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**UNIVERSITÄT  
BERN**

DEPARTMENT OF CLINICAL RESEARCH  
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# Jahresbericht Annual Report 2014

1994

20  
2014

DEPARTEMENT  
KLINISCHE FORSCHUNG

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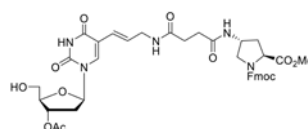
Members of the University of Bern and Inselspital can obtain a copy of this report online at: [www.dkf.unibe.ch](http://www.dkf.unibe.ch)

## Cover:

The coloured scanning electron microscopic image depicts a crystallised nucleoside analogue. Nucleoside analogues are molecules that act like nucleosides in DNA or RNA replication. The use of synthetic analogues ranges from inhibiting the action of viral reverse transcriptase and polymerases (e.g., in Hepatitis B and HIV) to the generation of nucleic acid-based enzymes (DNAzymes).

*Synthesis: Marcel Hollenstein (Department of Chemistry & Biochemistry)*

*Image: Christopher B. Jackson (IKELOS GmbH)*



# Contents

The DCR at a Glance / Das DKF auf einen Blick	2
Foreword – Director’s Report / Vorwort – Bericht des Direktors	3 / 4
Organisation	5
Organigram	6
DCR Sites	7
Key People	8
Core Facility	10
Technology Core Facilities	12
Technology Core Facilities / DCR Internal Research Groups	14
DCR Internal Research Groups	18
DCR Research Groups from the Inselspital	24
Key Events	46
Personnel Update	49

## 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 2014, 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.

We hope you enjoy our video presentations:  
[www.dkf.unibe.ch](http://www.dkf.unibe.ch) > Research  
> Research Groups  
> Facilities and Services > Core Facilities

## Das DKF auf einen Blick

Das Departement Klinische Forschung (DKF) ist ein Forschungsdepartement der Medizinischen Fakultät der Universität Bern.

Es wurde 1994 mit dem Auftrag gegründet, Forschenden vom Inselspital, Universitätsspital Bern und von der Medizinischen Fakultät eine optimale Infrastruktur zur Verfügung zu stellen. Im Jahr 2014 waren 47 unabhängige Forschungsgruppen dem DKF angeschlossen, die zusammen fast alle Bereiche der biomedizinischen Forschung abdecken.

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

Viel Vergnügen mit unseren Videopräsentationen:  
[www.dkf.unibe.ch](http://www.dkf.unibe.ch) > Forschung  
> Forschungsgruppen  
> Facilities und Dienstleistungen > Core Facilities





## Foreword – Director's Report



Dear readers and colleagues,

In 2014, the DCR celebrated its 20th anniversary. We were active in informing the general public about our research activities. On 6 November, we organised our first "Open House", which was very well attended. In addition, we also prepared short video presentations on the research activities of several of the DCR groups. The presentations can be found on the webpages of the DCR and I am convinced you will find them interesting to watch.

The DCR has grown continuously during the past years and, even more importantly, has increased its scientific and technological support to the affiliated scientists at the Inselspital, Bern University Hospital. We have been able to show that we are ready for the future challenges ahead of us!

This year, we welcomed two new research groups with a haematological focus: the Hematology (Adults) group led by the new Head of the Department of Hematology and Central Hematology Laboratory, Inselspital, Prof. Dr. Anne Angelillo-Scherrer, and the Experimental Haemostasis group led by Prof. Dr. Hans-Peter Kohler and PD Dr. Verena Schröder. In addition, we also provided laboratory space to the new research group of Prof. Dr. Kurt Lippuner from the Clinic of Osteoporosis. Some of these groups will be relocated in the near future to the new Murtenstrasse 40 premises. We wish these new DCR groups the best of success with their research activities.

As mentioned last year, the DCR also supports the bottom-up creation of research clusters. These clusters are composed of DCR and external groups who would like to organize common activities such as seminar series. In 2014, the "Cluster for Lung Development, Regeneration and Respiratory Diseases" was created with the inten-

tion to further support collaboration in a field that has a long and successful track record at the Faculty of Medicine. Next year will also see the creation of more such clusters, in particular one dedicated to cardiovascular science.

Among the core activities of the DCR, the Technology and Animal Core Facilities hold a central place. For this reason, a survey among the users of the facilities was carried out this year, in order to gain feedback regarding the specific services provided by the facilities. We were extremely pleased to hear that the vast majority of users was satisfied with the services. We also received some useful advice and suggestions for improvements of a few aspects of these services.

With regard to the animal facilities—the Central Animal Facility; the ESI, Experimental Surgery Unit; the CMF, Clean Mouse Facility—all three have undergone an increase in capacities and renovation work. These activities to support animal experimentation are now coordinated by the "Experimental Animal Center" task force of the Faculty of Medicine. This task force has been very active and will continue its work to address the major future challenges, such as the problem of lack of housing space for mice and rats, and the preparation of the new facility in the InselNord building, which is planned to open in 2019. We are also pleased to see that the activities of the CMF, Clean Mouse Facility are steadily increasing and have now achieved a level of security with the guaranteed financial support from the University Board of Directors and the Directorate of Teaching and Research, Inselspital.

New equipment also plays a key role for the Technology Core Facilities. This year, the Genomics facility acquired a new digital PCR system, allowing more accurate and sensitive measurements, while the Live Cell

Imaging (LCI) facility was granted financial support from an SNF R'Equip grant to purchase a new microfluidic system for microscopy experiments (PI: Prof. Dr. Olivier Guenat).

The last point I would like to emphasise here is the very successful start of the small Bioinformatics unit with Dr. Irene Keller and Dr. Cedric Simillion (under the supervision of Dr. Rémy Bruggmann). Several papers have already been published thanks to their expert analyses of the data generated from the different DCR groups and facilities. We plan to continue this unit and expand it, if possible, in the future.

Now in its twenties, the DCR has reached "adulthood". We are looking forward to working with you in the future to make it an even better place to perform relevant biomedical research. I would like to take this opportunity to say a warm thank you to all of you as well as to all the very motivated employees of the DCR. I wish you all the best for the coming year.

Prof. Dr. Hugues Abriel, MD PhD

## Vorwort – Bericht des Direktors

Liebe Leserinnen und Leser  
Liebe Kolleginnen und Kollegen

Im Jahr 2014 feierte das DKF seinen 20. Geburtstag. Aus diesem Anlass haben wir die breite Öffentlichkeit aktiv über unsere Forschungsarbeit informiert. Unser „Tag der offenen Türen“ fand am 6. November statt und war sehr gut besucht. Zusätzlich haben wir kurze Videopräsentationen zur Forschungstätigkeit mehrerer DKF Gruppen vorbereitet. Die Videos sind auf der DKF Homepage aufgeschaltet. Ich bin überzeugt, dass Sie diese sehr interessant finden werden.

Das DKF ist in den letzten Jahren kontinuierlich gewachsen und, was noch wichtiger ist, konnte sein Angebot an wissenschaftlicher und technologischer Unterstützung für die Forschenden des Inselspitals, Universitätsspital Bern, vergrössern. Wir konnten zeigen, dass wir bereit sind für die Herausforderungen der Zukunft!

In diesem Jahr durften wir zwei neue Forschungsgruppen mit einem hämatologischen Fokus im DKF willkommen heissen: die Gruppe Hämatologie (Erwachsene) der neuen Klinikdirektorin der Universitätsklinik für Hämatologie und Hämatologisches Zentrallabor, Inselspital, Frau Prof. Dr. Anne Angelillo-Scherrer und die Gruppe Experimentelle Hämostase unter der Leitung von Herr Prof. Dr. Hans-Peter Kohler und Frau PD Dr. Verena Schröder. Zudem haben wir auch der neuen Forschungsgruppe der Klinik für Osteoporose von Herr Prof. Dr. Kurt Lippuner Laborflächen zur Verfügung gestellt. Einige dieser Gruppen werden in naher Zukunft in die neuen Räumlichkeiten an der Murtenstrasse 40 verlegt werden. Wir wünschen diesen neuen DKF Gruppen viel Erfolg bei ihren Forschungsaktivitäten.

Wie bereits letztes Jahr erwähnt, möchte das DKF die Schaffung von Forschungsclusters fördern. Diese Clus-

ters setzen sich aus Forschungsgruppen innerhalb und ausserhalb des DKF zusammen, mit dem Ziel, gemeinsame Aktivitäten, wie Seminarreihen, zu organisieren. Im Jahr 2014 wurde der „Cluster for Lung Development, Regeneration and Respiratory Diseases“ geschaffen, mit der Absicht, die Zusammenarbeit in einem Bereich mit einer langen Erfolgsgeschichte an der Medizinischen Fakultät zu unterstützen. Im nächsten Jahr ist die Schaffung von weiteren Clusters geplant, insbesondere eines, welches der Herz-Kreislauf Wissenschaft gewidmet ist.

Bei den Kernaktivitäten des DKF nehmen die Technologie und Tier Core Facilities einen zentralen Platz ein. Aus dem Grund wurde dieses Jahr eine Umfrage unter den Nutzern der Einrichtungen durchgeführt, um ein Feedback zu den Dienstleistungen der Einrichtungen zu erhalten. Wir waren sehr erfreut zu hören, dass die überwiegende Mehrheit der Nutzer mit den Dienstleistungen zufrieden ist. Wir erhielten auch hilfreiche Vorschläge und Anregungen zur Verbesserung dieser Dienstleistungen.

Was die Tier Einheiten betrifft—Zentrale Tierställe; ESI, Experimental Chirurgische Station; CMF, Clean Mouse Facility—so waren für alle drei Kapazitätsvergrösserung und Umbauarbeiten angesagt. Diese Aktivitäten zur Unterstützung von Tierversuchen werden jetzt durch eine Task Force der Medizinischen Fakultät, dem „Experimental Animal Center“, koordiniert. Diese Arbeitsgruppe war sehr aktiv und wird ihre Arbeit fortsetzen, um die grossen Herausforderungen der Zukunft anzugehen, wie die fehlenden Kapazitäten zur Unterbringung von Mäusen und Ratten und die Planung der neuen Tierhaltungs-Einrichtung im Neubau InselNord, welche voraussichtlich im Jahr 2019 in Betrieb genommen werden kann. Wir freuen uns auch darüber, dass sich die Aktivi-

täten der CMF, Clean Mouse Facility stetig erhöhen und deren Betrieb nun durch die gewährleistete finanzielle Unterstützung der Universitätsleitung und der Direktion Lehre und Forschung des Inselspitals abgesichert ist.

Neue Geräte spielen eine Schlüsselrolle in den Technologie Core Facilities. Dieses Jahr konnte die Genomics Core Facility ein neues digitales PCR-System erwerben, das genauere und empfindlichere Messungen erlaubt. Der Live Cell Imaging (LCI) Core Facility wurde finanzielle Unterstützung durch einen Grant des SNF R'Equip Programms gewährt, welcher die Anschaffung eines neuen Microfluidic Systems für Mikroskopie Experimente ermöglicht (PI: Prof. Dr. Olivier Guenat).

Als letztes möchte ich hier den sehr erfolgreichen Start der kleinen Bioinformatik Einheit mit Dr. Irene Keller und Dr. Cedric Simillion (unter der Leitung von Dr. Rémy Bruggmann) hervorheben. Mehrere Manuskripte konnten bereits, dank ihrer fachmännischen Analyse von Daten, die in verschiedenen DKF Forschungsgruppen und Einheiten generiert wurden, veröffentlicht werden. Für die Zukunft planen wir, diese Einheit weiterzuführen und, wenn möglich, zu erweitern.

Jetzt, in seinem zwanzigsten, ist das DKF „erwachsen“ geworden. Wir freuen uns auf die weitere Zusammenarbeit mit Ihnen, um das DKF in Zukunft zu einem noch besseren Institut zu machen, an dem relevante biomedizinische Forschung durchgeführt werden kann. Ich möchte mich an dieser Stelle bei allen, insbesondere bei all den sehr motivierten Mitarbeitenden im DKF, ganz herzlich bedanken!



Prof. Dr. Hugues Abriel, MD PhD

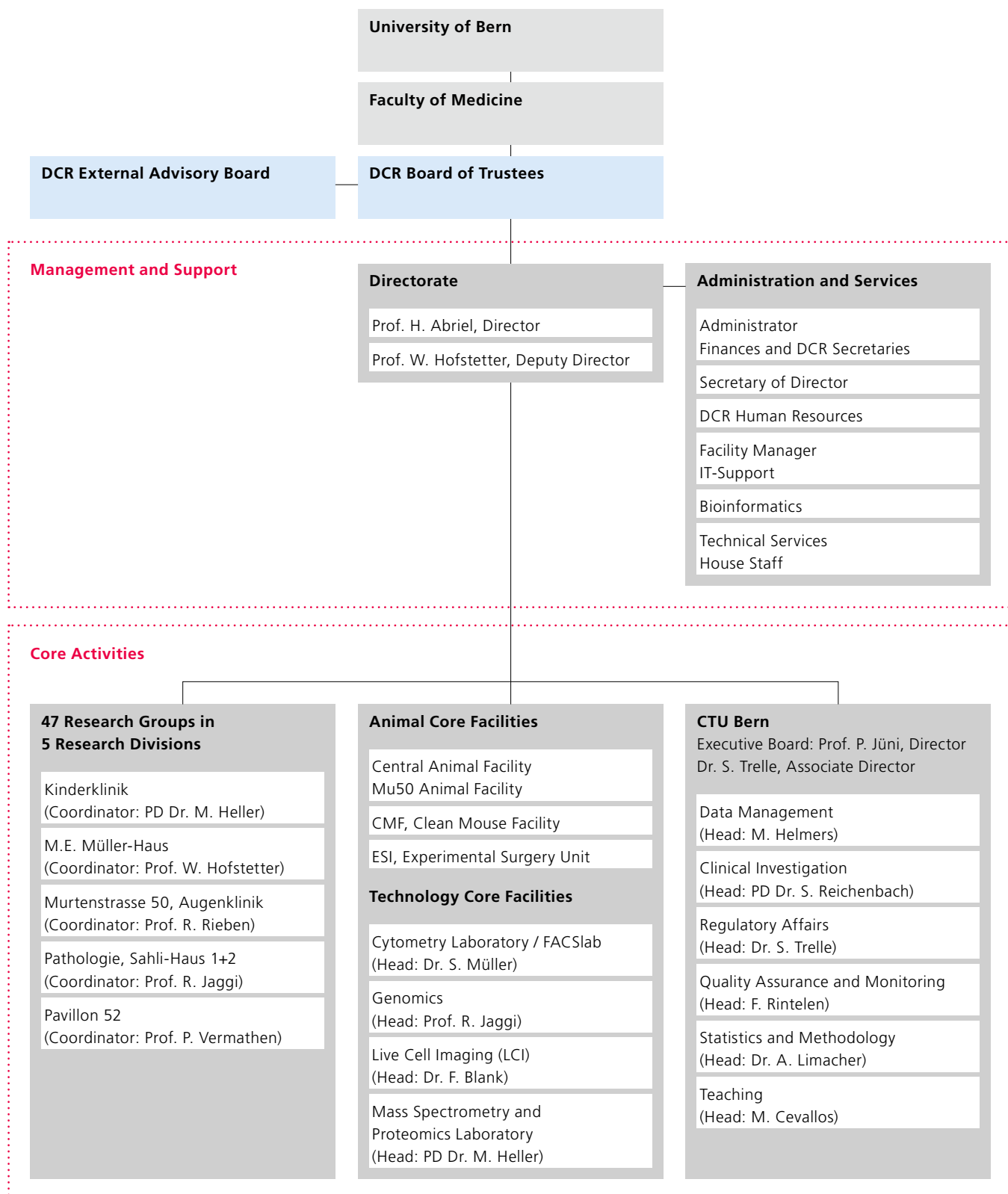
# Organisation

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 2014. The vast majority (42) of these groups are from clinics of the Inselspital, Bern University Hospital. The remainder (5) 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 5 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 2014







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



## Key People

### DCR Board of Trustees



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Chair

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Prof. Dr. Daniel Candinas  
Prof. Dr. Sabina Gallati  
Prof. Dr. Peter Jüni  
Prof. Dr. Christoph Müller  
Prof. Dr. Lutz-Peter Nolte

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Prof. Dr. Peter Eggli  
Prof. Dr. Matthias Gugger  
Prof. Dr. Anton Sculean  
Prof. Dr. Christian Seiler (since Aug.)  
Prof. Dr. Andreas Stuck (until July)  
Elisabeth Albertson (since Oct.)  
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Regula Käch (until Mar.)

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Prof. Dr. Hugues Abriel  
Director



Prof. Dr. Willy Hofstetter  
Deputy Director

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EPF Lausanne, Switzerland

Prof. Dr. Paul Klenerman  
University of Oxford, UK

Prof. Dr. Karl Schaller  
University of Geneva, Switzerland

Prof. Dr. Radek Skoda  
University of Basel, Switzerland

### Administration and Central Services

#### Administrator / Finances and DCR Secretaries

Basak Ginsbourger, Administrator  
Deborah Re, Secretary  
Ruth Scheuter, Secretary (until Mar.)  
Uyen Schmutz, Secretary  
Beatrix Stalder, Secretary (since Mar.)

