern. In addition, a strong emphasis is put on the development of translational approaches and the use of omics technologies.

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. Im Jahr 2013 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. Die Clinical Trials Unit (CTU) Bern ist auch dem DKF angegliedert. Ausserdem wird ein starkes Gewicht auf die Entwicklung von translationellen Ansätzen und der Anwendung von Omics-Technolgien gelegt.

Foreword – Director's Report

Dear readers and colleagues,

In this report, I would like to inform you about the important achievements of 2013. First, let me welcome to the DCR the new research group from the Department of Diagnostic, Interventional and Paediatric Radiology, Inselspital and wish the entire team every success in their research. This group is headed by Prof. Heverhagen and PD Dr. von Tengg-Kobligk.

I would also like to highlight the hiring of two expert bioinformaticians and one IT specialist in our efforts to establish a Bioinformatics unit. Their roles are to support the design of studies involving large data sets and to help analyse the data, in particular from the genomics, proteomics and metabolomics fields. This project will be financially supported for five years by the Directorate of Teaching and Research, Inselspital. The bioinformaticians have already been involved in many different projects and the first manuscripts are about to be submitted for publication. The necessity and usefulness of the new Bioinformatics unit has been proven within a very short time. This looks like it will be a huge success!

Another important project that was realised in 2013 was the significant increase in housing capacity for mice in the Central Animal Facility. This will make possible the recruitment of new researchers and the improvement of conditions for the existing research groups in the Faculty of Medicine. The allocation of the additional housing space will be coordinated by the newly created "Organisation of the Experimental Animal Centre" task force in the Faculty of Medicine. This good news is somewhat overshadowed by the fact that the demand for animal housing space is still extremely high and we are already aware that the increase achieved in 2013 will not suffice.

As already mentioned in last year's report, the DCR offers its research groups the possibility to build so-called "Research Clusters", with the aim of supporting collaborations and the organisation of educational activities. The "Regenerative Neuroscience" Research Cluster was particularly noteworthy in 2013, with the organisation of progress report meetings and other well-attended events. We would like to particularly encourage the creation of such clusters in the next years to come. Please contact me if you would be interested in working on such a project.

It is very important to us that a large part of the research performed at the DCR is carried out by young scientists. It is one of the key missions of the DCR to provide these young researchers with optimal conditions for their education. In 2013, 12 PhD and 2 MD/PhD students completed their dissertation in DCR research groups. This gives you an excellent illustration of the important role the DCR plays in educating the biomedical scientists of tomorrow.

Lastly, I would like to inform you that at the end of January 2014, we closed the DCR research division located on the Tiefenau hospital campus. The Tiefenau laboratories were the birthplace of the DCR, where pioneering research in the domain of cancer biology was performed. With time, the infrastructure aged and became increasingly inadequate, and the distance to the main Inselspital campus was also a disadvantage. For these reasons, and concomitantly with the retirement of the DCR Tiefenau Coordinator, Prof. Anne-Catherine Andres, it was decided to close this division. I would like to warmly thank Prof. Andres for her outstanding work at the DCR over her more than 20 years with us. We will miss her! At the same time, the research group "Vasoactive Peptide" ended its activities due to the retirement of its Head, Dr. Sidney Shaw. We wish him the very best for the future!

In 2014, the DCR will celebrate its 20th anniversary. Celebrations will mainly take place during the Day of Clinical Research, which will be held on 5 November 2014. In addition, we will organise an open day to give our researchers the possibility to present their activities to a broader public.

Without a doubt, 2013 was again a year full of activities and developments that will improve the quality of research that can be performed at the DCR. This has been the result of the hard work of many of the DCR employees. I would like to sincerely thank all of you for your excellent work for the department and the biomedical research community at the University of Bern.

Prof. Dr. Hugues Abriel, MD PhD

Vorwort – Bericht des Direktors

Liebe Leserinnen und Leser
Liebe Kolleginnen und Kollegen

In diesem Bericht möchte ich auf wichtige Ereignisse im Jahr 2013 hinweisen. Zuerst heisse ich die neue Forschungsgruppe des Universitätsinstituts für Diagnostische, Interventionelle und Pädiatrische Radiologie, Inselspital im DKF willkommen und wünsche dem ganzen Team eine erfolgreiche Forschungstätigkeit. Die Gruppe wird von den Herren Prof. Dr. Heverhagen und PD Dr. von Tengg-Kobligk geleitet.

Als nächstes darf ich Sie darüber informieren, dass wir in unserem Bestreben eine Bioinformatik Einheit aufzubauen, zwei ausgewiesene Bioinformatiker und einen IT-Spezialisten eingestellt haben. Ihre Aufgabe ist es, die Durchführung von Studien, in welchen grosse Datenmengen anfallen, zu unterstützen und bei der Analyse dieser Daten, insbesondere aus den Bereichen Genomics, Proteomics und Metabolomics, mitzuarbeiten. Dieses Projekt wird finanziell während fünf Jahren von der Direktion Lehre und Forschung, Inselspital getragen. Die Bioinformatiker waren bereits an vielen verschiedenen Projekten beteiligt, und die ersten Manuskripte werden in Kürze zur Veröffentlichung eingereicht. Die Notwendigkeit und der Nutzen der neuen Einheit Bioinformatik hat sich innerhalb kürzester Zeit bestätigt. Es sieht nach einem riesigen Erfolg aus!

Ein weiteres wichtiges Projekt, das 2013 umgesetzt werden konnte, ist die Erhöhung der Kapazität der Maushaltung in den Zentralen Tierställen. Dies wird die Rekrutierung neuer Forschender und die Verbesserung der Bedingungen für die bestehenden Forschungsgruppen in der Medizinischen Fakultäten ermöglichen. Die Zuteilung dieser zusätzlichen Haltungs-Kapazitäten wird durch die neu geschaffene Task Force „Organisation of the Experimental Animal Center" an der Medizinischen Fakultät koordiniert werden. Diese gute Nachricht wird von der Tatsache überschattet, dass die Nachfrage nach Tierhaltungs-Kapazitäten weiterhin sehr hoch ist, und wir sind uns bewusst, dass die 2013 erreichte Kapazitätserhöhung nicht genügen wird.

Wie bereits im letzten Jahresbericht erwähnt, bietet das DKF seinen Forschungsgruppen die Möglichkeit sogenannte „Forschungscluster" zu bilden, mit dem Ziel, Zusammenarbeiten und die Organisation gemeinsamer Weiterbildungsaktivitäten zu unterstützen. Der Cluster für „Regenerative Neurowissenschaft" ist im Jahr 2013 besonders aufgefallen durch die Organisation von „Progress Report" Treffen und weiteren gut besuchten Veranstaltungen. Wir möchten die Schaffung von Forschungsclusters in den nächsten Jahren speziell fördern. Bitte kontaktieren Sie mich, wenn Sie Interesse haben, in einem solchen Projekt mitzuwirken.

Es ist uns sehr wichtig, dass ein grosser Teil der Forschung im DKF durch junge Wissenschaftler ausgeführt wird. Es ist eine der Hauptaufgaben des DKF jungen Forschenden optimale Bedingungen für ihre Ausbildung zur Verfügung zu stellen. Im Jahr 2013 haben 12 PhD und 2 MD/PhD Studenten ihre Dissertationen in einer DKF Forschungsgruppe abgeschlossen. Dies ist ein ausgezeichnetes Beispiel dafür, welche wichtige Rolle das DKF in der Ausbildung der biomedizinischen Wissenschaftler von Morgen spielt.

Schliesslich möchte ich Ihnen mitteilen, dass per Ende Januar 2014 der DKF Forschungsbereich auf dem Areal des Tiefenauspitals geschlossen wurde. Die Tiefenaulabors waren die Geburtsstätte des DKF, wo bahnbrechende Forschung im Bereich der Krebsbiologie durchgeführt wurde. Mit der Zeit veraltete die Infrastruktur und wurde immer unzureichender und auch die Entfernung zum Inselspital war nachteilig. Aus diesen Gründen, und gleichzeitig mit der Pensionierung der Koordinatorin des DKF Bereichs Tiefenau, Frau Prof. Dr. Anne-Catherine Andres, wurde beschlossen, diesen Bereich zu schliessen. Ich bedanke mich ganz herzlich bei Frau Prof. Andres für die hervorragende Arbeit, die sie am DKF während mehr als 20 Jahren geleistet hat. Sie wird uns fehlen! Zur gleichen Zeit hat die Forschungsgruppe „Vasoaktive Peptide", wegen der Pensionierung ihres Leiters, Dr. Sidney Shaw, die Aktivitäten eingestellt. Wir wünschen ihm alles Gute für die Zukunft!

Im 2014 wird das DKF sein 20-jähriges Jubiläum feiern. Dieses Jubiläum wird hauptsächlich während des Tages der Klinischen Forschung am 5. November 2014 gefeiert. Bei dieser Gelegenheit wird zudem ein „Tag der offenen Tür" organisiert, der unseren Forschenden die Möglichkeit bieten wird, ihre Forschungsarbeiten einer breiten Öffentlichkeit zu präsentieren.

Zweifelsohne war auch das Jahr 2013 wiederum ein Jahr voller Aktivitäten und Entwicklungen, die dazu beitragen werden, die Qualität der Forschung, die im DKF getätigt wird, weiter zu steigern. Dies ist das Resultat der harten Arbeit, die von vielen DKF Mitarbeitenden geleistet wurde. Ich bedanke mich bei allen ganz herzlich für die ausgezeichnete Arbeit, die sie für das Departement und für die biomedizinische Forschungsgemeinschaft der Universität Bern geleistet haben!

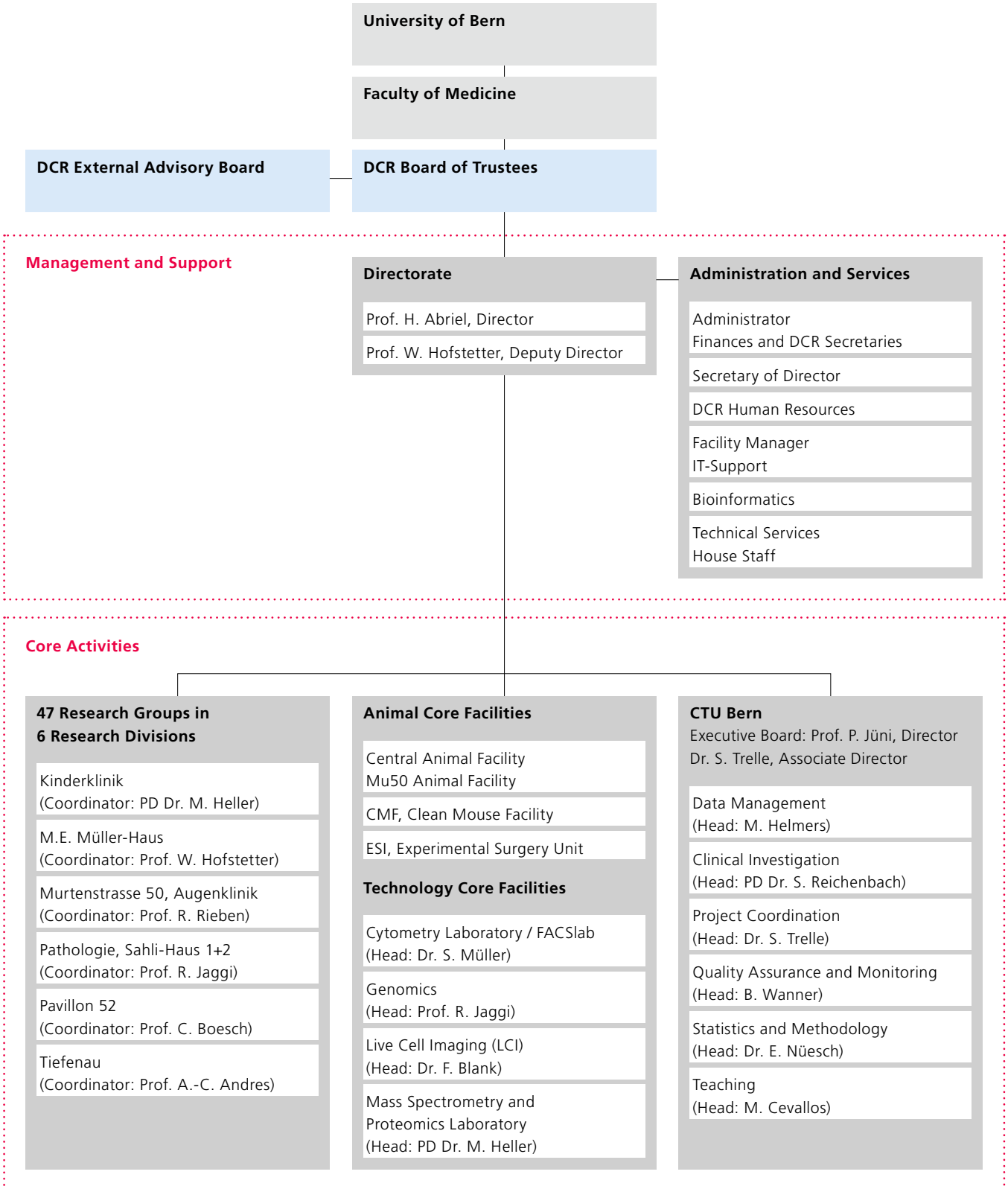
Prof. Dr. Hugues Abriel, MD PhD

Organisation

The role of the DCR is to provide optimal infrastructure and scientific support to its research groups, of which there were 47 at the end of 2013. The vast majority (40) of these groups are from clinics of the Inselspital, Bern University Hospital. The remainder (7) 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. Equally important, the DCR is responsible for operating Technology and Animal Core Facilities. It also hosts the Clinical Trials Unit (CTU) Bern. Furthermore, the groups of the department are supported by central services responsible for administration, informatics, technical support and bioinformatics.

Organigram

December 2013



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

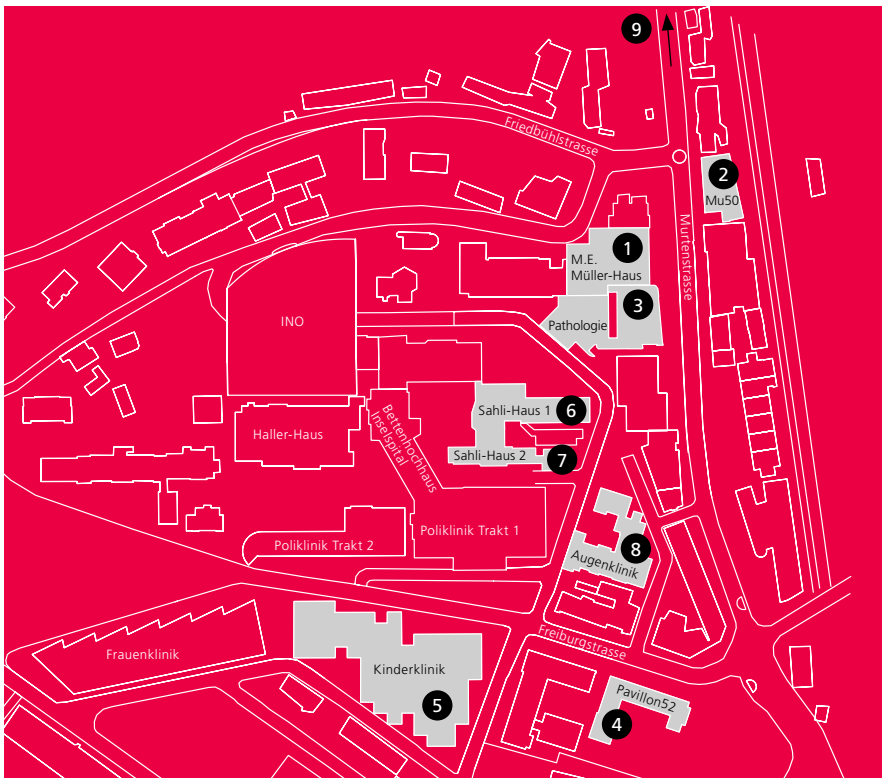
Sahli-Haus 2
Freiburgstrasse 14

8

Augenklinik
Freiburgstrasse 8

9

Tiefenau
Tiefenaustrasse 120c



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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 Core Facilities

Dr. Fabian Blank
Live Cell Imaging (LCI)

PD Dr. Manfred Heller
Mass Spectrometry and
Proteomics Laboratory

Prof. Dr. Rolf Jaggi
Genomics

Prof. Dr. Peter Jüni
Clinical Trials Unit (CTU)
Bern

Dr. Stefan Müller
Cytometry Laboratory /
FACSlab

Clinical Trials Unit (CTU) Bern

www.ctu-bern.ch

Achievements 2013

Data handling and management in clinical research is regulated with defined minimal standards such as restricted access (user management and role concept), electronic signature and audit trail. CTU Bern provides a powerful data management system for clinical studies but because it is a commercial software solution, it is often costly. As a second solution, we installed the REDCap system, developed by Vanderbilt University with support from the National Institutes of Health. The new system is easy to use, efficient and secure while being compliant with all regulatory requirements. We expect that it will be especially useful for observational studies and simple clinical trials.

Within the framework of National Research Programme 67 "End of Life", we were successful in receiving funding for a randomised controlled trial ("SENS Trial") together with the University Center for Palliative Care. This multicentre trial aims at evaluating whether a structured early palliative care intervention reduces stress in patients with advanced cancer. The trial was initiated in November and will run for three years.

The new Act on Research in Humans (Humanforschungsgesetz; HFG) introduces a risk-based categorisation of clinical trials. Together with the Federal Office of Public Health (BAG), we evaluated the feasibility of this approach for categorising (and regulating) clinical trials. We compared the newly proposed, structured categorisation procedure with an unstructured approach for risk-categorisation. All the major ethics committees and more than 130 sponsors of clinical trials participated. The project provided insights into the feasibility of the new categorisation procedure. In addition, it showed that it is possible to evaluate certain aspects of a new regulation before its implementation in a randomised controlled trial.

Several trials that we supported were completed in 2013. The most prominent one was the "PC-Trial" initiated by the Departments of Cardiology and Neurology. This international, multicentre trial published in the *New England Journal of Medicine* compared the effects of percutaneous closure of a patent foramen ovale to medical therapy in patients with a patent foramen ovale and ischemic stroke, transient ischemic attack (TIA), or a peripheral thromboembolic event. The primary outcome of the trials was a composite of death, nonfatal stroke, TIA or peripheral embolism. CTU Bern was responsible for data management, statistical analysis and write-up of the study report/publication.

Performance Report 2013

As in previous years, we were active in providing consultancy services, with more than 100 contacts in various clinical departments of the Inselspital. The increased inspections by Swissmedic and the increased sensitisation and appreciation of the value of quality assurance measures were probably the main reasons for an increase in demand for on-site monitoring services. For the other workflows (Statistics & Methodology, Clinical Investigation, Data Management), the number of new and running projects was stabile compared to previous years.

The increasing demand for courses in Good Clinical Practice and basic clinical research methodology continued in 2013. CTU Bern offers two types of courses in these areas: a one-day basic course and a two-day advanced add-on course. We were able to increase the number of courses and hosted four basic courses with

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Studies in medicine and MD at University of Bern. Training in internal medicine. SNF Postdoc and PROSPER Fellowship in Bristol (UK). Return to Bern in 2002. Since 2007, Founding Director, CTU Bern. Associate Professor (2009); Full Professor of Clinical Epidemiology (2010). Since 2013, Director, Institute of Social and Preventive Medicine, University of Bern.

Dr. Sven Trelle
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Studies in medicine (2002). Research Fellow at Department I of Internal Medicine, Cologne (DE) (2003-2005) and Institute of Social and Preventive Medicine, University of Bern (2005-2008). Since 2008, Associate Director, CTU Bern.

111 participants overall and two courses with 44 participants overall.

Finances 2013

As in previous years, the Inselspital provided core funding for senior staff and parts of our administration. Nevertheless, project funds and service charges needed to cover 75% of our budget. Thanks to revenues in previous years and acquisition of new projects, we were able to roughly break even. In addition, the Institute of Social and Preventive Medicine continued to support us with in-kind contributions.

Outlook 2014

Starting 1 January 2014, all health-related research in humans will be regulated by the new HFG, which introduces major changes not only for clinical trials but also for observational studies. These include new processes for approval of clinical research projects and new minimal standards for conducting all sorts of studies, including retrospective ones. We expect increased demand for services, especially for the Data Management and Monitoring workflows.

The Director of Teaching and Research, Inselspital commissioned CTU Bern to develop a set of standard operating procedures covering planning and conduct of clinical trials. The aim is to guarantee high quality and compliance with applicable regulatory requirements at the Inselspital. The focus will be on investigator-initiated trials. The set-up and first implementation phase of the project will be completed by the end of March 2014.

Staff Members

Prof. Dr. Peter Jüni, Director
Dr. Sven Trelle, Associate Director
Hafeezul Adnan, Project Manager
Vanessa Arn, Assistant
Dr. Daria Bochanek, Monitor
Renata Bünter, Clinical Research Coordinator
Myriam Cevallos, Clinical Research Associate
Dr. Michael Coslovsky, Statistician
Dr. Bruno da Costa, Statistician
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Muriel Helmers, Head, Data Management
Stefanie Hossmann, Monitor
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Regula Jaeggi, Clinical Research Coordinator
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Dr. Andreas Limacher, Statistician
Dr. Linda Nartey, Project Coordinator (until Sep.)
Dr. Eveline Nüesch, Head, Statistics and Methodology (since July)
Sabrina Patel, Central Data Monitor (until Sep.)
Nico Pfäffli, Research Associate
Julie Rat-Wirtzler, Statistician
PD Dr. Stephan Reichenbach, Head, Clinical Investigation
Ursina Sager, Clinical Research Coordinator
Timon Spörri, Research Associate
Malcolm Sturdy, Data Manager
Brigitte Wanner, Head, Quality Assurance and Monitoring
Janine Wyniger, Monitor
Serge Zaugg, Statistician
Katrin Ziegler, Data Manager

Selected Publications

Percutaneous closure of patent foramen ovale in cryptogenic embolism. Meier, B; Kalesan, B; Mattle, HP; Khattab, AA; Hildick-Smith, D; Dudek, D; Andersen, G; Ibrahim, R; Schuler, G; Walton, AS; Wahl, A; Windecker, S; Jüni, P (2013) in: N Engl J Med, 368(12), p. 1083-1091.

Anti-Mullerian hormone levels in girls and adolescents with Turner syndrome are related to karyotype, pubertal development and growth hormone treatment. Visser, JA; Hokken-Koelega, AC; Zandwijken, GR; Limacher, A; Ranke, MB; Fluck, CE (2013) in: Hum Reprod, 28(7), p. 1899-1907.

Prospective, multicenter validation of prediction scores for major bleeding in elderly patients with venous thromboembolism. Scherz, N; Mean, M; Limacher, A; Righini, M; Jaeger, K; Beer, HJ; Frauchiger, B; Osterwalder, J; Kucher, N; Matter, CM; Banyai, M; Angelillo-Scherrer, A; Lammle, B; Husmann, M; Egloff, M; Aschwanden, M; Bounameaux, H; Cornuz, J; Rodondi, N; Aujesky, D (2013) in: J Thromb Haemost, 11(3), p. 435-443.

Prevalence of cam and pincer-type deformities on hip MRI in an asymptomatic young Swiss female population: a cross-sectional study. Leunig, M; Jüni, P; Werlen, S; Limacher, A; Nuesch, E; Pfirrmann, CW; Trelle, S; Odermatt, A; Hofstetter, W; Ganz, R; Reichenbach, S (2013) in: Osteoarthritis Cartilage, 21(4), p. 544-550.

Effect of initial treatment strategy on survival of patients with advanced-stage Hodgkin›s lymphoma: a systematic review and network meta-analysis. Skoetz, N; Trelle, S; Rancea, M; Haverkamp, H; Diehl, V; Engert, A; Borchmann, P (2013) in: Lancet Oncol, 14(10), p. 943-952.

Comparative efficacy of pharmacological and non-pharmacological interventions in fibromyalgia syndrome: network meta-analysis. Nuesch, E; Hauser, W; Bernardy, K; Barth, J; Jüni, P (2013) in: Ann Rheum Dis, 72(6), p. 955-962.

Cytometry Laboratory / FACSlab

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Studies in microbiology at University of Bern; PhD (1996). Postdoc (2000-2001) in intestinal mucosal immunology at University of Bristol (UK); Head, Flow Cytometry Laboratory, School of Cellular and Molecular Medicine (2001). Since 2004, Senior Scientist in Gastroenterology at DCR; since 2010, Head, Cytometry Laboratory / FACSlab Core Facility.

Achievements 2013

The highlight of 2013 was certainly the installation of the ImageStream-X imaging flow cytometer in April. Since then, more than ten different research groups have run mainly pilot experiments with it and we have even started a collaboration with a research group from Geneva.

The other important event in 2013 was the upgrade of the 3-laser and 8-detector flow cytometer to a 5-laser and 18-detector system. Having now two virtually identical instruments provides increased capacity and more flexibility. Also, it is now less critical if one of the instruments needs to be serviced or repaired.

On the organisational side, the Windows login system was introduced for the flow cytometers on 1 January 2013. This login system allows more accurate assessment of the measuring times of each user and, as a consequence, enables us to bill them more accurately.

Furthermore, since summer, access to the FACSlab outside of the regular opening hours has been facilitated for all registered users. There is no need to organise badge and keys beforehand anymore.

As in 2012, we again conducted two FACS courses, worth 2 ECTS points for PhD students.

Performance Report 2013

Both sorting and sample acquisitions remained at the same high frequency as in 2012. Due to the upgrade of the old LSR II flow cytometer, acquisitions were better balanced between the two state-of-the-art cytometers. Since the upgrade itself was rather lengthy and tedious, and we unfortunately experienced a number of downtimes with the other instrument, it was not always easy to cope with the continuously high demand from our users.

In 2013, 68.8% of the FACS measurements were performed by researchers from clinics and 30.8% by researchers from university institutes. Usage by external people only made up 0.4%. Regarding cell sorting, these numbers were 45%, 54.1% and 0.9%, respectively. Interestingly, 68.9% of acquisitions and 45.5% of cell sorting were performed by or for users from DCR groups.

Finances 2013

While in 2012 we had a negative balance of CHF 6,000, expenses in 2013 were CHF 2,000 lower than revenues. The positive balance was achieved on the one hand by the modified usage fee system and on the other by charging the users for FlowJo software licences.

Outlook 2014

- The BD FACS ARIA III cell sorter will be equipped with a 561 nm yellow-green laser. This will allow the use of a wide variety of fluorescent proteins often used for transfections or as reporter genes.
- Due to strong demand, two FACS courses will already be conducted in spring 2014.
- Since the automated high recovery sample acquisition device connected to the upgraded flow cytometer now profits from the additional lasers and detectors, it is our aim to establish and evaluate flow cytometric array and screening protocols that might be of great interest for many researchers.

Staff Members

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

Live Cell Imaging (LCI)

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Dr. Fabian Blank
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MSc in Cell Biology (2003) at University of Bern; PhD in Structural Biology (2006). Postdocs at Institute of Anatomy, University of Bern (2007-2008) and Telethon Institute for Child Health Research, Perth (2008-2009) (AU). Since 2009, Senior Scientist, Pulmonary Medicine (Adults), DCR; since 2010, Commission Member, Microscopy Imaging Centre; since 2012, Head, Live Cell Imaging Core Facility, DCR.

Achievements 2013

Two projects were among the most important achievements for the establishment of the newest DCR Core Facility: 1. The purchase of a fully automated system for long-term live cell observation (Nikon BioStation CT), together with setting up a cell culture laboratory for the preparation and storage of living samples before, during and after imaging. 2. Organising funding (R'Equip grant in 2012) and purchase of a new laser scanning microscope (Zeiss LSM710), including the preparation of a new room for confocal live cell imaging with air conditioning, access to CO_2 and two powerful workstations for image processing with specific software (IMARIS, CL-Quant, etc.). In September, we celebrated completion with an opening event.

These achievements would not have been possible without the support of the Microscopy Imaging Centre (MIC). The MIC is the interfaculty platform that coordinates, prioritises and supports funding applications in the field of high-end microscopy, as well as organising access to microscopy equipment for all members of the University. The LCI is one of the units of the MIC. We also wish to thank Barbara Rothen-Rutishauser (University of Fribourg) and Thomas Geiser (Inselspital) for their invaluable support and their assistance in the acquisition of funds.

Performance Report 2013

Although not yet at full capacity, no less than 53 users from 25 different research groups acquired image data with the help of the LCI Core Facility and spent a total of 3,555 hours using its equipment during 2013. In addition, we provided two 2-day courses on fluorescence microscopy, laser scanning microscopy, immunofluorescence labelling and image processing for 30 students. Furthermore, we contributed to the cutting-edge lectures and practical parcours in light microscopy organised by the MIC.