#### Secretary of Director

Verena Frazao

#### DCR Human Resources

Silvia Rösselet

#### Facility Manager

Bernhard Grossniklaus

#### IT-Support

Michael Ackermann (since July)  
Oliver Schweizer (until June)  
Thomas Späti

#### Bioinformatics

Dr. Irene Keller  
Dr. Cedric Simillion  
David Andel (until Aug.)  
Ilker Romann (since Sep.)

#### Technical Services

Otto Aeby, Head DCR Maintenance

**Coordinators of Research Divisions**



**Prof. Dr. Anne-Catherine Andres**  
Tiefenau (until Jan.)



**Prof. Dr. Chris Boesch**  
Pavillon 52 (until Sep.)



**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



**Prof. Dr. Peter Vermathen**  
Pavillon 52 (since Sep.)

**Heads of Technology 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**  
CTU Bern



**Dr. Stefan Müller**  
Cytometry Laboratory /  
FACSlab

## Clinical Trials Unit (CTU) Bern

[www.ctu-bern.ch](http://www.ctu-bern.ch)

[www.dkf.unibe.ch/zentraler-dienst/93/](http://www.dkf.unibe.ch/zentraler-dienst/93/)

### Achievements 2014

The new Human Research Act (HRA; "Humanforschungsgesetz") introduced major changes in the regulation of clinical research, not only for clinical trials but also for observational studies including retrospective research projects. This new regulation was the driver for two projects carried out by CTU Bern, mostly in collaboration with the Directorate of Teaching and Research, Inselspital. The aim was to both support researchers to comply with the new regulation and to improve quality of conduct of clinical research projects. These projects addressed:

#### Standard operating procedures

At the end of 2013, the Directorate of Teaching and Research, Inselspital commissioned CTU Bern to develop a set of standard operating procedures (SOPs) and related documents covering aspects related to clinical trial conduct. The aim was to guarantee high quality and compliance with applicable regulatory requirements of clinical trials performed at the Inselspital. We were able to provide a first set of essential SOPs as planned over the course of 2014. The work is ongoing and additional documents will be produced during 2015.

#### Compliance of data management

CTU Data Management supports the Inselspital in assuring clinical research related data management is compliant with the HRA. CTU Bern developed different solutions in collaboration with the Inselspital: 1) The use of the existing REDCap system has increased massively. CTU Bern started empowering clinical researchers to build study databases on their own; 2) An additional system, secuTrial, was installed at the Inselspital and is being managed by CTU Bern. secuTrial is being used for more complex databases that cannot be implemented

using REDCap; and 3) additional solutions using MS Access/MS SQL as well as SharePoint infrastructure were set up in collaboration with the Inselspital to allow for HRA-compliant data management of small scale projects. By the end of 2014, 211 research databases of the Inselspital were checked to be HRA compliant or moved to one of the above-mentioned solutions.

Several clinical studies that we supported were completed in 2014. For example, the SWITCO 65+ cohort study completed follow-up and the study database was closed in the first half of 2014. SWITCO 65+ was a multicentre cohort study of inpatients and outpatients aged  $\geq 65$  years with an objective diagnosis of venous thromboembolism followed up for four years. CTU Bern was responsible for data management and statistical analyses. Another prominent example was the BIOSCIENCE trial. This multicentre trial published in the *Lancet* compared the effects of a biodegradable polymer sirolimus-eluting stent with a durable polymer everolimus-eluting stent in patients with chronic stable coronary artery disease or acute coronary syndromes. CTU Bern was responsible for data management, central and on-site monitoring, and statistical analysis.

### Performance Report 2014

As in previous years, we were active in providing consultancy services with again more than 100 contacts from various clinical departments of the Inselspital. The new HRA resulted in a sharp increase in consultations for the Data Management workflow.

The demand for courses in good clinical practice and basic clinical research methodology remained high. CTU Bern offers two types of courses: a one-day basic course and a two-day advanced add-on course. We were



Prof. Dr. Peter Jüni  
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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  
[sven.trelle@ctu.unibe.ch](mailto:sven.trelle@ctu.unibe.ch)

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.

able to further increase the number of courses and hosted five basic courses with 143 participants overall and three courses with 115 participants overall. In addition, CTU Bern was heavily involved in the setting up and conduct of a Certificate of Advanced Studies for Clinical Research Coordinators at Bern University of Applied Sciences.

### Finances 2014

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 2015

The impact of the HRA will remain high in 2015, especially for the Data Management and Monitoring workflows. We will expand our repertoire of courses (GCP refresher, hands-on training for data managers, introduction to statistics, protocol-writing workshop) and continue our involvement in specialist training (physiotherapists, clinical research coordinators). We hope to receive approval for several grant proposals in which CTU Bern was involved, including large-scale international trials.

### Staff Members

**Prof. Dr. Peter Jüni**, Director  
**Dr. Sven Trelle**, Associate Director  
**Hafeezul Adnan**, Project Manager  
**Vanessa Arn**, Assistant  
**Renata Bünter**, Clinical Research Coordinator  
**Dr. Lukas Bütikofer**, Statistician (since Aug.)  
**Myriam Cevallos**, Clinical Research Associate (until Dec.)  
**Dr. Michael Coslovsky**, Statistician (until Nov.)  
**Madeleine Dähler**, Clinical Research Coordinator  
**Regula Dänzer**, Clinical Research Coordinator (until July)

**Veronika Fiege**, Statistician (since Sep.)  
**Dr. Alan Haynes**, Statistician (since Sep.)  
**Dr. Dik Heg**, Senior Statistician  
**Muriel Helmers**, Head, Data Management  
**Stefanie Hossmann**, Monitor  
**Dr. Samuel Iff**, Statistician (until May)  
**Regula Jaeggi**, Clinical Research Coordinator  
**Lucia Kacina**, Monitor  
**Renata Klingelhöfer**, Financial Officer (until Jan.)  
**Thomas Knutti**, Financial Officer (until Jan.)  
**Dr. Andreas Limacher**, Head, Statistics  
**Lena Maurer**, Research Associate (since Mar.)  
**Dr. Eveline Nüesch**, Head, Statistics and Methodology (until Jul.)  
**Nico Pfäffli**, Research Associate (until Aug.)  
**Julie Rat-Wirtzler**, Data Manager  
**PD Dr. Stephan Reichenbach**, Head, Clinical Investigation  
**Felix Rintelen**, Head, Monitoring and Regulatory Affairs (since Nov.)  
**Martina Rothenbühler**, Statistician (since Aug.)  
**Dr. Dominique Rubi**, Data Manager (since July)  
**Ursina Sager**, Clinical Research Coordinator  
**Dr. Roger Schürch**, Statistician (since Nov.)  
**Timon Spörri**, Research Associate (until Sep.)  
**Dr. Malcolm Sturdy**, Data Manager  
**Brigitte Wanner**, Head, Quality Management  
**Miriam Wegmann**, Data Manager (since July)  
**Selina Wegmüller**, Research Associate (since Feb.)  
**Janine Wyniger**, Monitor  
**Adrian Wyss**, Data Manager (since Oct.)  
**Serge Zaugg**, Statistician  
**Katrin Ziegler**, Data Manager

### Acknowledgements in Publications

Fractional flow reserve-guided PCI for stable coronary artery disease. De, BB; Fearon, WF; Pijls, NH; Barbato, E; Tonino, P; Piroth, Z; Jagic, N; Mobius-Winckler, S; Rioufol, G; Witt, N; Kala, P; MacCarthy, P; Engstrom, T;

Oldroyd, K; Mavromatis, K; Manoharan, G; Verlee, P; Frobert, O; Curzen, N; Johnson, JB; Limacher, A; Nuesch, E; Juni, P (2014) in: *N Engl J Med*, 371(13), p. 1208-1217.

Integrating fragmented evidence by network meta-analysis: relative effectiveness of psychological interventions for adults with post-traumatic stress disorder. Gerger, H; Munder, T; Gemperli, A; Nuesch, E; Trelle, S; Juni, P; Barth, J (2014) in: *Psychol Med*, 44(15), p. 3151-3164.

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## Cytometry Laboratory / FACSlab

[www.facslab.unibe.ch](http://www.facslab.unibe.ch)

[www.dkf.unibe.ch/zentraler-dienst/48/](http://www.dkf.unibe.ch/zentraler-dienst/48/)

### Achievements 2014

In 2014, a yellow-green laser and additional detectors were installed in our BD FACS ARIA III cell sorter. Fluorescent proteins often used for transfection and as reporter genes, such as mCherry, red fluorescent protein (RFP) or dsRed, can now be detected accurately and efficiently for sorting purposes. In addition, the fluorescent spillover between the frequently used fluorochromes FITC and phycoerythrin (PE) can be minimised by exciting PE with the yellow-green instead of the blue laser.

For experiments with up to four colours, we now offer a BD FACSCalibur flow cytometer, which was moved from the DCR Rheumatology laboratory to our Core Facility, and which we thoroughly serviced and tested.

We observed increased demand to participate in our FACS course and needed to offer it four times in 2014.

### Performance Report 2014

Compared to 2013, FACS measurements increased by 10% and sorting by an impressive 40%! 66.7% of the FACS measurements were performed by researchers from Inselspital clinics

and 33.2% by researchers from University of Bern institutes. Use by external people made up only 0.1%. Cell sorting numbers were 64.5%, 33.5% and 2.0%, respectively. 67.4% of acquisitions and 63.6% of cell sorting were performed by DCR groups.

Due to frequent and heavy overbooking of our state-of-the-art flow cytometers, it was often difficult to find convenient time slots for measuring samples. Since November 2014, we now also charge for excessively booked time as soon as it exceeds actual time used by more than 30 mins. In this way, users should be motivated to more carefully estimate their required time, and the freed-up time can be booked by others.

### Finances 2014

The markedly increased use of our instruments was also reflected by increased revenues in 2014. In addition, the invoice for the yearly FlowJo software licence fee was covered by the "Ressourcenausschuss" of the Faculty of Medicine. Together, this resulted in a significant replenishment of our finances.



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

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

### Outlook 2015

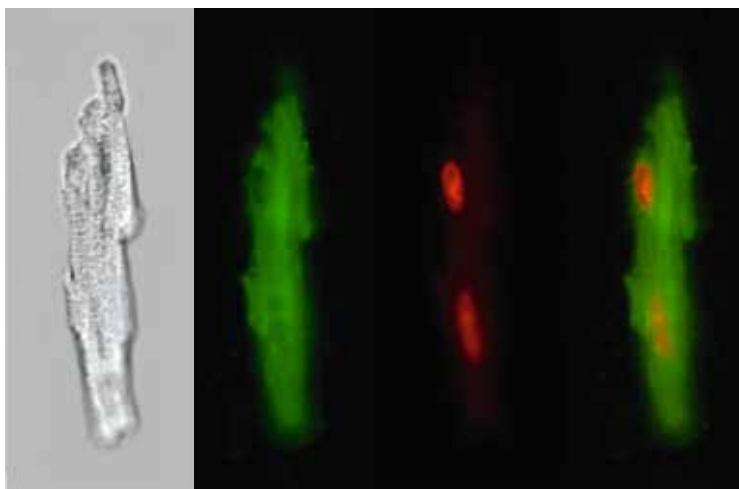
The FACS course will be adjusted in order to justify two ECTS points. In particular, this will mean that the final presentation will have to fulfil more stringent criteria.

The heavy use of our instruments requires shorter preventive maintenance intervals. This will be possible thanks to the improved financial situation.

We plan to develop, evaluate and post on our website specific protocols for analyses with our instruments, particularly for the ImageStream and the HyperCyt.

### Staff Members

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



## Live Cell Imaging (LCI)

[www.lci.dkf.unibe.ch/](http://www.lci.dkf.unibe.ch/)  
[www.dkf.unibe.ch/zentraler-dienst/92/](http://www.dkf.unibe.ch/zentraler-dienst/92/)

### Achievements 2014

Among the most important achievements in 2014 was the establishment and kick off of a new histology laboratory in our Core Facility. In this new laboratory, under the able guidance of Carlos Wotzkow, users have access to infrastructure, support and training in the field of sample preparation, embedding, cutting, immunohistochemistry and immunofluorescence.

Since its launch in 2012, the LCI Core Facility has been a unit of and is supported by the Microscopy Imaging Centre (MIC), an 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. In 2014, we launched a new practical MIC module, entitled "Immunohistochemistry, immunofluorescence and microscopy in paraffin embedded sections" ([www.mic.unibe.ch/teaching.php](http://www.mic.unibe.ch/teaching.php)) providing interested users with a lot of practical and theoretical knowledge in the field of histology.

Last but not least, we completely refurbished the LCI homepage, which now provides a regularly updated

overview of the current infrastructure, training, support and teaching in the LCI Core Facility.

### Performance Report 2014

A total number of 68 users (2013: 53) from 30 different research groups (2013: 25) acquired microscopy data with our help of the LCI Core Facility and spent a total of 6,177 booked hours (2013: 3,555) using its equipment during the last year. Furthermore, we provided one two-day MIC module on fluorescence microscopy, laser scanning microscopy, immunofluorescence labelling and image processing, and a five-day MIC module on immunohistochemistry and immunofluorescence in paraffin-embedded sections, for a total of 22 students. In addition, we contributed to cutting-edge lectures and the practical parours in light microscopy organised by the MIC.

### Finances 2014

In 2014, the LCI Core Facility collected CHF 28,250 (2013: CHF 18,750) in fees from confocal microscopy and



**Dr. Fabian Blank**  
[fabian.blank@dkf.unibe.ch](mailto:fabian.blank@dkf.unibe.ch)

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

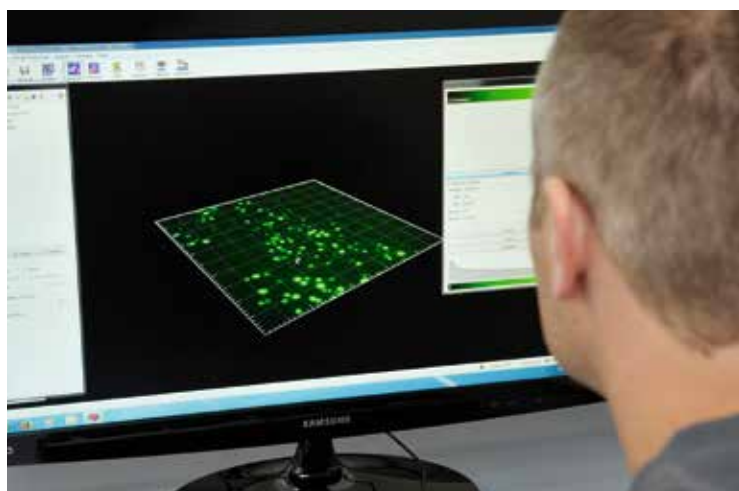
the Nikon Biostation. Expenses included a total of CHF 28,844 (2013: CHF 20,663) for repair, maintenance and disposables. Of this amount, the MIC kindly contributed CHF 3,207.60 to cover the repair of the Nikon Biostation CT and the Directorate of Teaching and Research, Inselspital covered CHF 16,584.70 for the 2014 IMARIS maintenance.

### Outlook 2015

For 2015, provision is made for the purchase of a new imaging system (brightfield/fluorescence or LSM) dedicated to monitoring microfluidic cell cultures in real time. Funding for this system is possible thanks to the help of Olivier Guenat, who received an SNF R'Equip grant and matching funds from the Inselspital "Fonds der Chefärztinnen und Chefärzte für Forschungsinfrastruktur".

### Staff Members

**Dr. Fabian Blank**, Head  
**Carlos Wotzkow**, Laboratory Technician



## Genomics (Core Facility)

[www.gcf.dkf.unibe.ch](http://www.gcf.dkf.unibe.ch)

## Molecular Biology (Research Group)

[www.molbiol.dkf.unibe.ch](http://www.molbiol.dkf.unibe.ch)



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

Studies and PhD (1982) at University of Bern. Postdoc (1984-1988) at Ludwig Institute for Cancer Research, Bern. Research (1988-1996) at Institute of Clinical and Experimental Cancer Research, Bern; several research residencies at University College, Dublin (IE). Habilitation (1990); Professor (1996) at University of Bern. Since 1996, Group Leader, DCR. Since 2010, Coordinator and since 2011, Head of Genomics Core Facility.

### Achievements 2014 / Outlook 2015

#### *Molecular Biology*

The majority of human breast cancer cells express the oestrogen (ER) and/or progesterone receptor. Hormone-bound receptors regulate transcription of numerous genes involved in the control of growth and proliferation. Anti-oestrogens like tamoxifen or repressors of oestrogen synthesis like letrozole efficiently inhibit these activities. Although receptor expression is limited to a subpopulation of cells in some tumours, they still respond to treatment. While ER-negative tumour cells cannot be a direct target for treatment, the mechanism by which proliferation is inhibited remains unclear. We developed methods to separate ER-positive and ER-negative cells from individual tumours. In 2015, we will measure gene expression in both subtypes. All the critical procedures have been tested and optimised. Material ("Schnellschnittmaterial") will be collected from surgical specimens from pathology. Subpopulations of these cells derived from single cancers have not been characterised before. The results will hopefully contribute to a better understanding of the mechanisms by which anti-oestrogens inhibit receptor-deficient tumour cells.

We compared the well-established recurrence score (Genomic Health) and our own RISK25 score in more than 200 prospective Swiss cancer specimens to investigate potential overlap. We also tested RISK25 and several other scores on 150 retrospective primary and recurrent cancers treated in Bern.

Our group has previously identified genes that potentially correlate with a response to letrozole but not to tamoxifen. In 2015, we will test and validate these genes in additional breast cancers from postmenopausal patients with primary breast cancer to determine

whether individual genes or a combination (score) are potentially predictive for a response to letrozole but not to tamoxifen.