Finances 2013

In 2013, the LCI Core Facility collected a total of CHF 18,750 in fees for confocal microscopy and the Nikon BioStation. Expenses included a total of CHF 20,663 for repair, maintenance and consumables. The MIC kindly contributed CHF 1,750 for consumables used in the microscopy course. In addition, CHF 16,000 of the IMARIS maintenance was covered by the Directorate of Teaching and Research, Inselspital.

Outlook 2014

Starting February 2014, Mr. Wotzkow (Tiefenau Labs), who already provided support for the facility during 2013, will work 90% in the LCI Core Facility in order to provide support for training, maintenance, teaching and coordination. We will establish a new histology lab, which will provide service, support and training in the field of embedding, cutting, immunohistochemistry and immunofluorescence. In addition, a refurbishment of our homepage is planned. Finally, additional courses on specific topics (advanced use of the LSM, image processing, histology) are in planning.

Staff Members

Dr. Fabian Blank, Head
Anna-Barbara Tschirren, Laboratory Technician
Carlos Wotzkow, Laboratory Technician

Genomics (Core Facility)

www.gcf.dkf.unibe.ch

Molecular Biology (Research Group)

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Prof. Dr. Rolf Jaggi
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Studies and PhD (1982) in Bern. Postdoc in Ludwig Institute for Cancer Research, Bern (1986-1988). Research in the Institute of Clinical and Experimental Cancer Research, Bern (1988-1996), several research periods in Ireland with Prof. Finian Martin, at University College, Dublin (1989-1992). Habilitation (1990); Professor (1996) at the University of Bern. Since 2010, Coordinator in DCR; since 2011, Head of Genomics Core Facility.

Achievements 2013

The majority of human breast cancer cells express the oestrogen and/or progesterone receptor. After hormone binding, these receptors act as transcription factors, regulating numerous genes and thereby stimulating cell proliferation. Anti-oestrogens like tamoxifen (Tam) or other drugs like letrozole (Let) that repress the synthesis of endogenous oestrogen may efficiently inhibit the actions of oestrogen. Many aspects of the underlying mechanisms are still not well understood. Interestingly, some tumours are inhibited by either Tam or Let to a similar degree, others seem to be resistant to one or both drugs, while still others may become resistant during treatment. Unfortunately, patients developing resistance have a poor prognosis and often die within five years. Moreover, many breast cancers express the oestrogen receptor (ER) in only a subpopulation of tumour cells, while the rest of the cells express no receptor and are therefore not directly targeted by the anti-oestrogen treatment. Many of these tumours seem to respond to treatment and tumours do not reappear.

Our group has identified potential target genes whose expression seems to be indicative of a response to Let but not to Tam. The impact of these genes will be further studied in other breast cancers. If the predictive impact of some or all of these genes can be corroborated, the genes can be used to identify a subgroup of patients whose outcome is superior when treated with Let rather than Tam. A certain predictive advantage of Let is only known for patients expressing low levels of ER. Another phenomenon that has not been well studied is the role of ER-deficient breast cancer cells in ER-positive cancers. Apparently, many of these cancers respond to anti-oestrogen treatment although the drugs only interfere with the ER.

The mechanistic aspects of how ER-deficient cells co-existing with ER-positive cells in the same tumours are inhibited are still not clear. A possible explanation is that the proliferation of receptor-deficient cells depends on a positive feedback from receptor-positive cells. Alternatively, ER expression might not be constitutive. This would result in both receptor-negative and receptor-positive cells in the same tumour at any one time. We plan to study ER-positive and -negative cells in a series of cancers co-expressing both cell types simultaneously. We will measure gene expression in both subtypes separately and study potential mechanisms of interaction that may explain why ER-negative cells are inhibited by anti-oestrogen treatments.

Performance Report 2013

Genomics

Our group is responsible for the DCR Genomics Core Facility and for the support of users from the Faculty of Medicine with two major instruments of the University's Genomics Facility: a low throughput Ion Torrent PGM instrument (located in our lab) and a high throughput Illumina HiSeq instrument (located in the Institute of Genetics, Vetsuisse Faculty). Last year, the Inselspital provided funding for the establishment of bioinformatics support and IT infrastructure for clinical groups setting up Next Generation Sequencing (NGS) projects. Several groups are receiving technical support during the experimental part of their studies and during processing, analysing and archiving their data. A new and powerful IT infrastructure was setup in the last two years by the Interfaculty Bioinformatics Unit (IBU) and by intensifying the collaboration with the Swiss Institute of Bioinformatics (Lausanne), who provide know-how, software and storage space for NGS data. The Genomics Core Facility collaborates closely with the IBU.

Finances 2013

Genomics

The Genomics Core Facility again had a working credit of CHF 15,000 from the DCR for consumables and equipment. Part of the money was used to set up and maintain the Ion Torrent platform and to test novel protocols and applications. We provide tailor-made solutions for reagents and chips for every research group, avoiding the accumulation of large stocks in several groups.

Outlook 2014

Genomics

A second laboratory technician started in January 2013, learnt all the applications on both NGS instruments and was very rapidly able to actively contribute to the support for both instruments of the Genomics Core Facility. It is planned that her salary for 2015 will be paid from overhead generated by the Illumina platform.

Molecular Biology

We will continue to validate the predictive score for Let, using additional breast cancer samples and separately measuring gene expression in ER-positive and ER-negative cells of the same tumours. The methodology will be further developed by preparing small sets of similar cells from fresh tumours, staining them with an antibody to the ER and separating cells according to colour by FACS. RNA will be isolated from each fraction and gene expression measured by qPCR, Nanostring and eventually RNA-Seq. The procedures are currently being tested with cells in culture. The protocols will be applied to cells derived from fresh breast cancers and later to frozen tissue from the Biobank Bern. The procedure should lead to a separate characterisation of ER-positive and ER-negative cells in single breast cancers.

Staff Members

Prof. Dr. Rolf Jaggi, Group Leader, Head of Genomics Core Facility
Dr. Irene Keller, Bioinformatician (Core Facility) (since July)
Michèle Ackermann, Laboratory Technician (Core Facility)
David Andel, IT Specialist (Core Facility) (since June)
Mariana Bustamante, PhD Student (Core Facility & Research Group) (since May)
Muriel Fragnière, Laboratory Technician (Core Facility & Research Group)

Collaborators

Molecular Biology

Aebi S, Lucerne Cantonal Hospital, Switzerland
Bubendorf L, University of Basel, Switzerland
Cathomas R, Graubünden Cantonal Hospital, Switzerland
Gautschi O, Lucerne Cantonal Hospital, Switzerland
Günthert A, Lucerne Cantonal Hospital, Switzerland
Kammler R, International Breast Cancer Study Group, Italy
Kristiansen G, University of Bonn, Germany
Pestalozzi B, Zurich, Switzerland
Popovici V, Masaryk University, Brno, CZ
Regan M, Dana-Farber Cancer Institute, USA
Vassella E, University of Bern, Switzerland

Grants

Amounts allocated for 2013:

Molecular Biology

- Swiss Cancer League: Molecular profiling from archival human breast cancer samples (R. Jaggi) CHF 66,867
- W.+H. Berger-Janser Foundation: Characterization of ER-negative cancer cells in ER-positive breast cancer (R. Jaggi) CHF 13,954
- SAKK 19/09: Bevacizumab, pemetrexed and cisplatin, or erlotinib and bevacizumab for advanced non-squamous NSCLC stratified by EGFR mutation status. A multicentre phase II trial including biopsy at progression (BIO-PRO trial) (R. Jaggi) CHF 20,109
- SAKK 26/10: Impact of Recurrence Score on Recommendations for Adjuvant Treatment of ER-positive Breast Cancer (R. Jaggi) CHF 10,000
- Various donors: (A. Günthert, R. Jaggi) CHF 24,690

Teaching Activities

- 1st-year medical students: Problem Based Learning (PBL)
- Selected topics in molecular pathology: Molecular processes of disease lecture
- Tumour biology: Genomics lecture

Publications

Molecular Biology

The need for transparency and good practices in the qPCR literature. Bustin, SA; Benes, V; Garson, J; Hellemans, J; Huggett, J; Kubista, M; Mueller, R; Nolan, T; Pfaffl, MW; Shipley, G; Wittwer, CT; Schjerling, P; Jaggi, R et al. (2013) in: Nature Methods 10(11), p. 1063-1067.

Mass Spectrometry and Proteomics Laboratory (Core Facility)

Protein and Cell Biology (Research Group) www.pmscf.dkf.unibe.ch

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

PhD in Chemistry/Biochemistry from the University of Bern (1994). Postdocs at University of Auckland (NZ) and Washington (US). Return to Switzerland in 1999 to University of Geneva, followed by three years as Senior Scientist at GeneProt Inc., Geneva, working on large-scale proteomics projects using LC-MS, MALDI-MS and robotics. Since 2003, Head of Proteomics and Mass Spectrometry Laboratory (PMSCF), a DCR Core Facility since 2008. Sixteen years experience in the use of mass spectrometry for protein analytics, proteomics and bioinformatics.

Achievements 2013

In February, we moved back to our refurbished laboratories in the Children's Hospital, Inselspital. At the same time, we installed two new high-performance LC-MS instruments (QExactive and LTQ Velos ETD, ThermoFisher Scientific), which were purchased in 2012 with funding from an SNF R'Equip grant and matching funds from the University. We implemented new data acquisition methods on these instruments and were able to quickly familiarise ourselves with their strengths and weaknesses. Together with the old LTQ orbitrap, we can now offer almost any state-of-the-art protein/proteome analysis protocol (data-independent, targeted and quantitative proteome analysis, intact protein mass measurements, etc.). The jump in analytical power has already enabled us to finish several projects and the data will be used to prepare several manuscripts (see below).

Marian Petrovic applied a data-independent acquisition method on the LTQ Velos to characterise the effect of doxorubicin on the proteome of the MCF7 breast cancer cell line. Doxorubicin is a DNA intercalating agent that has been used as an effective chemotherapeutic agent for the treatment of many types of solid tumours, including breast, lung, ovarian, prostate and bladder cancer. However, its use is severely limited due to side effects such as cardiotoxicity and heart failure, as well as dizziness, lack of concentration and cognitive deficits known as 'chemobrain'. To minimise the side effects in patients, biomarkers indicating treatment efficacy are critically needed and may provide new therapeutic targets for cancer. Marian Petrovic's work revealed that doxorubicin down-regulated several proteins involved in synaptic connections of the nervous system, which might potentially explain the chemobrain side effect. A manuscript is in preparation. Marian returned to Košice (SK) to finish his PhD, at the end of September.

Before Niurka Meneses left the DCR in March, she was able to finish the data analysis of the TRPM4 interactome (manuscript in preparation) and we performed some work on the characterisation of the chemical nature of formaldehyde-induced cross-linking of proteins using mass spectrometry. For the latter, it was paramount to have the new instrumentation available. The results require additional evaluation but should also result in a manuscript.

Natasha Buchs, François Achermann and Sophie Braga Lagache further developed the protocol for blood plasma microparticle isolation and subsequent proteome analysis. They made substantial progress in depleting classical serum proteins and being able to detect several hundred cellular proteins associated with these particles, not least due to the sensitivity provided by the new instrumentation. Currently, we are improving the reproducibility of the microparticle isolation and characterisation by means of electron microscopy. Additional activity went into the development of cell medium conditions to allow for shear stress experiments with endothelial cells, using a protocol to incorporate stable isotope labelled amino acids for quantitative protein chase experiments by mass spectrometry.

Performance Report 2013

Mass Spectrometry and Proteomics

Despite the move to the new laboratory, installation of new instrumentation and the subsequent time needed for familiarisation, we will break the previous year's sample throughput record on the LTQ orbitrap again (666 in 2011, >>1000 in 2012, 1694 in 2013). Including the analytical runs on the two new instruments, where we developed new methods and ran customer support samples in a ratio of roughly 3:2, we analysed close to 2000 samples in 2013!

Finances 2013

Mass Spectrometry and Proteomics

The Faculty of Medicine Resources Committee granted CHF 4,000 to cover some of our running costs. Thanks to the excellent use of our services by research groups from all over the university, we are able to generate sufficient funds to cover future maintenance costs ourselves. With money remaining from the R'Equip grant, we were able to purchase a replacement nano-LC system for the LTQ orbitrap system (installation in Jan. 2014).

Outlook 2014

We expect to receive about 600-700 plasma samples from volunteers who participated in a high-altitude study (organised by Jacqueline Pichler Hefti and Tobias Merz, Inselspital) aimed at better understanding the physiological processes taking place during hypobaric hypoxia and related symptoms, e.g., pulmonary vasoconstriction. As microparticle numbers and compositions are known to change during hypoxic stress, we plan to quantitate microparticle-associated protein expression in these samples. We have applied for third-party funding to finance new staff for the analyses. François Achermann's transfer from the Tiefenau Laboratories to our lab will be complete in February. He will take over some administrative and work-safety tasks, and support Sophie Braga Lagache in running the Core Facility.

Staff Members

PD Dr. Manfred Heller, Head
Dr. Niurka Meneses Moreno, Postdoctoral Fellow (Research Group) (until Mar.)
Dr. Cedric Simillion, Bioinformatician (Core Facility) (since July)
François Achermann, Laboratory Technician (Core Facility & Research Group) (since Oct.)
David Andel, IT Specialist (Core Facility) (since June)
Sophie Braga Lagache, Laboratory Assistant (Core Facility)
Natasha Buchs Tetkovic, Laboratory Technician (Core Facility & Research Group)
Marian Petrovic, visiting PhD student (Sciex Programme, Core Facility & Research Group) (until Sep.)

Collaborators

Müller M, Swiss Institute of Bioinformatics (Geneva), Switzerland
Jackson C, Inselspital, Switzerland
Pichler Hefti J, Inselspital, Switzerland

Grants

Amounts allocated for 2013:

Protein and Cell Biology

- SNF: In vivo relevance of the PY and PDZ-domain binding motifs of the cardiac sodium channel Nav1.5 (H. Abriel) CHF 13,230
- Sciex-NMS^{ch}: Quantification of new protein synthesis by endothelial cells under shear stress using SILAC method (M. Petrovic, M. Heller) CHF 48,000

Teaching Activities

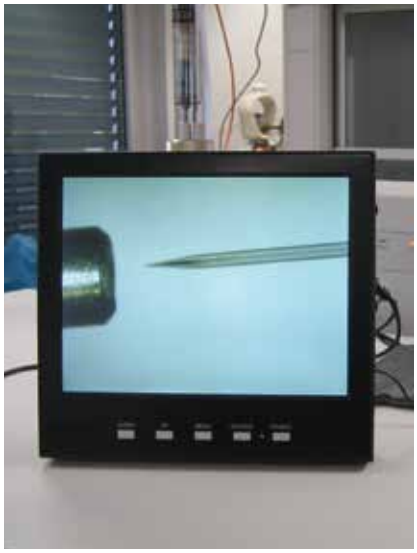
- Proteomics lectures: Tumour biology (Biomedical Engineering, Faculty of Medicine), Omics (Faculty of Science)
- MSc Bioinformatics: Planning and preparation of a specialised course in proteomics

Publications

The Aeromonas salmonicida subsp. salmonicida exoproteome: global analysis, moonlighting proteins and putative antigens for vaccination against furunculosis. Vanden Bergh, P; Heller, M; Braga Lagache, S; Frey, J (2013) in: Proteome Sci., 11(1), p. 44, e-pub ahead of print.

The Aeromonas salmonicida subsp. salmonicida exoproteome. Determination of the complete repertoire of Type-Three Secretion System effectors and identification of other virulence factors. Vanden Bergh, P; Heller, M; Braga Lagache, S; Frey, J (2013) in: Proteome Sci., 11(1), p. 42, e-pub ahead of print.

Nucleolar proteins regulate stage-specific gene expression and ribosomal RNA maturation in Trypanosoma brucei. Schumann Burkard, G; Käser, S; de Araujo, P; Schimanski, B; Naguleswaran, A; Knüsel, S; Heller, M; Roditi, I (2013) in: Mol. Microbiol., 88(4), p. 827-840.



Bone Biology & Orthopaedic Research

www.bonebiology.dkf.unibe.ch

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

Research Highlights 2013 / Outlook 2014

Bone Biology & Orthopaedic Research Group

Highlights of our research on bone cell biology, inflammatory diseases and molecular transport systems include:

- Interleukin-17 and TNFα induce the release of granulocyte-macrophage colony-stimulating factor (GM-CSF) by osteoblasts. The release of GM-CSF changes the local haematopoietic environment from differentiation/activation of osteoclastogenesis to proliferation of haematopoietic progenitors. We are investigating the implications for the development and progress of inflammatory diseases of the skeleton (NFP64, PhD project N. Ruef).
- We are studying the osseointegration and tissue reactions to newly developed biomaterials, composed of nano-fibers and CaP cements, with improved mechanical properties. A first pilot experiment with a CaP cement was initiated in rats (NFP64, PhD project N. Ruef).
- Studies on the expression and function of molecular transporters in bone lineage cells revealed iron transporters to be highly regulated during osteoclastogenesis. The role of iron in osteoclast differentiation and activation will be assessed (NCCR, PhD project W. Xie).
- TGFβ supports chondrogenesis in dedifferentiated primary articular chondrocytes up to a certain number of population doublings. Thereafter, the cells no longer form cartilage, even in the presence of TGFβ. The molecular reasons are as yet unknown (RMS, PhD project A. Tekari).
- Biofunctionalisation is a means to improve the osseointegration and turnover of CaP ceramic-based bone substitute materials. In a project lead by PD Dr. F. Klenke, the effects of growth factors like BMP2, VEGF, RANKL on the turnover of these materials are being characterised (SNF, PhD project J. Choy).

Osteo-Articular Research Group

Highlights of our research on cartilage biology and degeneration, and imaging techniques to assess osteoarthritic changes include:

- Expression patterns of S100A1 and S100B in human articular cartilage and primary human articular chondrocyte under dedifferentiating and redifferentiating conditions assessed via qRT-PCR, immunocytochemistry, FACS and Western blot identify both proteins as markers of chondrocytes differentiation status.
- Expression patterns of S100A1 and S100B are similar in normal and arthritic cartilage tissue, with both proteins being co-expressed with collagen type II in normal, and with collagen type I in arthritic cartilage.
- Comparative assessment of arthritic versus control whole joints of rats and rabbits using newly developed imaging measurement techniques demonstrated quantifiable differences in joint space, cartilage shape, thickness, contact area and surface roughness (collaboration with Kathryn Stok, ETH Zurich).
- An S100 cell-based ELISA assay was developed to investigate re-expression of S100 in human articular chondrocytes as a redifferentiation high throughput readout in a microplate format. The assay was validated by BMP4 induction of HAC redifferentiation (MSc thesis E. Schönholzer).

Group Members

Bone Biology & Orthopaedic Research Group
Prof. Dr. Willy Hofstetter, Group Leader
Dr. Rainer Egli, Senior Scientist
Dr. Antoinette Wetterwald, Senior Scientist
Silvia Dolder, Laboratory Technician
Mark Siegrist, Laboratory Technician
John Choy, PhD Student
Nina Ruef, PhD Student (since Feb.)
Adel Tekari, PhD Student
Wenjie Xie, PhD Student

Osteo-Articular Research Group
PD Dr. Dobrila Nesic, Group Leader
Dr. Jose Diaz Romero, Senior Scientist
Dr. Aurélie Quintin, Research Assistant (until Feb.)

Clinician with projects in the group
PD Dr. Frank Klenke, Clinical Research Associate

Collaborators

Aeberli D, Inselspital, Switzerland
Fuster D, Inselspital, Switzerland
Kohl S, Inselspital, Switzerland
Koller B, Scanco Medical AG, Switzerland
Luginbuehl R, RMS Foundation, Switzerland
Müller R, ETH Zurich, Switzerland
Schäfer B, Geistlich Pharma AG, Switzerland
Sebald HJ, theSpinecenter (Thun), Switzerland
Sebald W, University of Würzburg, Germany
Seitz M, Inselspital, Switzerland
Siebenrock KA, Inselspital, Switzerland
Stok K, ETH Zurich, Switzerland
Zulliger M, Scanco Medical AG, Switzerland
Zumstein M, Inselspital, Switzerland
Zwerina J, Dresden University of Technology, Germany

Grants

Amounts allocated for 2013:

Bone Biology & Orthopaedic Research
- SNF: NCCR TransCure sub-project: Role of ion transporter TRPV6 and other transporters in bone homeostasis (M. Hediger, W. Hofstetter) CHF 70,000
- SNF: NFP64 – Nanofibres reinforced bone substitute materials: Effect of delayed fibre degradation on cells and tissues (R. Luginbuehl, K. Maniura, W. Hofstetter)
- SNF: Biofunctionalization of β-Tricalcium Phosphate Ceramics for the Repair of Osseous Defects (F. Klenke, W. Hofstetter) CHF 80,000
- SNF: Osteoclastogenesis and chronic inflammatory rheumatic disorders, (M. Seitz, D. Aeberli, B. Engelhardt, JV Stein, W. Hofstetter)
- ITI Foundation: Functionalization of CaP bone substitutes with growth factors (F. Klenke, W. Hofstetter)
- RMS: Cartilage Tissue Formation of Cells Seeded on Structured Scaffolds in Physiological Conditions (W. Hofstetter) CHF 70,000
- Alfred und Anneliese Sutter-Stöttner Stiftung: Heilung von Frakturen in osteoporotischen Knochen (W. Hofstetter) CHF 87,000

Osteo-Articular Research
- AO Foundation: Start up grant S-11-96N – S100 as a cellular marker for chondrogenicity of human articular chondrocytes (D. Nesic, M. Zumstein) CHF 36,000

Teaching Activities

- MSc Biomedical Engineering: Tissue Engineering course (Nesic)
- MSc Biomedical Engineering: Osteology course (Hofstetter)
- 3rd-year dentistry students: Pathophysiology – Skeleton (Hofstetter)
- 1st-year medical students: Molecular biology practical courses (Hofstetter)
- 2nd-year medical students: Kidney block – Calcium and phosphate metabolism (Hofstetter)
- 3rd-year biomedical and cell biology students: Pathology of the musculoskeletal system (Nesic)

Publications

In vitro cytotoxicity of silver nanoparticles on osteoblasts and osteoclasts at antibacterial concentrations. Albers, CE; Hofstetter, W; Siebenrock, KA; Landmann, R; Klenke, FM (2013) in: Nanotoxicology, 7(1), p. 30-36.

Interleukin-17A stimulates granulocyte-macrophage colony-stimulating factor release by murine osteoblasts in the presence of 1,25-dihydroxyvitamin D(3) and inhibits murine osteoclast development in vitro. Balani, D; Aeberli, D; Hofstetter, W; Seitz, M (2013) in: Arthritis Rheum, 65(2), p. 436-446.

Mitogen-activated protein kinase 2 regulates physiological and pathological bone turnover. Braun, T; Lepper, J; Ruiz, HG; Hofstetter, W; Siegrist, M; Lezuo, P; Gaestel, M; Rumpler, M; Thaler, R; Klaushofer, K; Distler, JH; Schett, G; Zwerina, J (2013) in: J Bone Miner Res, 28(4), p. 936-947.

Modulation of human osteoblasts by metal surface chemistry. Hofstetter, W; Sehr, H; de, WM; Portenier, J; Gobrecht, J; Hunziker, EB (2013) in: J Biomed Mater Res A, 101(8), p. 2355-2364.

Prevalence of cam and pincer-type deformities on hip MRI in an asymptomatic young Swiss female population: a cross-sectional study. Leunig, M; Juni, P; Werlen, S; Limacher, A; Nuesch, E; Pfirrmann, CW; Trelle, S; Odermatt, A; Hofstetter, W; Ganz, R; Reichenbach, S (2013) in: Osteoarthritis Cartilage, 21(4), p. 544-550.

Expression of antagonists of WNT and BMP signaling after non-rigid fixation of osteotomies. Montjovent, MO; Siegrist, M; Klenke, F; Wetterwald, A; Dolder, S; Hofstetter, W (2013) in: Bone, 53(1), p. 79-86.

Cardiovascular Research

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

Studies in biology at the University of Bern; PhD in Immunology (1992). SNF postdoc in Leiden (NL) working on xenotransplantation (1994-1997). Involved in several EU research projects since then. Return to Bern in 1997 to establish a research group. Habilitation (2002); Associate Professor (2007). Since 2005, Group Leader, Cardiovascular Research, DCR.

Research Highlights 2013 / Outlook 2014

In 2013, Claudia Dührkop and Anjan Bongoni successfully defended their PhD theses. Claudia Dührkop's work focused on ischemia/reperfusion (I/R) injury, for which she refined a rat hind limb model. Her data showed that the complement system is not the key player in I/R injury of skeletal muscle tissue. Oedema as well as myocyte necrosis and apoptosis in limbs subjected to prolonged ischemia followed by reperfusion could not be prevented by the complement inhibitor APT070, which is a complement receptor 1 derived construct. Also low molecular weight dextran sulfate, a potent inhibitor of the complement and coagulation cascades, had no effect. Both APT070 and low molecular weight dextran sulfate did what they are supposed to do; they prevented complement deposition in the tissue but this had no effect on oedema and tissue damage. In contrast, C1 Inhibitor, a plasma-derived protein that inhibits the complement, coagulation and kinin cascades, protected the hind limbs almost completely from I/R injury. Protection correlated with the prevention of bradykinin receptor b1 upregulation in the tissue. Therefore, we concluded from this series of experiments that skeletal muscle I/R injury may, at least in part, depend on activation of the kinin cascade and that preoperative, systemic treatment with C1 inhibitor may potentially be used in a clinical setting to prevent skeletal muscle I/R injury in the context of elective surgery.

Anjan Bongoni's thesis was a continuation of our work on xenotransplantation. Using an extracorporeal perfusion system, developed together with the Department of Plastic and Hand Surgery, Inselspital to prolong the survival of amputated extremities, we perfused porcine limbs with whole human blood. Both wildtype and limbs transgenic for the human complement regulator CD46 and human HLA-E were used. Anjan Bongoni's analysis of the perfused tissue, together with in vitro experiments with porcine aortic endothelial cells, revealed that human CD46 indeed attenuates activation of human complement on the porcine cells and may help to prolong the survival of porcine xenografts in a human recipient. In addition, he showed that the porcine asialo-glycoprotein receptor 1 (ASGR-1) is present not only on pig liver endothelial cells, as previously known, but also on porcine endothelial cells from the aorta and the femoral artery. ASGR-1 may thus be the key molecule for activation and scavenging of human platelets on the porcine vasculature. Finally, he also showed that the lectin pathway of complement is involved in xenorejection of porcine cells by human plasma.

In 2014, we will continue our xenotransplantation research in collaboration with the Ludwig-Maximilian University of Munich (DE). Another focus will be the development of an in vitro assay in which endothelial cells are cultured under flow on the inner surface of microchannels on a microfluidics chip.

Group Members

Prof. Dr. Robert Rieben, Group Leader
Dr. Yara Banz, Research Associate (Pathology)
PD Dr. Jana Ortmann, Research Associate (Tiefenau Hospital)
Julie Denoyelle, Laboratory Technician
Jane Shaw-Boden, Laboratory Technician
Uyen Schmutz, Web Administrator
Mai Abdelhafez, PhD Student (since Nov.)
Anjan Bongoni, PhD Student
Claudia Dührkop, PhD Student (until Oct.)
Shengye Zhang, PhD Student

Collaborators

Bovin N, Korchagina E, Institute of Bioorganic Chemistry, Russia
Constantinescu MA,
Gajanayake T, Vögelin E, Inselspital, Switzerland
Gorantla V, University of Pittsburgh Medical Center, USA
Guenat O, University of Bern, Switzerland
Jenni HJ, Inselspital, Switzerland
Khattab A, Inselspital, Switzerland
Klymiuk N, Wolf E, University of Munich, Germany
Miescher S, Spirig R, Spycher M, CSL Behring AG, Switzerland
Ruder T, University of Zurich, Switzerland
Seebach J, Geneva University Hospital, Switzerland
Vemula P, inStem, India

Grants

Amounts allocated for 2013:

- SNF: Endothelial cell protection – The role of heparan sulfate proteoglycans and complement in pathophysiology and prevention of ischemia / reperfusion injury (R. Rieben) CHF 100,000
- SNF: Composite tissue preservation by extracorporeal blood perfusion and vascular cytoprotection to extend the time limit to replantation or transplantation (E. Vögelin, M.A. Constantinescu, R. Rieben) CHF 75,000
- CSL Behring: Effects and mechanisms of anti-inflammatory treatment by plasma products to attenuate ischemia/reperfusion injury (R. Rieben) CHF 100,000
- 3R Research Foundation: Development of an in vitro system to grow and investigate vascular endothelial cells under physiological flow conditions (R. Rieben) CHF 30,000

Teaching Activities

- MSc Biomedical Sciences: Elective module – Induction of transplantation tolerance in composite tissue allotransplantation
- Medical students: Elective course 5034 – Ihr Partner im Labor: Forschung auf den Gebieten Organtransplantation, Chirurgie und Herzinfarkt
- PhD students in Graduate School for Cellular and Biomedical Sciences: Immunology tutorial
- High school students: Patenschaften für Maturaarbeiten (5 students with 2-week lab stay each)

Publications

Combined inhibition of complement C5 and CD14 markedly attenuates inflammation, thrombogenicity, and hemodynamic changes in porcine sepsis. Barratt-Due, A et al. (2013) in: J Immunol, 191(2), p. 819-827.

Activation of the lectin pathway of complement in pig-to-human xenotransplantation models. Bongoni, AK et al. (2013) in: Transplantation, 96(9), p. 791-799.

Development of a bead-based multiplex assay for the simultaneous detection of porcine inflammation markers using xMAP technology. Bongoni, AK; Lanz, J; Rieben, R; Banz, Y (2013) in: Cytometry A, 83(7), p. 636-647.

C1 esterase inhibitor reduces lower extremity ischemia/reperfusion injury and associated lung damage. Duehrkop, C et al. (2013) in: PLoS One, 8(8), p. e72059.

Use of dextran sulfate in tourniquet-induced skeletal muscle reperfusion injury. Duehrkop, C; Denoyelle, J; Shaw, S; Rieben, R (2013) in: J Surg Res, in press, doi: 10.1016/j.jss.2013.10.012.

Ischemia/reperfusion injury: effect of simultaneous inhibition of plasma cascade systems versus specific complement inhibition. Duehrkop, C and Rieben, R (2013) in: Biochem Pharmacol, in press, doi: 10.1016/j.jss.2013.10.012.

Effect of pressure-controlled intermittent coronary sinus occlusion (PICSO) on myocardial ischaemia and reperfusion in a closed-chest porcine model. Khattab, AA et al. (2013) in: EuroIntervention, 9(3), p. 398-406.

Microsurgery and liver research: Lumbricus terrestris, a reliable animal model for training? Leclere, FM; Lewbart, GA; Rieben, R; Vogelin, E (2013) in: Clin Res Hepatol Gastroenterol, 37(2), p. 166-170.

Ischemia/reperfusion injury of porcine limbs after extracorporeal perfusion. Muller, S et al. (2013) in: J Surg Res, 181(1), p. 170-182.

Edema is a sign of early acute myocardial infarction on post-mortem magnetic resonance imaging. Ruder, TD et al. (2013) in: Forensic Sci Med Pathol, 9(4), p. 501-505.

Botulinum toxin A and B raise blood flow and increase survival of critically ischemic skin flaps. Schweizer, DF et al. (2013) in: J Surg Res, 184(2), p. 1205-1213.

Reconstituted high-density lipoprotein modulates activation of human leukocytes. Spirig, R et al. (2013) in: PLoS One, 8(8), p. e71235.

Regulatory Sequences of the Porcine THBD Gene Facilitate Endothelial-Specific Expression of Bioactive Human Thrombomodulin in Single- and Multitransgenic Pigs. Wuensch, A et al. (2013) in: Transplantation, in press, doi: 10.1097/TP.0b013e3182a95cbc.

Ion Channels and Channelopathies

www.ionchannels.dkf.unibe.ch

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 the Lausanne University Hospital, a post-doc at Columbia University (US). In 2002, SNF Professor and start of independent research studying the role of ion channels in human disorders. Since 2009, Professor of Pathophysiology, University of Bern and DCR Director. Since 2012, member of the National Research Council of the SNF.

Research Highlights 2013 / Outlook 2014

Our research group studies the roles of ion channels in cardiac and neurological disorders. Disorders such as cardiac arrhythmias or chronic pain may be caused by either mutations in the genes coding for the ion channel subunits or dysregulation of their functions. These disorders are hence called 'channelopathies'.

In 2013, Cédric Laedermann obtained his PhD based on two studies that were published this year. His main study published in the *Journal of Clinical Investigation* revealed new molecular and cellular mechanisms implicating voltage-gated sodium channels in neuropathic pain in a mouse model with nerve injuries. This work was the result of a fruitful collaboration with the group of Isabelle Decosterd (Pain Center, University Hospital of Lausanne).

Further, we investigated the roles of ion channels in cardiac arrhythmias. In the frame of the SNF-funded SCOPES collaboration with Russian geneticists, Valentin Sottas published a study on the characterisation of genetic variants of the cardiac sodium channel Nav1.5 leading to sudden cardiac death. Diana Shy and Ludovic Gillet have been working on the molecular and functional characterisation of Nav1.5 using new genetically modified mouse models that we generated with the support of the SNF and the EU FP7 "EUTrigTreat" project.

The channel TRPM4 is also the focus of many of our current studies as part of the "NCCR TransCure". Ninda Syam investigated the biochemical alterations of TRPM4 variants found in patients with cardiac arrhythmias and revealed the molecular determinants of TRPM4 glycosylation, while Yassine Amarouch is currently working on several new compounds identified in the TransCure project that have either blocking or activating properties on this channel. This work is performed in close collaboration with the groups of Jean-Louis Reymond (chemistry) and Matthias Hediger (screening facility) at the University of Bern.

In 2013, our group was involved in the organisation of two international meetings. In June, the 2nd meeting on cardiac and neurological channelopathies was held in Moscow, gathering together close to 50 Russian, French, and Swiss basic and clinical scientists. In October, with the support of the SNF, we organised a small international exploratory workshop in Beatenberg (CH) on the topic of computational tools to investigate genetic channelopathies.

Both ion channels, Nav1.5 and TRPM4, will be the focus of our studies in 2014. Ninda Syam will defend her thesis work before autumn 2014. This year will also be the last year of the EUTrigTreat project, with a closing general assembly to be held in June 2014 in Berlin (DE). We also plan to be active in submitting the proposal for a continuation of SNF funding for the second phase (years 5-8) of the TransCure project. Finally, Valentin Sottas will spend 6 months in the laboratory of André Kléber at Harvard University in Boston (US) on a Doc.Mobility stipend from the SNF.

Group Members

Prof. Dr. Hugues Abriel, Group Leader
Dr. Jean-Sébastien Rougier, Senior Teaching and Research Assistant
Dr. M. Yassine Amarouch, Postdoctoral Fellow
Dr. Ludovic Gillet, Postdoctoral Fellow
Maria Essers, Laboratory Technician
Sabine Nafzger, Laboratory Technician (since Oct.)
Louis Amport, Secretary (until July)
Deborah Felder, Secretary (since Aug.)
Verena Frazao, Secretary
Morgan Chevalier, PhD Student (since July)
Cedric J. Laedermann, PhD Student (until July)
Diana A. Shy, PhD Student
Valentin Sottas, PhD Student
Ninda Syam, PhD Student

Collaborators

Barò I, French National Research Agency, CNRS, France
Bezzina C, University of Amsterdam Academic Medical Centre, The Netherlands
Decosterd I, University of Lausanne, Switzerland
Hatem SN, French National Research Agency, INSERM, France
Hediger M, NCCR TransCure, Switzerland
Kucera JP, University of Bern, Switzerland
Lehnart SE, FP7 EUTrigTreat Consortium, University of Göttingen, Germany
Reymond JL, NCCR TransCure, Switzerland
Swan H, University of Helsinki, Finland
Sychov O, SNF SCOPES Project, Ukraine
Zaklyazminskaya EV, SNF SCOPES Project, Russia
Zambelli T, ETH Zurich, Switzerland

Grants

Amounts allocated for 2013:

- SNF: In vivo relevance of the PY and PDZ-domain binding motifs of the cardiac sodium channel Nav1.5 (H. Abriel) CHF 84,658
- SNF: Molecular determinants of Nav 1.5 multiprotein complexes in cardiac cells (H. Abriel) CHF 178,573
- SNF: Roles of ion channel-interacting proteins in cardiac channelopathies (H. Abriel, E.V. Zaklyazminskaya, O.S. Sychov) CHF 54,000
- SNF: NCCR TransCure subproject: Physiology, pharmacology and pathophysiology of the calcium-activated non-selective cation TRPM4 channel (M. Hediger, H. Abriel) CHF 227,023
- European: EUTrigTreat – Identification and therapeutic targeting of common arrhythmia trigger mechanisms (S. Lehnart, H. Abriel) CHF 74,255
- UniBern Forschungsstiftung (H. Abriel) CHF 12,844

Teaching Activities

- Dentistry students: Coordination of pathophysiology lectures
- Dentistry students: Kidney and electrolytes pathophysiology
- MSc Biomedical Sciences: Ion channels in cardiac diseases
- BSc Life Sciences: Cardiac ion channels in health and disease

Publications

Biochemical, single-channel, whole-cell patch clamp, and pharmacological analyses of endogenous TRPM4 channels in HEK293 cells. Amarouch, MY; Syam, N; Abriel, H (2013) in: Neurosci Lett, 541, p. 105-110.

A Phosphoinositide 3-Kinase (PI3K)-serum- and glucocorticoid-inducible Kinase 1 (SGK1) Pathway Promotes Kv7.1 Channel Surface Expression by Inhibiting Nedd4-2 Protein. Andersen, MN et al. (2013) in: J Biol Chem, 288(52), p. 36841-36854.

Dysregulation of voltage-gated sodium channels by ubiquitin ligase NEDD4-2 in neuropathic pain. Laedermann, CJ et al. (2013) in: J Clin Invest, 123(7), p. 3002-3013.

beta1- and beta3- voltage-gated sodium channel subunits modulate cell surface expression and glycosylation of Nav1.7 in HEK293 cells. Laedermann, CJ; Syam, N; Pertin, M; Decosterd, I; Abriel, H (2013) in: Front Cell Neurosci, 7, p. 137.

Molecular genetics and functional anomalies in a series of 248 Brugada cases with 11 mutations in the TRPM4 channel. Liu, H et al. (2013) in: PLoS One, 8(1), p. e54131.

A-kinase anchoring protein Lbc coordinates a p38 activating signaling complex controlling compensatory cardiac hypertrophy. Pérez López, I et al. (2013) in: Mol Cell Biol, 33(15), p. 2903-2917.

Mice carrying ubiquitin-specific protease 2 (Usp2) gene inactivation maintain normal sodium balance and blood pressure. Pouly, D et al. (2013) in: Am J Physiol Renal Physiol, 305(1), p. F21-F30.

Proteasome inhibitor (MG132) rescues Nav1.5 protein content and the cardiac sodium current in dystrophin-deficient mdx (5cv) mice. Rougier, JS; Gavillet, B; Abriel, H (2013) in: Front Physiol, 4, p. 51.

Characterization of 2 genetic variants of Na(v) 1.5-arginine 689 found in patients with cardiac arrhythmias. Sottas, V et al. (2013) in: J Cardiovasc Electrophysiol, 24(9), p. 1037-1046.

Mammary Gland Biology and Carcinogenesis

www.dkf.unibe.ch/research-group/2/

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

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

Research Highlights 2013 / Outlook 2014

Eph 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.

This transgenic model serves as a tool to investigate the role of EphB4/ephrin-B2 signalling in the control of the mammary stem cell niche. We have shown that mammary glands of truncated ephrin-B2 transgenic mice contain significantly more stem cells and alveolar ER-positive progenitor cells. In contrast, overexpression of EphB4 results in an augmentation of the luminal and bi-potent precursor cell fractions. Thus, ephrin-B2 derived signalling is involved in the control of the stem cell niche and a balanced EphB4-ephrin-B2 signalling is required for the regulation of cell fate decisions.

Characterisation of signal transduction pathways involved in the EphB4/ephrin-B2-induced phenotypes by microarray analyses revealed that the deregulated transgene expression in the luminal and basal cells affects mainly the wnt-signaling pathway and regulators of cell adhesion/migration in the progenitor and stem cell fractions. Thus, the phenotypic consequences are most probably due to an indirect effect by which the MMTV-controlled EphB4 activation in differentiating epithelial cells influences the stem/progenitor cells, which then differentiate abnormally. Taken together, our results demonstrate that EphB4-ephrin-B2 signalling is indispensable for mammary stem cell homeostasis and correct cell fate decisions.

Group Members

Prof. Dr. Anne-Catherine Andres, Group Leader
Dr. Philip Känel, Postdoctoral Fellow (until Nov.)
Dr. Robert Strange, Consultant
François Achermann, Laboratory Technician
Carlos Wotzkow, Laboratory Technician

Collaborators

Djonov V, University of Bern, Switzerland

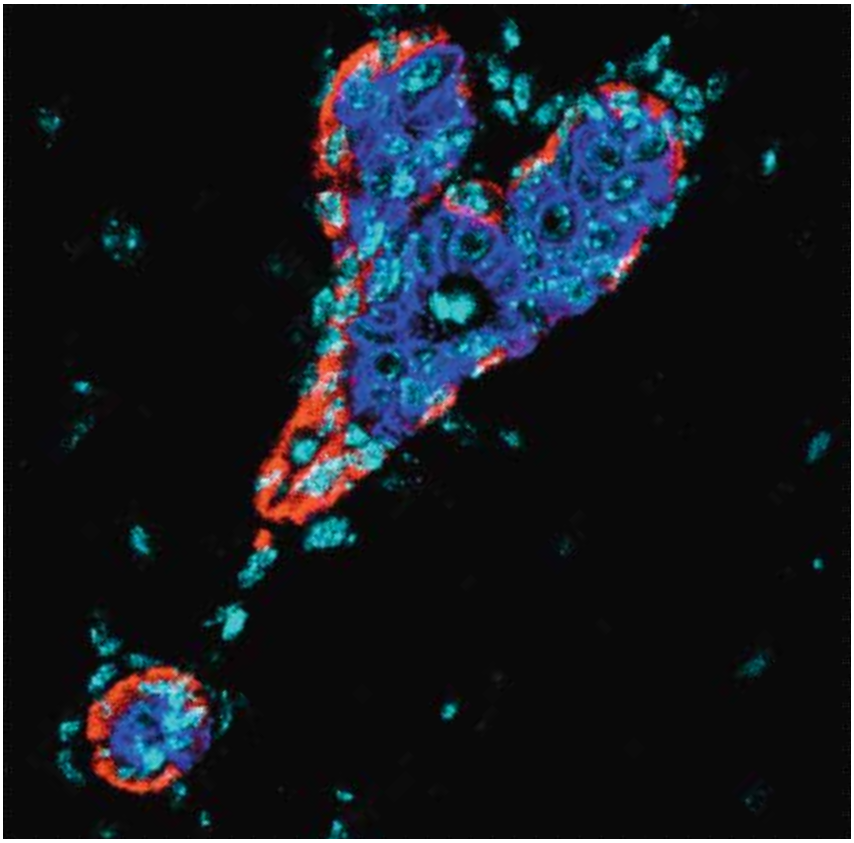
Grants

Amounts allocated for 2013:

- SNF: The role of EphB4 and ephrin-B2 in the control of the mammary gland stem/progenitor cell population (A.-C. Andres) CHF 64,000
- Swiss Cancer League: The molecular mechanisms provoking the ephrin-B2 induced deregulation of the mammary stem cell niche and leading to metastatic tumour growth (A.-C. Andres) CHF 50,000
- Schweizerische Stiftung für Klinisch-Experimentelle Tumorforschung: Transgenic mouse models to study the molecular mechanisms leading to the invasive phenotype of mammary tumors (A.-C. Andres) CHF 40,000

Teaching Activities

- Member, Biological Systems Commission, Graduate School for Cellular and Biomedical Sciences
- Member, Commission for MSc Biomedical Sciences curriculum
- BSc and MSc Biomedical Sciences: Organiser and teacher, Tumour biology programme
- 1st-year medical students: Organiser and teacher, Developmental Biology programme; Transgenic seminar – Cell death of multicellular organisms lecture
- 1st-year veterinary medicine students: Transgenic animals lecture
- Graduate School for Cellular and Biomedical Sciences: Molecular biological methods in clinical diagnosis practical course
- MSc Bioengineering: Molecular biology practical course
- 1st-year medical students: Elective module – Genetic mutations: cyto- and molecular genetics



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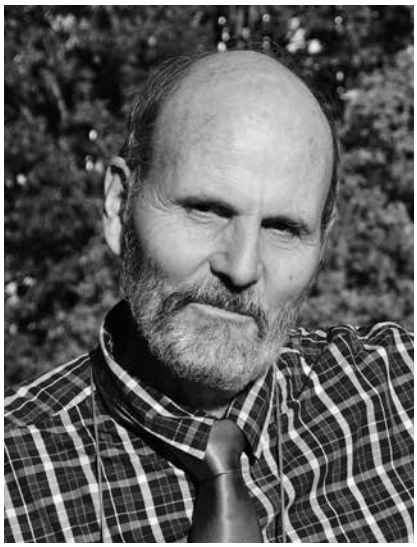

Prof. Dr. Rudolf Brenneisen
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Fed. dipl. in Pharmaceutical Sciences and PhD at the University of Bern. Head, Department of Phytochemistry & Pharmacognosy, Institute of Pharmacy, University of Bern (1981); Habilitation and Privatdozent (1988). Vice-Director, Institute of Pharmacy (1990-91). Associate Professor 1993. Since 1997, Group Leader, Phytopharmacology, Bioanalytics and Pharmacokinetics Group, DCR. President, Swiss Academy of Pharmaceutical Sciences. Since 2008, President, Swiss Committee for Drugs of Abuse Testing. Since 2009, President, Swiss Taskforce for Cannabinoids in Medicine.

Research Highlights 2013 / Outlook 2014

Highlights of our research include:

In *Bryophyllum pinnatum* (a perennial plant with tocolytic and sedative properties), we were able to identify new bufadienolides by LC/MS^n, with concentrations in the subtoxic range. Comparison of a flavonoid fraction to oxybutynin (standard medication for an overactive bladder) showed a reduction in human bladder contraction in vitro from 20% to 10%.

In the largest clinical trial so far (120 subjects) with i.v. Δ^9-tetrahydrocannabinol (THC), it could be shown that this main constituent of cannabis triggers paranoid thoughts in vulnerable individuals. The mechanism of action causing paranoia is the generation of negative affect and confusing anomalous experiences, which should be targets in clinical intervention.

In mid 2014, the research activities will stop due to the retirement of the group leader.

Group Members

Prof. Dr. Rudolf Brenneisen, Group Leader
Dr. Christian Lanz, Laboratory Supervisor, Research Assistant
Dr. Umut Soydaner, Postdoctoral Fellow, BNF Program (Apr.-Nov.)
Ilgü Öztürk, Postgraduate Fellow, BNF Program (since Oct.)

Collaborators

Freeman D, University of Oxford, UK
Gasser P, Solothurn, Switzerland
Hamburger M, University of Basel, Switzerland
Morrison P, King's College London, UK
Schnelle M, Weleda AG, Switzerland
Von Mandach U, University Hospital Zurich, Switzerland
Wüest A, Paracelsus Hospital Richterswil, Switzerland

Grants

Amounts allocated for 2013:

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

Teaching Activities

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

Publications

Two new flavonol glycosides and a metabolite profile of Bryophyllum pinnatum, a phytotherapeutic used in obstetrics and gynaecology. Furer, K; Raith, M; Brenneisen, R; Mennet, M; Simoes-Wust, AP; von, MU; Hamburger, M; Potterat, O (2013) in: Planta Med, 79(16), p. 1565-1571.

Acute effects of intravenous heroin on the hypothalamic-pituitary-adrenal axis response: a controlled trial. Walter, M; Gerber, H; Kuhl, HC; Schmid, O; Joechle, W; Lanz, C; Brenneisen, R; Schachinger, H; Riecher-Rossler, A; Wiesbeck, GA; Borgwardt, SJ (2013) in: J Clin Psychopharmacol, 33(2), p. 193-198.

Safety and efficacy of LSD-assisted psychotherapy in participants with anxiety associated with life-threatening diseases: A randomized active placebo-controlled phase 2 pilot study. Gasser, P; Holstein, P; Michel, Y; Doblin, R; Yazar-Klosinski, B; Passie, T; Brenneisen, R. In: J Nervous Mental Dis, in press.

DCR Research Groups from the Inselspital

Forty research groups from departments of the Inselspital were affiliated with the DCR at the end of 2013. Below is a list of the groups and the names of the Chairs of Departments and/or Group Leaders. Fifteen of the groups are featured on the following pages. Other groups will be featured in future annual reports.

Anaesthesiology: Prof. Dr. Frank Stüber, Dr. Christoph Lippuner

Angiology: Prof. Dr. Iris Baumgartner, Prof. Dr. Nicolas Diehm

Audiology: Prof. Dr. Marco Caversaccio, Prof. Dr. Martin Kompis, PD Dr. Pascal Senn

Cardiology: Prof. Dr. Bernhard Meier, Prof. Dr. Stephan Windecker, Prof. Dr. Yves Allemann, Prof. Dr. Paul Mohacsi, PD Dr. Stefano Rimoldi, PD Dr. Claudio Sartori, Prof. Dr. Urs Scherrer, Prof. Dr. Christian Seiler, Prof. Dr. Thomas M. Suter, PD Dr. Hildegard Tanner

Cardiovascular Surgery: Prof. Dr. Thierry Carrel, Prof. Dr. Hendrik Tevaearai, PD Dr. Florian Dick, Dr. Sarah Longnus, Dr. Henriette Most, PD Dr. Olaf Stanger

Cranio-Maxillofacial Surgery: Prof. Dr. Tateyuki Iizuka, Dr. Nicola Saulacic, Dr. Benoît Schaller

Dermatology: Prof. Dr. Luca Borradori, Dr. Bertrand Favre, PD Dr. Robert Hunger, Prof. Dr. Dagmar Simon, Prof. Dr. Nikhil Yawalkar

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

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

Endocrinology of the Breast: PD Dr. Petra Stute

Endometriosis and Gynaecological Oncology: Prof. Dr. Michel D. Müller, Prof. Dr. Nick A. Bersinger

Endometrium & Ovary: Prof. Dr. Michael von Wolff

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

Gastroenterology / Mucosal Immunology: Prof. Dr. Andrew Macpherson, Prof. Dr. Kathy McCoy, Dr. Markus Geuking, PD Dr. Jan Hendrik Niess, Prof. Dr. Frank Seibold

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

Haematology / Oncology (Paediatrics): Prof. Dr. Kurt Leibundgut, PD Dr. Alexandre Arcaro, Prof. Dr. Beatrice U. Müller

Hand Surgery: Prof. Dr. Esther Vögelin

Hepatology: Prof. Dr. Jean-François Dufour, PD Dr. Andrea De Gottardi, Prof. Dr. Jeff Idle, PD Dr. Nasser Semmo, Dr. Guido Stirnimann

Human Genetics: Prof. Dr. Sabina Gallati, Dr. Johannes Lemke, PD Dr. André Schaller

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

Magnetic Resonance Spectroscopy and Methodology, AMSM: Prof. Dr. Chris Boesch, Prof. Dr. Roland Kreis, Prof. Dr. Peter Vermathen

Nephrology and Hypertension: Prof. Dr. Bruno Vogt, PD Dr. Geneviève Escher, Prof. Dr. Brigitte Frey, PD Dr. Daniel Fuster, Prof. Dr. Uyen Huynh-Do, Prof. Dr. Stephan Krähenbühl, Prof. Dr. Markus Mohaupt, PD Dr. Andreas Pasch, Prof. Dr. Dominik Uehlinger

Neurology: Prof. Dr. Claudio L. Bassetti, Prof. Dr. Antoine Adamantidis, Prof. Dr. Marcel Arnold, Prof. Dr. Alain Kaelin, Prof. Dr. Heinrich Mattle, Prof. Dr. René Müri, Prof. Dr. Kaspar Schindler

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

Nuclear Medicine: Prof. Dr. Thomas M. Krause, PD Dr. Martin A. Walter

Oncology / Haematology (Adults): Prof. Dr. Martin Fey, Dr. Urban Novak, Prof. Dr. Thomas Pabst

Ophthalmology: Prof. Dr. Sebastian Wolf, PD Dr. Volker Enzmann, PD Dr. Ute Wolf-Schnurbusch, PD Dr. Martin Zinkernagel

Orthopaedic Surgery: Prof. Dr. Klaus-Arno Siebenrock, Prof. Dr. Ernst B. Hunziker

Plastic Surgery: Prof. Dr. Mihai Constantinescu, Prof. Dr. Dominique Erni, Dr. Maziar Shafighi

Prenatal Medicine: Prof. Dr. Daniel Surbek, Dr. Andreina Schoeberlein, Dr. Marc Baumann

Psychosomatic Medicine: Prof. Dr. Roland von Känel

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

Pulmonary Medicine (Paediatrics): Prof. Dr. Nicolas Regamey, PD Dr. Philipp Latzin

Radiation Oncology: Prof. Dr. Daniel Aebersold, PD Dr. Yitzhak Zimmer, PD Dr. Kathrin Zaugg

Radiology: Prof. Dr. Johannes Heverhagen, PD Dr. Hendrik von Tengg-Kobligk

Rheumatology: Prof. Dr. Peter M. Villiger, PD Dr. Frauke Förger, Dr. Stefan Kuchen, Prof. Dr. Michael Seitz, Prof. Dr. Beat Trueb

Thoracic Surgery: Prof. Dr. Ralph A. Schmid, PD Dr. Steffen Frese, Dr. Sean R.R. Hall, Dr. Thomas Marti, Dr. Renwang Peng

Tumor-Immunology: Prof. Dr. Adrian Ochsenbein

Urology: Prof. Dr. George Thalmann, Dr. Marco Cecchini, PD Dr. Katia Monastyrskaya

Visceral and Transplantation Surgery: Prof. Dr. Daniel Candinas, PD Dr. Deborah Keogh-Stroka, Prof. Dr. Guido Beldi, Dr. Lukas Brügger

Cardiology

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Prof. Dr. Bernhard Meier
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Studied medicine at University of Zurich (1975); board certified in Internal Medicine (1980) and Cardiology (1983). Cardiology training at Emory University (US). Head, Invasive Cardiology, University Hospital, Geneva (1983-1992). Chair and Professor of Cardiology (1992); rotating Chair (2001), Inselspital. Involved in coronary angioplasty since the first case in 1977. Currently, Chair of Cardiology, Inselspital.

Prof. Dr. Stephan Windecker
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MD (1992) at University of Heidelberg (DE). FMH certification in Cardiology. Currently, Professor of Invasive Cardiology, University of Bern and Chief of Cardiology, Inselspital; Head of Research and Group Leader, DCR. President-Elect, European Association of Percutaneous Cardiovascular Interventions.

Prof. Dr. Yves Allemann
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Studied medicine at Universities of Neuchâtel and Lausanne; MD (1986). FMH certification in Internal Medicine (1994) and Cardiology (1998). Since 2002, Head, Outpatient Clinic, Department of Cardiology, Inselspital. Since 2008, Assistant Professor at University of Bern.

Research Highlights 2013 / Outlook 2014

Allemann/Scherrer/Rimoldi/Sartori Groups

Assisted reproductive technology (ART) induces vascular dysfunction in children, the underlying mechanisms and long-term consequences of which are unknown. We generated mice by ART and found that they display endothelial dysfunction and increased vascular stiffness, resulting in arterial hypertension. Progeny of male ART mice also exhibited vascular dysfunction, suggesting underlying epigenetic modifications. Indeed, ART mice had altered methylation at the promoter of the eNOS gene in the aorta, which correlated with decreased vascular eNOS expression and NO synthesis. Administration of a deacetylase inhibitor normalised vascular gene methylation and function, and resulted in progeny without dysfunction. Finally, ART mice fed a high-fat diet had roughly a 25% shorter life span than control mice. This highlights the potential of ART to induce vascular dysfunction and shorten life span, as well as demonstrating an urgent need to debate related ethical and societal issues.

Mohacsi Group

We aim to minimise the side effects of immunosuppression (increased susceptibility to infections, cancer and nephro-/neurotoxicity) often observed in heart transplant (HTx) patients by studying mechanisms for optimisation of tailored immunosuppressive therapy. In collaboration with the Department of Clinical Chemistry, we investigated whether genetic polymorphisms in drug metabolism, transport and targets of immunosuppressants affect the drug dose required to achieve therapeutic blood trough drug levels in cardiac allograft recipients. In a second project, together with the Centre of Excellence for Prevention of Organ Failure, we studied the clinical application of a novel blood test using genomic and proteomic biomarkers to predict and detect graft rejection in HTx patients.