### Performance Report 2014 / Outlook 2015

#### *Genomics*

The Genomics Core Facility supported users of the Faculty of Medicine in running their sequencing projects. The experimental part of low throughput studies on the Ion Torrent PGM and high throughput studies on the Illumina Hi-Seq was carried out by the Core Facility technician. Support was also offered with planning, quality control, primary analysis and detailed evaluation. The Inselspital funded two bioinformaticians, one IT specialist (60%) and one technician. Further support was provided by the Molecular Biology technician. The Core Facility collaborated with the Head of the Interfaculty Bioinformatics Unit, who established an active collaboration with the Swiss Institute of Bioinformatics, where copies of data from Bern are archived.

Approximately 860 libraries were produced and sequenced on the HiSeq in 2014; 282 from researchers associated with the Faculty of Medicine (DCR: 210 libraries, 6 groups; Inselspital: 40 libraries, 2 groups; Institute of Pathology: 32 libraries, 2 groups). In addition, several hundred small libraries and 40 sequencing runs were analysed on the Ion Torrent.

After the first year of full operation of the two sequencing platforms, it seems that the majority of researchers have a preference for high throughput sequencing (lower costs per nucleotide, more complete sequence information, well-accepted data). Very likely, the preference to use Illumina will continue in 2015, as novel and cheaper protocols are becoming available. The Ion Torrent will still remain

the best choice for diagnostic projects (mutation, deletion or rearrangement analysis).

The Vetsuisse Faculty has bought a new HiSeq instrument and the Faculty of Science a MiSeq. They will substantially increase the sequencing capacity of the Illumina platforms in 2015. We therefore expect an increased workload for technical support. On the other hand, the demand for the Ion Torrent will probably remain similar or decrease. As the Inselspital has purchased a PGM and a MiSeq, many diagnostic projects will be carried out in the clinics.

### Finances 2014

#### Genomics

The Genomics Core Facility had a working credit of CHF 15,000 from the DCR for repairs, maintenance and new equipment, and for establishing new protocols. One of the two technicians was busy most of her time with the HiSeq instrument located at the Vetsuisse Faculty. A new technician will need to be hired for the Inselspital position.

### Staff Members

**Prof. Dr. Rolf Jaggi**, Group Leader, Head of Genomics Core Facility

**Dr. Irene Keller**, Bioinformatician (Core Facility)

**Michèle Ackermann**, Laboratory Technician (Core Facility)

**David Andel**, IT Specialist (Core Facility) (until Aug. 2014)

**Ilker Romann**, IT Specialist (Core Facility) (from Sep. 2014)

**Mariana Bustamante**, PhD Student (Research Group)

**Muriel Fragnière**, Laboratory Technician (Research Group & Core Facility)

### Collaborators

**Aebi S**, Lucerne Cantonal Hospital, Switzerland

**Cathomas R**, Graubünden Cantonal Hospital, Switzerland

**Gautschi O**, Lucerne Cantonal Hospital, Switzerland

**Günthert A**, Lucerne Cantonal Hospital, Switzerland

**Krestel H, Nirrko A**, Inselspital, Switzerland

**Kristiansen G**, University of Bonn, Germany

**Pestalozzi B**, Zurich, Switzerland

**Popovici V**, Masaryk University, Czech Republic

**Rohr S**, University of Bern, Switzerland

Adjuvant Treatment of ER-positive Breast Cancer (R. Jaggi) CHF 22,468

– Various donors: (R. Jaggi) CHF 11,193

### Teaching Activities

- 1st year medical students: Problem Based Learning
- Selected topics in molecular pathology: Molecular Processes of Disease lecture

### Publications

#### *Molecular Biology*

Comprehensive validation of published immunohistochemical prognostic biomarkers of prostate cancer-what has gone wrong? A blueprint for the way forward in biomarker studies. Huber, F; Montani, M; Sulser, T; Jaggi, R; Wild, P; Moch, H; Gevensleben, H; Schmid, M; Wyder, S; Kristiansen, G (2015) in: Br J Cancer, 112(1), p. 140-148.

### Grants

#### Amounts allocated for 2014:

#### *Molecular Biology*

- W.+H. Berger-Janser Foundation: Characterization of ER-negative cancer cells in ER-positive breast cancer (R. Jaggi) CHF 52,011
- SAKK 26/10: Impact of Recurrence Score on Recommendations for



# Mass Spectrometry and Proteomics Laboratory (Core Facility)

## Protein and Cell Biology (Research Group)

[www.pmscf.dkf.unibe.ch](http://www.pmscf.dkf.unibe.ch)

### Achievements 2014 / Outlook 2015

#### *Mass Spectrometry and Proteomics & Protein and Cell Biology*

We finalised the protocol development for the proteome analysis of blood plasma microparticles. With our protocol, we routinely achieve excellent reproducibility in protein quantity measurements (CVs typically smaller than 10%). We have so far identified 2,267 products of genes that are associated with human plasma microparticles, of which 422 proteins are plasma-membrane associated, including many cell markers. These markers allow us to produce a quantitative cell profile of the origin of the microparticles. With this work, we won a poster prize at the DCR Day of Clinical Research on 5 November 2014 and Manfred Heller gave an oral presentation at the yearly meeting of the Swiss Group for Mass Spectrometry on 30 October 2014.

We also developed a new data acquisition method on the QExactive mass spectrometer that records an electronic archive of microparticle-associated proteins from individual samples with a single LC-MS/MS run. The archives can be searched by specialised software for the presence of any protein of interest (target) and extraction of quantitative information of such targets is possible. These achievements will allow us to screen hundreds of individual plasma samples from clinical studies of vascular disease patients, in order to glean a better understanding of the role of microparticles in such diseases. We kindly ask clinicians to contact us, if they are interested in collaborating in this research field.

#### **Proteomics service portfolio**

Together with other developments in our laboratory, we can now offer the following proteomics services:

- Standard sample preparation for LC-MS/MS (in-gel, in-solution, and on-beads digestion, as well as protein concentration of conditioned cell media)
- Protein identification based on protein or genetic sequence databases
- PTM analysis
- Relative/absolute protein quantification (isotope labelled or label free) by means of data-dependent acquisition (discovery mode), or targeted approaches such as selected reaction monitoring (SRM), selected ion monitoring (SIM), and data-independent acquisition (DIA)
- De-novo sequencing of polypeptides
- Intact mass determination of proteins up to a size of about 150 kDa
- Basic statistical evaluation of proteomics data

#### **Plans for 2015**

In 2015, we are hoping for financial support from the SNF to allow us to recruit additional staff and tackle the microparticle project in collaboration with clinics of the Inselspital. Furthermore, we are about to develop an automated in-gel digestion with direct coupling to LC-MS/MS protocol, in collaboration with CTC Analytics AG, Zwingen. If successful, this will help us to acquire more reproducible data for many customer samples. In addition, we intend to finalise the development of a new protocol for global proteome and phospho-proteome analyses.

#### **Performance Report 2014**

*Mass Spectrometry and Proteomics*  
As described above, we invested considerable time in the development of new analytical tools. In total, with all our customer samples, we performed roughly 1,600 analytical runs on our three nanoLC-MS/MS instruments this year.



**PD Dr. Manfred Heller**  
[manfred.heller@dkf.unibe.ch](mailto:manfred.heller@dkf.unibe.ch)

PhD in Biochemistry (1994) at University of Bern. Postdocs at University of Auckland (NZ) and Washington, Seattle (US). Return to Switzerland in 1999 to University of Geneva, followed by three years as Senior Scientist at GeneProt Inc., Geneva and DiagnoSwiss, Monthey. Since 2003, Head of Proteomics and Mass Spectrometry Laboratory, a DCR Core Facility since 2008. Seventeen years of experience in mass spectrometry, proteomics and bioinformatics.



### Finances 2014

*Mass Spectrometry and Proteomics*  
 We experienced a year of relatively few invoiced instrument breakdowns (two instruments under warranty). This comfortable situation allowed us to put aside most of the fee-for-service income from this year and our financial situation is very sound.

### Staff Members

**PD Dr. Manfred Heller**, Group Leader (Research Group) and Head (Core Facility)

**François Achermann**, Laboratory Technician (Core Facility & Research Group), Radio-safety and JHE Deputy and Biosafety Officer, DCR

**Sophie Braga Lagache**, Laboratory Assistant (Core Facility & Research Group)

**Natasha Buchs Tetkovic**, Laboratory Technician (Core Facility & Research Group)

**Dr. Cedric Similion**, Bioinformatician (Core Facility)

**Ilker Romann**, IT specialist (Core Facility) (since Sep.)

### Collaborators

**Böhm G**, CTC Analytics AG, Switzerland

**Jackson C**, Inselspital, Switzerland

**Müller M**, Swiss Institute of Bioinformatics, Switzerland

### Grants

None for 2014.

### Teaching Activities

- MSc Biomedical Sciences: Tumour Biology – proteomics lecture
- MSc Biology: From Genomes to Metabolomes – proteomics lecture
- MSc in Bioinformatics: Mass Spectrometry to Systems Biology course

### Publications

A low-affinity penicillin-binding protein 2x variant is required for heteroresistance in *Streptococcus pneumoniae*. Engel, H; Mika, M; Denapate, D; Hakenbeck, R; Muhlemann, K; Heller, M; Hathaway, LJ; Hilty, M (2014) in: *Antimicrob Agents Chemother*, 58(7), p. 3934-3941.

*Streptococcus pneumoniae* detects and responds to foreign bacterial peptide fragments in its environment. Hathaway, LJ; Battig, P; Reber, S; Rotzetter, JU; Aebi, S; Hauser, C; Heller, M; Kadioglu, A; Muhlemann, K (2014) in: *Open Biol*, 4, p. 130224.

Genome-wide identification of pathogenicity factors of the free-living amoeba *Naegleria fowleri*. Zysset-Burri, DC; Muller, N; Beuret, C; Heller, M; Schurch, N; Gottstein, B; Wittwer, M (2014) in: *BMC Genomics*, 15, p. 496.



## Bone Biology & Orthopaedic Research

[www.bonebiology.dkf.unibe.ch](http://www.bonebiology.dkf.unibe.ch)  
[www.dkf.unibe.ch/forschungsgruppe/1/](http://www.dkf.unibe.ch/forschungsgruppe/1/)



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

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

### Research Highlights 2014 / Outlook 2015

#### Bone Biology & Orthopaedic Research Group

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

- In vivo experiments in a rat model to investigate the osseointegration and turnover of composite materials of poly-lactate nano-fibres and CaP cement. Particular attention was paid to safety issues and a pathological analysis of all organs was performed (NFP64, PhD project N. Ruef).
- Studies of the highly regulated process of iron transport in osteoclast lineage cells. We found increased levels of iron to inhibit osteoclastogenesis while stimulating macrophage proliferation and differentiation. Furthermore, levels of transcripts encoding the molecular components of iron homeostasis and storage were dependent on the differentiation states (NCCR, PhD project W. Xie).
- Fracture repair in osteoporotic bone is not impaired as compared to healthy bone with normal density and structure. It is not clear, however, how long-term treatment of patients with bisphosphonates affects the healing process. We are studying the path of bone repair in osteoporotic bones treated with bisphosphonates in rigid and non-rigid fixation (PhD project M. Hauser).
- Investigation into why articular chondrocytes expanded in monolayer culture lose their potential for chondrogenesis in the absence of exogenous growth factors. Auto- and paracrine TGF- $\beta$  signalling has been identified as an essential component for cartilage formation. Further characterisation of this pathway and identification of other components are the focus of further studies (RMS, R. Egli).
- Detailed studies of the mechanisms of the effects of bone morphogenetic proteins and their agonists in integration and turnover of materials. Bio-functionalisation is a means to improve the osseointegration and turnover of CaP ceramic-based bone substitute materials. (SNF, PhD project J. Choy; PI: F. Klenke).

#### Osteo-Articular Research Group

Highlights of our research on cartilage biology and degeneration include:

- Studies of the calcium-binding proteins S100A1 and S100B, which are expressed in normal human articular cartilage. Both proteins show diminished expression during the process of osteoarthritic cartilage degeneration and both proteins are gradually lost during expansion in monolayer (de-differentiation), yet only S100A1 is re-expressed in pellets (re-differentiation). Loss of S100B expression suggests irrevocable change of cells after isolation.
- We discovered a direct correlation between the percentage of S100-positive human articular chondrocytes and deposition of proteoglycan in micro-mass pellet culture, establishing S100 as a marker of their chondrogenic potential in vitro.

**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

**Michel Hauser**, PhD Student  
(since June)

**Nina Ruef**, PhD Student (since Feb.)

**Adel Tekari**, PhD Student (until Apr.)

**Wenjie Xie**, PhD Student

*Osteo-Articular Research Group*

**PD Dr. Dobrila Nestic**, Group Leader

*Clinician with projects in the Group*

**PD Dr. Frank Klenke**, Project Leader

**Collaborators**

**Aeberli D**, Inselspital, Switzerland

**Fuster D**, Inselspital, Switzerland

**Kohl S**, Inselspital, Switzerland

**Luginbuehl R**, RMS Foundation,  
Switzerland

**Schäfer B**, Geistlich Pharma AG,  
Switzerland

**Schär M**, Inselspital, Switzerland

**Sebald HJ**, theSpinecenter (Thun),  
Switzerland

**Seitz M**, Inselspital, Switzerland

**Siebenrock KA**, Inselspital,  
Switzerland

**Stok K**, ETH Zurich, Switzerland

**Zumstein M**, Inselspital, Switzerland

**Grants****Amounts allocated for 2014:**

*Bone Biology & Orthopaedic Research*

– SNF: NCCR TransCure sub-project:  
Role of ion transporter TRPV6 and  
other transporters in bone homeo-  
stasis (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. Mani-  
ura, W. Hofstetter) CHF 83,000

– SNF: Biofunctionalization of  
 $\beta$ -Tricalcium Phosphate Ceramics  
for the Repair of Osseous Defects  
(F. Klenke, W. Hofstetter)

– SNF: Osteoclastogenesis and chronic  
inflammatory rheumatic disorders  
(M. Seitz, D. Aeberli, B. Engelhardt,  
J.V. 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 35,000

– 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. Nestic, M. Zumstein)  
CHF 24,000

**Teaching Activities**

- MSc Biomedical Engineering:  
Tissue Engineering course (Nestic)
- MSc Biomedical Engineering:  
Osteology course (Hofstetter)
- 3rd-year dentistry students: Patho-  
physiology – Skeleton (Hofstetter)
- 1st-year medical students: Mole-  
cular biology practical courses  
(Hofstetter)
- 2nd-year medical students: Kidney  
block – Calcium and phosphate  
metabolism (Hofstetter)
- 3rd-year biomedical and cell biolo-  
gy students: Pathology of the  
musculoskeletal system (Nestic)

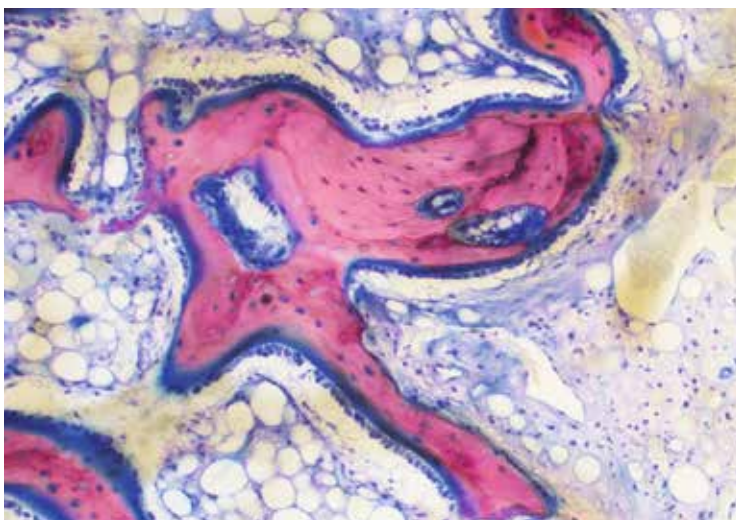
**Publications**

Incorporation of RANKL promotes  
osteoclast formation and osteoclast  
activity on beta-TCP ceramics. Choy, J;  
Albers, CE; Siebenrock, KA; Dolder, S;  
Hofstetter, W; Klenke, FM (2014) in:  
*Bone*, 69, p. 80-88.

S100A1 and S100B expression  
patterns identify differentiation status  
of human articular chondrocytes.  
Diaz-Romero, J; Quintin, A; Schoen-  
holzer, E; Pauli, C; Despont, A; Zum-  
stein, MA; Kohl, S; Nestic, D (2014) in:  
*J Cell Physiol*, 229(8), p. 1106-1117.

Chondrocytes expressing intracel-  
lular collagen type II enter the cell  
cycle and co-express collagen type I  
in monolayer culture. Tekari, A;  
Luginbuehl, R; Hofstetter, W; Egli, RJ  
(2014) in: *J Orthop Res*, 32(11),  
p. 1503-1511.

TREM-1 deficiency can attenuate  
disease severity without affecting  
pathogen clearance. Weber, B;  
Schuster, S; Zysset, D; Rihs, S; Dick-  
greber, N; Schurch, C; Riether, C;  
Siegrist, M; Schneider, C; Pawelski, H;  
Gurzeler, U; Ziltener, P; Genitsch, V;  
Tacchini-Cottier, F; Ochsenbein, A;  
Hofstetter, W; Kopf, M; Kaufmann, T;  
Oxenius, A; Reith, W; Saurer, L;  
Mueller, C (2014) in: *PLoS Pathog*,  
10(1), p. e1003900.