Suter Group

We seek to improve the prevention and clinical management strategies for cancer drug-associated cardiovascular side effects. It is a worrisome fact that ischemia and cardiotoxic compounds can lead to cellular damage and irreversible decline of cardiac function. Thus, it is critically important to understand the cardiovascular complications of cancer therapies to provide better diagnostics and therapy. In the lab, we investigated mechanisms of cardiotoxicity of old and new anti-cancer therapies in rodent and human iPSC-derived cardiomyocytes in 3D-culture conditions.

Tanner Group

One focus of our research is the early detection of arrhythmias in general and of atrial fibrillation in particular. We compared different screening tools and algorithms for the detection of atrial tachyarrhythmia. The most feared complications of atrial fibrillation are thromboembolic events, which could be prevented by anticoagulation. Therefore, we will develop and validate a probability score for early detection of atrial fibrillation in patients at risk. We developed novel tools for long-term monitoring, since conventional external loop-recorders have the inconvenience of artifacts, skin irritation and especially poor P-wave detection. Oesophageal long-term electrocardiography may overcome such limitations. We also established a cardiac-arrhythmia genetic programme to study the novel molecular basis of primary arrhythmia syndromes and sudden cardiac death.

Prof. Dr. Paul Mohacsi
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MD at University of Zurich. Postdoc at Stanford University Medical Center (US). Since 1993, Medical Director, Heart Failure and Cardiac Transplantation and Head of Research, Department of Cardiology, Inselspital. Konsiliarus in Transplantation Immunology (2008-2012) at University of Freiburg (DE). Visiting Professor (2008, 2011) at University of British Columbia (CA). EMBA at University of Zurich (2009). Since 2013, Full Professor and Chief Cardiologist, University of Bern.

PD Dr. Stefano Rimoldi
stefano.rimoldi@insel.ch

MD (2001) at University of Bern. FMH certification in Internal Medicine (2007) and Cardiology (2012). Postdoc at University of Lausanne (2010-2011). Since 2013, Chief Resident, Inselspital. Venia legendi (2013).

PD Dr. Claudio Sartori
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MD (1991) at University of Lausanne. FMH certification in Internal Medicine (2000). Postdoc at University of California, San Francisco (US). Since 2003, Assistant Professor at University Hospital Lausanne (CHUV). Currently, Visiting Professor at Department of Cardiology, Inselspital.

Group Members

Prof. Dr. Bernhard Meier, Chair

Prof. Dr. Yves Allemann, Group Leader
PD Dr. Stefano Rimoldi, Group Leader
PD Dr. Claudio Sartori, Group Leader
Prof. Dr. Urs Scherrer, Group Leader
Dr. Emrush Rexhaj, Senior Scientist
Dr. Robert von Arx, Clinical Research Associate
Dr. David Cerny, Clinical Research Associate
Dr. Andreia Schmidt, Postdoctoral Fellow (since Feb.)
Dr. Rodrigo Soria Maldonado, Postdoctoral Fellow
Elisa Bouillet, Laboratory Technician

Prof. Dr. Paul Mohacsi, Group Leader
Dr. Raschid Setoud, Postdoctoral Fellow
Alexia Roschi, Laboratory Technician

Prof. Dr. Christian Seiler, Group Leader, Deputy Chair
Dr. Nicolas Brugger, Research Associate
Dr. Stefano de Marchi, Research Associate
Dr. Steffen Glökler, Research Associate
Dr. Michael Stoller, Research Associate
PD Dr. Tobias Traupe, Research Associate

Prof. Dr. Thomas M. Suter, Group Leader
Dr. Christian Zuppinger, Research Associate

PD Dr. Hildegard Tanner, Group Leader
Dr. Argelia Medeiros Domingo, Research Associate (since Aug.)
Dr. Fabian Noti, Research Associate (since Jan.)
PD Dr. Laurent Roten, Research Associate
Dr. Jens Seiler, Research Associate
Dr. Helge Servatius, Research Associate (since Aug.)

Prof. Dr. Stephan Windecker, Head of Research, Group Leader
PD Dr. Thomas Pilgrim, Consultant
Dr. Lorenz Räber, Consultant
Dr. Giulio G. Stefanini, Research Associate
Dr. Stefan Stortecky, Consultant
Dr. Massanori Taniwaki, Visiting Research Fellow

Dr. Jürg Fuhrer, Head of Rhythmology (since July)

Collaborators

Abriel H, University of Bern, Switzerland
Bailey D, University of Glamorgan, UK
Berger W, University of Zurich, Switzerland
Cabello Fernández G, University of Tarapacá, Chile
Duru F, University Hospital Zurich, Switzerland
Fuster D, University of Bern, Switzerland
Haas C, University of Zurich, Switzerland
Häberlin A, University of Bern, Switzerland
Hagl C, Grinninger C, Ludwig Maximilian University of Munich, Germany
Largiadèr C, Inselspital, Switzerland
Martinelli L, Frigerio M, Niguarda Hospital, Italy
McManus B, Wilson-McManus J, University of British Columbia, Canada
Merkely B, Semmelweis University, Hungary
Messerli FH, St. Luke's-Roosevelt Hospital Center, USA
Pratali L, National Research Council (Pisa), Italy
Raio L, University of Bern, Switzerland
Sawyer, DB, Vanderbilt University Medical Center, USA
Sola J, CSEM SA, Switzerland
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Villena M, University of St. Andrés, Bolivia
Willhelm M, University of Bern, Switzerland

Prof. Dr. Urs Scherrer
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MD (1975) at University of Zurich. Postdoc at UT Southwestern Medical School, Dallas (US). Director of Research Laboratory, CHUV, Lausanne (1990-2011). Honorary Professor of Medicine, University of Lausanne. Currently, Visiting Professor, Department of Cardiology, Inselspital. Published first report demonstrating foetal programming of vascular dysfunction in humans.

Prof. Dr. Christian Seiler
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Studied medicine at University of Bern (1979-1985). Postdoc in USA at University of Texas Health Science Center (1990-1992). Since 1997, Director of Echocardiography; since 1998, Staff Physician Interventional Cardiology, Department of Cardiology, Inselspital. PD (1997); Associate Professor (2000); Full Professor (2010). Co-Head, Faculty of Medicine MSc curriculum. Vice President, Bern Cantonal Ethics Committee.

Prof. Dr. Thomas M. Suter
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MD at University of Zurich (1986). Cardiology and CCU/ICU Fellowship in internal medicine at Zurich University. In the USA, fellowships in cardiovascular physiology and cardiology at Boston University (1992-1998); internship at Brigham and Women's Hospital, Boston (1998). Since 2005, Associate Professor, University of Bern.

PD Dr. Hildegard Tanner
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MD (1994) at University of Bern; FMH certification in Internal Medicine (2001) and Cardiology (2003). Research fellow in electrophysiology (1997-1999) and cardiology fellow (2000-2003) in Bern. Research fellow in electrophysiology (2003-2005) at Heart Center, University of Leipzig (DE). Since 2005, Attending Electrophysiologist, Department of Cardiology, Inselspital. Venia docendi (2009).

Grants

Amounts allocated for 2013:

- SNF: Systemic Vascular Function in Young, Healthy Offspring of Preeclampsia (Y. Allemann, S. Rimoldi, C. Sartori, U. Scherrer) CHF 115,000
- SNF: Insulin-resistance in offspring of assisted reproductive technologies (C. Sartori, S. Rimoldi, Y. Allemann, U. Scherrer) CHF 140,000
- SNF: Genetic determinants in sudden infant death syndrome and sudden unexplained death syndrome (C. Haas, W. Berger, A. Medeiros) CHF 137,000
- Swiss Foundation for Pacemaker and Electrophysiology: Screening of silent atrial fibrillation in patients with prolonged atrial electromechanical interval and high thromboembolic risk; development and validation of a probability score to diagnose atrial fibrillation with extensive screening (L. Roten, H. Tanner, J. Seiler) CHF 20,000
- CTI: Body-on-the-Plate – An Integrated Ready-To-Use Platform For Investigating Multi Organ Toxicity (C. Zuppinger) CHF 63,000
- Pfizer Prize for Cardiovascular Research: Vascular Dysfunction in ART Children (S. Rimoldi, U. Scherrer, Y. Allemann, C. Sartori) CHF 15,000
- Swiss Heart Foundation: Screening of silent atrial fibrillation in patients with prolonged atrial electromechanical interval and high thromboembolic risk; development and validation of a probability score to diagnose atrial fibrillation with extensive screening (L. Roten, H. Tanner, J. Seiler) CHF 60,000
- Swiss Transplant Cohort Study: Evaluation of genomic and proteomic blood biomarkers for diagnosis of heart/kidney allograft rejection (P. Mohacsi) CHF 30,000

Five Selected Publications

Oxidative-nitrosative stress and systemic vascular function in highlanders with and without exaggerated hypoxemia. Bailey, DM; Rimoldi, SF; Rexhaj, E; Pratali, L; Salinas, SC; Villena, M; McEneny, J; Young, IS; Nicod, P; Allemann, Y; Scherrer, U; Sartori, C (2013) in: Chest, 143(2), p. 444-451.

Adjuvant bevacizumab-containing therapy in triple-negative breast cancer (BEATRICE): primary results of a randomised, phase 3 trial. Cameron, D; Brown, J; Dent, R; Jackisch, C; Mackey, J; Pivot, X; Steger, GG; Suter, TM; Toi, M; Parmar, M; Laeufle, R; Im, YH; Romieu, G; Harvey, V; Lipatov, O; Pienkowski, T; Cottu, P; Chan, A; Im, SA; Hall, PS; Bubuteishvili-Pacaud, L; Henschel, V; Deurloo, RJ; Pallaud, C; Bell, R (2013) in: Lancet Oncol, 14(10), p. 933-942.

The optimal lead insertion depth for esophageal ECG recordings with respect to atrial signal quality. Haeberlin, A; Niederhauser, T; Marisa, T; Goette, J; Jacoment, M; Mattle, D; Roten, L; Fuhrer, J; Tanner, H; Vogel, R (2013) in: J Electrocardiol, 46(2), p. 158-165.

Mice generated by in vitro fertilization exhibit vascular dysfunction and shortened life span. Rexhaj, E; Paoloni-Giacobino, A; Rimoldi, SF; Fuster, DG; Anderegg, M; Somm, E; Bouillet, E; Allemann, Y; Sartori, C; Scherrer, U (2013) in: J Clin Invest, 123(12), p. 5052-5060.

Mechanisms and drug therapy of pulmonary hypertension at high altitude. Scherrer, U; Allemann, Y; Rexhaj, E; Rimoldi, SF; Sartori, C (2013) in: High Alt Med Biol, 14(2), p. 126-133.

Cardiovascular Surgery

www.cardiovascular-research.ch

Prof. Dr. Thierry Carrel
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Studied medicine at University of Bern. Clinical training in General Surgery, FMH (1990); Cardiovascular Surgery, FMH (1993) in Basel and Bern. Habilitation in Zurich (1993). Fellowships at clinics in Paris (FR), Hannover (DE) and Helsinki (FI). Joined Clinic for Thoracic and Cardiovascular Surgery, Inselspital as Senior Attending in 1995; since 1999, Head and Chair, Department of Cardiovascular Surgery.

Prof. Dr. Hendrik Tevaearai Stahel
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Studied medicine at University of Lausanne. Clinical training in General Surgery, FMH (1995) and Cardiovascular Surgery, FMH (2002). Research fellowship (1999-2001) at Duke University (US). Since 2003, Senior Attending, Department of Cardiovascular Surgery, Inselspital; since 2005, Head of Research and Development.

PD Dr. Florian Dick
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Studied medicine at Universities of Basel and Paris (FR). Clinical training in General Surgery, FMH (2005) including a Vascular Surgery specialisation. Joined Department of Cardiovascular Surgery, Inselspital as Resident in 2004; Attending since 2006. Spent one year in Vascular Surgery Research Group, Imperial College London (UK). Since returning, Head of Vascular Surgery Research (2010) and Senior Attending (2012).

Research Highlights 2013 / Outlook 2014

Our research focuses on the following projects:

Donation after Cardiac Declaration of Death (DCDD)

Since its formation in 2009, this group aims to identify and evaluate strategies to promote the use of DCDD cardiac grafts. In 2013, the SNF and the Swiss Heart Foundation awarded funding to this group, fostering its further development and expansion in 2014.

Myocardial Recovery

In this project, we continue to investigate beneficial as well as maladaptive changes of unloading on normal and failing myocardium. We use a small animal model that mimics the changes induced by an assist device, which is implanted in severe heart failure. We seek to elucidate the ways in which novel molecular therapeutic strategies may contribute to enhancing the beneficial impact of unloading and potentially induce myocardial recovery. In 2013, the group focused on ex vivo testing of the therapeutic use of the $\beta\gamma$-inhibitor Gallein on isolated failing cardiac myocytes both from our small animal model and from human samples. We assessed the effect of this small molecule in advanced heart failure as well as in unloaded myocardium.

Limb Ischemia/Reperfusion

This project evaluates the molecular pathways underpinning muscle cell death of skeletal muscle and future pathways to protect ischemic muscle against reperfusion injury. The experimental phase was completed in 2013 and a manuscript is in preparation for publication in early 2014.

Clinical Research: Cardiac

Research focuses on a variety of topics including the flow and degeneration of biological valve prostheses, 4D aortic imaging, complications and long-term outcome of aortic surgery, cardiorenal syndromes and mechanisms of intraoperative renal damage, mini extra corporeal circulation (MECC), cardioplegia and myocardial metabolism (ischemia-reperfusion injury). We have initiated the Bern Aortic Registry (BeAR).

Clinical Research: Vascular

Research focuses on optimised management strategies to improve clinical outcomes of symptomatic and juxtarenal abdominal aortic aneurysm repair. Based on our experience of how to achieve close to 100% patient follow-up during cross-sectional surveys, these patient series demonstrated in addition that mortality may be significantly underestimated if long-term survival is only estimated using the Kaplan Meier method, which is based on incomplete follow-up information. This led to the proposition of a follow-up index, which should help to appraise the validity of survival figures. The second research focus is on the validation of a novel scoring system for postoperative complications.

Dr. Sarah Longnus
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Studied biology at University of Western Ontario (CA); PhD at Department of Pathology and Laboratory Medicine, James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research, University of British Columbia (CA). Postdoc positions in Boston (US) and Nice (FR). Since 2009, Group Leader, Cardiovascular Surgery, DCR.

Dr. Henriette Most
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Studied medicine at Charité Medical School, Berlin (DE). Joined Department of Cardiovascular Surgery, Inselspital as Resident in 2005. Postdoc (2008-2009) at Thomas Jefferson University (US). Returned to Inselspital in 2010 to continue training in cardiovascular surgery. Clinical commitments as well as Group Leader, Cardiovascular Surgery, DCR.

PD Dr. Olaf Stanger
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Studied medicine in Vienna (AT), Lund (SW) and London (UK). Licensed GP, specialised in General Surgery and Cardiac Surgery; FETCS. Worked at Departments of Cardiac Surgery, University Hospitals Graz (AT) (1995-2001) and Salzburg (AT) (2001-2011). Consultant Cardiac Surgeon, London; Senior Clinical Lecturer, Imperial College; Clinical Research Lead, Cardiovascular Biomedical Research Unit, Brompton (UK) (2011-2013). MBA (Health Care). Since 2013, Consultant, Department of Cardiovascular Surgery, Inselspital.

Group Members

Prof. Dr. Thierry Carrel, Chair
Prof. Dr. Hendrik Tevaearai Stahel, Head of Research and Development
Prof. Dr. Martin Czerny, Group Leader (until Aug.)
PD Dr. Florian Dick, Group Leader
Dr. Sarah Longnus, Group Leader
Dr. Henriette Most, Group Leader
PD Dr. Olaf Stanger, Group Leader (since Apr.)
Dr. Regula von Allmen, Research Associate
Dr. Xuebin Fu, Postdoctoral Fellow (since Nov.)
Dr. Stéphanie Lecaudé, Postdoctoral Fellow
Martina Bona, Assistant Data Manager (since Aug.)
Nadja Dalla Vecchia, Data Manager
Brigitta Gahl, Statistician
Johannes Graf, Assistant Data Manager (since July)
Bettina Kohler, Data Manager
Laetitia Krummen, Data Manager (since June)
Monika Sperisen, Data Manager
Sorin Ciocan, Laboratory Technician
Nithya Devapragash, Laboratory Technician (since Nov.)
Céline Ferrié, Laboratory Technician (until May)
Veronika Mathys, Laboratory Technician (until Nov.)
Barbara Schweizer, Laboratory Assistant
Adrian Segiser, Laboratory Technician
Laura Seidel, Secretary
Monika Dornbierer, MD-PhD Student

Collaborators

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Flück M, Balgrist University Hospital, Switzerland
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Greenhalgh R, Imperial College London, UK
Guzzela L, Schmid M, ETH Zurich, Switzerland
Hedhammar M, Swedish University of Agricultural Sciences, Sweden
Ullrich N, University of Bern, Switzerland

Grants

Amounts allocated for 2013:

- Swiss Heart Foundation: Improving cardiac tolerances to ischemia and reperfusion with microRNA (S. Longnus) CHF 65,000
- Forschungs-Grant des Inselspitals für Nachwuchsforschende: Combination of Mechanical Unloading with Molecular Therapy for Enhanced Adrenergic Response to Generate Myocardial Recovery (H. Most) CHF 80,000
- European Society for Vascular Surgery Research: Salvage of ischaemic peripheral muscle from reperfusion injury by fibre-targeted overexpression of focal adhesion kinase: Validating an emerging concept of post ischemia conditioning (R. von Allmen, F. Dick) € 30,000

Five Selected Publications

Dynamic patterns of ventricular remodeling and apoptosis in hearts unloaded by heterotopic transplantation. Brinks, H et al. (2013) in: J Heart Lung Transplant, e-pub ahead of print: doi: 10.1016/j.healun.2013.10.006.

Early troponin T and prediction of potentially correctable in-hospital complications after coronary artery bypass grafting surgery. Gober, V et al. (2013) in: PLoS One, 8(9), p. e74241.

Anisotropically oriented electrospun matrices with an imprinted periodic micropattern: a new scaffold for engineered muscle constructs. Guex, AG et al. (2013) in: Biomed Mater, 8(2), p. 021001.

Mild hypothermia during global cardiac ischemia opens a window of opportunity to develop heart donation after cardiac death. Stadelmann, M et al. (2013) in: Transpl Int, 26(3), p. 339-348.

Type A aortic dissection after nonaortic cardiac surgery. Stanger, O et al. (2013) in: Circulation, 128(15), p. 1602-1611.

Cranio-Maxillofacial Surgery

www.dkf.unibe.ch/research-group/57/

Research Highlights 2013 / Outlook 2014

The regenerative pathways during periosteal distraction osteogenesis (PDO) may be influenced by the local environment. A series of experiments was performed to evaluate the ability of periosteum to generate bone tissue where there is none. The contribution of periosteum was assessed using a rat calvaria model with either intact or excised periosteum and the application of resorbable collagen membrane. Significant differences were observed between the groups. The presence of periosteum was necessary for the bone formation, while the application of collagen membrane was not.

The nature and kinetics of bone formation can be impaired or delayed by the applied rate of PDO. An initial experiment aimed to estimate the benefit of gradual versus immediate periosteal elevation. The results indicated a positive influence of gradual compared to immediate elevation. A novel rabbit model was established to assess the influence of these different rates. The goal was to elucidate the interplay between the mechanics and biology of bone formation. Two morphological patterns of bone formation were observed: originating from the old bone surface (low rate) and from the periosteum (high rate). A longer consolidation period was necessary to reach the difference in bone volume between the two groups, as demonstrated on the micro CT. Increased expression was found for BMP2 in bone (slow rate) and for RunX2 in periosteum (high rate).

New population-based implant methodology was designed to advance the state-of-the-art approaches by combining shape and bone quality information. This computational method was developed for the case of mandibular locking fixation plates to optimise the parameters of plate angle and screw position. Significant improvement in the available bone thickness was observed with the proposed implants compared to the standard plates, without compromising the bone mineral density around the screws. An angle and screw separation of 129° and 9 mm for females and 121° and 10 mm for males are more suitable designs than the commercially available 120° and 9 mm.

The incidence of infection following mandibular fractures involving alveolus was estimated by comparison of 1-day and 5-day postoperative courses of antibiotics. The 59 patients were randomly assigned to two groups. Six of the 30 patients in the 5-day group (20%) and six of the 29 in the 1-day group (21%) developed local wound infections throughout the 6-month observation period. In the present patient population, a 1-day postoperative course of antibiotics was as effective in preventing infective complications as a 5-day regimen.

Prof. Dr. Tateyuki Iizuka
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MD and DDS in Germany; PhD in Medicine (1992). Since 1996, Associate Professor at Helsinki University (FI). Since 2000, Professor of Cranio-Maxillofacial Surgery at University of Bern; since 2006, Chair. Lecturer at Helsinki University (since 1998), External Professor at Osaka (JP) Dental University (since 2005) and National University of Singapore (since 2006).

Dr. Nikola Saulacic
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DDS and MSc at University of Belgrade (RS); European PhD (2005) at University of Santiago de Compostela (ES). Research and Teaching Associate at University of Geneva (2006-2007). Since 2007, Research Associate, Cranio-Maxillofacial Surgery, Inselspital and since 2009, Clinic for Oral Surgery and Stomatology, University of Bern. Since 2012, Group Leader, Cranio-Maxillofacial Surgery, DCR.

Dr. Benoît Schaller
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MD at University of Bern (2000) and DMD at University of Zurich (2007). FMH certification in Oral and Maxillofacial Surgery (2010). Since 2007, Research Associate, Cranio-Maxillofacial Surgery, DCR; since 2013, Group Leader.

Group Members

Prof. Dr. Tateyuki Iizuka, Chair
Dr. Nikola Saulacic, Head of Research, Group Leader
Dr. Benoît Schaller, Group Leader
Dr. Eliane Brolese, Research Assistant
Dr. Maiko Haga-Tsujimura, Research Assistant (until Oct.)
Dr. Peng Jiambo, Research Assistant
Dr. Ken Nakahara, Research Assistant
Dr. Kosaku Sawada, Research Assistant (since Nov.)
Caroline-Dominique Zürcher, Secretary

Collaborators

Buser D, University of Bern, Switzerland
Hofstetter W, University of Bern, Switzerland
Koch R, Synthes GmbH, Switzerland
Mataga I, University of Niigata, Japan
Mallaun M, Straumann AG, Switzerland
Nolte LP, University of Bern, Switzerland
Scolozzi P, University of Geneva, Switzerland
Sculean A, University of Bern, Switzerland
Wahl G, University of Bonn, Germany

Grants

Amounts allocated for 2013:

- ITI Foundation: Comparing autogenous cortical bone in vertical augmentation and single-stage implant placement to staged procedure: A dog study (K. Nakahara, M. Haga-Tsujimura, K. Sawada, T. Iizuka, N. Saulacic) CHF 35,821
- Straumann AG: Augmentation techniques in vertical alveolar defects for single-stage implant placements: A comparative animal study (K. Nakahara, T. Iizuka, N. Saulacic) CHF 21,411

Five Selected Publications

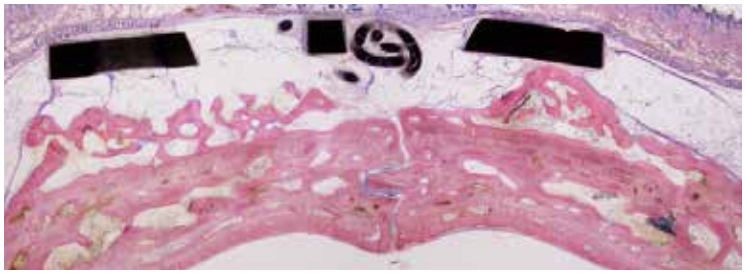
Population-based design of mandibular fixation plates with bone quality and morphology considerations. Bousleiman, H; Iizuka, T; Nolte, LP; Reyes, M (2013) in: Ann Biomed Eng, 41(2), p. 377-384.

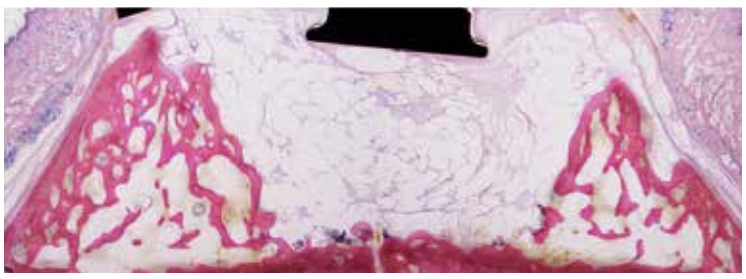
Impact of bone harvesting techniques on cell viability and the release of growth factors of autografts. Miron, RJ; Gruber, R; Hedbom, E; Saulacic, N; Zhang, Y; Sculean, A; Bosshardt, DD; Buser, D (2013) in: Clin Implant Dent Relat Res, 15(4), p. 481-489.

Relative contributions of osteogenic tissues to new bone formation in periosteal distraction osteogenesis: histological and histomorphometrical evaluation in a rat calvaria. Saulacic, N; Hug, C; Bosshardt, DD; Schaller, B; Buser, D; Haeniwa, H; Iizuka, T (2013) in: Clin Implant Dent Relat Res, 15(5), p. 692-706.

Analysis of new bone formation induced by periosteal distraction in a rat calvarium model. Saulacic, N; Schaller, B; Iizuka, T; Buser, D; Hug, C; Bosshardt, DD (2013) in: Clin Implant Dent Relat Res, 15(2), p. 283-291.

The role of postoperative prophylactic antibiotics in the treatment of facial fractures: a randomized, double-blind, placebo-controlled pilot clinical study. Part 2: Mandibular fractures in 59 patients. Schaller, B; Soong, PL; Zix, J; Iizuka, T; Lieger, O (2013) in: Br J Oral Maxillofac Surg, 51(8), p. 803-807.





Gastroenterology / Mucosal Immunology

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Prof. Dr. Andrew Macpherson
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Studied biochemistry (PhD, 1983) and medicine (MB, 1985) at University of Cambridge (UK). Research Group Leader and Senior Medical Staff at University Hospital Zurich (1998-2004). Professor of Medicine (2004-2008) at McMaster University (CA). Since 2008, Chief of Gastroenterology and Co-Chair, Department of Visceral Surgery and Medicine, Inselspital.

Prof. Dr. Kathy McCoy
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Studied immunology (PhD, 1997) at Otago University and Malaghan Institute of Medical Research (NZ). Postdoc (1998-2000) and Senior Research Scientist/Group Leader (2000-2006) at Institute for Experimental Immunology, University Hospital Zurich. Assistant Professor (2006-2010) and Director of Axenic/Gnotobiotic Facility (2008-2010) at McMaster University (CA). Since 2010, DCR Group Leader, Gastroenterology / Mucosal Immunology.

Dr. Markus Geuking
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Studied molecular biology and immunology (PhD, 2006) at University of Zurich and ETH Zurich. Postdoctoral Fellow (2006-2010) at McMaster University (CA). Since 2010, DCR Group Leader, Gastroenterology / Mucosal Immunology.

Research Highlights 2013 / Outlook 2014

Our research groups strive to understand the molecular and cellular immune mechanisms involved in regulating host-microbial mutualism.

Macpherson Group

We investigate the dynamics of intestinal microbial colonisation at steady state. We measure important parameters, such as bacterial proliferation, retention of bacteria in different niches and shedding of bacteria. Furthermore, we study the stratification of bacteria within the gut and determine the dynamics of bacteria within the mucus layer lining the gut epithelium. Although live bacteria are compartmentalised to mucosal sites under homeostatic conditions, bacterial products can penetrate to systemic sites. Therefore, we are investigating the metabolic handshake between the host and its microbiota, using state-of-the-art metabolomics technology. We are also looking at the impact microbial exposure during pregnancy has on the development of the immune system of the offspring after birth.

McCoy Group

We have observed that in the absence of microbes, the pathways that normally repress the production of IgE antibodies are disrupted, resulting in elevated serum IgE levels in germ-free mice, which reflects immune dysregulation. We have shown that the complexity of the microbiota present early in life is instrumental in instructing a normal immune regulatory status. A critical threshold of microbial complexity has to be reached early during colonisation to ensure proper induction of immune regulation. Furthermore, we could demonstrate that this immune dysregulation in the absence of intestinal microbes also results in increased susceptibility to oral but not systemic antigen-induced anaphylaxis. This is the first experimental demonstration of a mechanism that could be an underlying cause of the observations described in the "hygiene hypothesis". We are now investigating the role of the innate immune system in sensing this microbial complexity and the signals involved in correcting the observed dysregulation.