## Cardiovascular Research

[www.cvrc.dkf.unibe.ch](http://www.cvrc.dkf.unibe.ch)

[www.dkf.unibe.ch/forschungsgruppe/61/](http://www.dkf.unibe.ch/forschungsgruppe/61/)



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

Studies in Biology at 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 2014 / Outlook 2015

For several years already, our research group has been closely collaborating with the Department of Plastic and Hand Surgery, Inselspital. The aim of one of our projects is to find new ways to prevent rejection of vascularised composite allografts, in particular transplanted hands. The problem in hand transplantation is that the graft recipients need lifelong systemic immunosuppression to prevent rejection of the allograft. However, conventional immunosuppression has considerable side effects. For example, over the years it may lead to a higher incidence of cancer or to kidney or liver failure. We therefore aim at developing novel techniques for local immunosuppression. In collaboration with the groups of Praveen Vemula, Bangalore (IN), and Jeffrey Karp, Boston (US), we developed and tested a hydrogel that can be locally injected into the grafted limb and which only delivers the immunosuppressant (Tacrolimus) when needed because of a rejection reaction. In a series of rat experiments, we were able to show that a single localised dose of enzyme-responsive hydrogel improves long-term survival of a vascularised composite allograft. All Lewis rats treated with the Tacrolimus-hydrogel at day 1 post transplantation did not reject their hind limb from Brown Norway rat donors for at least 100 days.

We continued our work on xenotransplantation in collaboration with the partners of the DFG Transregio Collaborative Research Center 127 (DE), through whom we have access to transgenically modified pigs and porcine cells. Anjan Bongoni, who finished his PhD in the last days of 2013 and continued as a postdoc until the end of August 2014, investigated the effect of human CD46 expression on porcine endothelial cells. In particular, he showed that hCD46 not only prevents activation and deposition of human complement on porcine endothelial cells, as expected, but also prevents the switch of the endothelial cell to a procoagulant and anti-fibrinolytic phenotype.

The link between the plasma cascade systems—complement, coagulation, kinin/kallikrein and fibrinolysis—and their interactions with endothelial cells will continue to be in the focus of our research in 2015. These investigations will be performed in vitro in cell culture models, in vivo in the rat hind limb ischemia/reperfusion injury model, and in pig limb perfusions, both autologous and xenogeneic. In addition, the rat hind limb transplantations will be continued in order to bring local, on-demand immunosuppression closer to clinical application.





### Group Members

**Prof. Dr. Robert Rieben,**  
Group Leader

**Dr. Yara Banz,** Research Associate  
(Pathology)

**PD Dr. Jana Ortmann,** Research  
Associate (Tiefenau Hospital)

**Dr. Anjan Bongoni,** Postdoc  
(until Aug.)

**Julie Denoyelle,** Laboratory  
Technician and MSc Student

**Alain Despont,** Laboratory  
Technician (since Feb.)

**Jane Shaw-Boden,** Laboratory  
Technician

**Uyen Schmutz,** Secretary and Web  
Administrator

**Mai Abdelhafez,** PhD Student

**Shengye Zhang,** PhD Student

**Rahel Klossner,** Intern (since July)

### Collaborators

**Abicht J, Reichart B,** Ludwig  
Maximilian University of Munich,  
Germany

**Ahrens H, Niemann H,** Friedrich  
Loeffler Institute, Germany

**Ayares D,** Revivacor Inc., USA

**Bovin N, Korchagina E, Titov A,**  
Russian Academy of Sciences, Russia

**Constantinescu MA, Olariu R,**  
Inselspital, Switzerland

**Gajanayake T, Schnider J, Sutter D,**  
Vögelin E, Inselspital, Switzerland

**Guenat O,** University of Bern,  
Switzerland

**Jenni HJ,** Inselspital, Switzerland

**Karp JM,** Harvard Medical School, USA

**Khattab A,** Inselspital, Switzerland

**Klymiuk N, Wolf E, Wünsch A,**  
Ludwig Maximilian University of  
Munich, Germany

**Miescher S, Spirig R, Spycher M,**  
CSL Behring AG, Switzerland

**Seebach J,** Geneva University  
Hospital, Switzerland

**Vemula P,** inStem, India

### Grants

#### Amounts allocated for 2014:

- SNF: Endothelial cell protection in xenotransplantation and ischemia/reperfusion injury: Assessing the effect of multiple transgenes and the pathophysiological role of the plasma cascade systems (R. Rieben) CHF 29,000
- SNF: Endothelial cell protection: The role of heparan sulfate proteoglycans and complement in pathophysiology and prevention of ischemia/reperfusion injury (R. Rieben) CHF 62,413
- 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 45,000
- Gottfried und Julia Bangerter-Rhyner-Stiftung: A Novel Therapeutic Method Targeting Local Immunosuppression in Composite Tissue Allotransplantation (E. Vögelin, R. Rieben, T. Gajanayake) CHF 20,000

### 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
- BSc in Life Sciences: Practical Course in Immunology
- PhD students in Graduate School for Cellular and Biomedical Sciences: Immunology tutorial
- High school students: Patenschaften für Maturaarbeiten (3 students with 2-week lab stay each)

### Publications

Complement dependent early immunological responses during ex vivo xenoperfusion of hCD46/HLA-E double transgenic pig forelimbs with human blood. Bongoni, AK et al. (2014) in: Xenotransplantation, 21(3), p. 230-243.

Use of dextran sulfate in tourniquet-induced skeletal muscle reperfusion injury. Duehrkop, C; Denoyelle, J; Shaw, S; Rieben, R (2014) in: J Surg Res, 187(1), p. 150-161.

Refinement of tourniquet-induced peripheral ischemia/reperfusion injury in rats: comparison of 2 h vs 24 h reperfusion. Duehrkop, C and Rieben, R (2014) in: Lab Anim, 48(2), p. 143-154.

A single localized dose of enzyme-responsive hydrogel improves long-term survival of a vascularized composite allograft. Gajanayake, T et al. (2014) in: Sci Transl Med, 6(249), p. 249ra110.

Regulatory sequences of the porcine THBD gene facilitate endothelial-specific expression of bioactive human thrombomodulin in single- and multi-transgenic pigs. Wuensch, A et al. (2014) in: Transplantation, 97(2), p. 138-147.



# Ion Channels and Channelopathies

[www.ionchannels.dkf.unibe.ch](http://www.ionchannels.dkf.unibe.ch)  
[www.dkf.unibe.ch/forschungsgruppe/66/](http://www.dkf.unibe.ch/forschungsgruppe/66/)



**Prof. Dr. Hugues Abriel**  
[hugues.abriel@dkf.unibe.ch](mailto:hugues.abriel@dkf.unibe.ch)

## Research Highlights 2014 / Outlook 2015

The main goal of our research is to elucidate the genetic, molecular and cellular mechanisms underlying human diseases caused by malfunction of ion channels, so called 'channelopathies'. Cardiac diseases such as arrhythmias or neurological disorders such as chronic pain may be caused by either mutations in the genes coding for the ion channel subunits or dysregulation of their functions.

In 2014, Ninda Syam obtained her PhD based on her studies related to the biochemical regulation of the ion channel TRPM4 and the characterisation of TRPM4 genetic variants found in patients with cardiac arrhythmias. A new student, Beatrice Bianchi, has taken her place. In the framework of phase 2 of the NCCR TransCure, she will investigate other genetic variants of TRPM4 causing arrhythmias and start to study the role of this channel in multiple sclerosis. She will address the question of whether newly developed TRPM4 compounds may reduce the severity of multiple sclerosis in a mouse model. M. Yassine Amarouch also left the group to take up a university position in Morocco. He will be replaced in 2015 by Lijo Cherian Ozhathil, a new TransCure postdoctoral fellow, who will characterise new compounds that have either blocking or activating properties on TRPM4. This work will be done in close collaboration with the group of Jean-Louis Reymond (Department of Chemistry and Biochemistry).

Another main focus of our group is the cardiac sodium channel Nav1.5, which is known to be involved in a myriad of cardiac disorders, in particular arrhythmias. Diana Shy and Ludovic Gillet published two important studies in the journals *Circulation* and *HeartRhythm*, describing the molecular and cellular determinants underlying the targeting and function of different populations of Nav1.5 channels in cardiac cells. These studies were mainly supported by the SNF and by the EU FP7 EuTrigTreat project. In a collaboration with Heikki Swan and Elisabeth Widen (FI), we also published a study reporting on a new exercise-induced arrhythmic phenotype caused by a mutation in the gene encoding Nav1.5.

Both ion channels Nav1.5 and TRPM4 will continue to be the focus of our studies in 2015. Diana Shy and Valentin Sottas will defend their theses during the year and we will look for PhD students to continue their work. Our group will also be more involved in the second phase of the NCCR TransCure, as Hugues Abriel will take over the directorship of this network.

Training both as a biologist at ETH Zurich and physician at University of Lausanne. After two years at 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, SNF National Research Council.

### Group Members

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



### Collaborators

Bezzina C, University of Amsterdam Academic Medical Centre, 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  
 Remme CA, University of Amsterdam Academic Medical Center, Netherlands  
 Reymond JL, NCCR TransCure, Switzerland  
 Swan H, University of Helsinki, Finland  
 Widen E, University of Helsinki, Finland  
 Zaklyazminskaya EV, Moscow, Russia  
 Zambelli T, ETH Zurich, Switzerland

### Grants

#### Amounts allocated for 2014:

- SNF: Molecular determinants of Nav 1.5 multiprotein complexes in cardiac cells (H. Abriel) CHF 305,500
- SNF: NCCR TransCure subproject: Physiology, pharmacology and pathophysiology of the calcium-activated non-selective cation TRPM4 channel (M. Hediger, H. Abriel) CHF 186,900
- SNF: Interdisciplinary project: Force-controlled patch clamp (T. Zambelli, H. Abriel) CHF 61,400
- European Union: EUTrigTreat – Identification and therapeutic targeting

of common arrhythmia trigger mechanisms (S. Lehnart, H. Abriel) CHF 75,900

### Teaching Activities

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

### Publications

Late cardiac sodium current can be assessed using automated patch-clamp. Chevalier, M; Amuzescu, B; Gawali, V; Todt, H; Knott, T; Scheel, O; Abriel, H (2014) in: *F1000Res*, 3, p. 245.

Expression, purification, and projection structure by single particle electron microscopy of functional human TRPM4 heterologously expressed in *Xenopus laevis* oocytes. Clemenccon, B; Fine, M; Luscher, B; Baumann, MU; Surbek, DV; Abriel, H; Hediger, MA (2014) in: *Protein Expr Purif*, 95, p. 169-176.

Cardiac-specific ablation of synapse-associated protein SAP97 in mice decreases potassium currents but not sodium current. Gillet, L; Rougier, JS; Shy, D; Sonntag, S; Mougnot, N; Essers, M; Shmerling, D; Balse, E; Hatem, SN; Abriel, H in: *Heart Rhythm*, e-pub ahead of print: doi: 10.1016/j.hrthm.2014.09.057.

Ubiquitin-specific protease USP2-45 acts as a molecular switch to promote

alphadelta-1-induced downregulation of Ca<sub>v</sub>1.2 channels. Rougier, JS; Albesa, M; Syam, N; Halet, G; Abriel, H; Viard, P in: *Pflugers Arch*, e-pub ahead of print.

PDZ domain-binding motif regulates cardiomyocyte compartment-specific Nav1.5 channel expression and function. Shy, D; Gillet, L; Ogrodnik, J; Albesa, M; Verkerk, AO; Wolswinkel, R; Rougier, JS; Barc, J; Essers, MC; Syam, N; Marsman, RF; van Mil, AM; Rotman, S; Redon, R; Bezzina, CR; Remme, CA; Abriel, H (2014) in: *Circulation*, 130(2), p. 147-160.

p.L1612P, a Novel Voltage-gated Sodium Channel Nav1.7 Mutation Inducing a Cold Sensitive Paroxysmal Extreme Pain Disorder. Suter, MR; Bhuiyan, ZA; Laedermann, CJ; Kuntzer, T; Schaller, M; Stauffacher, MW; Roulet, E; Abriel, H; Decosterd, I; Wider, C in: *Anesthesiology*, e-pub ahead of print.

A Gain-of-Function Mutation of the SCN5A Gene Causes Exercise-Induced Polymorphic Ventricular Arrhythmias. Swan, H; Amarouch, MY; Leinonen, J; Marjamaa, A; Kucera, JP; Laitinen-Forsblom, PJ; Lahtinen, AM; Palotie, A; Kontula, K; Toivonen, L; Abriel, H; Widen, E (2014) in: *Circ Cardiovasc Genet*, (6): p. 771-781.

Glycosylation of TRPM4 and TRPM5 channels: molecular determinants and functional aspects. Syam, N; Rougier, JS; Abriel, H (2014) in: *Front Cell Neurosci*, 8, p. 52.

# DCR Research Groups from the Inselspital

Forty-two research groups from departments of the Inselspital were affiliated with the DCR at the end of 2014. Below is a list of the groups and the names of the Chairs of Department, Heads of Research/Laboratory and/or Group Leaders. Nine 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, PD Dr. Martin Luginbühl, PD Dr. Andreas Vogt

**Angiology:** Prof. Dr. Iris Baumgartner

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

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

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

**Clinical Radiopharmacy:** Prof. Dr. Thomas M. Krause, PD Dr. Martin A. Walter

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

**Dermatology:** Prof. Dr. Luca Borradori, Prof. Dr. Robert Hunger, Dr. Christoph Schlapbach, Dr. Dagmar Simon, Prof. Dr. Nikhil Yawalkar

**Endocrinology of the Breast:** PD Dr. Petra Stute

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

**Endocrinology / Diabetology / Metabolism (Paediatrics):**

Prof. Dr. Primus Mullis, Prof. Dr. Christa Flück, PD Dr. Jean-Marc Nuoffer

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

**Endometrium & Ovary:**

Prof. Dr. Michael von Wolff

**Experimental Haemostasis:**

Prof. Dr. Hans-Peter Kohler, PD Dr. Verena Schröder

**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 Voegelin

**Hematology (Adults):** Prof. Dr. Anne Angelillo-Scherrer, Prof. Dr. Gabriela Baerlocher, PD Dr. Johanna Anna Kremer Hovinga Strebel, PD Dr. Elisabeth Oppliger Leibundgut

**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, PD Dr. André Schaller

**Intensive Care 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, 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. Urs Fischer, Prof. Dr. Heinrich Mattle, Prof. Dr. René Müri, Prof. Dr. Kaspar Schindler, PD Dr. Michael Schüpbach

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

**Oncology / Haematology (Adults):**

Prof. Dr. Martin Fey, PD 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, Prof. Dr. Marius Keel, PD Dr. Dobrila Nesic

**Osteoporosis:** Prof. Dr. Kurt Lippuner

**Plastic Surgery:** Prof. Dr. Mihai Constantinescu, PD Dr. Maziar Shafiqhi

**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

**Pulmonary Medicine (Paediatrics):**

Prof. Dr. Thomas Geiser, PD Dr. Philipp Latzin

**Radiation Oncology:** Prof. Dr. Daniel

Aebersold, PD Dr. Yitzhak Zimmer, Dr. Michaela Medová, 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. Burkhard Möller, Prof. Dr. Michael Seitz, Prof. Dr. Beat Trueb, Dr. Daniel Yerly

**Thoracic Surgery:** Prof. Dr. Ralph A.

Schmid, 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, Prof. Dr. Katia Monastyrskaya

**Visceral and Transplantation Surgery:**

Prof. Dr. Daniel Candinas, PD Dr. Deborah Keogh-Stroka, Dr. Vanessa Banz, Prof. Dr. Guido Beldi, Dr. Lukas Brügger

# Anaesthesiology

[www.anaesthesiologie.insel.ch/de/forschungresearch/](http://www.anaesthesiologie.insel.ch/de/forschungresearch/)  
[www.dkf.unibe.ch/research-group/85/](http://www.dkf.unibe.ch/research-group/85/)

## Research Highlights 2014 / Outlook 2015

We have different research groups that investigate a variety of topics in the context of anaesthesiology and pain medicine.

### Stüber/Lippuner Group

We focus on the genetic predisposition for perioperative morbidity and mortality, with a special interest in the field of inflammation/immunology, cardiovascular research, pharmacogenetics and pain medicine. Our projects embrace the influence of genomic variations from the molecular level to the clinical phenotype. We aim to link basic with clinical research. The anaesthesia genetic biobank of patients and healthy donors was strongly expanded during 2014 and association studies showed single nucleotide polymorphisms that enhance the risk of post-operative nausea and vomiting. This and additional genetic association studies will be continued in 2015 to explore the impact of our genome on perioperative risks. Additional projects in the field of the modulation of the human immune system through anaesthesia/surgery successfully started in 2014 and will be continued in 2015. For example, the role of miRNAs in pain and the immune defence will be explored in more detail.

### Luginbühl Group

In cooperation with the Department of Anaesthesiology, University Medical Center Groningen (UMCG) (NL), a novel triple interaction model of sevoflurane, propofol and remifentanyl was developed and presented at the 2014 annual meeting of the International Society for Anaesthetic Pharmacology in New Orleans (US). The model forms a link between intravenous and inhalation anaesthetics in combination with opioids. It allows us to estimate the anaesthetic potency of any combination of the three drugs and to convert a propofol-remifentanyl combination into an equipotent sevoflurane-remifentanyl combination. It will be used in the revised version of Smart Pilot View® (Dräger Medical, DE), an anaesthesia drug display, which may be useful to optimise titration of anaesthetics during surgery. In 2014, the enrolment of patients for the Smart Pilot Utility Trial, a two-centre open-label observational study in cooperation with the UMCG, was completed in Bern (enrolment in Groningen is still active). In 2015, a follow-up study on the potency of other opioids in combination with propofol and sevoflurane will be started in Bern.

### Vogt Group

The focus of our group is on the investigation of pulmonary gas exchange, using the multiple inert gas elimination technique (MIGET) based on micropore membrane inlet mass spectrometry (MMIMS). Since 2011, we have been working on an SNF-funded project to assess the clinical applicability of using MMIMS-MIGET to record rapid changes in respiratory and circulatory distribution in patients. This translational research project is composed of three parts: 1) An in vitro lung model using oxygenators for gas exchange to investigate MMIMS-MIGET under laboratory conditions; 2) An animal lung injury series showing the highly resolved time course of the ventilation-to-perfusion distribution in two types of lung damage (lavage lung injury and autologous clot injury), using MMIMS-MIGET; and 3) A clinical study in cardiac and thoracic surgery patients to assess, for the first time, feasibility and safety in clinical patients.



**Prof. Dr. Frank Stüber**  
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MD (1988) at Kiel University (DE). Postdoc (1990-1991) at University of Alabama at Birmingham (US). Venia docendi (1999); Vice Director Anaesthesiology (2001-2008), University of Bonn (DE). Since 2001, Visiting Associate Professor, University of Texas, Houston (US). Since 2008, Full Professor and Chair, Department of Anaesthesiology and Pain Medicine; since 2013, Vice Medical Director, Inselspital.



**Dr. Christoph Lippuner**  
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Studied biology at ETH Zurich (2002); Dr. rer. nat. (2005) at Max Planck Institute for Infection Biology, Humboldt University of Berlin (DE). Postdoc (2005-2007) at Netherlands Cancer Institute, Amsterdam. Group Leader (2007-2009), Albert-Ludwigs University, Freiburg (DE). Postdoc (2009-2012), University of Zurich. Since 2012, Head of Laboratory, Anaesthesiology Research Group, DCR.



**PD Dr. Martin Luginbühl**  
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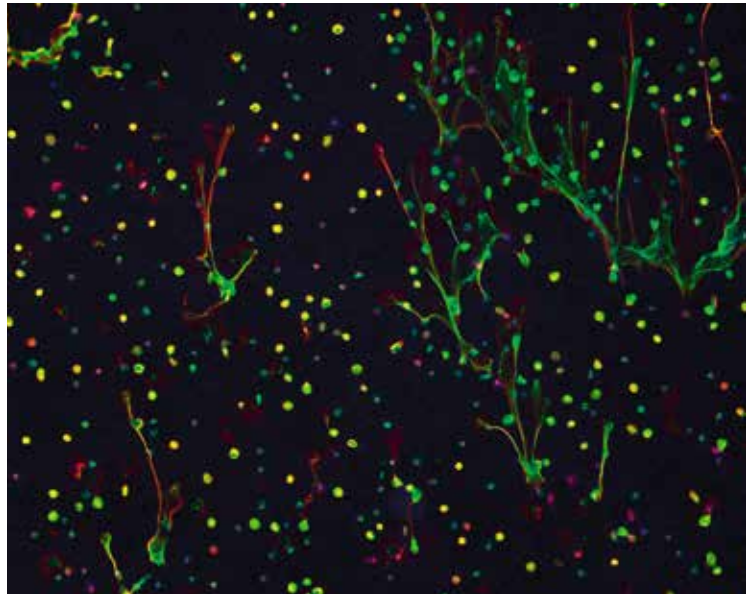
MD (1986) at University of Bern. FMH Anaesthesiology (1994); venia docendi (2008). Since 2011, Head, Department of Anaesthesia, Spital Netz Bern, Tiefenau and Ziegler.





PD Dr. Andreas Vogt  
andreas.vogt@insel.ch

MD (1989) at University of Bern; Diploma of the European Academy of Anaesthesiology (1999). Research fellowship (2007) at Department of Anaesthesiology, Johannes Gutenberg University, Mainz (DE). Venia docendi (2014) at University of Bern. Since 2014, Senior Attending, Head of Anaesthesia for General, Thoracic and Liver Transplantation Surgery, Inselspital.



### Group Members

**Prof. Dr. Frank Stüber**, Chair  
**Dr. Christoph Lippuner**, Head of Laboratory  
**PD Dr. Martin Luginbühl**, Group Leader  
**PD Dr. Andreas Vogt**, Group Leader

**PD Dr. Malte Book**, Consultant  
**Dr. Daniel Gerber**, Resident  
**Prof. Dr. Ulrike Stamer**, Attending  
**Dr. Stefanie Wenger**, Resident  
**Dr. Rolf Lauber**, Bio-Engineer  
**Volker Hartwich**, Research Associate  
**Dr. Zhang Lan**, Research Associate  
**Rakesh Vasireddy**, Research Associate  
**Dr. Balamurugan Varadarajan**, Postdoctoral Fellow  
**Dr. Tingting Wen**, Postdoctoral Fellow  
**Dr. Xianghong Zhang**, Postdoctoral Fellow  
**Sibylle Rohrbach**, Technical Assistant  
**Marcel Schiff**, Technical Assistant  
**Mirela Vitanescu**, Technical Assistant (since Nov.)  
**Loreen Erass**, Study Nurse  
**Ruth Lobsiger**, Secretary  
**Matthias Staiger**, MD Student

### Selected Collaborators

**Baumgardner J**, Oscillology LLC, USA  
**McCoy K**, University of Bern, Switzerland  
**Platzer M**, Leibniz Institute for Age Research – Fritz Lipmann Institute, Germany

**Struys MMRF**, University Medical Center Groningen, Netherlands  
**Vereecke H, Proost H**, University Medical Center Groningen, Netherlands

### Selected Grants

**Amounts allocated for 2014:**

- Scherbath Foundation: Modulation of the gut inflammasome by different anaesthetic concepts (F. Stüber, K. McCoy) CHF 75,000
- Gottfried and Julia Bangerter-Rhyner Foundation: Multiple Inert Gas Elimination Technique Based on Micropore Membrane Inlet Mass Spectrometry for Real Time VA/Q Distribution Evaluation: A Prospective, Observational Clinical Study in Cardiac and Thoracic Surgery (A. Vogt) CHF 50,000

### Selected Publications

Tramadol and O-Desmethyl Tramadol Clearance Maturation and Disposition in Humans: A Pooled Pharmacokinetic Study. Allegaert, K; Holford, N; Anderson, BJ; Holford, S; Stüber, F; Rochette, A; Troconiz, IF; Beier, H; de Hoon, JN; Pedersen, RS; Stamer, U in: Clin Pharmacokinetics, e-pub ahead of print.

A response surface model approach for continuous measures of hypnotic and analgesic effect during sevoflurane-remifentanyl interaction:

quantifying the pharmacodynamic shift evoked by stimulation. Heyse, B; Proost, JH; Hannivoort, LN; Eleveld, DJ; Luginbuhl, M; Struys, MM; Vereecke, HE (2014) in: Anesthesiology, 120(6), p. 1390-1399.

8p23 beta-defensin copy number determination by single-locus pseudo-gene-based paralog ratio tests risk bias due to low-frequency sequence variations. Zhang, X; Muller, S; Moller, M; Huse, K; Taudien, S; Book, M; Stüber, F; Platzer, M; Groth, M (2014) in: BMC Genomics, 15, p. 64.

Inflammatory mediators influence the expression of nociceptin and its receptor in human whole blood cultures. Zhang, L; Stüber, F; Stamer, UM (2013) in: PLoS One, 8(9), p. e74138.

Genome-wide association study of survival from sepsis due to pneumonia: an observational cohort study. Rautanen, A et al. in: Lancet Respir Med, e-pub ahead of print: doi: 10.1016/S2213-2600(14)70290-5.

# Cardiovascular Surgery

[www.cardiovascular-research.ch](http://www.cardiovascular-research.ch)  
[www.dkf.unibe.ch/forschungsgruppe/8/](http://www.dkf.unibe.ch/forschungsgruppe/8/)

## Research Highlights 2014 / Outlook 2015

Our research focuses on the following projects:

### Cardiac donation after circulatory death (DCD)

The DCD project is currently the major research topic of our unit. We aim to identify and evaluate strategies to promote the use of DCD cardiac grafts. 2014 was marked by a *Nature Reviews Cardiology* publication and the Young Investigator Award at the annual meeting of the European Association for Cardio-Thoracic Surgery. Also, a new direction was explored, with an investigation of the changes in miRNA occurring during DCD-associated ischemia-reperfusion processes.

### Ventricular unloading and myocardial recovery

We continued to investigate the possible mechanisms leading to beneficial or maladaptive changes following unloading on normal and failing myocardium. Using a heterotopic transplantation model that mimics the changes induced by an assist device in cases of severe heart failure, we seek novel molecular therapeutic strategies that may contribute to enhancing the beneficial impact of unloading and potentially induce myocardial recovery.

### 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. Due to restructuring, we are now focusing on a collaboration with the Balgrist University Hospital, Zurich.

### Vascular tissue engineering

In 2014, thanks to two collaborations with groups in Sweden, we initiated a research project that aims at creating small diameter arterial vessels based on decellularisation and repopulation processes.

### Clinical research

2014 was marked by the restructuring of our data management team. Clarified flow charts and standard operating procedures were developed to facilitate scientific as well as administrative (ethics, finance, regulatory) processes.

The Cardiac Clinical Research Group focused on an internal registry, looking at several topics including flow and degeneration of biological valve prostheses, outcome after aortic surgery, cardiorenal syndromes and mechanisms of intra-operative renal damage, MECC, value of troponin after cardiac surgery, cardioplegia and myocardial metabolism (ischemia-reperfusion injury).

The Vascular Clinical Research Group focused on management strategies to improve clinical outcomes of symptomatic and juxtarenal abdominal aortic aneurysm repair. Based on our close to 100% patient follow-up during cross-sectional surveys, our patient series demonstrated that mortality may be significantly underestimated if long-term survival is estimated using only the Kaplan Meier method, which is based on incomplete follow-up information. This led to the proposition of a follow-up index (FUI), which should help appraise the validity of survival figures. We also focused on the validation of a novel scoring system for postoperative complications.



**Prof. Dr. Thierry Carrel**  
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Studied medicine at University of Bern; clinical training in General Surgery, FMH (1990) and 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 Tevæearai 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 at Swiss Institute for Experimental Cancer Research (1988-1990) and Duke University (US) (1999-2001). Executive MBA in St. Gallen (2007). Since 2003, Senior Attending, Department of Cardiovascular Surgery, Inselspital. Since 2005, Head of Research and Development, Cardiovascular Surgery, DCR. Since 2008, CEO of Swiss Cardio Technologies AG.



**PD Dr. Florian Dick**  
 florian.dick@insel.ch

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).



**Dr. Sarah Longnus**  
sarah.longnus@insel.ch

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**  
henriette.most@insel.ch

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**

Studied medicine in Vienna (AT), Lund (SE) and London (UK). Licensed GP, specialised in General Surgery and Cardiac Surgery; FETCS. Worked in Austria at Departments of Cardiac Surgery University Hospitals Graz (1995-2001) and Salzburg (2001-2011). Consultant Cardiac Surgeon, London; Senior Clinical Lecturer, Imperial College, London; Clinical Research Lead, Cardiovascular Biomedical Research Unit, Brompton (UK) (2011-2013). MBA (Health Care). Consultant (2013-2014), Department of Cardiovascular Surgery, Inselspital.

### Group Members

**Prof. Dr. Thierry Carrel**, Chair  
**Prof. Dr. Hendrik Tevaearai Stahel**, Head of Research and Development  
**PD Dr. Florian Dick**, Group Leader  
**Dr. Sarah Longnus**, Group Leader  
**Dr. Henriette Most**, Group Leader  
**PD Dr. Olaf Stanger**, Group Leader (until Oct.)

**Dr. Florian Schönhoff**, Research Associate

**Dr. Regula von Allmen**, Research Associate

**Dr. Bernhard Winkler**, Research Associate (since Dec.)

**Dr. Xuebin Fu**, Postdoctoral Fellow

**Dr. Stéphanie Lecaudé**, Postdoctoral Fellow

**Martina Bona**, Assistant Data Manager

**Nadja Dalla Vecchia**, Data Manager

**Brigitta Gahl**, Statistician

**Johannes Graf**, Assistant Data Manager

**Alan Haynes**, Data Manager (since Nov.)

**Bettina Kohler**, Data Manager

**Laetitia Krummen**, Data Manager

**Monika Sperisen**, Data Manager

**Sorin Ciocan**, Laboratory Manager

**Albert Dashi**, Research Technician (Feb.-Oct.)

**Nithya Devapragash**, Laboratory Technician (until Feb.)

**Dr. Silvan Jungi**, Research Assistant (since Oct.)

**Natalia Méndez Carmona**, Laboratory Technician (since May)

**Barbara Schweizer**, Laboratory Assistant

**Adrian Segiser**, Laboratory Technician

**Sara Baumberger**, Secretary (since Mar.)

**Laura Seidel**, Secretary (until Jan.)

**Emilie Farine**, PhD Student (since Mar.)

**Petra Niederberger**, PhD Student (since Mar.)

### Selected Collaborators

**Brügger J**, EPF Lausanne, Switzerland

**Flück M**, Balgrist University Hospital, Switzerland

**Hedhammar M**, KTH Royal Institute of Technology, Sweden

**Holgerson S**, University of Gothenburg, Sweden

**Most P**, Heidelberg University Hospital, Germany

### Selected Grants

**Amounts allocated for 2014:**

- SNF: Improving cardiac tolerance to warm ischemia: The role of metabolic modulation in protection against lethal reperfusion injury (S. Longnus) CHF 88,000

### Selected Publications

Dynamic patterns of ventricular remodeling and apoptosis in hearts unloaded by heterotopic transplantation. Brinks, H; Giraud, MN; Segiser, A; Ferrie, C; Longnus, S; Ullrich, ND; Koch, WJ; Most, P; Carrel, TP; Tevaearai, HT (2014) in: J Heart Lung Transplant, 33(2), p. 203-210.

Clinical performance of a sutureless aortic bioprosthesis: five-year results of the 3f Enable long-term follow-up study. Englberger, L; Carrel, TP; Doss, M; Sadowski, J; Bartus, K; Eckstein, FF; Asch, FM; Martens, S (2014) in: J Thorac Cardiovasc Surg, 148(4), p. 1681-1687.

Plasma-functionalized electrospun matrix for biograft development and cardiac function stabilization. Guex, AG; Frobert, A; Valentin, J; Fortunato, G; Hegemann, D; Cook, S; Carrel, TP; Tevaearai, HT; Giraud, MN (2014) in: Acta Biomater, 10(7), p. 2996-3006.

Heart transplantation with donation after circulatory determination of death. Longnus, SL; Mathys, V; Dornbierer, M; Dick, F; Carrel, TP; Tevaearai, HT (2014) in: Nat Rev Cardiol, 11(6), p. 354-363.

Protective Effect of Focal Adhesion Kinase against Skeletal Muscle Reperfusion Injury after Acute Limb Ischemia. Flück, M; von Allmen, RS; Ferrié, C; Tevaearai, H; Dick, F in: Eur J Vasc Endovasc Surg, e-pub ahead of print: doi: 10.1016/j.ejvs.2014.11.011.

## Clinical Radiopharmacy

[www.nukmed.insel.ch/de/forschung/pd-dr-med-ma-walter/](http://www.nukmed.insel.ch/de/forschung/pd-dr-med-ma-walter/)  
[www.dkf.unibe.ch/forschungsgruppe/91/](http://www.dkf.unibe.ch/forschungsgruppe/91/)

### Research Highlights 2014 / Outlook 2015

Our group is dedicated to developing highly innovative radiopharmaceuticals and testing their clinical usefulness. Since our beginning in 2011, we have established a Chemistry Unit (Department of Chemistry and Biochemistry), a Biology Unit (Haller-Haus) and a Clinical Unit (INO-building, Inselspital).

#### Chemistry Unit

In 2014, our Chemistry Unit designed and synthesised new radiotracers for tumour imaging and therapy. Lorenz Meier introduced a method to improve tumour uptake, utilising synergies of multiple targeting functions. Cristina Olariu developed a radioactive label to follow tracers in the body over long intervals. Her work was published in *Biomaterials*—the leading journal in clinical applications of bio-related materials—and featured in public media, such as *10vor10*. Using our new peptide synthesiser, Myriam Bergmann created a library of tumour-targeting ligands and Andrea Grotzky developed a class of imaging tracers carrying up to a thousand-fold the radioactivity of tracers currently used in the clinic. The approach was patented in 2014.