Geuking Group

We have previously shown that intestinal bacterial colonisation induces strong regulatory T cell (Treg) and interleukin-10 (IL-10) responses to ensure immune homeostasis following colonisation. Based on these findings, we are now studying the antigen-specificity requirements for efficient Treg induction, using genetically modified *E. coli* strains expressing a particular T cell epitope. Furthermore, we have observed that there is a very early induction of IL-10 following colonisation in the absence of a functional Treg compartment. We are now investigating the degree to which this very early IL-10 induction can compensate for the absence of Treg and how this protects from lethal inflammation.

Niess Group

Mononuclear phagocytes are a heterogeneous cell population in the lamina propria of the small and large intestine that actively recognise constituents of the intestinal microbiota. We are investigating if these populations can be distinguished by the expression of the IL-10-like cytokine IL-19. We aim to determine if phagocyte-derived IL-19 contributes to the maintenance of intestinal homeostasis in the presence of a commensal microbiota.

PD Dr. Jan Hendrik Niess
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Studied medicine (MD, 2002) at Friedrich Schiller University, Jena (DE). Postdoctoral Fellow (2001-2006) at Massachusetts General Hospital, Harvard Medical School, Boston (US). Group Leader and training in internal medicine and gastroenterology (2006-2012) at Ulm University (DE). Since 2012, Attending Physician, Department of Visceral Surgery and Medicine, Inselspital.

Group Members

Prof. Dr. Andrew Macpherson, Chief of Gastroenterology, Co-Chair
Prof. Dr. Kathy McCoy, Group Leader
Dr. Markus Geuking, Group Leader
PD Dr. Jan Niess, Group Leader

Dr. Julia Cahenzli, Postdoctoral Fellow
Dr. Stephanie Ganal, Postdoctoral Fellow (since Sep.)
Dr. Mercedes Gomez de Aguero, Postdoctoral Fellow
Dr. Li Hai, Postdoctoral Fellow
Dr. Chunlan Huang, Postdoctoral Fellow (since Sep.)
Dr. Melissa Lawson, Postdoctoral Fellow
Dr. Francesca Ronchi, Postdoctoral Fellow (since Feb.)
Dr. Yasuhiro Uchimura, Postdoctoral Fellow
Prof. Dr. Reiner Wiest, Senior Consultant
Pascal Juillerat, Consultant
Beatrice Flogerzi, Laboratory Technician
Madeleine Wyss, Laboratory Technician
Yasmin Köller, PhD Student
William Kwong Chung, PhD Student
Sandra Rupp, PhD Student
Anna Steinert, PhD Student (since Dec.)

Collaborators

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Powrie F, University of Oxford, UK
Santamaria P, University of Calgary, Canada
Sauer U, ETH Zurich, Switzerland
Stecher B, Ludwig Maximilian University, Germany

Grants

Amounts allocated for 2013:

- SNF: Compartmentalisation of commensal intestinal microbes and host IgA immunity in maintaining host-microbial mutualism (A. Macpherson) CHF 237,000
- SNF: The role of antigen-specific and toll-like receptor-dependent de novo generation of inducible regulatory T cells in the induction of intestinal immune homeostasis (M. Geuking) CHF 176,741
- SNF: Shaping of the innate immune system during neonatal exposure to commensal intestinal microbes (A. Macpherson) CHF 157,410
- SNF: Investigation into the impact of environmental microbes on regulation of IgE and allergic disease (K. McCoy) CHF 72,000
- SNF: Marie Heim-Vögtlin postdoctoral fellowship: Microbiota-mediated fine-tuning of the threshold of intestinal inflammasome activation in host- microbial mutualism (A. Macpherson, K. McCoy) CHF 111,667
- European Research Council: Mechanisms of hygiene-mediated immune dysregulation and impact on the susceptibility to allergic and autoimmune diseases (K. McCoy) CHF 300,000

Five Selected Publications

Microbial-immune cross-talk and regulation of the immune system. Cahenzli, J; Balmer, ML; McCoy, KD (2013) in: Immunology, 138(1), p. 12-22.

Intestinal microbial diversity during early-life colonization shapes long-term IgE levels. Cahenzli, J; Koller, Y; Wyss, M; Geuking, MB; McCoy, KD (2013) in: Cell Host Microbe, 14(5), p. 559-570.

Stratification and compartmentalisation of immunoglobulin responses to commensal intestinal microbes. Macpherson, AJ and McCoy, KD (2013) in: Semin Immunol, 25(5), p. 358-363.

Sex differences in the gut microbiome drive hormone-dependent regulation of autoimmunity. Markle, JG; Frank, DN; Mortin-Toth, S; Robertson, CE; Feazel, LM; Rolle-Kampczyk, U; von, BM; McCoy, KD; Macpherson, AJ; Danska, JS (2013) in: Science, 339(6123), p. 1084-1088.

Pathological bacterial translocation in liver cirrhosis. Wiest, R; Lawson, M; Geuking, M (2014) in: J Hepatol, 60(1), p. 197-209.

Haematology / Oncology (Paediatrics)

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Prof. Dr. Kurt Leibundgut
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Medical Diploma (1981) and MD (1986) at University of Zurich. PD (2000) and Associate Professor (2009) at University of Bern. Since 2011, Head of Division, Paediatric Haematology and Oncology, Department of Paediatrics, Inselspital. Since 2003, Director, Paediatric and Adult Stem Cell Transplantation Program, Inselspital.

PD Dr. Alexandre Arcaro
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Diploma in biology at University of Lausanne (1992). PhD at University of Fribourg (1995). Postdocs at Ludwig Institute for Cancer Research, University College London (UK) (1995-1996) and University of Lausanne (1998-2000). Lecturer (2000-2003) at Imperial College London. Oberassistent (2004-2009) at University Children's Hospital Zurich. PD (2008) at University of Zurich. Since 2010, Group Leader/Oberassistent, Haematology / Oncology (Paediatrics), DCR and PD at University of Bern.

Prof. Dr. Beatrice U. Müller

Medical Diploma (1991) and MD (1995) at University of Basel. Postdoc (1997-2002) at Harvard University, Boston, (US). PD (2007) and Professor (2010) at University of Bern. Since 2013, Group Leader, Haematology / Oncology (Paediatrics), DCR.

Research Highlights 2013 / Outlook 2014

We are involved in several projects aiming to identify molecular targets for the development of novel therapies for childhood cancer, with an emphasis on embryonal tumours (medulloblastoma, neuroblastoma), glioma and leukaemia (ALL, AML). We are also involved in several clinical studies in paediatric cancer patients. A summary of the main studies of 2013 is presented below.

Clinical Research: Neuropsychology/-Cognition

Since the 2010 implementation of a neuropsychological care programme at the Division of Haematology and Oncology, Department of Paediatrics, Inselspital, we have acquired extensive experience with the assessment and remediation training of cognitive functioning in both children with brain tumours and those with other oncological diseases. We hope that this work will not only improve knowledge of the cognitive late effects of cancer and its treatment but also be seminal for future cognitive rehabilitation efforts to improve academic achievement of these children.

Clinical Research: Fever in Neutropenia

Under the lead of Prof. Dr. Roland Ammann, a variety of international and national prospective and retrospective clinical studies are being performed, with the aim to improve supportive care in children with chemotherapy-induced fever in neutropenia.

Laboratory Research

We identified novel molecular targets for the development of targeted therapies in neuroblastoma using RNA interference screening. Our studies revealed that targeting the fibroblast growth factor receptor 2 (FGFR2) could sensitise neuroblastoma cells to cisplatin, a commonly used chemotherapeutic agent. In addition, an autocrine signalling loop involving fibroblast growth factor 2 (FGF-2) and FGFR2 was described in primary neuroblastoma and neuroblastoma cell lines.

We evaluated novel pharmacological inhibitors of the class IA phosphoinositide 3-kinase p110α (PIK3CA) gene in glioma. Over-expression of p110α could be documented in primary tumours at the protein level, which correlated with the expression of the epidermal growth factor receptor (EGFR) and the activation of the mammalian target of rapamycin (mTOR) pathway. In addition, pharmacological inhibitors of p110α or RNA interference (RNAi) inhibited the proliferation and survival of cell lines and primary cultures from glioma patients in vitro and in vivo.

We also investigated the molecular mechanism of action of the above-mentioned inhibitors in cancer cell lines with activating mutations in the PIK3CA gene. We could show that pharmacological inhibitors of p110α or RNAi inhibited the survival of PIK3CA-mutant cell lines through the induction of apoptosis and autophagy. The induction of cell death was dependent on a shift in the balance of the expression of pro- and anti-apoptotic Bcl-2 family proteins.

Group Members

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Valeriya Dimitrova, PhD Student
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Zlobec I, University of Bern, Switzerland

Grants

Amounts allocated for 2013:

- SNF: Investigating the function of phosphoinositide 3-kinase isoforms in the mTOR pathway and drug resistance in human cancer (A. Arcaro) CHF 133,640
- SNF: (2011-2014) Deregulation of the master transcription factor PU.1 by a complex of distant regulatory elements in AML patients (B. Müller) CHF 110,333
- Beatrice Borer Foundation: Neuropsychologic/-cognitive evaluation of children with brain tumors and other pediatric malignancies (K. Leibundgut) CHF 130,000
- Berner Stiftung für krebskranke Kinder und Jugendliche: (K. Leibundgut) CHF 268,000
- European Commission: ASSET (A. Arcaro) CHF 240,000
- Oncosuisse: Transcriptional dysregulation during myeloid transformation in AML (B. Müller) CHF 74,475
- Pediatric Oncology Group (USA) and Swiss Paediatric Oncology Group: Clinical research, multicenter studies (K. Leibundgut) CHF 69,237
- Stiftung für klinisch-experimentelle Tumorforschung: Identification and characterisation of leukemia stem cells in pediatric acute lymphoblastic leukemia using a novel in vivo model (A. Arcaro, K. Leibundgut) CHF 67,000
- Stiftung zur Krebsbekämpfung: Novel molecular targets for medullo-blastoma in relation to c-Myc (A. Arcaro) CHF 10,000

Five Selected Publications

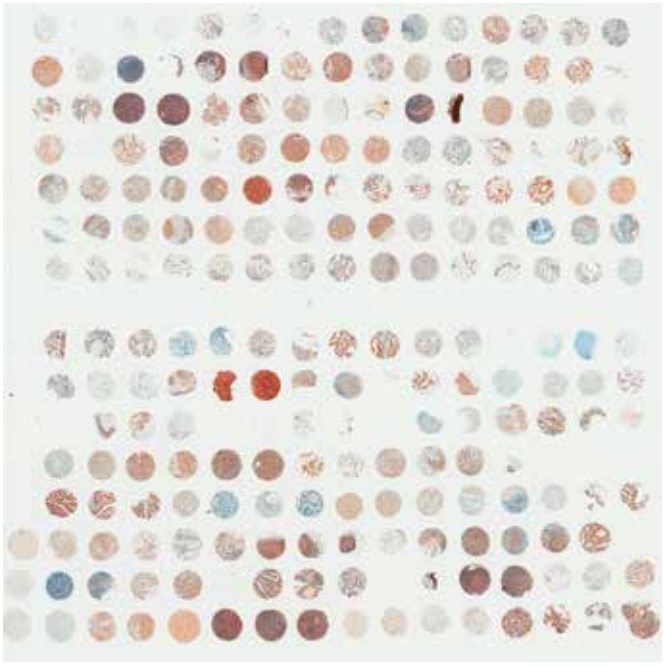
Involvement of autophagy in the response of tumor cells to PtdIns3K inhibitors: therapeutic implications. Arcaro, A (2013) in: Autophagy, 9(4), p. 607-608.

Different fever definitions and the rate of fever and neutropenia diagnosed in children with cancer: a retrospective two-center cohort study. Binz, P; Bodmer, N; Leibundgut, K; Teuffel, O; Niggli, FK; Ammann, RA (2013) in: Pediatr Blood Cancer, 60(5), p. 799-805.

Emerging metabolic targets in the therapy of hematological malignancies. Leni, Z; Parakkal, G; Arcaro, A (2013) in: Biomed Res Int, 2013.

RNA interference screening identifies a novel role for autocrine fibroblast growth factor signaling in neuroblastoma chemoresistance. Salm, F et al. (2013) in: Oncogene, 32(34), p. 3944-3953.

Targeting the phosphoinositide 3-kinase p110-alpha isoform impairs cell proliferation, survival, and tumor growth in small cell lung cancer. Wojtalla, A et al. (2013) in: Clin Cancer Res, 19(1), p. 96-105.



Hepatology

www.swissliver.ch/de/E-Commerce/Forschungsgruppen

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Mathematical (1984) and medical (1986) degrees at University of Geneva. Research fellow (1991-1995) at Tufts University (US) and GI-fellowship (1995-1997) at New England Medical Center, Boston (US). Return to Switzerland in 1997. Since 2011, Chief of Hepatology and Co-Chair, Department of Visceral Surgery and Medicine, Inselspital.

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PhD in biochemistry at University of London (UK). Professor of Pharmacogenetics (1988-1995); Chair, Department of Pharmacological Sciences (1992-1995); Head, School of Clinical Medical Sciences (1991-1995), University of Newcastle (UK). Professor of Medicine and Molecular Biology (1995-2004), Norwegian University of Science and Technology, Trondheim (NO). Since 2003, Visiting Professor, University of Bern. Scientific Contractor, Laboratory of Metabolism, NCI, Bethesda (US).

Research Highlights 2013 / Outlook 2014

Treatment of Refractory Ascites

Refractory ascites is accumulation of fluid (ascites) in the abdominal cavity that cannot be managed with the standard therapy of diet and diuretics. It is predominantly caused by cirrhosis but may also occur as a complication of cancer or chronic heart failure. Refractory ascites is associated with marked abdominal distension, pain, shortness of breath, increased risk of hernia and spontaneous bacterial peritonitis. Treatment options are limited to repeated paracentesis or the implantation of a transjugular intrahepatic portosystemic shunt. The alfapump is a novel device that pumps ascites fluid from the abdominal cavity to the bladder, where it is passed naturally from the body through normal urination, thereby preventing accumulation of ascites and the onset of associated symptoms. The alfapump has reduced median number of paracentesis procedures per month from 3.4 pre-implantation to 0.2 post-implantation. In line with the positive clinical outcomes, quality of life of patients was shown to improve. The Inselspital is leading a clinical study, in collaboration with the liver clinics in Barcelona, Leipzig, Homburg-Saar and Frankfurt, to assess performance and safety of the alfapump for the treatment of refractory ascites.

Metabolomics of Hepatocellular Carcinoma

A considerable number of metabolomic investigations into hepatobiliary diseases have been published in the last two to three years. The accumulated data, together with our own findings, have allowed us to generate a working model for the metabolic fluxes and reprogramming that occur in hepatobiliary diseases as they progress through various stages towards hepatocellular carcinoma (HCC). We have obtained insights into the role that various gene expression patterns may play in governing hepatic metabolism in HCC tumours. An interesting observation is that the Warburg effect in HCC appears to be small; of the order of a four-fold shift from mitochondrial oxidation to cytosolic aerobic glycolysis. This contrasts with Warburg's original observations in an experimental rat liver tumour of a 100-fold shift. Our studies support the concept of a core metabolomic phenotype in hepatobiliary disease, with elevated plasma bile acids and attenuated plasma lysophosphatidylcholines. Our data also support the conclusion that there is a metabolic reprogramming towards fatty acid β-oxidation as an energy source in certain HCC tumours. We propose that the laying down of hepatic triglyceride stores in the precursor stages of NASH/NAFLD provides a rich energy source for future HCC. In collaboration with our clinical hepatology colleagues, we are in the process of investigating the first of several such precursor diseases, chronic hepatitis C, using our array of metabolomic tools, specifically GCMS and UPLC-ESI-QTOFMS.

The outlook for 2014 includes the addition of other such diseases, for example, alcoholic liver disease and chronic hepatitis B. Such studies should furnish new insights into the pathobiology of HCC and generate candidate biomarkers for early detection of HCC.

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Lilian Smith, Secretary

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Grants

- SNF: Hint1, Hint2 a closer look at mechanisms (J.-F. Dufour)
- SNF: Sinergia: Metabolic pathways governing liver carcinogenesis and regeneration (J.-F. Dufour)
- European Commission: Fatty liver: Inhibition of progression (FLIP) (J.-F Dufour)
- Oncosuisse: Hepatocarcinogenic roles of mTOR, raptor and rapamycinsin absence of Pten (J.-F. Dufour)
- Inselspital: Innovation Funds: Alfa-Pump (A. De Gottardi)
- ITL, UK: HCC metabolomics (J. Idle)
- NIH: Radiation metabolomics (J. Idle)
- Walter and Gertrud Siegenthaler Foundation: T cell responses in HCV infection (N. Semmo)

Five Selected Publications

Tissue metabolomics of hepatocellular carcinoma: tumor energy metabolism and the role of transcriptomic classification. Beyoglu, D et al. (2013) in: Hepatology, 58(1), p. 229-238.

IL28B expression depends on a novel TT/-G polymorphism which improves HCV clearance prediction. Bibert, S et al. (2013) in: J Exp Med, 210(6), p. 1109-1116.

Radiofrequency ablation suppresses distant tumour growth in a novel rat model of multifocal hepatocellular carcinoma. Erös de Bethlenfalva-Hora, C et al. (2014) in: Clin Sci (Lond), 126(3), p. 243-252.

Hepatitis B and C in Switzerland – healthcare provider initiated testing for chronic hepatitis B and C infection. Fretz, R et al. (2013) in: Swiss Med Wkly, 143, p. w13793.

Recommendations for the management of hepatitis C virus infection among people who inject drugs. Robaeys, G et al. (2013) in: Clin Infect Dis, 57 Suppl 2, p. S129-S137.

Magnetic Resonance Spectroscopy and Methodology, AMSM

www.amsm.dkf.unibe.ch

Research Highlights 2013 / Outlook 2014

Magnetic resonance imaging (MRI) and spectroscopy (MRS) are powerful and extremely versatile methods for non-invasive studies and diagnostic examinations in humans. Our group uses these methods primarily in prospective studies, and combines methodological development with applications to study physiology and pathology, together with the underlying mechanisms, in situ. Three SNF grants with PIs in our group, six SNF grants in collaboration with other groups, and one EU project define the direction of our research.

A major success this year was the fact that three PhD students successfully defended their theses. Thanks to new grants, we were able to hire three new PhD students and one postdoc.

An SNF grant on insulin resistance, a major research topic of our group, was successfully renewed. While insulin resistance is a major cause of cardiovascular diseases such as stroke and myocardial infarction, we study the effects of chronic or acute exercise and different kinds of carbohydrates, lipids and amino acids on muscle and liver metabolism. We have several strong collaborations on this topic (with endocrinology, diabetology, and hepatology groups of the Inselspital, with preclinical institutes of the University of Bern, and with groups of the Universities of Lausanne, Pittsburgh, Lyon, and Tübingen).

Another SNF grant aims at the development of acquisition and synergistic post-processing methods. This is tailored to the observation of brain metabolism but is transferable to other organs. In collaboration with ETH Zurich, exchange processes between amide protons and water were studied in brain and muscle. In 2013, one PhD student defended her thesis on optimal experimental designs based on Cramér-Rao minimal error bounds and one PhD student started on this project.

Renal function in native and transplanted kidneys is investigated by multi-modal MRI and MRS in another SNF project. Reproducibility studies employing functional MR methods, such as diffusion-weighted imaging, arterial spin labelling and oxygen-dependent MRI were performed. In collaborations with ARTORG groups, image post processing was developed to minimise motion artefacts. For detection of renal ectopic lipids, MRS and MRI methods were optimised.

High-resolution magic angle spinning (HR-MAS) techniques are being developed to correlate tissue spectra in vivo and vitro. HR-MAS allows the metabolic characterisation of tissues like brain, muscle, prostate, breast, liver and kidney. Several HR-MAS studies were performed on biopsies and analysed by 'metabonomical' methods.

TRANSACT (TRAnsforming Magnetic Resonance Spectroscopy into A Clinical Tool) is an EU-funded Marie Curie Initial Training Network (www.transact-itn.eu). It aims at improving and automating MRS so that the clinical use of MRS becomes more robust and widespread. The aim of our subproject is the definition and automatic recognition of spectral quality so that radiologists without specific methodological knowledge will be better able to use MRS in their every day diagnostic work.

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Studied physics at ETH Zurich; PhD with Kurt Wüthrich. Studies in medicine, Swiss State License and MD at University of Zurich. Postdoc at University Children's Hospital Zurich (1985-1990). Since 1991, Professor at University of Bern; DCR since 1995; Department of Diagnostic, Interventional and Paediatric Radiology, Inselspital since 2011. Visiting Professor (2006) at Université Lyon 1 (FR). President of MR Societies (ESMRMB 1997, ISMRM 2001). Silver medallist (ISMRM) and Fellow (ISMRM and ESMRMB). President of SNF Research Commission, University of Bern (2008-2013). Since 2013, Member, SNF National Research Council.

Prof. Dr. Roland Kreis
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Studied chemistry at ETH Zurich; PhD with Richard Ernst. Postdoc and Boswell Fellow in USA at Caltech and HMRI (1989-1992). At University of Bern since 1992; Habilitation (2000); Titular Professor, later converted to Associate Professor (2006). Fellow of ISMRM (2011) and ESMRMB (2012).

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Group Members

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Prof. Dr. Peter Vermathen, Group Leader
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Karin Zwygart-Brügger, Technician
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Christine Bolliger, PhD Student (until Apr.)
Andreas Boss, PhD Student (until May)
Vaclav Brandejsky, PhD Student (until Apr.)
Gaëlle Diserens, PhD Student
Sila Dokumaci, PhD Student
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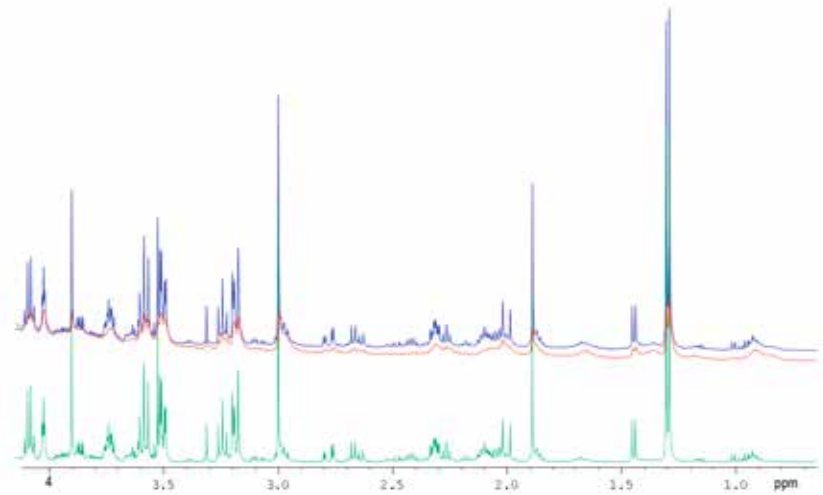
Grants

Amounts allocated for 2013:

- SNF: Multi-nuclear magnetic resonance spectroscopy (MRS) and imaging (MRI) on a clinical whole-body MR-system: Insulin resistance, ageing, and physical activity. Follow-up grant: Multi-nuclear magnetic resonance spectroscopy (MRS) and imaging (MRI) on a clinical whole-body MR-system: Lipid organelles and mitochondria (both C. Boesch) CHF 79,295
- SNF: Magnetic Resonance Techniques to Investigate Human Brain Physiology: Acquisition and Postprocessing Tools to Advance Spectroscopy at Clinical and High Magnetic Fields (R. Kreis) CHF 87,000
- SNF: Advanced multi-modal MR Imaging and Spectroscopy for Comprehensive Characterization of Renal Function in Native and Transplanted Kidneys (P. Vermathen) CHF 118,260
- European Commission: TRANSACT-ITN (R. Kreis) CHF 23,864



Five Selected Publications

On the use of Cramer-Rao minimum variance bounds for the design of magnetic resonance spectroscopy experiments. Bolliger, CS; Boesch, C; Kreis, R (2013) in: Neuroimage, 83, p. 1031-1040.

Magnetization exchange observed in human skeletal muscle by non-water-suppressed proton magnetic resonance spectroscopy. Macmillan, EL; Boesch, C; Kreis, R (2012) in: Magn Reson Med, 70(4), p. 916-924.

Does normalized signal intensity of cervical discs on T2 weighted MRI images change in whiplash patients? Ulbrich, EJ; Anon, J; Hodler, J; Zimmermann, H; Sturzenegger, M; Anderson, SE; Boesch, C (2013) in: Injury, e-pub ahead of print: doi: 10.1016/j.injury.2013.11.009.

Living Renal Allograft Transplantation: Diffusion-weighted MR Imaging in Longitudinal Follow-up of the Donated and the Remaining Kidney. Eisenberger, U; Binser, T; Thoeny, HC; Boesch, C; Frey, FJ; Vermathen, P in: Radiology, e-pub ahead of print, doi: 10.1148/radiol.13122588.

Coffee consumption attenuates short-term fructose-induced liver insulin resistance in healthy men. Lecoultre, V; Carrel, G; Egli, L; Binnert, C; Boss, A; MacMillan, EL; Kreis, R; Boesch, C; Darimont, C; Tappy, L in: Am.J.Clin.Nutr., e-pub ahead of print, doi: 10.3945/ajcn.113.069526.

Nephrology and Hypertension

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Research Highlights 2013 / Outlook 2014

2013 was a year of transition for our department. With the arrival of the Clinical Pharmacology Group (based in Basel and Bern), led by Prof. Krähenbühl, knowledge in drug action and toxicity, realisation of phase I clinical studies and aspects of energy metabolism in experimental animals and humans were gained. The laboratory Head, Prof. Frey, retired at the end of September and was replaced by PD Dr. Escher. In addition to her work on cholesterol reverse transport, she is adapting gas chromatography and mass spectrometry methods for the quantification of bile acids and oxysterols in human sera and mice tissues.

The Vogt Group investigates renal mechanisms leading to sodium retention during decompensated cirrhosis, especially changes occurring in single renal tubules. A lot of effort is being invested in developing in vitro microperfusion, a method established only in two other laboratories in the world, for the analysis of the movements of ions across the isolated nephron segment.

The Fuster Group strives to elucidate the physiological and pathophysiological roles of sodium/proton exchangers and the plasma membrane proton pump (V-ATPase) in the kidney, bone and endocrine pancreas. In a study published in *PNAS* this year, the group showed that the sodium/proton exchanger NHA2 is a critical player for insulin secretion in β-cells.

The Huynh-Do Group analyses Eph receptors and ephrin signalling in healthy and disease states. They unravelled important signalling pathways downstream of the oncogenic and angiogenic EphB1 and EphA2 receptors, and also showed that EphB4 signalling is central for maintenance of podocyte homeostasis during acute Thy1 nephritis. The establishment of an intra-uterine growth restriction model to study kidney development in the mouse is ongoing.

The Mohaupt Group focussed on the regulation of aldosterone production in pregnancy and preeclampsia via VEGF signalling and sFlt-1. They demonstrated that the aldosterone-sodium relationship is desensitised in pregnancy, as is blood pressure control. They are currently analysing factors affecting blood pressure and renal function in the Swiss population, and trying to understand the protective mechanisms in pregnancy to overcome the proatherosclerotic effect of high aldosterone levels.

PD Dr. Pasch received the "Heuberger Winterthur Young Entrepreneur Award" for the development of a test to measure calcification propensity of patient serum in vitro. His group investigates the calcification prevention mechanism of sodium thiosulfate, a compound that has been shown to prevent the development of vascular calcifications in uremic rats and haemodialysis patients.

The Uehlinger Group estimated red blood cell life span using carbon monoxide content of exhaled end-expiratory air and biotinylated red blood cells in normal subjects and patients on renal replacement therapy. Preparation of a clinical multicentre trial to test a new vascular access for dialysis (bone anchored port) is ongoing.

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Jahnen-Dechent W, Pecks U, RWTH Aachen University, Germany
Karlsson M, University of Uppsala, Sweden
Karumanchi S, Harvard Medical School, USA
Lingappa V, University of Mysore, India
Swiss Systemic Lupus Erythematosus Cohort, Switzerland
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Studied medicine at University of Bonn (DE). Postdocs at University of Erlangen-Nuremberg (DE) (1991-1992, 1994-1997), University of Florida, Gainesville (US) (1992-1994) and University of Bern (1997-2001). Lecturer, University of Bern (2001-2004). Visiting Professor at University of Nottingham (UK) and BIDMC Harvard Medical School, Boston (US) (2009). Since 2005, Group Leader, Inselspital.

PD Dr. Andreas Pasch
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MD (2000) at University of Tübingen (DE). Internal medicine resident at Bruderholz Cantonal Hospital (2000-2001, 2002-2004). Postdoc (2001-2002) at Children's Hospital Freiburg (DE). Resident and postdoc (2004-2007); Attending Physician Nephrology (2007-2010), Inselspital. Postdoc (2010-2011) at RWTH Aachen University (DE). Since 2011, Attending Physician, Inselspital. Venia docendi at University of Bern (2012).

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Studied medicine at University of Bern. Research stays in the USA at E. Squibb & Sons Ltd, Princeton (1987) and University of California, San Francisco (1989-91), and in Sweden at University of Uppsala (2008). Since 2008, Head Physician, Blood Purification Methods, Inselspital.

Schütz D, Cendres+Métaux, Switzerland
Scolari F, University of Brescia, Italy
Smith E, Monash University, Australia
Sviridov D, Baker IDI, Australia
Swiss Transplant Cohort Study, Switzerland
Van Goor H, University of Groningen, The Netherlands
Weitz G, AlloCyte Pharmaceuticals AG, Switzerland

Grants

Amounts allocated for 2013:

- SNF: Sodium retention in cholestatic mice (B. Vogt) CHF 90,000
- SNF: Functional MRI and kidney (M. Burnier, B Vogt) CHF 190,000
- SNF: Molecular mechanisms of mitochondrial toxicity of drugs (S. Krähenbühl) CHF 100,000
- SNF: Statin-induced skeletal muscle toxicity: role of statin transport into myocytes and of the IGF-1R signaling pathway (S. Krähenbühl) CHF 120,000
- SNF: Is Fetal and Placental Size, Blood Pressure and Overall Pregnancy Outcome Determined by Aldosterone Production and Salt Intake (M. Mohaupt) CHF 150,000
- SNF: Blood pressure and the kidney: interface between genes and environment (M. Bochud, M. Mohaupt) CHF 200,000
- SNF: Red blood cell survival in patients with renal failure – assessment and therapy modelling implications (D. Uehlinger) CHF 70,000
- SNF: Quest for biological function (D. Fuster) CHF 96,000
- SNF: NCCR Kidney.CH (F. Verrey, B. Vogt, D. Fuster, U. Huynd-Do, A. Pasch) CH 325,000
- SNF: NCCR TransCure (M. Hediger, B. Vogt, D, Fuster) CHF 210,000
- CTI: C-Terminal Agrin Fragments as novel renal biomarkers to improve patient care (U. Huynh-Do, C. Wagner, S. Hettwer) CHF 80,000
- CTI: Eine neue Klasse von Oligonucleotidpräparaten zur Behandlung der Duchenne Muskeldystrophie (B. Frey-von Matt) CHF 145,000
- CTI: LFA1 inhibitors (G. Weitz, S. Krähenbühl) CHF 80,000
- CTI: Clinical study as a prerequisite for the commercial launch of the Novel Body Access (D. Uehlinger) CHF 70,000
- Amgen AG: EVOLVE (A. Pasch) CHF 20,000
- Professor Dr Max Cloëtta Foundation: Medical Research Position Award (D. Fuster) CHF 115,000
- European Commission: IKPP-CO-FUND (U. Huynh-Do) CHF 453,300

Five Selected Publications

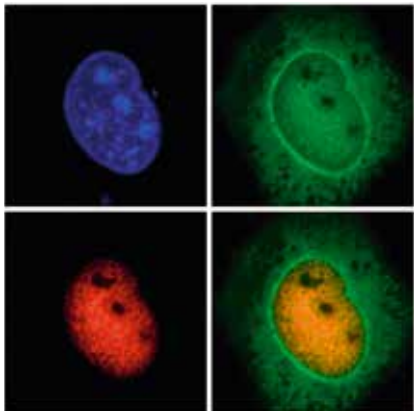
Sodium/hydrogen exchanger NHA2 is critical for insulin secretion in beta-cells. Deisl, C et al. (2013) in: Proc Natl Acad Sci U S A, 110(24), p. 10004-10009.

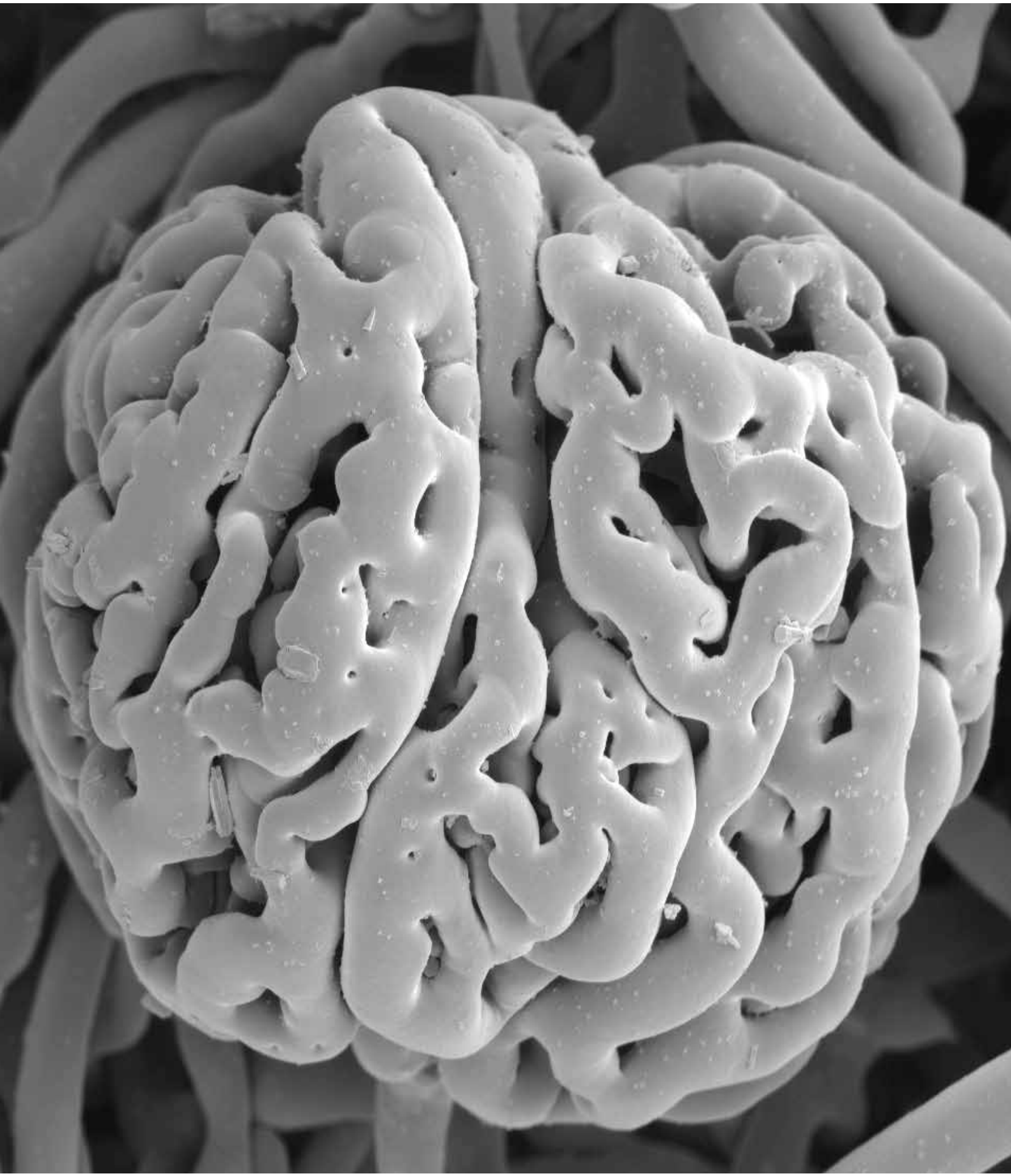
Vascular endothelial growth factor-A and aldosterone: relevance to normal pregnancy and preeclampsia. Gennari-Moser, C et al. (2013) in: Hypertension, 61(5), p. 1111-1117.

Effect of dark chocolate on renal tissue oxygenation as measured by BOLD-MRI in healthy volunteers. Pruijm, M et al. (2013) in: Clin Nephrol, 80(3), p. 211-217.

Phosphatase and tensin homolog regulates stability and activity of EphB1 receptor. Rodriguez, S and Huynh-Do, U (2013) in: FASEB J, 27(2), p. 632-644.

Evidence for a role of sterol 27-hydroxylase in glucocorticoid metabolism in vivo. Vogeli, I et al. (2013) in: J Endocrinol, 219(2), p. 119-129.





Neurology

www.neuro-bern.ch
www.dkf.unibe.ch/forschungsgruppe/14/

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MD at University of Basel (1985); neurology residency in Bern/Lausanne. FMH certification (1992). Research fellowships in neurophysiology (1985-1986) at University of Basel and sleep medicine (1995-1996) at University of Michigan, Ann Arbor (US). Venia docendi (1997). Professor and Vice-Chair of Neurology, University Hospital Zurich (2001-2009). Director, Neurocenter of Southern Switzerland (2009-2011). Since 2012, Full Professor of Neurology, Chair, Department of Neurology, Inselspital.

Prof. Dr. Antoine Adamantidis
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PhD (2005) at University of Liege (BE). Postdoc (2006-2010) at Stanford University School of Medicine, Palo Alto (US). Since 2010, Assistant Professor, Department of Psychiatry, Douglas Mental Health University Institute, McGill University, Montreal (CA). Since 2013, Assistant Professor, Department of Neurology, Inselspital.

Research Highlights 2013 / Outlook 2014

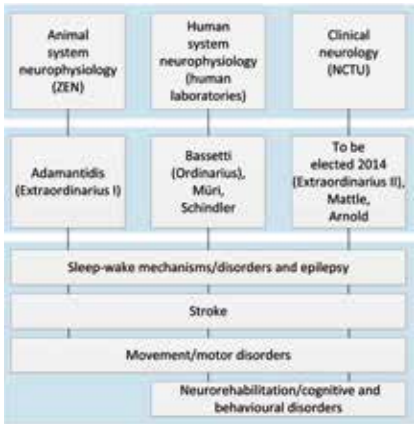
The main research approaches and topics of the Department of Neurology are shown in the figure below. Additional research groups are active in the areas of multiple sclerosis, muscle disorders, autonomic disorders, headache, and vestibular disorders. The main research platforms include the Center for Experimental Neurology (Zentrum für experimentelle Neurologie; ZEN), Human Neurophysiology Laboratories, Perception and Eye Movement Laboratory, and the newly created Neuro-Clinical Trial Unit (NCTU).

Highlights 2013

- Prof. Adamantidis was selected by the Faculty of Medicine for the newly created tenure track assistant professorship in system neurophysiology and joined the department in December 2013, where he now directs the ZEN. The main goal of his research is to understand the dynamics of the neural circuit controlling sleep and wake states, to delineate brain wiring and functions. To achieve this, molecular tools are combined with in vitro and in vivo electrophysiology to optogenetically control genetically targeted cell populations in the mouse brain.
- The renovation and enlargement of the ZEN was completed. It now includes a new molecular laboratory, rat and mice sleep recording facilities, and an animal functional assessment room.
- The Sleep and Epilepsy Group founded a research network ("Bern Network for Epilepsy Sleep and Consciousness", BENESCO), which currently includes teams from Bern, Fribourg, Solothurn, and Lugano. The group received two new SNF grants.
- The Stroke Group published a multicentre international randomised trial on stroke prevention in patent foramen ovale in the *N Engl J Med*. The Stroke Unit was opened and the Stroke Center was certified in the field of highly specialised medicine. The first animal stroke experiments were performed. The group received one new SNF grant.
- Dr. Schüpbach of the Movement/Motor Disorders Group published a study in the *N Engl J Med* on the favourable effect on outcome of deep brain stimulation also in patients with early-stage Parkinson's disease. A new human electroneuromyography (ENMG) laboratory/centre was opened.
- The Neurorehabilitation/Cognitive and Behavioral Disorders Group started two new projects in the framework of the Center for Cognition, Memory, and Learning (CCLM). They intensified their collaboration with the ARTORG Gerontechnology and Rehabilitation Group in the field of higher visual functions.

Outlook 2014

- Prof. Kaelin was selected as the new director of the Neurocenter of Southern Switzerland. His experimental animal group studying levodopa-induced dyskinesias in rats will move with him. Dr. Schüpbach will replace him as group leader.
- The ZEN will be enlarged by two additional rooms for optogenetics research.
- The NCTU team will hire a clinical study coordinator and a biostatistician.
- The new Human Sleep-Wake and Epilepsy Center should be completed. A multichannel near-infrared-spectroscopy (NIRS) and a high density EEG machine will be acquired.



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MD (1994) at University of Bern; neurology residency in Bern, FMH certification (2000). Research fellowships in clinical neurology at Lariboisière Hospital, Université Paris VII (FR) (2005). Venia docendi (2007). Since 2010, Associate Professor of Neurology; since 2012, Co-Chair, Stroke Center, Department of Neurology, Inselspital.

Prof. Dr. Alain Kaelin
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MD (1991) at University of Bern; neurology residency in Bern. FMH certification (1997). Fellowship (1999-2001) in movement disorder and neurophysiological research at National Institute of Neurological Disorders and Stroke, Bethesda, (US). Venia docendi (2004). Since 2008, Senior Attending and Head, Movement Disorders Center, Department of Neurology, Inselspital; Associate Professor (2012).

Prof. Dr. Heinrich Mattle
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MD (1976) at University of Zurich; neurology residency in Zurich. FMH certification (1985). Fellowships in neuroradiology (1988-1990) at Harvard University, Boston (US). Venia docendi (1990). Since 1990, Vice-Chair, Department of Neurology, Head of Outpatient Clinics, Founder and Co-Chair of Stroke Center, Inselspital; Associate Professor (1996).

Group Members

Sleep-Wake Mechanisms/Disorders and Epilepsy Group
Prof. Dr. Claudio L. Bassetti, Group Leader
Prof. Dr. Antoine Adamantidis, Group Leader (since Dec.)
Prof. Dr. Kaspar Schindler, Senior Consultant, Group Leader (since July)
Prof. Dr. Johannes Mathis, Senior Consultant
Dr. Heidemarie Gast, Consultant
PD Dr. Arto Nirkko, Consultant
Dr. Lino Nobili, External Consultant
Dr. Thomas Horvath, Research Assistant
Dr. Andreas Steimer, Physicist
Dr. Francesca Baracchi, Postdoctoral Fellow
Dr. Ertugrul Cam, Postdoctoral Fellow
Dr. Bo Gao, Postdoctoral Fellow
Dr. Svitlana Palchykova, Postdoctoral Fellow
Dr. Frédéric Zubler, Postdoctoral Fellow
Aleksandra Hodor, PhD Student
Maria Pace, PhD Student

Movement/Motor Disorders Group
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Prof. Dr. Mathias Sturzenegger, Senior Consultant
Dr. Michael Schüpbach, Consultant
Prof. Dr. Claudio L. Bassetti
Dr. Niklaus Meier, Consultant
Prof. Dr. Jean-Marc Burgunder, External Consultant
Dr. Christine Capper-Loup, Postdoctoral Fellow
Susanne Sgroi, PhD Student

Stroke Group
Prof. Dr. Heinrich Mattle, Group Leader
Prof. Dr. Marcel Arnold, Senior consultant, Group Leader
Prof. Dr. Claudio L. Bassetti
Prof. Dr. Werner Z'Graggen, Senior Consultant
PD Dr. Urs Fischer, Consultant
Dr. Oliver Findling, Consultant
Dr. Aikaterini Galimanis, Consultant
Dr. Simon Jung, Consultant
Dr. Marie-Louise Mono, Consultant
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Neurorehabilitation/Cognitive Disorders Group
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Dr Tim Vanbellingen, Postdoctoral Fellow
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Rahel Schumacher, PhD Student

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Lammers GJ, Leiden University Medical Centre, The Netherlands
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Medical school at University of Bern (1989-1995); National MD-PhD programme, Institute of Neuroinformatics, ETH Zurich and University of Zurich (1996-1999); Doctorates at Faculty of Mathematics/Natural Sciences (PhD) and Medical Faculty (MD), University of Zurich (1999). Research Fellow (2006-2007) at Epileptology Center, University of Bonn (DE). Venia docendi (2010). Since 2013, Associate Professor and Head of Epilepsy Center, Department of Neurology, Inselspital.

Thaler D, Kent D, Tufts Medical Center, USA
Tafti M, Franken P, University of Lausanne, Switzerland

Grants

Amounts allocated for 2013:
(SNF grants only)

- SNF: Sleep apnea and stroke, human (C. Bassetti) CHF 200,000
- SNF: Restless leg and cardiovascular risk, human/animal (M. Manconi, C. Bassetti) CHF 100,000
- SNF: Swiss study of initial decompressive craniectomy versus best medical treatment of spontaneous supratentorial intracerebral hemorrhage (SWITCH), human (U. Fischer) CHF 174,000
- SNF: Cerebral perfusion, vasospasm, subarachnoid hemorrhage, human (J. Beck, W. Z'Graggen) CHF 120,000
- SNF: Aphasia and co-speech gestures, human (R. Müri) CHF 146,000
- SNF: Bilingualism, human (J.-M. Annoni, R. Müri) CHF 100,000
- SNF: Fatigue in autommune diseases, animal (A. Fontana, H. Gast) CHF 50,000
- SNF: Motion and spatial neglect, human (T. Nyffeler, R. Müri) CHF 108,000
- SNF: Enhancement of sensory processing by attention, human (R. Ptak, R. Müri) CHF 110,000
- SNF: Neural basis of praxis production, human (S. Bohlhalter, R. Müri) CHF 110,000
- SNF: Etiology, diagnosis, treatment of cervicocerebral artery dissections, human (M. Arnold) CHF 650,000
- SNF: Imaging large scale neuronal networks in epilepsy, human (M. Seeck, K. Schindler) CHF 115,000

Five Selected Publications

Sleep deprivation before stroke is neuroprotective: a pre-ischemic conditioning related to sleep rebound. Cam, E; Gao, B; Imbach, L; Hodor, A; Bassetti, CL (2013) in: Exp Neurol, 247, p. 673-679.

Synchronization and desynchronization in epilepsy: controversies and hypotheses. Jiruska, P; de, CM; Jefferys, JG; Schevon, CA; Schiff, SJ; Schindler, K (2013) in: J Physiol, 591(4), p. 787-797.

Factors that determine penumbral tissue loss in acute ischaemic stroke. Jung, S; Gilgen, M; Slotboom, J; El-Koussy, M; Zubler, C; Kiefer, C; Luedi, R; Mono, ML; Heldner, MR; Weck, A; Mordasini, P; Schroth, G; Mattle, HP; Arnold, M; Gralla, J; Fischer, U (2013) in: Brain, 136(12), p. 3554-3560.

Percutaneous closure of patent foramen ovale in cryptogenic embolism. Meier, B; Kalesan, B; Mattle, HP; Khattab, AA; Hildick-Smith, D; Dudek, D; Andersen, G; Ibrahim, R; Schuler, G; Walton, AS; Wahl, A; Windecker, S; Juni, P (2013) in: N Engl J Med, 368(12), p. 1083-1091.

Neurostimulation for Parkinson's disease with early motor complications. Schuepbach, WM; Rau, J; Knudsen, K; Volkmann, J; Krack, P; Timmermann, L; Halbig, TD; Hesekamp, H; Navarro, SM; Meier, N; Falk, D; Mehdorn, M; Paschen, S; Maarouf, M; Barbe, MT; Fink, GR; Kupsch, A; Gruber, D; Schneider, GH; Seigneuret, E; Kistner, A; Chaynes, P; Ory-Magne, F; Brefel, CC; Vesper, J; Schnitzler, A; Wojtecki, L; Houeto, JL; Bataille, B; Maltete, D; Damier, P; Raoul, S; Sixel-Doering, F; Hellwig, D; Gharabaghi, A; Kruger, R; Pinsker, MO; Amtage, F; Regis, JM; Witjas, T; Thobois, S; Mertens, P; Kloss, M; Hartmann, A; Oertel, WH; Post, B; Speelman, H; Agid, Y; Schade-Brittinger, C; Deuschl, G (2013) in: N Engl J Med, 368(7), p. 610-622.


DELL
HEKA

Nuclear Medicine

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MD (1979) at Freiburg medical school (DE). Residencies in pathology, internal medicine, radiology and nuclear medicine (1979-1992). Vice-Chair at Departments of Nuclear Medicine, University Hospital Freiburg (DE) (1993-1999) and Bonn (DE) (2000-2001). Since 2001, Chair, Department of Nuclear Medicine, Inselspital. Since 2013, President, Swiss Society of Nuclear Medicine.

PD Dr. Martin A. Walter
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Training in medical schools of London (UK), Zurich and Münster (DE) (1995-2001). Residencies in nuclear medicine and endocrinology, University Hospital Basel (2002-2007). Research Fellow (2007-2009) at Department of Pharmacology, UCLA (US). Attending Physician at University Hospital Basel (2009-2010). Since 2010, Attending Physician and Head of Nuclear Medicine Research, DCR; Assistant Professor at Department of Pharmacology, UCLA.

Research Highlights 2013 / Outlook 2014

The development and optimisation of radioactive tracers for cancer imaging and treatment is the main focus of our research group. One of our major tenets is performing research driven by true clinical demand. Towards this aim, our group comprises chemists, biochemists, biologists and medical doctors, working closely together during the entire development process.

In 2013, we established laboratories for the synthesis of new tracers at the Department of Chemistry. At Haller-Haus we set up a radiochemistry laboratory for radioactive labelling of these compounds and a biology laboratory for their in vitro evaluation. To allow long-term in vivo studies, we are currently building an animal housing system. Finally, within the Nuclear Medicine Routine Laboratories at the INO building, we set up two GMP-conform sterile flow benches for the clinical translation of new radiotracers.

In our chemistry laboratories, Dr. Grotzky developed a class of imaging molecules carrying more than a thousand-fold the radioactivity of molecules currently used in the clinic. In parallel, Dr. Olariu developed multi-functional radioactive gold nanoparticles, which can be used for various purposes, e.g., tumour imaging and in vivo cell tracking. Finally, Dr. Meier worked on optimising tumour targeting of gold-based nanoparticles.

In the biochemistry laboratories, Dr. Cescato developed systems for controlled drug delivery with our nanoparticle platforms, enabling simultaneous targeted application of radioactivity and medication. In parallel, Dr. Taelman worked on stimulating the expression of various target molecules to improve the uptake of our radiotracers into the tumour cell. Meanwhile, his project has successfully passed all in vitro and in vivo tests, and together with our collaborators, Christoph Stettler and Aurel Perren, we are preparing a clinical translation at the Inselspital for 2014.

Our two clinicians, Dr. Radojewski and Dr. Marincek supported the entire research group by performing all the animal experiments in our new facilities, while also working on their own clinical research projects.

Finally, our epidemiologist, Dr. Gloy, is performing a systematic review and meta-analysis on the toxicity profile of radioiodine. With over 17,000 abstracts and 3,300 full papers screened, this is one of the largest systematic reviews ever performed. This huge project made fast progress in 2013. It is performed in collaboration with groups from Bern, Basel and Aarau, and is funded by the Federal Office of Public Health.

With all the exciting projects mentioned above, we expect 2014 to be a very fruitful year. First, we will take full advantage of our new infrastructure by extensively evaluating the variety of our new compounds in vitro and in vivo. Then, we expect the results from one of the largest systematic reviews ever performed. Finally, we are looking forward to the first clinical translation of a new imaging and treatment approach developed in Bern. Our entire group is grateful to all our collaborators and supporters who made these exciting projects possible.

Group Members

Prof. Dr. Thomas Krause, Chair
PD Dr. Martin A. Walter, Group Leader
Dr. Renzo Cescato, Postdoctoral Fellow
Dr. Viktoria Gloy, Postdoctoral Fellow
Dr. Andrea Grotzky, Postdoctoral Fellow
Dr. Lorenz Meier, Postdoctoral Fellow
Dr. Cristina Olariu, Postdoctoral Fellow
Dr. Vincent Taelman, Postdoctoral Fellow
Dr. Nicolas Marincek, House Staff
Dr. Piotr Radojewski, House Staff

Collaborators

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Czernin J, University of California, Los Angeles, USA
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Rochlitz C, University Hospital Basel, Switzerland
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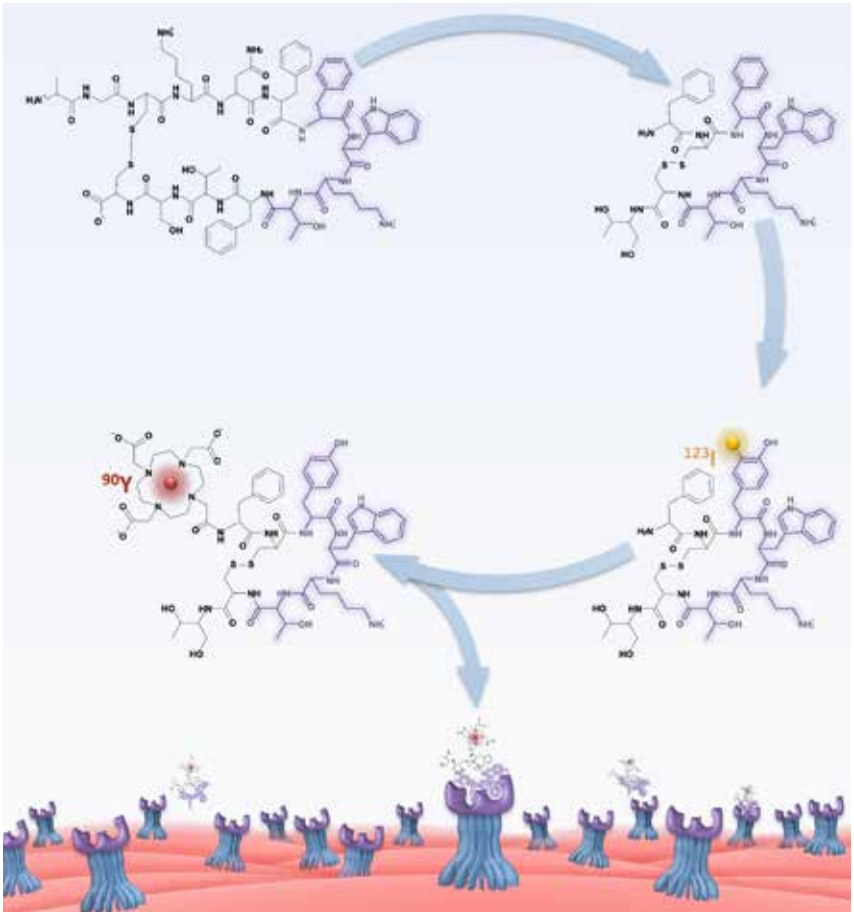
Grants

Amounts allocated for 2013:

- SNF Ambizione: Somatostatin-coupled Nanoparticles for Cancer Imaging and Therapy (M. Walter) CHF 102,000
- Bernese Cancer League: A Gold-198 based Nanoparticle Platform for the Treatment of Neuroendocrine Cancers (M. Walter) CHF 51,000
- Opo-Foundation: Drug-based stimulation of somatostatin receptor expression (M. Walter) CHF 30,000
- CTI: Polymeric Nanogels for Targeted Cancer Imaging (M. Walter) CHF 284,000



- Oncosuisse/Cancer League: A Multifunctional Nanoparticle Platform for Combined Radiotherapy and Targeted Delivery of Sirolimus (M. Walter) CHF 166,000
- Ruth & Arthur Scherbarth-Foundation: Polymeric Nanogels for Molecular Targeted Cancer Imaging (M. Walter) CHF 30,000
- Stiftung zur Krebsbekämpfung: Instrumentation funds for Laboratory Equipment (M. Walter) CHF 49,000
- Federal Office of Public Health (BAG): Safety Profile of Radioiodine Therapy (SPRINT): Systematic Review and Meta-Analysis (M. Walter) CHF 55,000
- Gebauer Stiftung: Instrumentation Funds for Laboratory Equipment (M. Walter) CHF 83,000

Five Selected Publications

Somatostatin-based radiotherapy with [90Y-DOTA]-TOC in neuroendocrine tumors: long-term outcome of a phase I dose escalation study. Marincek, N et al. (2013) in: J Transl Med, 11, p. 17.