#### Biology Unit

Our Biology Unit developed methods to improve tumour targeting via manipulation of molecular targets. Renzo Cescato established a novel system for controlled drug delivery. Vincent Taelman developed a method to up-regulate specific target molecules that significantly improves the tumour uptake of radiotracers. The clinical translation of his approach aims to make ineligible patients eligible for targeted therapies and is currently ongoing in cooperation with the Clinical Trials Unit (CTU) Bern and the Institute of Pathology, as well as the Departments of Endocrinology, Diabetes and Clinical Nutrition, and Medical Oncology, Inselspital. In a similar approach, Nadia Sanchez is translating this method to increase tumour uptake of conventional chemotherapeutics. Piotr Radojewski and Nicolas Marincek translated many of our new tools from cells to animals, further facilitating clinical translation.

#### Clinical Unit

Our Clinical Unit evaluated the benefits and harms of radiotracers in patients. Viktoria Gloy coordinated a systematic review and meta-analysis on the toxicity of radioiodine of over 17,000 abstracts and 3,300 papers. This project—one of the largest systematic reviews in medicine—is funded by the Federal Office of Public Health and made rapid progress in 2014. It is conducted in collaboration with the Clinical Trials Unit (CTU) Bern, the Institute of Pathology and several key departments at the Inselspital as well as other national and international groups.

2014 was a very successful year for us. The establishment of key infrastructure resulted in rapid growth and innovation in all three Units, allowing us to develop new techniques and expand the boundaries of our field. Our projects are fully integrated within the Inselspital and conducted in collaboration with national and international experts. Our first innovations are now published, patented and on the path to clinical translation. We are grateful to all our collaborators and supporters who made this exciting progress possible.



**Prof. Dr. Thomas M. Krause**  
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MD (1979) at University of 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 of Swiss Society of Nuclear Medicine.



**PD Dr. Martin A. Walter**  
martin.walter@dkf.unibe.ch

Medical studies (1995-2001) in London (UK), Zurich and Münster (DE). Residency in Nuclear Medicine and Endocrinology (2002-2007) and Attending (2009-2010) at University Hospital Basel. Fellowships with inventors of DOTATOC therapy (Helmut R. Mäcke; 2005-2007) and PET technology (Michael Phelps; 2007-2009). Since 2010, Attending Physician, Inselspital and Head, Clinical Radiopharmacy, DCR. Since 2011, Assistant Professor in Pharmacology, University of California, Los Angeles (US).



**Dr. Renzo Cescato**  
renzo.cescato@dkf.unibe.ch

PhD in Biochemistry and Cell Biology (1995) at University of Basel. Postdoc in Alzheimer's disease research at CNS Department, Sandoz/Novartis (1996-1999). Research Fellow, Institute of Pathology; Tutor, Faculty of Medicine, University of Bern; Executive Board Member, Federal Coordination Commission for Occupational Safety (2001-2012). Since 2012, Coordinator, Biology Unit, Clinical Radiopharmacy, DCR.





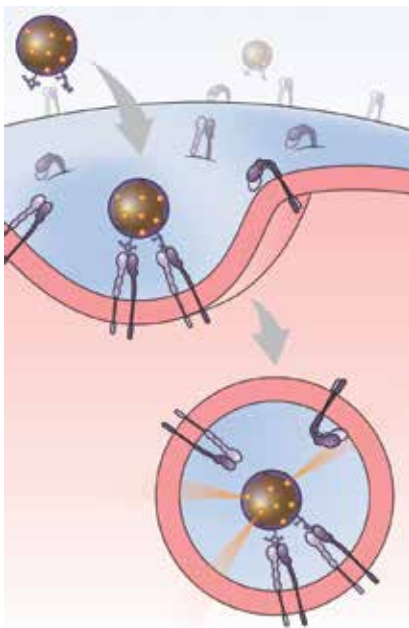
**Dr. Viktoria Gloy**  
viktoria.gloy@dkf.unibe.ch

MSc in Nutrition and Food Science (2007) at Kiel University (DE); DSc in Nutrition and Food Science (2011) at ETH Zurich. Since 2011, Research Associate, Basel Institute for Clinical Epidemiology and Biostatistics. Since 2012, Coordinator, Clinical Unit, Clinical Radiopharmacy, DCR.



**Dr. Lorenz Meier**  
lorenz.meier@med.unibe.ch

PhD in Chemistry (1998) at ETH Zurich. Post-docs at Departments of Non-metallic Materials, ETH Zurich, and Chemistry, Zurich University of Applied Sciences (1998-2008). Senior Scientist in industry (2008-2010). Lecturer on Colloidal Principles for Applications (2000-2011) and Clay Minerals (since 2006) at ETH Zurich. Since 2011, Coordinator, Chemistry Unit, Clinical Radiopharmacy, DCR.



### Group Members

**Prof. Dr. Thomas M. Krause**, Chair  
**PD Dr. Martin A. Walter**,  
Group Leader  
**Dr. Renzo Cescato**, Coordinator  
Biology Unit  
**Dr. Viktoria Gloy**, Coordinator  
Clinical Unit  
**Dr. Lorenz Meier**, Coordinator  
Chemistry Unit  
**Dr. Myriam Bergmann**, Postdoctoral  
Fellow  
**Dr. Andrea Grotzky**, Postdoctoral  
Fellow  
**Dr. Cristina I. Olariu**, Postdoctoral  
Fellow  
**Dr. Nadia Sanchez**, Postdoctoral  
Fellow  
**Dr. Vincent F. Taelman**, Postdoctoral  
Fellow  
**Dr. Nicolas Marincek**, Research  
Assistant  
**Dr. Piotr Radojewski**, Research  
Assistant  
**Dr. Petar-Marko Spanjol**, Research  
Assistant  
**Maria Umlauft**, Research Assistant  
**Stefanie Alépée**, Secretary  
**Sarah Loretan**, Secretary  
**Doris Riedo**, Secretary

### Selected Collaborators

**Ben-Shlomo A**, Cedars-Sinai Medical  
Center, USA  
**Beyesmann J**, Ulm University,  
Germany  
**Czernin J**, University of California,  
Los Angeles, USA  
**Mäcke HR**, University Hospital  
Freiburg, Germany  
**Segura T**, University of California,  
Los Angeles, USA

### Selected Grants

**Amounts allocated for 2014:**

- SNF: RGD-coupled Nanohydrogels for Molecular Targeted Imaging of  $\alpha_v\beta_3$  Integrin Expressing Tumors (M. Walter) CHF 52,000
- Bernese Cancer League: A Gold-198 based Nanoparticle Platform for the Treatment of Neuroendocrine cancers (M. Walter) CHF 50,000
- CTI: Polymeric Nanogels for Targeted Cancer Imaging (M. Walter) CHF 97,000
- Federal Office of Public Health (BAG): Safety Profile of Radioiodine Therapy

(SPRINT): Systematic Review and Meta-Analysis (M. Walter) CHF 63,000

- Helmut Horten Foundation: Germanium-dotted Gold Nanoparticles for Cell Tracking (M. Walter) CHF 128,000
- Oncosuisse/Cancer League: A Multifunctional Nanoparticle Platform for Combined Radiotherapy and Targeted Delivery of Sirolimus (M. Walter) CHF 132,000

### Selected Publications

F-RB390: Innovative ligand for imaging the T877A androgen receptor mutant in prostate cancer via positron emission tomography (PET). Bertolini, R et al. in: Prostate, e-pub ahead of print: doi: 10.1002/pros.22919.

Prevalence, characteristics, and publication of discontinued randomized trials. Kasenda, B et al. (2014) in: JAMA, 311(10), p. 1045-1051.

Indium-111 labeled gold nanoparticles for in-vivo molecular targeting. Ng, QK et al. (2014) in: Biomaterials, 35(25), p. 7050-7057.

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

Survival after somatostatin based radiopeptide therapy with 90Y-DOTATOC vs. 90Y-DOTATOC plus 177Lu-DOTATOC in metastasized gastrinoma. Dumont, RA et al. in: Am J Nucl Med Mol Imaging, e-pub ahead of print.



## Dermatology

[www.dermatologie.insel.ch/de/lehreundforschung/](http://www.dermatologie.insel.ch/de/lehreundforschung/)  
[www.dkf.unibe.ch/research-group/72/](http://www.dkf.unibe.ch/research-group/72/)

### Research Highlights 2014 / Outlook 2015

#### Allergies

In the two rare pustular skin disorders with systemic involvement, acute generalised exanthematous pustulosis and generalised pustular psoriasis, we found that the interleukin (IL) 17A/F was highly expressed by the innate immune cells neutrophils and mast cells. Our findings provide a rationale for a therapeutic approach with modern antibodies against IL-17A/F.

The heat shock protein (HSP) 90 plays an important role in cell survival, cytokine signalling and immune responses. We therefore investigated its potential involvement in the chronic inflammatory skin disease psoriasis. Our data showed that the inducible isoform HSP90 $\alpha$  is significantly up-regulated in epidermal keratinocytes and mast cells of lesional skin. Interestingly, patients treated with ustekinumab, a human monoclonal antibody neutralising IL-12 and IL-23, exhibited reduced HSP90 expression in psoriatic skin in parallel with clinical resolution of psoriasis. Our findings provide a rationale for a novel therapeutic approach in psoriasis with HSP90 inhibitors.

In mice, T helper type 9 (TH9) cells, which specifically produce IL-9, mediate tumour immunity and participate in autoimmune and allergic inflammation. We characterised human TH9 cells and found that most memory TH9 cells were skin tropic or skin resident. Many of them were stimulated by the opportunistic fungus *Candida albicans*. IL-9 production was transient and preceded the up-regulation of other inflammatory cytokines, such as interferon- $\gamma$ , IL-9, IL-13 and IL-17, by skin-tropic T cells. IL-9-producing T cells were increased in the skin lesions of psoriasis, suggesting that these cells may also contribute to human inflammatory skin diseases.

Although due to different causes, eczematous skin lesions of atopic dermatitis and allergic or irritant contact dermatitis are characterised by the same typical clinical signs. We investigated the expression of IL-17 and markers of tissue remodelling in these acute skin lesions. We found that in contrast to other cytokines, IL-17 as well as IL-21 and IL-22, were expressed in all eczema subtypes independent of their pathogenesis. There was a correlation between the expression of the tissue remodelling markers tenascin C and matrix metalloproteinase 9 with IL-17+ T cells and neutrophils, respectively; the latter responding to IL-17.

#### Plakins and the cytoskeleton

Plakins are intracellular proteins that interact with various elements of the cytoskeleton and critically regulate the cytoarchitecture of cells. They play a crucial role in the maintenance of the integrity of tissues such as the skin and muscles that are subjected to mechanical stress. We characterised the complex interaction of the plakins plectin with several types of intermediate filaments by various approaches, including a recently developed novel and rapid binding method based on the expression of fluorescent proteins in mammalian cells (FluoBACE). Finally, we found that the plakins BPAG1-a and -b associate with the microtubule plus-end-binding proteins EB1 and EB3 and modulate vesicular transport, Golgi apparatus structure and cell migration in myoblasts.



**Prof. Dr. Luca Borradori**  
 luca.borradori@insel.ch

MD (1986) at University of Bern; Resident in Dermatology (1989-1993) at University Hospitals of Paris (FR), Lausanne and Geneva. Postdoc at National Cancer Institute, NIH, Bethesda (US) (1993-1995) and Division of Cell Biology, Netherlands Cancer Institute (NL) (1995-1997). Since 2005, Associate Professor, Geneva University Hospitals. Since 2008, Chair and Head, Department of Dermatology, Inselspital.



**Prof. Dr. Rober Hunger**  
 robert.hunger@insel.ch

Studied medicine (1984-1990) at Universities of Freiburg (DE) and Bern; MD-PhD (1996) at University of Bern; board certification in Dermatology (2001). Postdoc (2001-2003) at Department of Dermatology, University of California, Los Angeles (US). Since 2011, Associate Professor, Department of Dermatology, Inselspital.



**Dr. Christoph Schlapbach**  
 christoph.schlapbach@insel.ch

MD (2008) and MD-PhD (2012) at University of Bern. Postdoc at Harvard Skin Disease Research Center, Boston (US) (2011-2012). Since 2012, Resident and Group Leader, Department of Dermatology, Inselspital.



**Prof. Dr. Dagmar Simon**  
dagmar.simon@insel.ch

MD (1989) at Friedrich Schiller University Jena (DE). Research fellowship (1991-1992) at Women's College Hospital, University of Toronto (CA). Board certifications in Dermatology (1993) and Allergy and Clinical Immunology (2003); PD (2006) at University of Bern. Since 2010, Associate Professor, Department of Dermatology, Inselspital.



**Prof. Dr. Nikhil Yawalkar**  
nikhil.yawalkar@insel.ch

MD (1988) at University of Basel. Board certifications in Dermatology (1995) and Allergy and Clinical Immunology (1998) at University of Bern. Postdocs in USA at Department of Dermatology, University of California, San Francisco School of Medicine (1995) and Harvard Skin Disease Research Center, Boston (2000-2002). Since 2006, Associate Professor, Department of Dermatology, Inselspital.

### Group Members

**Prof. Dr. Luca Borradori**, Chair and Head, Group Leader

**Prof. Dr. Robert Hunger**, Group Leader

**Dr. Christoph Schlapbach**, Group Leader

**Prof. Dr. Dagmar Simon**, Group Leader

**Prof. Dr. Nikhil Yawalkar**, Group Leader

**Dr. Bertrand Favre**, Laboratory Head

**Dr. Kexiang Yan**, Postdoctoral Fellow (until Aug.)

**Nadja Begré**, Laboratory Technician  
**Ursula Läderach**, Laboratory Technician

**Evelyne Seger**, Laboratory Technician  
**Claire Micossé**, PhD Student (since Apr.)

**Kseniia Poliakova**, PhD Student (until June)

**Rahel Thomi**, PhD Student

### Selected Collaborators

**Hertl M**, Philipp University of Marburg, Germany

**Liem R**, Columbia University, USA

**Shafighi M**, Inselspital, Switzerland

**Simon HU**, University of Bern, Switzerland

**Ugguccioni MG**, Institute for Research in Biomedicine, Switzerland

### Selected Grants

Amounts allocated for 2014:

None above CHF 50,000

### Selected Publications

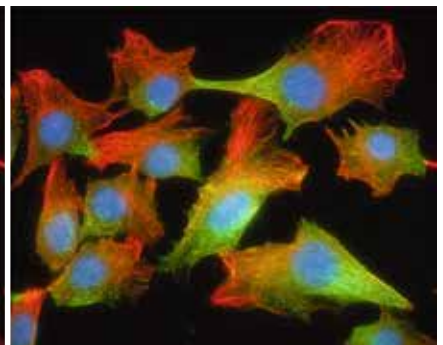
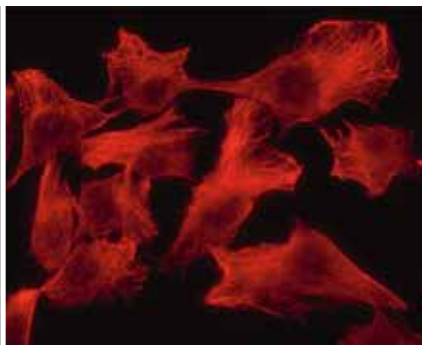
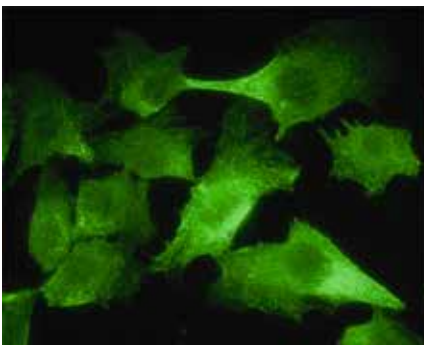
Interaction of plectin with keratins 5 and 14: dependence on several plectin domains and keratin quaternary structure. Bouameur, JE; Favre, B; Fontao, L; Lingasamy, P; Begre, N; Borradori, L (2014) in: *J Invest Dermatol*, 134(11), p. 2776-2783.

High expression of FOXP3 in primary melanoma is associated with tumour progression. Gerber, AL; Munst, A; Schlapbach, C; Shafighi, M; Kiermeir, D; Husler, R; Hunger, RE (2014) in: *Br J Dermatol*, 170(1), p. 103-109.

Th17 cells and tissue remodeling in atopic and contact dermatitis. Simon, D; Aeberhard, C; Erdemoglu, Y; Simon, HU (2014) in: *Allergy*, 69(1), p. 125-131.

Increased expression of heat shock protein 90 in keratinocytes and mast cells in patients with psoriasis. Kakeda, M; Arock, M; Schlapbach, C; Yawalkar, N (2014) in: *J Am Acad Dermatol*, 70(4), p. 683-690.

Human TH9 cells are skin-tropic and have autocrine and paracrine proinflammatory capacity. Schlapbach, C; Gehad, A; Yang, C; Watanabe, R; Guenova, E; Teague, JE; Campbell, L; Yawalkar, N; Kupper, TS; Clark, RA (2014) in: *Sci Transl Med*, 6(219), p. 219ra8.



## Experimental Haemostasis

[www.dkf.unibe.ch/research-group/96/](http://www.dkf.unibe.ch/research-group/96/)



**Prof. Dr. Hans-Peter Kohler**  
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### Research Highlights 2014 / Outlook 2015

Our research focuses on two topics:

#### Coagulation factor XIII

We study aspects of the biochemistry of coagulation factor XIII (FXIII), its role in clot formation in cardiovascular disease and in congenital FXIII deficiency. We have shown that the FXIII activation peptide (AP-FXIII) is released into the circulation upon FXIII activation by thrombin but it was not known whether this free AP-FXIII had any function. We were able to demonstrate that free AP-FXIII reduces any further FXIII activation and delays fibrin crosslinking, suggesting that free AP-FXIII may have a functional role as a regulator of FXIII activation and fibrin stabilisation.

In the FXIII A-subunit dimer, the first 37 amino acids form the AP-FXIII and cross the intersubunit interface. Our aim was therefore to investigate whether the AP-FXIII is important for the stability of the FXIII A-subunit dimer. We expressed FXIII A-subunit variants with stepwise deletions of amino acids of the AP-FXIII from the N-terminus. We found that variants with deletions of 11 or more N-terminal amino acids were not expressed. Therefore, this part of AP-FXIII must be crucial for stability of the FXIII protein. Furthermore, with increasing number of deleted amino acids, the expressed variants showed reduced thermal stability and increased susceptibility towards thrombin activation. Our data showed for the first time that AP-FXIII is important for FXIII stability and regulates FXIII activation.

In other work, we characterised a large cohort of patients from Pakistan with congenital FXIII deficiency. We identified several novel mutations leading to this rare bleeding disorder, which give further clues to the structure/function relationship of FXIII protein domains.

#### Interactions between the complement system and blood coagulation

Mannan-binding lectin-associated serine protease 1 (MASP-1) of the complement lectin pathway has been suggested to interact with coagulation due to its similarity to thrombin. We and others have shown that MASP-1 can cleave the thrombin substrates fibrinogen, FXIII, TAFI and the PAR4 receptor on endothelial cells. In 2014, we demonstrated that MASP-1 induces clot formation in plasma and whole blood via prothrombin activation. We identified several cleavage sites for MASP-1 in the prothrombin molecule and will continue working on the exact mechanism of prothrombin activation by MASP-1 in 2015. Through bypassing the upstream coagulation cascade, MASP-1 might represent a link between inflammatory conditions and thrombotic complications.

This year, we also showed for the first time that plasma levels of complement MASP-1 and MASP-2 are elevated in patients with type 1 diabetes. MASP levels correlated with those of glycosylated haemoglobin and decreased when glycaemic control was improved. We hypothesise that elevated MASP levels might contribute to the increased risk of thrombotic complications in diabetes patients.

MD (1991) at University of Bern. Clinical training in internal medicine; FMH certification in Internal Medicine (1998). Research fellowship (1996-1998) at University of Leeds (UK). Venia docendi (2001); Titular Professor (2006); Honorary Professor (2007) at University of Bern. Head of Internal Medicine, Department of Emergency Medicine, Inselspital (2000-2006). Since 2000, Group Leader, Experimental Haemostasis (FXIII Research Group), DCR and Inselspital. Since 2008, Head and Chair of Medicine, Spital Netz Bern, Tiefenau and Ziegler.



**PD Dr. Verena Schröder**  
verena.schroeder@insel.ch

MSc in Pharmacy (1999) at University of Basel; PhD (2003) at University of Basel with research conducted at Laboratory for Thrombosis Research, DCR. Postdocs at University of Bern (2003-2008) and University of Leeds (UK) (2008-2010). Since 2010, Senior Researcher and Group Leader, Experimental Haemostasis, DCR; venia docendi 2013.

### Group Members

**Prof. Dr. Hans-Peter Kohler,**  
Group Leader  
**PD Dr. Verena Schröder,**  
Group Leader  
**Dr. Helena Handrková,**  
Postdoctoral Fellow  
**Lorenz Jenny,** PhD Student

### Selected Collaborators

**Ajjan R,** University of Leeds, UK  
**Borhany M,** National Institute of  
Blood Diseases and Bone Marrow  
Transplantation, Pakistan  
**Dobó J, Gál P,** Hungarian Academy  
of Sciences, Hungary  
**Lam W,** Emory University and Georgia  
Institute of Technology, USA  
**Thiel S,** Aarhus University, Denmark

### Selected Grants

#### Amounts allocated for 2014:

- SNF: Further characterisation of the activation steps of blood coagulation factor XIII, the role of its activation peptide and B-subunits, and their impact on clot formation, structure and lysis (H.-P. Kohler) CHF 125,495
- SNF: Interactions between complement and coagulation in cardio- and cerebrovascular diseases: Role of MASP-1 in clot formation (V. Schröder) CHF 102,836

### Selected Publications

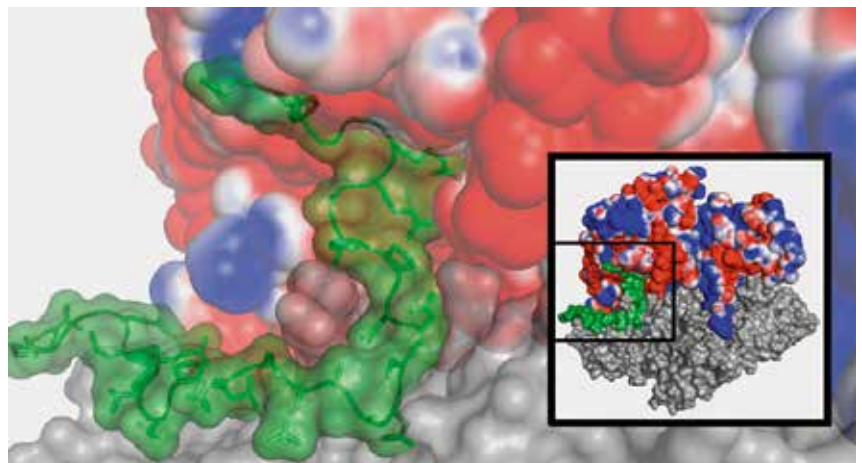
Congenital factor XIII deficiency in Pakistan: characterization of seven families and identification of four novel mutations. Borhany, M; Handrkova, H; Cairo, A; Schroeder, V; Fatima, N; Naz, A; Amanat, S; Shamsi, T; Peyvandi, F; Kohler, HP (2014) in: Haemophilia, 20(4), p. 568-574.

Multiple roles of complement MASP-1 at the interface of innate immune response and coagulation. Dobo, J; Schroeder, V; Jenny, L; Cervenak, L; Zavodszky, P; Gal, P (2014) in: Mol Immunol, 61(2), p. 69-78.

Hypofibrinolysis in type 2 diabetes: the role of the inflammatory pathway and complement C3. Hess, K; Alzahrani, SH; Price, JF; Strachan, MW; Oxley, N; King, R; Gamlen, T; Schroeder, V; Baxter, PD; Ajjan, RA (2014) in: Diabetologia, 57(8), p. 1737-1741.

Free factor XIII activation peptide affects factor XIII function. Schroeder, V; Handrkova, H; Dodt, J; Kohler, HP in: Br J Haematol, e-pub ahead of print: doi: 10.1111/bjh.13144.

Plasma levels of MASP-1 and MASP-2 are elevated in type 1 diabetes and correlate with glycaemic control. Jenny, L; Ajjan, R; King, R; Thiel, S; Schroeder, V in: Clin Exp Immunol, e-pub ahead of print: doi: 10.1111/cei.12574.





# Neurology

[www.neuro-bern.ch](http://www.neuro-bern.ch)

[www.dkf.unibe.ch/forschungsgruppe/14/](http://www.dkf.unibe.ch/forschungsgruppe/14/)

## Research Highlights 2014 / Outlook 2015

In 2014, our department founded two new research units: the Center for Experimental Neurology (ZEN) and the Neuro Clinical Trial Unit (NCTU). The ZEN, led by Antoine Adamantidis, was officially inaugurated on 24 October 2014. It includes a new molecular laboratory, rat and mice sleep-recording facilities, and an animal functional assessment room. In 2015, the ZEN will be enlarged by two additional rooms for optogenetic research. The NCTU, led by Urs Fischer, represents a platform of the Bern Neurocentre to promote and professionalise high quality clinical research, adopting national and international guidelines. The NCTU works in close cooperation with the Clinical Trials Unit (CTU) Bern. In the next year, there will be a closer interaction, following the decision by the DCR to reorganise CTU Bern. In 2014, we also integrated the Psychosomatic research group of Roland von Känel.

A total of eighteen SNF grants are running in our department, thirteen with yearly funding higher than CHF 50,000 (see Selected Grants). Of these eighteen grants, seven were newly awarded in 2014 (four with funding starting 2015): four to the Sleep and Epilepsy Group, two to the Neurorehabilitation Group and one to the Stroke Group.

### Stroke Group

This group has a research focus on the management of acute ischemic and haemorrhagic stroke, on its prevention and on biomarkers of cerebrovascular diseases. In 2014, the world's largest series of cervicocerebral artery dissections was published as a result of a multicentre translational Special Program University Medicine (SNF-SPUM) project. A new SNF grant received in 2014 led to the initiation of the first

multicentre randomised trial on decompressive hemicraniectomy in intracerebral haemorrhage (SWITCH).

### Sleep-Wake Mechanisms/Disorders and Epilepsy Group

The Experimental Sleep Group studies the dynamics of the neural circuit controlling sleep and wake states in order to delineate brain wiring and functions. Molecular tools are combined with in vitro and in vivo electrophysiology to optogenetically control genetically targeted cell populations in the mouse brain. The Clinical Translational Sleep Group studies the effects of sleep apnoea and other sleep disorders on stroke in humans, on the effect of sleep modulation on stroke outcome in rodents, and on the etio-pathophysiology of narcolepsy. The Clinical Epilepsy Group focuses on the dynamics of epileptic brains, by mathematical analysis of intracranially recorded electric brain signals (EEG) in order to improve diagnostics and therapies. A paper published in 2014 showed that removing those parts of EEG-derived functional networks where information flow is largest during seizures is associated with better seizure control.

### Movement/Motor Disorders Group

This group has a research focus on deep brain stimulation. In a proof of concept study published in 2014, it was shown for the first time that it is possible to provide directional deep brain stimulation using segmented electrodes, resulting in a better therapeutic window of stimulation. This study was carried out in collaboration with Claudio Pollo from the Department of Neurosurgery. In 2014, Michael Schüpbach took over the lead of the Movement Disorders Center.



Prof. Dr. Claudio L. Bassetti  
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MD (1985) at University of Basel; 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. *Clinical and animal research, sleep, stroke.*



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. *Animal research, sleep.*



Prof. Dr. Marcel Arnold  
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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, University of Paris 7 (FR), (2005). Venia docendi (2007). Since 2010, Associate Professor of Neurology. Currently Chair, Stroke Center, Department of Neurology, Inselspital. *Clinical research, stroke.*





**Prof. Dr. Urs Fischer**  
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MD (2000) at University of Bern; Neurology residency in Bern; FMH certification (2007). Research fellowship (2008) and MSc (2009) in Clinical Neurology, University of Oxford (UK). Venia docendi (2011). Since 2014, Associate Professor. Since 2014, Head Neurological Emergency Team and Head Neuro Clinical Trial Unit, Department of Neurology, Inselspital. *Clinical research, stroke.*



**Prof. Dr. Heinrich Mattle**  
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MD (1976) at University of Zürich; Neurology residency in Zurich; FMH certification (1985). Fellowships in Neuroradiology (1988-1990) at Harvard University, Boston (US). Venia docendi (1990). Since 1990, Vice-Chair and Head Out-patient Clinic, Department of Neurology, Inselspital. Associate Professor of Neurology (1996). *Clinical research, stroke and multiple sclerosis.*



**Prof. Dr. René Müri**  
rene.mueri@insel.ch

MD (1984) at University of Bern; Neurology residency in Bern and Basel; FMH certification (1991). Postdoc at INSERM U 289, Hôpital de la Salpêtrière, Paris (FR) (1993-1995). Venia Docendi (1997). Since 2004, Senior Attending and Head, Unit of Cognitive and Restorative Neurology, Department of Neurology, Inselspital. Associate Professor of Neurology (2008). *Clinical research, visuo-perception/eye movement, neurorehabilitation.*

### Neurorehabilitation/Cognitive Disorders Group

This group has a research focus on the physiology and pathophysiology of perception and eye movement, gerontechnology and neurorehabilitation. In 2014, Roger Kalla joined the group as a new senior researcher. His research field is the vestibular system and cognition.

### Neuropsychosomatic Group

This group has a research focus on neuropsychosomatics and the biology of stress in cardiovascular diseases, and their rehabilitation. In papers published in 2014, it was shown that chocolate with 72% cocoa content mitigates stress-triggered hormone and coagulation reactivity related to human stress responses.

### Group Members

*Sleep-Wake Mechanisms/Disorders and Epilepsy Group*

**Prof. Dr. Claudio L. Bassetti**,  
Group Leader

**Prof. Dr. Antoine Adamantidis**,  
Group Leader (ZEN)

**Prof. Dr. Kaspar Schindler**,  
Consultant, Group Leader

**Prof. Dr. Johannes Mathis**, Senior  
Consultant

**Dr. Heidemarie Gast**, Consultant

**Prof. Dr. Arto Nirkko**, Consultant

**Dr. Thomas Horvath**, Research  
Assistant

**Dr. Michael Oberholzer**, Research  
Assistant

**Dr. Andrea Seiler**, Research Assistant

**Dr. Francesca Baracchi**, Postdoctoral  
Fellow (ZEN)

**Dr. Simone Duss**, Postdoctoral Fellow

**Dr. Thomas Gent**, Postdoctoral  
Fellow (ZEN)

**Dr. Andreas Steimer**, Postdoctoral  
Fellow

**Dr. Frédéric Zubler**, Postdoctoral  
Fellow

**Dr. Carolina Gutierrez Herrera**,  
Research Associate (ZEN)

**Laura Facchin**, PhD Student (ZEN)

**Marta Pace**, PhD Student (ZEN)

*Movement/Motor Disorders Group*

**PD Dr. Michael Schüpbach**,  
Group Leader

**Prof. Dr. Claudio L. Bassetti**,  
Head of Department

**Prof. Dr. Kai Rösler**, Senior Consultant  
**Prof. Dr. Mathias Sturzenegger**,  
Senior Consultant

**Dr. Ines Debove**, Consultant

**Dr. Lenard Lachenmayer**, Consultant

**Dr. Niklaus Meier**, Consultant

*Stroke Group*

**Prof. Dr. Marcel Arnold**,  
Group Leader

**Prof. Dr. Urs Fischer**, Group Leader

**Prof. Dr. Heinrich Mattle**,  
Group Leader

**Prof. Dr. Werner Z'Graggen**,  
Group Leader

**Prof. Dr. Claudio L. Bassetti**,  
Head of Department

**PD Dr. Simon Jung**, Senior Consultant

**Dr. Anne Broeg**, Consultant

**Dr. Aikaterini Galimanis**, Consultant

**Dr. Barbara Goeggel-Simonetti**,  
Consultant

**Dr. Mirjam Heldner**, Consultant

**Dr. Kai Liesirova**, Consultant

**Dr. Julia Meisterernst**, Consultant

**Dr. Maire-Luise Mono**, Consultant

**Marianne Kormann**, Study Nurse

**Andrea Surtmann**, Study Nurse

*Neurorehabilitation/Cognitive Disorders Group*

**Prof. Dr. René Müri**, Group Leader

**PD Dr. Klemens Gutbrod**, Senior  
Research Associate

**PD Dr. Roger Kalla**, Senior  
Consultant

**Dr. Manuel Bertschi**, Postdoctoral  
Fellow

**Dr. Tim Vanbellinggen**, Postdoctoral  
Fellow

**Diego De Leon Rodriguez**,  
PhD Student

**Noëmi Eggenberger**, PhD Student

**Simone Hopfner**, PhD Student

**Matthias Lüthi**, PhD Student

**Basil Preisig**, PhD Student

**Rahel Schumacher**, PhD Student

*Neuro CTU Group*

**Prof. Dr. Urs Fischer**, Group Leader  
**Dr. Corrado Bernasconi**, Co-Chair  
NCTU

**Dr. Stephanie Lerch**, Co-Chair NCTU  
**PD Dr. Michael Schüpbach**,  
Vice-Chair

**Prof. Dr. Jürgen Beck**, Consultant

**Prof. Dr. Thomas Dierks**, Consultant

**Dr. Sebastian Grunt**, Consultant

**Dr. Christian Kamm**, Consultant

**Prof. Dr. Schindler**, Consultant



**Prof. Dr. Kaspar Schindler**  
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MD (1995) at University of Bern; 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); Neurology residence in Zurich and Bern; FMH certification (2005). 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. *Clinical research, epilepsy.*



**PD Dr. Michael Schüpbach**  
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MD (1995) at University of Bern; Resident (1996-1999) at Institute of Physiology, Bern; Neurology residency in Bern; FMH certification (2002). Research fellowship (2003-2008) at Salpêtrière Hospital, Paris (FR). Since 2008, Attending Physician; since 2010, Chair, DBS program; since 2014, Chair, Movement Disorders Center, Department of Neurology, Inselspital. Venia docendi (2014). *Clinical research, movement disorders.*



**Prof. Dr. Roland von Känel**  
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MD (1993) at University of Bern (1993); residency in Internal Medicine; FMH certification (1999); residency in Psychiatry and Psychotherapy, FMH certification (2008). Postdoc (1999-2001) at University of California, San Diego (US). Chair, Psychosomatic Medicine (2004-2014). Associate Professor of Somato-Psychosocial Medicine (2004-2012); Full Professor of Psychosomatic Medicine (2012-2014), Inselspital. Since 2014, Head, Clinic Barmelweid. *Clinical research, neuropsychosomatics.*