Somatostatin-based radiopeptide therapy with [(177)Lu-DOTA]-TOC versus [(90)Y-DOTA]-TOC in neuroendocrine tumours. Romer, A et al. (2014) in: Eur J Nucl Med Mol Imaging, 41(2), p. 214-222.

1,2,3-Triazoles as amide bond mimics: triazole scan yields protease-resistant peptidomimetics for tumor targeting. Valverde, IE et al. (2013) in: Angew Chem Int Ed Engl, 52(34), p. 8957-8960.

Cohort study of somatostatin-based radiopeptide therapy with [(90)Y-DOTA]-TOC versus [(90)Y-DOTA]-TOC plus [(177)Lu-DOTA]-TOC in neuroendocrine cancers. Villard, L et al. (2012) in: J Clin Oncol, 30(10), p. 1100-1106. Featured in: (2012) Nat Rev Clin Oncol, 9(5), p. 250.

Practical Guidance on Peptide Receptor Radionuclide Therapy (PRRNT) for Neuroendocrine Tumours. Bal, CS et al. (2013) in: International Atomic Energy Agency, IAEA Human Health Series No. 20.

Ophthalmology

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PhD in engineering (1988) and MD (1990) at RWTH Aachen (DE). Lecturer (1992-1993) at Schepens Eye Research Institute, Boston (US). Board certification in Ophthalmology (1994). Venia docendi (1995). Professor for Ophthalmology at University of Leipzig (DE) (1999-2004). Since 2005, Chair, Department of Ophthalmology, Inselspital.

Research Highlights 2013 / Outlook 2014

In 2013, research continued in a number of projects, including retinal degeneration, pathophysiology and stem cell-based endogenous and exogenous regeneration. The ultimate goal is to thereby achieve better understanding and possible treatment of age-related macular degeneration (AMD) and retinitis pigmentosa (RP). The main focus in the last year was on the development of a zebrafish-based retinal degeneration/regeneration model using the photoreceptor-specific toxin N-methyl-N-nitrosourea (MNU) to pharmacologically induce the degeneration. Visual acuity measurements, and histological and immunohistochemical staining for apoptosis and proliferation were performed. A characteristic sequence of retinal changes was observed: Apoptosis of photoreceptors occurred three days after MNU treatment, resulting in a significant photoreceptor cell loss. Consequently, proliferation was seen in the inner and outer nuclear layer. Not only a complete histological but also a functional regeneration occurred within 30 days after the initial treatment. In 2014, we will intensify this research to characterise the underlying pathways and, especially, to identify differences and similarities to the mouse, where the same degeneration model exists. This might give us the possibility to actively modulate endogenous regeneration in the mammalian retina.

In the macular pigment (MP) project, we investigate the treatment of age-related maculopathy patients with dietary supplementation to increase MP density and consequently modify the natural course of the disease. A study using two-wavelength retinal autofluorescence measurements has started with 500 patients. The estimated primary completion date is December 2015.

Additionally, we initiated research in retinal vein occlusion (RVO), a common vascular disorder of the retina with controversial pathogenesis. It is the occurrence of macular oedema in RVO that most frequently leads to visual loss. Significantly elevated vitreous levels of soluble cytokines have been found in vitreous samples of patients suffering from RVO. Our group established a mouse model of RVO using laser photocoagulation to produce thrombosis within the targeted retinal vein. By means of fluorescein angiography and optical coherence tomography, we were able to describe the time course of retinal vein occlusion in the mouse in vivo. Furthermore, we were able to show invasion and activation of macrophages and microglia in the affected areas of the retina. In 2014, we are planning to quantify macrophage influx into the retina and to qualitatively describe processes by FACS analysis. Moreover, investigation of the role of CCL5, CCL7, IL-6, IL-8, and VEGF in this experimental RVO model is pending. CX3CR-GFP+/+ mice will be used to elucidate the origin of the activated antigen-presenting cells in the retina in this model. Ultimately, a better understanding of the contribution of the innate immune system to the pathophysiology of RVO may provide clues to alternative treatment modalities.

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PhD in cell biology (1995) and postdoc (1995-2000) at University of Leipzig (DE). Postdoc (2001-2005) and Assistant Professor (2005-2006) at University of Louisville (US). Since 2006, Head of Research, Department of Ophthalmology, Inselspital. Venia Docendi (2010).

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PD Dr. Martin Zinkernagel
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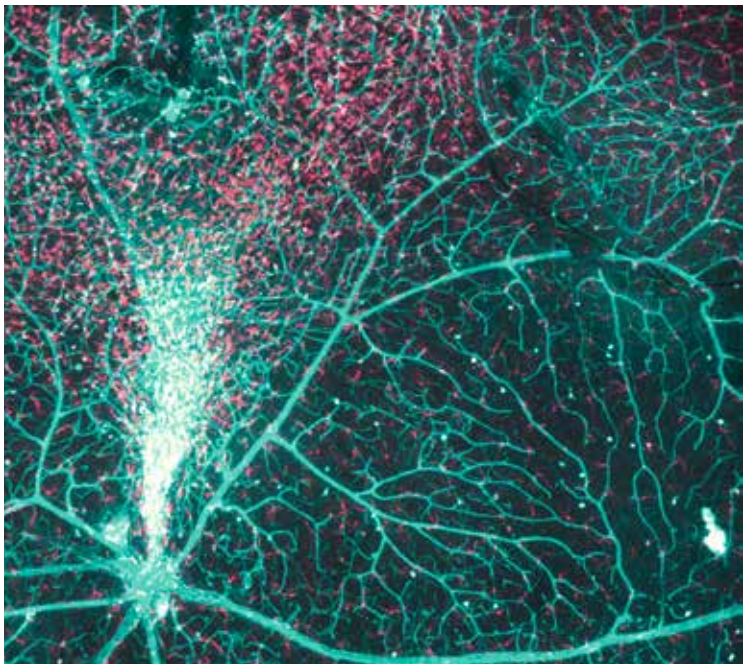

Group Members

Prof. Dr. Sebastian Wolf, Chair
PD Dr. Volker Enzmann, Head of Research, Group Leader
PD Dr. Ute Wolf-Schnurrbusch, Group Leader
PD Dr. Martin Zinkernagel, Group Leader
Dr. Andreas Ebneter, Research Associate
Dr. Markus Tschopp, Research Assistant
Federica Bisignani, Laboratory Technician
Agathe Duda, Laboratory Technician
Monika Kilchenmann, Laboratory Technician
Anita Zenger, Study Nurse
Dr. Cavit Agca, Postdoctoral Fellow (since Oct.)
Jasmin Balmer, PhD Student
Chantal Dysli, PhD Student
Muriel Dysli, PhD Student
Miriam Reisenhofer, PhD Student

Collaborators

Jazwinska A, University of Fribourg, Switzerland
Reichenbach A, University of Leipzig, Germany

Grants

Amounts allocated for 2013:

- SNF: The Role of Macular Pigment in Patients With Age-Related Macular Degeneration (S. Wolf) CHF 100,000
- Fritz Tobler Foundation: Endogenous regeneration capacity of the retinal Müller glia in the mammalian retina (V. Enzmann) CHF 40,800
- Inselspital (Lehre & Forschung): Role of the immune system in experimental vein occlusion (M. Zinkernagel) CHF 64,000
- Velux: Role of Macular Pigment (U. Wolf-Schnurrbusch) CHF 66,000
- Peter Mayor Gedächtnisstiftung: Exploring retinal degeneration and regeneration with the model organism zebrafish (M. Tschopp) CHF 13,000
- OPOS Foundation: Microglia in experimental retinal vein occlusion (A. Ebneter, M. Zinkernagel) CHF 100,000

Selected Publications

Presence of the Gpr179(nob5) allele in a C3H-derived transgenic mouse. Balmer, J; Ji, R; Ray, TA; Selber, F; Gassmann, M; Peachey, NS; Gregg, RG; Enzmann, V (2013) in: Mol Vis, 19, p. 2615-2625.

Three-year results of visual outcome with disease activity-guided ranibizumab algorithm for the treatment of exudative age-related macular degeneration. Lala, C; Framme, C; Wolf-Schnurrbusch, UE; Wolf, S (2013) in: Acta Ophthalmol, 91(6), p. 526-530.

Characteristics of rod regeneration in a novel zebrafish retinal degeneration model using N-methyl-N-nitrosourea (MNU). Tappeiner, C; Balmer, J; Iglicki, M; Schuerch, K; Jazwinska, A; Enzmann, V; Tschopp, M (2013) in: PLoS One, 8(8), p. e71064.

Detection of Chlamydia and complement factors in neovascular membranes of patients with age-related macular degeneration. Wolf-Schnurrbusch, UE; Hess, R; Jordi, F; Stuck, AK; Sarra, GM; Wolf, S; Enzmann, V (2013) in: Ocul Immunol Inflamm, 21(1), p. 36-43.

Prenatal Medicine

www.dkf.unibe.ch/research-group/19/

Prof. Dr. Daniel Surbek
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MD (1988) at University of Basel. Specialist in obstetrics and gynecology (1996). Visiting Scientist (1996) at Johns Hopkins University, Baltimore and Children's Hospital of Philadelphia (US). Research Fellow (2000) at Kings College Hospital London (UK). Sub-specialist in maternal-fetal medicine (2000). Habilitation at University of Basel (2002). Since 2005, Co-Chair and Full Professor of Obstetrics and Gynecology, Head of Obstetrics and Foeto-Maternal Medicine, Inselspital.

Dr. Andreina Schoeberlein
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MS in agriculture (1990), PhD in animal genomics (1993) at ETH Zurich. Postdocs in veterinary medicine, genetics (1994-1996) at University of Liège (BE) and cardiovascular surgery (1996-2001) at University Hospital Zurich. Research scientist at Laboratories for Prenatal Medicine, University Hospital Basel (2001-2005) and Inselspital (2005-2009). Since 2009, Co-Head, Laboratory for Prenatal Medicine, DCR; Group Leader, Stem Cell Research.

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MD at University of Geneva and Bern (1996); Research Fellow (2000-2002) at Perinatal Biology Group, University of Medicine and Dentistry, New Jersey (US). Specialist in obstetrics and gynecology, Inselspital (2010). Currently, Senior Fellow at Department of Obstetrics and Gynaecology, Inselspital and Co-PI, NCCR TransCure.

Research Highlights 2013 / Outlook 2014

Stem Cell Research

Cerebral palsy, with its severe lifelong disability, typically arises from oligodendrocyte damage due to preterm birth or birth asphyxia leading to periventricular leukomalacia. Our major research focus is on the development of peripartum stem cell transplantation strategies for neuroregeneration in peripartum brain damage due to hypoxia or preterm birth. We assessed the developmental plasticity of umbilical cord tissue-derived mesenchymal stem cells (MSC), and were recently able to show that these cells differentiate ex vivo into neural cell lines including oligodendrocyte precursors. In addition, MSC from preterm birth umbilical cord have an even higher differentiation potential. Currently, we are addressing the mechanism of immunomodulatory and neuroproliferative effects in culture models. To determine the effect and mechanism of stem cell-mediated neuroregeneration, we use a newborn rat model of combined peripartum hypoxic-inflammatory brain damage. Subcutaneous administration of *E.coli*-derived lippopolysaccharides followed by left carotid artery ligation and defined hypoxia (8% O_2, 40 min) was performed on early postnatal rats. Different therapeutic approaches were chosen, including neural stem cell and MSC transplantation, with or without erythropoietin (EPO) or preimplantation factor (PIF). Administration of stem cells alone and in combination with EPO reduced the extent of the damage, as assessed by immunohistochemistry. Functional tests show a significant reduction of unilateral spastic paresis. Current experiments aim to elucidate the neuroregenerative mechanism of MSC at different transplantation time points. This work is being carried out in collaboration with the DCR "Regenerative Neuroscience" Research Cluster (Enzmann/Grandgirard/Widmer).

Preeclampsia Research

Foetal programming in preeclampsia leads to cardiovascular and metabolic diseases in offspring later in life. This phenomenon and its prevention is a major focus of our project, which is part of the large SNF NCCR TransCure. In 2013, we assessed the role of specific transmembrane transporters (Glut1/3, Glut9, OAT4, SVCT2 and DMT1) in the placenta in the preeclampsia pathway. Transporter mRNA expression under specific conditions was determined. Transwell membrane assays, vesicle assays generated with human placental membranes, and patch clamp assays were used to determine functional transmembrane transport capacity. In addition, we set up an ex-vivo placental perfusion model to measure transport capacity. Currently, we are using a transgenic liver-specific Glut9-knockout mouse model to further examine mechanistic issues. In experiments in collaboration with chemists and structural biologists, we are testing potential compounds and their effects on preeclampsia pathogenesis and foetal programming.

Group Members

Prof. Dr. Daniel Surbek, Co-Chair, Head of Research
Dr. Andreina Schoeberlein, Co-Head of Research, Group Leader
Dr. Marc Baumann, Group Leader, Senior Fellow
Dr. Martin Müller, Research Associate
PD Dr. Luigi Raio, Research Associate, Senior Consultant
Dr. Arjun Jain, Postdoctoral Fellow (until Oct.)
Dr. Marianne Jörger-Messerli, Postdoctoral Fellow
Dr. Benjamin Lüscher, Postdoctoral Fellow
Judith Herbst, Research Midwife
Ursula Reinhart, Laboratory Technician
Ruth Sager, Laboratory Technician
Camilla Marini, PhD Student
Byron Oppliger, PhD Student
Ramesh Perjasamy, PhD Student (until Sep.)
Soleen Ghafoor, MD Student (until Mar.)
Prof. Dr. Henning Schneider, Research Associate (retired)

Collaborators

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Grants

Amounts allocated for 2013:

- SNF: NCCR TransCure sub-project (D. Surbek, M. Baumann) CHF 167,000
- SNF: Systemic vascular function in offsprings of preeclampsia (Y. Allemann, L. Raio) CHF 120,000
- Eagle Foundation: Perinatal stem cell transplantation for brain injury (D. Surbek, A. Schoeberlein) CHF 30,000
- Cryo-Save: Umbilical cord stem cells for neuroregeneration (D. Surbek, M. Messerli) CHF 50,000

Five Selected Publications

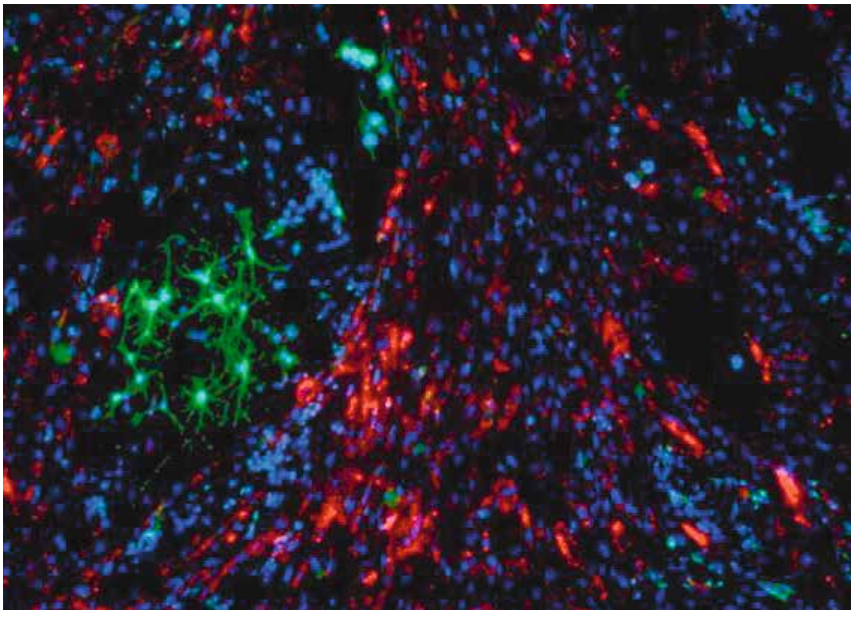
Placental ABCA1 and ABCG1 expression in gestational disease: pre-eclampsia affects ABCA1 levels in syncytiotrophoblasts. Baumann, M; Korner, M; Huang, X; Wenger, F; Surbek, D; Albrecht, C (2013) in: Placenta, 34(11), p. 1079-1086.

Stem cells from umbilical cord Wharton's jelly from preterm birth have neuroglial differentiation potential. Messerli, M; Wagner, A; Sager, R; Mueller, M; Baumann, M; Surbek, DV; Schoeberlein, A (2013) in: Reprod Sci, 20(12), p. 1455-1464.

High acceptance rate of hybrid allogeneic-autologous umbilical cord blood banking among actual and potential Swiss donors. Wagner, AM; Krenger, W; Suter, E; Ben, HD; Surbek, DV (2013) in: Transfusion, 53(7), p. 1510-1519.

Normotensive Blood Pressure in Pregnancy: The Role of Salt and Aldosterone. Gennari-Moser, C; Escher, G; Kramer, S; Dick, B; Eisele, N; Baumann, M; Raio, L; Frey, FJ; Surbek, D; Mohaupt, MG (2013) in: Hypertension, e-pub ahead of print: doi: 10.1161/01.hyp.36.2.149.

Use of human embryonic stem cells and umbilical cord blood stem cells for research and therapy: a prospective survey among health care professionals and patients in Switzerland. Wagner, AM; Krenger, W; Holzgreve, W; Burkli, P; Surbek, DV (2013) in: Transfusion, e-pub ahead of print: doi: 10.1111/trf.12137.



Radiation Oncology

www.dkf.unibe.ch/forschungsgruppe/21/

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MSc in biology (1988) at Tel Aviv University (IL). PhD (1994) and researcher (1994-1995) at Weizmann Institute (IL). Postdoc (1995-1996) at Ciba-Geigy, Basel. Research Associate (1997-2000) at Tel Aviv University. Since 2000, Head, Radiation Oncology Research Group, DCR. Venia docendi (2013).

PD Dr. Kathrin Zaugg
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MD (1992) at University of Zurich; PhD (2007) at University of Toronto (CA). Board exam in Radiation Oncology (1997). Fellowships in palliative care (2000) at Harvard Medical School, Boston (US) and radiation oncology (2000-2002) at Princess Margaret Hospital, Toronto (CA). Venia legendi (2012) at University of Zurich. Currently, Senior Consultant and Principal Investigator, Department of Radiation Oncology, Inselspital.

Research Highlights 2013 / Outlook 2014

Zimmer Group

The receptor tyrosine kinase MET is a major molecular target in clinical oncology. Our group primarily focuses on studying molecular mechanisms underlying tumour cells resistance to MET targeting, as well as MET signalling to pathways responding to DNA damage. With our continuing interest in the signalling crosstalk between MET and the DNA damage response, we finalised a discovery posttranslational proteomics study ("PTMScan"). It aimed to identify phosphorylation, ubiquitination and acetylation changes in tumour cells in response to the small molecule inhibitor EMD1214063, which is currently under clinical evaluations, combined with ionising radiation. In parallel to ongoing bioinformatics analysis, we also started a series of biological validations for some of the findings, using the SRM methodology (PhD project, Eleonora Orlando, co-supervision Y. Zimmer / R. Aebersold).

The PTMScan study identified a novel phosphorylation site on MET, which might play an important role in MET-related responses to DNA damage. A newly funded project aiming at the validation and investigation of the biological significance of phosphorylation at this site will start in 2014 (Medová). With respect to tumour cells radiosensitisation by MET targeting (emphasis on gastric carcinoma), we are currently finalising a study demonstrating senescence as a major biological endpoint of this combined treatment modality.

Finally, an extensive collaboration with Merck Serono focusing on genomic/transcriptomic studies in head and neck tumours was established (D. Aebersold / Y. Zimmer).

Zaugg Group

We utilise the discriminating characteristics of the tumour cell as a platform for designing novel therapies. Tolerance of chronic low oxygen environments (hypoxia) is a major distinguishing characteristic of the tumour cell in the body. Hand in hand with hypoxia tolerance is an alteration of the metabolism. It is our belief that increased efforts at understanding and intervening with the pathway(s) leading to hypoxia tolerance will provide anti-cancer therapies both on their own and in combination with radiotherapy.

We recently published a study identifying carnitine palmitoyltransferase 1C (CPT1C) as a novel p53 target gene in vitro and in vivo. CPT family members regulate the transport of free fatty acids into the mitochondria, where they get access to beta-oxidation. Loss of function of CPT1C was generated in mouse embryonic stem cells. Importantly, these cells readily succumbed to cell death under hypoxic conditions, whereas control cells were resistant. Using transient knock-down models for CPT1C, the same striking in vitro effect was found in different human cancer cell lines. Furthermore, using a murine tumour model (NF1/p53 heterozygotes), we found that loss of CPT1C leads to a significant increase in survival of these mice, strongly supporting our hypothesis that CPT1C plays a key role in carcinogenesis. The mechanism of action by which CPT1C protects cancer cells from hypoxia is currently under investigation.

Group Members

Prof. Dr. Daniel M. Aebersold, Chair

PD Dr. Yitzhak Zimmer, Head of Research, Group Leader
Dr. Michaela Medová, Senior Research Associate

Melanie Leuener Tombolini, Laboratory Technician (since May)
Bruno Streit, Laboratory Technician (until Aug.)
Paola Francica, PhD Student
Astrid Glück, PhD Student (since May)
Kei Mikami, PhD Student
Lluís Nisa, MD-PhD Student (since Jan.)
Eleonora Orlando, PhD Student (since Nov.)

PD Dr. Kathrin Zaugg, Group Leader (since Aug.)
Dr. Jianhua Feng, Senior Research Associate (since Aug.)
Ning Chang, PhD Student (since Aug.)

Collaborators

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Keogh-Stroka D, University of Bern, Switzerland
Mak T, University of Toronto, Canada
Rushing E, University Hospital Zurich, Switzerland
Tschan M, University of Bern, Switzerland

Grants

Amounts allocated for 2013:

- SNF: CPT1C as novel key regulator of cancer metabolism and carcinogenesis: deciphering mechanisms and signaling pathways (K. Zaugg) CHF 195,000
- SNF: The link between aberrant MET signaling and DNA repair pathways in liver tumor cells as a target for sensitization to DNA damaging agents (Y. Zimmer) CHF 100,000
- Swiss Cancer League: Dose-rate effect of novel radiation technologies: relevance for the clinical use (K. Zaugg) CHF 50,000
- Novartis Foundation: The link between aberrant MET signaling and DNA repair pathways in liver tumor cells as a target for sensitization to DNA damaging agents (Y. Zimmer) CHF 20,000
- Ruth & Arthur Scherbarth Foundation: The relevance of p53 status to the response of tumor cells to MET inhibitors and to their sensitization via MET targeting (M. Medová) CHF 10,000
- Stiftung Klinisch-Experimentelle Tumorforschung: MET signalling under hypoxic conditions: emphasis on tumor radioresistance (Y. Zimmer) CHF 61,400

Five Selected Publications

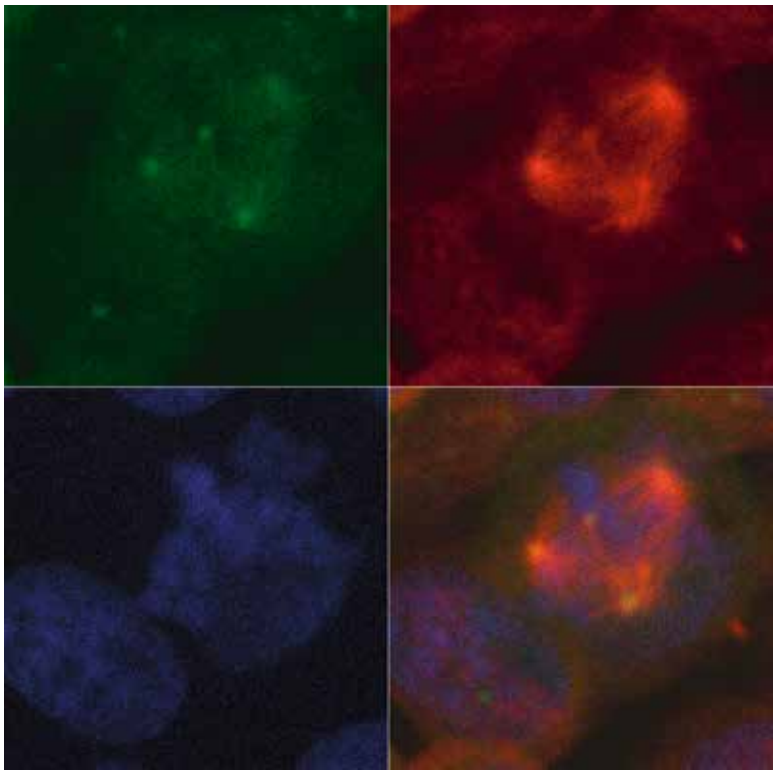
The Molecular Crosstalk between the MET Receptor Tyrosine Kinase and the DNA Damage Response-Biological and Clinical Aspects. Medová, M; Aebersold, DM; Zimmer, Y (2013) in: Cancers (Basel), 6(1), p. 1-27.

The novel ATP-competitive inhibitor of the MET hepatocyte growth factor receptor EMD1214063 displays inhibitory activity against selected MET-mutated variants. Medová, M et al. (2013) in: Mol Cancer Ther, 12(11), p. 2415-2424.

Depletion of the novel p53-target gene carnitine palmitoyltransferase 1C delays tumor growth in the neurofibromatosis type I tumor model. Sanchez-Macedo, N et al. (2013) in: Cell Death Differ, 20(4), p. 659-668.

Targeting of the MET receptor tyrosine kinase by small molecule inhibitors leads to MET accumulation by impairing the receptor downregulation. Leiser, D et al. (2013) in FEBS Lett, e-pub ahead of print: doi: 10.1016/j.febslet.2013.12.025.

Using state variables to model the response of tumour cells to radiation and heat: a novel multi-hit-repair approach. Scheidegger, S; Fuchs, HU; Zaugg, K; Bodis, S; Füchslin, RM (2013) in: Comput Math Methods Med, e-pub ahead of print: doi: 10.1155/2013/587543.



Thoracic Surgery

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MD at University of Zurich; Residency, Division of Surgery (1988-1994). Fellowship (1994-1995) at Department of Thoracic and Cardiovascular Surgery, Washington University Medical School, St. Louis (US). Staff Surgeon, Division of Surgery, University Hospital Zurich (1996-1999). Since 1999, Professor of Surgery, Chair, Department of Thoracic Surgery, Inselspital.

Research Highlights 2013 / Outlook 2014

Frese Group

We studied how lung cancer cells can be sensitised for receptor-mediated apoptosis. In another project, we discovered that low doses of the topoisomerase I inhibitor irinotecan (known for its use in chemotherapy of metastatic cancer) is able to efficiently suppress the autoimmune disease systemic lupus erythematosus in mice, which led to the initiation of a clinical study.

Hall Group

There is emerging evidence to suggest that the tumour (mesenchymal) microenvironment acts in concert with the cancer cell-centric changes driving tumour phenotype. We have recently identified rare mesenchymal stromal cells in primary human lung adenocarcinomas and are interested in how these cells promote tumour growth. Initially, mesenchymal stromal cells were shown to possess broad immunomodulatory properties. We postulate that these cells may act as key effectors in regulating the composition and function of infiltrating leukocytes within the tumour microenvironment, tipping the balance towards immunosuppression. Therefore, our aim is to use a combined pharmacological and genetic approach (patient-derived samples and inducible mouse models of human lung adenocarcinoma) to determine the potential of this tumour-derived mesenchymal subset to serve as a novel therapeutic target in lung cancer. In a second project, we are interested in identifying cell subsets that are critical for lung regeneration. To achieve this, we plan to utilise genetic fate mapping tools to identify cellular hierarchies in alveolar development and cell fate during injury and alveolar regeneration.

Marti and Peng Groups

Lung cancer is the most common cause of cancer-related mortality worldwide. More than 80% of lung tumours are non-small-cell lung cancers (NSCLC). It has been postulated that tumour initiation and propagation are mediated by so-called 'tumour-initiating cells' (TICs) that can self-renew and spawn differentiated progeny. The DNA damage response (DDR) is a complex signalling network that maintains genome integrity, essential for the proper function and survival of all organisms. We were able to identify TICs in cell lines and primary NSCLC samples. Subsequent analysis indicated that factors of the DDR and nucleotide synthesis pathways are deregulated in TICs. Our aim is to identify differentially regulated DDR factors in TICs compared to tumour bulk cells, which will subsequently allow us to identify novel targets for pharmacological or genetic intervention to treat lung cancer.

Resistance to chemotherapy is the major cause of therapeutic failure in NSCLC. Our previous findings indicate that chemotherapy resistance is linked to a subpopulation of cells with stem cell-like features, i.e. TICs. We plan to isolate chemotherapy-resistant cells from primary patient samples after exposure to chemotherapeutics used in the clinical setting. Characterisation of the selected subpopulation should provide insights into the mechanism of chemoresistance and lead to new therapeutic targets in NSCLC.

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MD at Friedrich-Schiller University of Jena (DE). Scholarship from Max-Planck Society. At DCR, University of Bern and Department of Thoracic Surgery, Inselspital (2000-2013); Staff Surgeon (2007-2013). Rotations to hospitals in Solothurn and Interlaken (2002-2006) while DCR Group Leader. DKF Research Prize (2003). Certification in General Surgery (2007); Venia docendi (2011).

Dr. Sean R.R. Hall
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PhD in Pharmacology and Toxicology at Queen's University (CA). Postdoc (2008-2010) at Brigham and Women's Hospital, Harvard Medical School (US). Senior Scientist (2011) at NeoStem Inc, Boston (US). Senior Scientist (2011-2012) at Erasmus Medical Center, Division of Transplantation and Intestinal Surgery, Rotterdam (NL). Since 2013, Group Leader, Department of Thoracic Surgery, Inselspital.

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PhD in biochemistry at Chinese Academy of Sciences, Beijing (CN). Research scientist (1998-2005) at Max Planck Institute, Göttingen (DE) and Visiting Scholar (1999) at Dartmouth Medical School (US). Group Leader at ETH Zurich (2006-2010). Since 2012, Group Leader, Department of Thoracic Surgery, Inselspital.

Group Members

Prof. Dr. Ralph A. Schmid, Chair
PD Dr. Steffen Frese, Group Leader (until Oct.)
Dr. Sean R.R. Hall, Group Leader (since Feb.)
Dr. Thomas M. Marti, Group Leader
Dr. Renwang Peng, Group Leader
Laurène Froment, Laboratory Technician
Selina Steiner, Laboratory Technician (until Dec.)
Dr. Gregor Kocher, Clinical Fellow
Andreas Keil, PhD Student
Liang Shunqing, PhD Student (since Sept.)
Colin Tièche, PhD Student (since Nov.)

Collaborators

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Nakatsu K, Queen's University, Canada
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Grants

Amounts allocated for 2013:

- DCR Grant-in-Aid: Role of immune preactivated mesenchymal stromal cells (MSCs) in reversing impaired lung immune function and subsequent chronic inflammation due to exposure to cigarette smoke (S. Hall) CHF 10,000
- Cancer League Canton Bern: Targeting tumor initiating cells in lung cancer (T.M. Marti, R. Peng) CHF 10,000
- China Scholarship Council Fellowship: Identify therapeutic targets in lung cancer stem cells (R.A. Schmid, R. Peng for L. Shun-Qing) CHF 12,000

Five Selected Publications

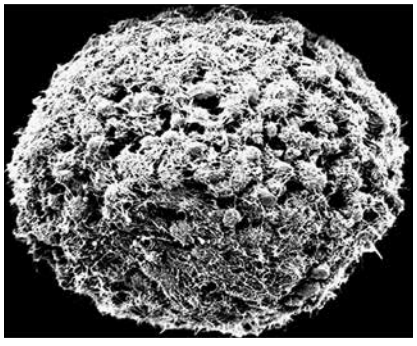
Suppression of OCT4B Enhances Sensitivity of Lung Adenocarcinoma A549 Cells to Cisplatin via Increased Apoptosis. Cortes-Dericks, L; Yazd, EF; Mowla, SJ; Schmid, RA; Karoubi, G (2013) in: Anticancer Res, 33(12), p. 5365-5373.

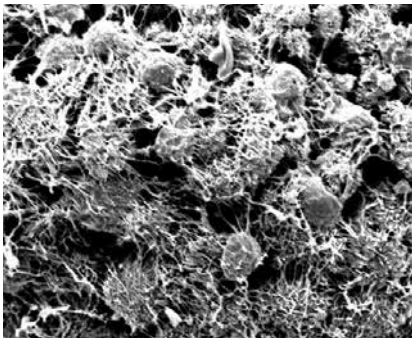
Identification and isolation of small CD44-negative mesenchymal stem/progenitor cells from human bone marrow using elutriation and polychromatic flow cytometry. Hall, SR; Jiang, Y; Leary, E; Yavanian, G; Eminli, S; O'Neill, DW; Marasco, WA (2013) in: Stem Cells Transl Med, 2(8), p. 567-578.

Overestimation of hematopoietic stem cell frequencies in human liver grafts. Hall, SR; Pedroza-Gonzalez, A; Pan, Q; Tilanus, HW; de, JJ; Wagemaker, G; van der Laan, LJ (2013) in: Hepatology, 57(6), p. 2547-2549.

Mesenchymal stromal cells improve survival during sepsis in the absence of heme oxygenase-1: the importance of neutrophils. Hall, SR; Tsoyi, K; Ith, B; Padera, RF, Jr.; Lederer, JA; Wang, Z; Liu, X; Perrella, MA (2013) in: Stem Cells, 31(2), p. 397-407.

Support of Hepatic Regeneration by Trophic Factors from Liver-derived Mesenchymal Stromal/Stem Cells. Fouraschen, S; Hall, S; de Jonge, J; van der Laan, LJW in Methods in Molecular Biology, published by Humana Press, entitled "Animal Models for Stem Cell Therapy" (accepted for publication).





Visceral and Transplantation Surgery

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Prof. Dr. Daniel Candinas
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Board examination (1987) and MD (1991) at University of Zurich. Fellowships in Birmingham (UK) (1993-1994) and Harvard Medical School, Boston (US) (1994-1995). Staff Surgeon at University Hospital Zurich (1996-1999) and Queen Elizabeth Hospital, Birmingham (1999-2002). Venia docendi (1997) at University of Zurich. Since 2002, Chair, Department of Visceral and Transplantation Surgery, Inselspital.

PD Dr. Deborah Keogh-Stroka
deborah.stroka@dkf.unibe.ch

Studied biology (MSc 1996) at Harvard University, Boston (US) and natural sciences/genetics (PhD 1998) at University of Vienna (AT). Postdocs at Institute of Physiology, University of Zurich (1998-1999) and Department of Surgery, University of Birmingham (UK) (1999-2002). Since 2002, Laboratory Head, Visceral and Transplantation Surgery, DCR. Venia docendi (2011).

Prof. Dr. Guido Beldi
guido.beldi@insel.ch

Board examination (1998); MD (2000) at University of Bern. Fellowships in Berlin (DE) (2004) and at Liver Center, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston (US) (2006-2007). FMH certification in Surgery (2005); Staff Surgeon since 2008, Department of Visceral Surgery and Medicine, Inselspital. Venia docendi (2009) and Associate Professor (2012).

Research Highlights 2013 / Outlook 2014

Focus on regenerative medicine of liver and sphincter muscle, and treatment of gastrointestinal tumours

The adult liver retains its ability to self-maintain its optimal mass in response to injury or resection. However, in some instances it does not regenerate, which can lead to organ failure. Our research focuses on improving liver regeneration following two approaches: firstly, a gene therapy approach using in vivo siRNAs targeting components of the Hippo signalling pathway, and secondly, isolating liver-derived Lgr5$^+$ stem cells for reconstitution of diseased liver tissue (Stroka/Candinas/Keogh).

Purinergic signalling and liver regeneration is another primary research focus. We have published the impact of extracellular nucleotides on natural killer (NK) cell cytotoxicity. Modulation of NK cell-mediated cytotoxicity and altered NK maturation explains impaired liver regeneration in immunodeficient mice. We are now exploring the modulation of effector functions by extracellular purines on other innate lymphoid cells. In particular, IL-22 secretion by NK cells is altered in mice null for CD39 compared to wild-type controls. As IL-22 has potent hepatoprotective properties, we are exploring the impact of IL-22 on liver regeneration (Beldi).

We are also investigating the use of adipocyte-derived stem cells (ADSCs) for skeletal (sphincter) muscle regeneration. We established methods for ADSC culture conditions, differentiation and characterisation. ADSCs have been injected into damaged skeletal muscle in an established mouse crush injury model. Next, we will investigate if pre-differentiation of ADSCs improves morphological and functional regeneration. We hypothesise that Lgr5$^+$-expressing cells—a reserve stem cell population in other tissues—might also play a role in skeletal muscle regeneration (Brügger).

Highlights of our research on new approaches for treatment of liver cancer include targeting the NAD$^+$-dependent deacetylase SIRT1 (Stroka) and YAP1 of the Hippo pathway (Banz). In collaboration with the Radiation Oncology Group (Aebersold/Zimmer), we are studying the effect of radiation-induced liver disease, a limiting factor for the use of ionising radiation in the treatment of liver tumours (Stroka).

Ongoing studies bridging clinical and basic research

- In collaboration with psychologists from the University of Neuchâtel, our study "communication in the operating room" has shown that case-relevant communication protects from deep surgical site infections such as anastomotic insufficiency or intraabdominal abscess formation. For 2014, we are planning a large prospective multicentre trial to improve intraoperative communication (Beldi).
- The feasibility of intraoperative radiation therapy for gastrointestinal cancers of the pancreas and rectum (Gloor).
- The impact of preoperative oral glutamine intake on the immunocompetence and outcomes of malnourished patients undergoing major abdominal surgery due to malignancies (Schnüriger).
- Evaluation of the accuracy of predicted ablation volume in a porcine liver model and a review of patients undergoing computer-assisted liver surgery (Banz).

Dr. Lukas Brügger
lukas.bruegger@insel.ch

MD (1992) at University of Bern: Board-certified surgeon, FMH (2001). Research fellowship on stem cell therapy for (sphincter) muscle regeneration at Laboratory for Stem Cell Therapy and Tissue Engineering, Urology, University Hospital Zurich (2010-2012). Joined Coloproctology Division, Inselspital in 2006; Senior Attending since 2013. Principle Investigator, Nano-Tera project on smart muscles for incontinence treatment.

Group Members

Prof. Dr. Daniel Candinas, Co-Chair, Head
PD Dr. Deborah Keogh-Stroka, Laboratory Head, Group Leader
Prof. Dr. Guido Beldi, Group Leader
Dr. Lukas Brügger, Group Leader
Dr. Vanessa Banz, Staff Surgeon
Prof. Dr. Beat Gloor, Co-Head
Dr. Adrian Keogh, Research Assistant
PD Dr. Beat Schnüriger, Consultant
PD Dr. Eliane Angst, Staff Surgeon
Prof Dr. Daniel Inderbitzin, Staff Surgeon
Dr. Roman Inglin, Staff Surgeon
Dr. Thomas Malinka, Staff Surgeon
Dr. Peter Studer, Junior Doctor
Andreas Furer, Laboratory Technician
Cynthia Furer, Laboratory Technician
Anita Born, Laboratory Technician
Sarah Overney, Laboratory Technician
Lilian Smith, Secretary
Gabriel Cantanhede, Visiting Fellow (since Apr.)
Michel Dosch, MD Student
Agata Gorecka, PhD Student (since Apr.)
Ramesh Kudira, PhD Student
Giulio Loforese, PhD Student
Dr. Simone Portmann, PhD Student (Jan.-Sep.)

Collaborators

Adams D, University of Birmingham, UK
Beutler B, University of Texas Southwestern Medical Center, USA
Cerny A, Clinica Luganese SA, Switzerland
Djafarzadeh S, Inselspital, Switzerland
Eberli D, University Hospital Zurich, Switzerland
Ferran C, Harvard Medical School, USA
Halazonetis T, University of Geneva, Switzerland
Kanse S, University of Oslo, Norway
Macphersen A, McCoy K, University of Bern, Switzerland
Montani M, Tschan M, University of Bern, Switzerland
Robson S, Harvard Medical School, USA
Tschan F, University of Neuchâtel, Switzerland
Zimmer Y, Aebersold D, University of Bern, Switzerland

Grants

Amounts allocated for 2013:

- SNF: Natural killer cell function after liver resection: the role of extracellular ATP (G. Beldi) CHF 25,167
- SNF: NTPDase1/CD39 and innate lymphoid cells in liver injury and repair (G. Beldi) CHF 84,370
- SNF: Relating human factor aspects during surgery to surgical site infection (G. Beldi) CHF 75,790
- Forschungs-Grant des Inselspitals/ Universitätsspitals Bern für Nachwuchsforschende: Targeting YAP1 of Hippo pathway to control the growth of hepatocellular carcinoma (V. Banz) CHF 80,000
- Fresenius Kabi: The impact of preoperative oral glutamine intake on the immunocompetence and outcomes of malnourished patients undergoing major abdominal surgery due to malignancies – A randomized, placebo-controlled pilot study (B. Schnüriger) CHF 18,000
- Johnson & Johnson: Hepato-pancreato-biliary fellowships (B. Gloor) CHF 100,000
- Ruth & Arthur Scherbarth Foundation: Novel stem cell therapy for anal sphincter regeneration (L. Brügger) CHF 80,000
- Strauss Foundation: Adult Stem Cells for Regenerative Medicine (D. Stroka, D. Candinas) CHF 250,000

Five Selected Publications

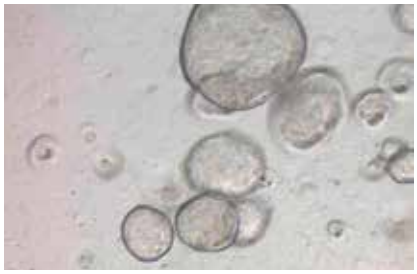
Promotion of liver regeneration by natural killer cells in a murine model is dependent on extracellular adenosine triphosphate phosphohydrolysis. Graubardt, N et al. (2013) in: Hepatology, 57(5), p. 1969-1979.

Inhibition of SIRT1 impairs the accumulation and transcriptional activity of HIF-1alpha protein under hypoxic conditions. Laemmle, A et al. (2012) in: PLoS One, 7(3), p. e33433.

Incision length for kidney transplantation does not influence short- or long-term outcome: a prospective randomized controlled trial. Malinka, T; Banz, VM; Wagner, J; Candinas, D; Inderbitzin, D (2013) in: Clin Transplant, 27(5), p. E538-E545.

Antitumor effect of SIRT1 inhibition in human HCC tumor models in vitro and in vivo. Portmann, S et al. (2013) in: Mol Cancer Ther, 12(4), p. 499-508.

Elevated liver regeneration in response to pharmacological reduction of elevated portal venous pressure by terlipressin after partial hepatectomy. Fahrner, R et al. (2013) in Transplantation (in press).



Key Events

Swiss Youth in Science: "Biology and Medicine" Study Week
17-23 Mar.

Seminar for students of the Kantonsschule Solothurn
2 July

Omics kick-off meeting of the DCR
11 Sep.

Information Event: What scientists from the Faculty of Medicine should know about how to apply to the Swiss National Science Foundation (SNSF)
2 Dec.

"Clinical Research" symposium for biomedical sciences students of the University of Fribourg
9 Dec.

Welcome Event 2013
29 May

As in the past, around 60 interested DCR newcomers attended this event, which in the future will take place yearly.

Day of Clinical Research 2013
5-6 Nov. 2013

A large and interested audience followed the presentations of **Prof. Dr. Nicholas Fisk** (Faculty of Health Sciences, University of Queensland, Australia) entitled "Biological and Translational Implications of Gestational Stem Cells" and **Prof. Dr. Henry Markram** (EPF Lausanne, Switzerland) entitled "The Human Brain Project".

Seven candidates applied for the Johanna Dürmüller-Bol DCR Research Prize 2013 (funded by the Johanna Dürmüller-Bol Foundation) and 173 abstracts were submitted for the DCR Poster Prizes and the Research Prize Alumni MedBern.

The winners were (left to right in photo below):

- Research Prize Alumni MedBern – Prof. Dr. Tobias Nef representing **Michael Jäger** (ARTORG Center)
- Best patient-oriented project – **Dr. Michael Nagler** (Department of Hematology and Central Hematology Laboratory, Inselspital)
- Johanna Dürmüller-Boll DCR Research Prize – **Dr. Marta Roccio** (Department of Ear, Nose and Throat Diseases, Head and Neck Surgery, Inselspital and Audiology, DCR)
- Best laboratory-oriented project – **Stefan Hahnewald** (Department of Ear, Nose and Throat Diseases, Head and Neck Surgery, Inselspital and Audiology, DCR)
- Best project by a medical student – **Christoph Flury** (Department of Medical Oncology, Inselspital and Tumor-Immunology, DCR)

The next Day of Clinical Research will be held 4-5 November 2014.

DKF Research Conferences 2013

With an average of 72 visitors each month, the DKF Research Conferences continue to be very successful. In 2013, we were pleased to present the following speakers:

4 Feb. – Prof. Dr. Luciano Gattinoni
University of Milan, Italy
Stress and strain within the lung: Not just for researchers!

4 Mar. – Dr. Ramzi Ajjan
University of Leeds, UK
Atherothrombosis in diabetes: The role of the fibrin network

8 Apr. – Prof. Dr. Tony Wyss-Coray
Stanford University School of Medicine, USA
Young blood for old brains – can we rejuvenate the brain?

6 May – Prof. Dr. Thomas Brunner
University of Constance, Germany
Local glucocorticoid synthesis in the intestinal epithelium and its role in the regulation of inflammatory diseases

3 June – Prof. Dr. Walter L. Miller
University of California, San Francisco, USA
New aspects of androgen biosynthesis: Collaborations between San Francisco and Bern

1 July – Prof. Dr. Jacques S. Beckmann
Swiss Institute of Bioinformatics, Lausanne, Switzerland
Clinical bioinformatics: A paradigm change in medicine

2 Sep. – Prof. Dr. Frank J. Gonzalez
National Cancer Institute, Bethesda, USA
The role of intestinal microbiota and nuclear receptors in metabolic diseases: Studies using genetically-modified mice and metabolomics

7 Oct. – Prof. Dr. Olaf Blanke
EPF Lausanne and University Hospital Geneva, Switzerland
Turning the body and self inside out: Bodily self-consciousness relies on multisensory brain mechanisms including cardiac signals

4 Nov. – Prof. Dr. J. J. Neefjes
Netherlands Cancer Institute, Amsterdam and Leiden University Medical Center, The Netherlands
Finding new functions for old anti-cancer drugs and the manipulation of the immune system

2 Dec. – Prof. Dr. Lynne E. Maquat
University of Rochester, USA
Human long non-coding RNA and mRNA function in normal and disease-associated cellular metabolism

In 2014, DKF Research Conferences will take place as usual every first Monday of the month from 5-6 pm, followed by an apéro.

Personnel Update

Academic Degrees

The following academic degrees where awarded to DCR group members:

Full Professor

Prof. Dr. Anne Angelillo-Scherrer
Department of Hematology and Central Hematology Laboratory, Inselspital

Professor

Prof. Dr. Mihai Constantinescu
Plastic Surgery

Prof. Dr. Paul Mohacsi
Cardiology

Associate Professor

Prof. Dr. Guido J. F. Beldi
Visceral and Transplantation Surgery

Prof. Dr. Peter Vermathen
Magnetic Resonance Spectroscopy and Methodology, AMSM

Prof. Dr. Esther Vögelin
Hand Surgery

Titular Professor

Prof. Dr. Karin Fattinger
Internal Medicine

Prof. Dr. Michael Reinert
Neurosurgery

Lecturer (Privatdozent)

PD Dr. Matthias Hänggi
Intensive Medicine

PD Dr. Frank Klenke
Bone Biology & Orthopaedic Research

PD Dr. Marcel Menke
Ophthalmology

PD Dr. Tobias M. Merz
Intensive Medicine

PD Dr. Elisabeth Oppliger-Leibundgut
Experimental Haematology (Adults)

PD Dr. Jana Ortmann
Cardiovascular Research

PD Dr. Laurent Roten
Cardiology

PD Dr. André Schaller
Human Genetics

PD Dr. Pascal Senn
Audiology

PD Dr. Maziar Shafighi
Plastic Surgery

PD Dr. Stijn Vandenberghe
Cardiovascular Surgery

PD Dr. Torsten A. Willenberg
Angiology

PD Dr. Yitzhak Zimmer
Radiation Oncology

PD Dr. Martin Zinkernagel
Ophthalmology

PhD

(supervisors in brackets)

Christine Bolliger
(Prof. Dr. Roland Kreis)
Novel combinations of acquisition and processing methods for the quantification of brain metabolites by in vivo ^{1}H magnetic resonance spectroscopy

Anjan Bongoni
(Prof. Dr. Robert Rieben)
Functional evaluation of multiple human transgenes to overcome immunological and coagulation barriers associated with pig-to-human xenotransplantation

Andreas Boss
(Prof. Dr. Chris Boesch)
Application of multinuclear magnetic resonance spectroscopy for the non-invasive investigation of skeletal muscle and liver metabolism

Jamal-Eddine Bouameur
(Prof. Dr. Luca Borradori)
Characterization of the interaction of plectin with intermediate filaments and its regulation by phosphorylation

Vaclav Brandejsky
(Prof. Dr. Chris Boesch)
Studies of metabolism by means of ^{1}H magnetic resonance spectroscopy

Claudia Dührkop-Sisewitz
(Prof. Dr. Robert Rieben)
Anti-inflammatory treatment prevents local and systemic effects of skeletal muscle ischemia/reperfusion injury

Franziska Maria Gisler
(Prof. Dr. Sabina Gallati)
Heterogeneity in cystic fibrosis: Analyses of phenotype modifications on interactomic levels in cystic fibrosis

Tamara Hilmenyuk
(Prof. Dr. Adrian Ochsenbein)
Malignant lymphoma B cells induce dysfunctional cytotoxic T cells

Christopher Benjar Jackson
(Prof. Dr. Sabina Gallati)
Characterisation of molecular pathomechanisms in mitochondrial disorders

Tohid Pirbodaghi
(PD Dr. Stijn Vandenberghe)
Speed modulation of rotary blood pumps: Experimental evaluation

Simone Portmann
(PD Dr. Deborah Stroka)
Inhibition of SIRT1 impairs primary liver cancer growth

Mina Rezaei
(Prof. Dr. Brigitte Frey, Dr. Thomas Andrieu)
Regulation of 11β-hydroxysteroid dehydrogenase type 2 by miRNA

MD PhD

(supervisors in brackets)

Florian Singer
(Prof. Dr. Urs Frey, Prof. Dr. Thomas Geiser)
Inert gas washout to assess airway function: From bench to bedside

Peter Studer
(PD Dr. Deborah Stroka)
A20: The cross road of survival, cell cycle and metabolism in the liver

Awards

The following DCR group members received awards in 2013:

Anjan Kumar Bongoni
Cardiovascular Research
IXA-TTS Young Investigator Travel Award, 12th Congress of the International Xenotransplantation Association: "Ex vivo xenoperfusion of (hCD46 & HLA-E)-double transgenic porcine forelimbs with whole, heparinized human blood: Study of early immunological responses"

Prof. Dr. Thierry Carrel
Cardiovascular Surgery
2013 Leonardo Da Vinci Award for Training Excellence

Monika Dornbierer
Cardiovascular Research
Best Poster Award, AGLA & Cardiovascular Biology Meeting 2013: "Heart transplantation with donation after cardiac death: Biochemical and hemodynamic parameters predict contractile recovery in a rat model"

Christoph Flury
Tumor-Immunology
DCR Poster Prize for best project by a medical student: "Combined inhibition of BCR/ABL-and CD27-signaling eradicates chronic myeloid leukemia cells"

Stefan Hahnewald
Audiology
DCR Poster Prize for best laboratory-oriented project: "First steps towards a gapless interface between auditory neurons and multi-electrode arrays in vitro"

Dr. Elisabeth Kieninger
Pulmonary Medicine (Paediatrics)
Benoît Pochon Prize: "Clinical impact and pathophysiology of viral infections and early lung disease in cystic fibrosis"

Ramesh Kudira
Visceral and Transplantation Surgery
Ethicon Travel Award, Annual Meeting SGG-SGVC-SASL 2013

Giulio Loforese
Visceral and Transplantation Surgery
EASL Young Investigator Award, EASL 2013 International Liver Congress

Giulio Loforese
Visceral and Transplantation Surgery
Award for Best Oral Presentation, Swiss Surgical Annual Meeting

Giulio Loforese
Visceral and Transplantation Surgery
Ethicon Travel Award, Annual Meeting SGG-SGVC-SASL 2013

PD Dr. Thomas Nyffeler
Neurology
Dr. Stefano Rimoldi
Cardiology
Pfizer Research Prize 2013: Honoured for excellent work in cardiology and neurology

PD Dr. Andreas Pasch
Nephrology and Hypertension
Heuberger Winterthur Young Entrepreneur Award

Dr. Marta Roccio
Audiology
Johanna Dürmüller-Bol DCR Research Prize: "Reactivation of dormant inner ear stem cells through modulation of cell cycle and developmental regulators"

Prof. Dr. Barbara Rothen
Pulmonary Medicine (Adults)
Ypsomed Innovation Prize (2nd prize): "Neue Bio-Printing Plattform für ein 3D-Lungengewebe der Luft-Blut-Schranke"

PD Dr. Andreas Schoenenberger
Geriatrics / Medicine of Ageing
Vontobel Prize 2013: "Predictors of functional decline in elderly patients undergoing transcatheter aortic valve implantation (TAVI)"

Dr.Christian Schürch
Tumor-Immunology
Best thesis 2012, Graduate School for Cellular and Biomedical Sciences: "Immune surveillance of cancer stem cells in chronic myeloid leukemia"

Dr. Christian Schürch
Tumor-Immunology
Research Award 2013, Hemmi-Stiftung: "CD27 as a novel therapeutic target in acute myeloid leukemia" progression"

Diana Shy
Ion Channels and Channelopathies
Denise Escande Poster Award, Denis Escande Symposium 2013: "PDZ domain-binding motif of the cardiac sodium channel Nav1.5 regulates compartment-specific channel expression and cardiac conduction"

Staff Changes

New Staff

Dr. Jörg Arnoldi
Head of Laboratory (50%), Plastic and Hand Surgery (since Nov.)

Luca Bologna
Doctoral Student (100%), Experimental Haematology (Adults) (since Aug.)

Mariana Bustamante Eduardo
Doctoral Student (100%), Molecular Biology and Genomics (since May)

Raja El Adnani Prince
Doctoral Student (100%), Haematology (since Aug.)

Deborah Felder
DCR Secretary (100%), Administration (since May)

Nicola Grimm
Apprentice (100%), DCR Maintenance (since Aug.)

Joël Grosjean
Laboratory Technician (40%), Urology (since June)

Dr. Eva-Maria Hau-Grosch
Research Assistant (50%), Pediatric Surgery (since Sep.)

Sophie Lagache Braga
Laboratory Technician (100%), Mass Spectrometry and Proteomics Laboratory (since Jan.)

Prof. Dr. Kathy McCoy
Head of Research (100%), Gastroenterology / Mucosal Immunology (since Jan.)

Marta Pace
Research Assistant (100%), Neurology (since Jan.)

Dr. Mina Rezaei
Postdoctoral Fellow (100%), Nephrology and Hypertension (since Sep.)

Uyen Schmutz
DCR Secretary (10%), Administration (since Aug.)

Oliver Schweizer
IT-Support (60%), Administration (since Mar.)

Corinne Sidler-Mantoux
Laboratory Technician (40%), Oncology / Haematology (Adults) (since June)

Retirement

Prof. Dr. Brigitte Frey
Laboratory Head (100%), Nephrology and Hypertension (until Sep.)

Prof. Dr. Ernst B. Hunziker
Group Leader (100%), Orthopaedic Surgery (until July)

Dr. Sidney Shaw
Group Leader (100%), Vasoactive Peptide (until Sep.)

Internal Reallocation

Jane Shaw-Boden
Laboratory Technician (50%), Cardiovascular Research (since Jan.)

Resignations

Dr. Marco Alves
Postdoctoral Fellow (100%), Pulmonary Medicine (Paediatrics) (until Apr.)

Louis Amport
DCR Secretary (10%), Administration (until July)

Barbara Bencivenga
Apprentice (100%), DCR Maintenance (until Aug.)

Michele Cibien
IT-Support (60%), Administration (until Mar.)

Dr. Sebastian Grunt
Research Assistant (50%), Neuropediatrics (until Aug.)

Michael Jäger
Doctoral Student (100%), Psychiatry (until Sep.)

Dr. Svitlana Palchykova
Research Assistant (50%), Neurology (until Mar.)

José Schranz
DCR Secretary (70%), Administration (until Apr.)

Deborah Shan
Laboratory Technician (40%), Oncology / Haematology (Adults) (until Apr.)

DCR Director: Prof. Dr. Hugues Abriel
Coordination: Verena Frazao
Editing: Leah Witton, wordsmith.ch@gmail.com
Photos: DCR; Susi Bürki and Tanja Kocher, Inselspital
Typesetting: Nadine Wüthrich
Print: Stämpfli Publikationen AG