**Prof. Dr. Roland Wiest**, Consultant  
**Prof. Dr. Werner Z'Graggen**, Consultant

#### *Neuropsychosomatic Group*

**Prof. Dr. Roland von Känel**, Group Leader  
**PD Dr. Stefan Begré**, Consultant  
**Dr. Niklaus Egloff**, Consultant  
**Dr. En-Young Wagner Cho**, Postdoctoral Fellow  
**Rebecca E. Meister**, PhD Student  
**Fiorenza A. Meyer**, PhD Student  
**Mary Princip**, PhD Student  
**Kathleen Schwarzkopf**, PhD Student

#### **Selected Collaborators**

**Andrzejak R**, Pompeu Fabra University, Spain  
**Annoni J-M, Albrecht U**, University of Fribourg, Switzerland  
**Bacon SL**, Concordia University, Canada  
**Baumann C**, University Hospital Zurich, Switzerland  
**Beck J, Gralla J, Meier B, Pollo C, Raabe A, Schroth G, Wiest R**, Inselspital, Switzerland  
**Bloch J, Hirt L**, University Hospital of Lausanne, Switzerland  
**Bousser MG, Debette S, Stapf C**, University of Paris 7, France  
**Brandt T, Grond-Ginsbach C**, University of Heidelberg, Germany  
**Burdakov D**, National Institute for Medical Research, UK  
**Burgunder JM**, Siloah Clinic, Switzerland  
**Deuschl G**, University of Kiel, Germany  
**Diniz Behn C**, Colorado School of Mines, USA  
**Gabriels L, Nuttin B**, Catholic University of Leuven, Belgium  
**Hamel E, Jones B, Seguela P, Williams S**, McGill University, Canada  
**Hartmann A**, Pitié-Salpêtrière Hospital, France  
**Henke K, Mast F, Mosimann UP, Nef T**, University of Bern, Switzerland  
**Huber R**, University Children's Hospital Zurich, Switzerland  
**Kaelin A**, Neurocenter of Southern Switzerland  
**Korotkova T, Ponomarenko P**, NeuroCure, Germany  
**Lammers GJ**, Leiden University Medical Centre, Netherlands  
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**Luppi PH**, University Lyon 1, France

**Lyrer P, Engelter S**, University of Basel, Switzerland  
**Malan L**, North-West University, South Africa  
**Manconi M, Cereda C, Fulda S, Galati S**, Neurocenter of Southern Switzerland  
**Massimini M**, University of Milan, Italy  
**Mausbach BT**, University of California, San Diego, USA  
**Mormann F**, University Hospital of Bonn, Germany  
**Nedeltchev K, Khatami R, Remonda L**, Cantonal Hospital Aarau/Barmelweid Clinic, Switzerland  
**Nobili L, Niguarda Hospital, Italy**  
**Nyffeler T, Bohlhalter S**, Lucerne Cantonal Hospital, Switzerland  
**Pollo C**, Inselspital, Switzerland  
**Ptak R**, University of Geneva, Switzerland  
**Stam J, Coutinho J**, University of Amsterdam, Netherlands  
**Tatlitsumak T**, University of Helsinki, Finland  
**Thaler D, Kent D**, Tufts Medical Center, USA  
**Thurston RC**, University of Pittsburgh, USA  
**Vesper J, Schnitzler A**, University Hospital Düsseldorf, Germany  
**Wiest R**, Inselspital, Switzerland  
**Wirtz PH**, University of Konstanz, Germany

#### **Selected Grants**

**Amounts allocated above CHF 50,000 for 2014:**  
*(four SNF grants with funding starting 2015 are excluded)*

- SNF: Bayesian Infer. Approach to Intracranial EEG Seizure Dynamics (K. Schindler) CHF 140,000
- SNF: Imaging neuronal networks in epilepsy, (M. Seeck, R. Wiest, K. Schindler) CHF 115,000
- SNF: Cervicocerebral Artery Dissection (EDIT-CAD-2 Study) (M. Arnold) CHF 657,776
- SNF: Swiss study of initial decompressive craniectomy (SWITCH) (U. Fischer) CHF 178,609
- SNF: Restless leg and cardiovascular risk, human/animal (M. Manconi, C. Bassetti) CHF 100,000
- SNF: Aphasia and co-speech gestures, human (R. Müri) CHF 146,000
- SNF: Bilingualism, human (J.-M. Annoni, R. Müri) CHF 100,000

- SNF: 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: Myocardial Infarction – Stress Prevention Intervention, (R. von Känel) CHF 120,000
- SNF: Sleep loss and sleep disorders, impact on stroke (C. Bassetti) CHF 200,000
- SNF: Slow wave sleep and memory traces (J. Mathis) CHF 70,000
- Swiss Heart Foundation: Sleep loss/disorders, impact on stroke outcome. (C. Bassetti) CHF 94,640
- Swiss Heart Foundation: Secondary prevention program for stroke victims. (S. Jung) CHF 50,000
- Swiss Heart Foundation: The brain heart interaction in acute stroke (H. Mattle) CHF 94,828
- Swiss Heart Foundation: Design of a new clinical score, circulation stroke (M. Heldner) CHF 50,000
- Swiss Heart Foundation: Swiss study of initial decompressive craniectomy (SWITCH) (J. Beck) CHF 100,000
- Research Grant of the Inselspital: EEG dynamics during wakefulness and sleep (H. Gast) CHF 80,000
- HFSP: Behavioral multitasking and coordination (A. Adamantidis) CHF 218,310
- Tropos: Sleep disorders and stroke outcome (C. Bassetti) CHF 60,000
- Volkswagen Foundation: Intracranial pressure and vestibular function (R. Gürkov, R. Kalla) EUR 75,900



### Selected Publications

Eye movements discriminate fatigue due to chronotypical factors and time spent on task – a double dissociation. Cazzoli, D; Antoniadou, CA; Kennard, C; Nyffeler, T; Bassetti, CL; Muri, RM (2014) in: PLoS One, 9(1), p. e87146.

Unconscious relational encoding depends on hippocampus. Duss, SB; Reber, TP; Hanggi, J; Schwab, S; Wiest, R; Muri, RM; Brugger, P; Gutbrod, K; Henke, K (2014) in: Brain, 137(Pt 12), p. 3355-3370.

Acute post-stroke blood pressure relative to premonitor levels in intracerebral haemorrhage versus major ischaemic stroke: a population-based study. Fischer, U; Cooney, MT; Bull, LM; Silver, LE; Chalmers, J; Anderson, CS; Mehta, Z; Rothwell, PM (2014) in: Lancet Neurol, 13(4), p. 374-384.

Baclofen facilitates sleep, neuroplasticity, and recovery after stroke in rats. Hodor, A; Palchykova, S; Baracchi, F; Noain, D; Bassetti, CL (2014) in: Ann Clin Transl Neurol, 1(10), p. 765-777.

Directional deep brain stimulation: an intraoperative double-blind pilot study. Pollo, C; Kaelin-Lang, A; Oertel, MF; Stieglitz, L; Taub, E; Fuhr, P; Lozano, AM; Raabe, A; Schupbach, M (2014) in: Brain, 137(Pt 7), p. 2015-2026.

Dark chocolate intake buffers stress reactivity in humans. Wirtz, PH; von Känel R; Meister, RE; Arpagaus, A; Treichler, S; Kuebler, U; Huber, S; Ehlert, U (2014) in: J Am Coll Cardiol, 63(21), p. 2297-2299.

Detecting Functional Hubs of Ictogenic Networks. Zubler, F; Gast, H; Abela, E; Rummel, C; Hauf, M; Wiest, R; Pollo, C; Schindler, K in: Brain Topogr, e-pub ahead of print.

Familial occurrence and heritable disorders of connective tissue in cervical artery dissection. Debetto S et al. (2014) in: Neurology, 83(22), p. 2023-31.

# Radiation Oncology

[www.dkf.unibe.ch/forschungsgruppe/21/](http://www.dkf.unibe.ch/forschungsgruppe/21/)

## Research Highlights 2014 / Outlook 2015

### Zimmer/Medová Group

In 2014, we continued our focus on the MET receptor tyrosine kinase as a target in cancer. In a collaboration with the IMSB/ETH Zurich, we applied targeted phosphoproteomics using SRM-based technology to extensively characterise the impact of MET inhibition, alone and in combination with irradiation. We monitored and quantified changes of selected ATM/ATR/DNA-PK substrates in various cell lines and under various experimental setups. The first part of this study is expected to be finalised in early 2015. We also began a study on a previously unreported phosphorylation of a serine residue within a conserved SQ motif on MET. An antibody against this phosphosite was raised and we will continue its characterisation in 2015. We will also investigate various MET variants in which the particular serine has been replaced by an alanine. In our investigations of the crosstalk between MET and the DNA damage response, we made further observations confirming the role of FoxM1 in cellular senescence and DNA damage following MET inhibition in preclinical models of gastric cancer. We also progressed with projects aiming to elucidate the role of ubiquitination on particular lysine residues on the H2AX histone in response to DNA damage following MET inhibition. In the first phase of a project with Merck Serono and the Institute of Pathology, we identified several MET mutations in tumour samples of a cohort of 200 patients with head and neck carcinoma. In 2015, we expect to finalise correlations between various clinical readouts and the presence of the mutations, and to complete the second phase of the project by performing transcriptomic analysis via RNASeq on the same patients.

### Zaugg Group

New technologies have revolutionised radiation oncology in the last decade. By administering the treatment dose to patients using novel techniques, such as Intensity Modulated Radiation Therapy or RapidArc Therapy, dose conformity to the tumour is increased and damage to healthy tissue is decreased. These benefits are achieved through radiation fields that are highly spatially and temporally regulated, by either modifying dose rate (pulse amplitude) or pulse repetition frequency (pulse frequency). Furthermore, technical achievements in the last year allow us to deliver the treatment dose significantly faster compared with standard radiation techniques (1 min versus up to 20 mins). There is increasing evidence that modulation of dose rate and delivery time affects tumour cell survival. The clinical significance of this observation and the underlying molecular mechanisms are still unclear. Therefore, our most recent project aims to: 1) determine the dose-rate effect (extremely high vs standard/low) on cellular survival and mode of cell death in various cell systems; 2) profile the changes in gene expression on different tumour cell lines when modulating dose rate, pulse repetition frequency and delivery time; 3) validate and quantify the differential activation of specific pathways; and 4) elucidate the mechanisms underlying different molecular responses to modulated radiation beams. This study will provide the first results on how high dose-rate application of ionising radiation and shortened delivery time can impact tumour cell survival and normal tissue responses, as part of a future radio-oncological technology.



**Prof. Dr. Daniel M. Aebersold**  
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MD (1994) at University of Basel. Postdoc (2000-2002) at Weizmann Institute of Science, Rehovot (IL). FMH certification in Radiation Oncology (2004); *venia docendi* (2004). Since 2007, Full Professor, Chair, Department of Radiation Oncology, Inselspital.



**PD Dr. Yitzhak Zimmer**  
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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, DCR. *Venia docendi* (2013).



**Dr. Michaela Medová**  
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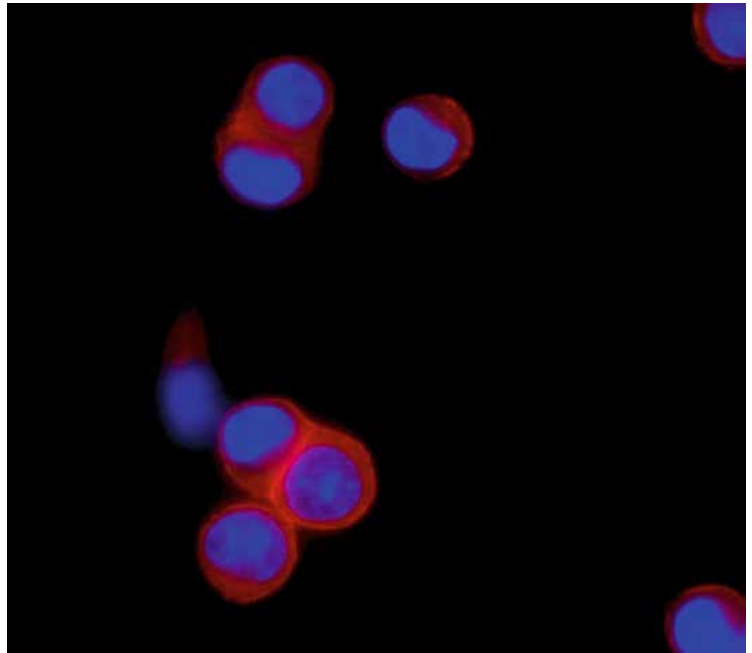
MSc in Biomedical Physics (2006) and Journalism (2006) at Comenius University, Bratislava (SK); PhD (2010) at University of Bern. Postdoc (2011-2013) at University of Bern. Since 2013, Principal Investigator and Co-Group Leader, Radiation Oncology, DCR.





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. Venia legendi 2012 at University of Zurich. Since 2013, Senior Consultant and Principal Investigator, Department of Radiation Oncology, Inselspital.



### Group Members

Prof. Dr. Daniel M. Aebersold, Chair

PD Dr. Yitzhak Zimmer, Head of Research, Group Leader

Dr. Michaela Medová, Co-Group Leader

Melanie Leuner-Tombolini,  
Laboratory Technician

Paola Francica, PhD Student

Astrid Glück, PhD Student

Jonas Koch, PhD Student (since July)

Kei Mikami, PhD Student (until Oct.)

Lluís Nisa, MD-PhD Student

Eleonora Orlando, PhD Student

Michaela Poliaková, PhD Student  
(since Nov.)

PD Dr. Kathrin Zaugg, Group Leader

Dr. Jianhua Feng, Senior Research Associate

Ning Chang, PhD Student

Dorota Dudka, PhD Student (since Nov.)

### Selected Collaborators

Aebersold R, ETH Zurich, Switzerland

Bladt F, Blaukat A, Merck Serono GmbH, Germany

Delorenzi M, Swiss Institute of Bioinformatics Lausanne, Switzerland

Giger R, Inselspital, Switzerland

Perren A, University of Bern, Switzerland

### Selected Grants

Amounts allocated for 2014:

- SNF: Impact of MET inhibition on the DDR-related phosphoproteome (Y. Zimmer, M. Medová) CHF 187,000
- SNF: Carnitine Palmitoyl-Transferase 1C (CPT1C) as Novel Key regulator of Cancer Metabolism and Carcinogenesis: Deciphering Mechanisms and Signalling Pathways (K. Zaugg) CHF 195,000
- Merck Serono: MET mutations and RNASeq of HNSCC (Y. Zimmer, D. Aebersold) CHF 365,598
- Werner und Hedy Berger-Janser Foundation: Characterisation of a novel putative ATM/ATR/DNA-PK phosphorylation site on the MET receptor tyrosine kinase (M. Medová) CHF 128,532
- Swiss Cancer League: Dose-rate effect of novel radiation technologies: relevance for the clinical use (K. Zaugg) CHF 76,000

### Selected Publications

Late toxicity and five year outcomes after high-dose-rate brachytherapy as a monotherapy for localised prostate cancer. Ghadjar, P; Oesch, SL; Rentsch, CA; Isaak, B; Cihoric, N; Manser, P; Thalmann, GN; Aebersold, DM (2014) in: Radiat Oncol, 9, p. 122.

Targeting of the MET receptor tyrosine kinase by small molecule inhibitors leads to MET accumulation by impairing the receptor downregulation. Leiser, D; Pochon, B; Blank-Liss, W; Francica, P; Gluck, AA; Aebersold, DM; Zimmer, Y; Medova, M (2014) in: FEBS Lett, 588(5), p. 653-658.

Biological, diagnostic and therapeutic relevance of the MET receptor signaling in head and neck cancer. Nisa, L; Aebersold, DM; Giger, R; Zimmer, Y; Medova, M (2014) in: Pharmacol Ther, 143(3), p. 337-349.



## Rheumatology

www.ria.insel.ch  
 www.rheumabern.ch  
 www.dkf.unibe.ch/research-group/23/

### Research Highlight 2014 / Outlook 2015

Our research focuses on complex questions of the immune system and on regulation of growth and differentiation of specific cell types. In 2014, basic research was divided into six projects, each with a separate group leader:

The **Förger Group** analysed the role of gamma delta T cells in pregnant patients with rheumatic diseases. Pregnancy-related disease improvement in patients with rheumatoid arthritis was reflected by a reduced pro-inflammatory cytokine profile of Vδ1 and Vδ2 cells. A manuscript was submitted for publication. In the coming years, this group plans to investigate changes of antigen-specific T cell responses during pregnancy in patients with rheumatoid arthritis.

The **Kuchen Group** investigated expression, processing and immunoregulatory function of small nucleolar RNA 104 (Snord104) and its derivatives. They found high levels of Snord104-derived small RNA fragments in haematopoietic cells and tissues of mice and humans, and proved their miRNA function. Preliminary data from Snord104-deficient mice indicate that Snord104-derived miRNAs contribute to immune homeostasis by acting as essential negative regulators of immune receptor signalling.

The **Seitz Group** examined the mechanisms of inhibition of osteoclastogenesis by anti-TNF treatment in inflammatory rheumatic disorders. It was hypothesised that this inhibition might be mediated by reduced mobilisation of osteoclast precursor cells from bone marrow into peripheral tissues and by reduced attachment of these cells to peripheral bone tissue, with subsequently reduced differentiation into mature osteoclasts.

The **Trueb Group** investigated the function of a novel growth factor receptor, FgfrL1, found in cartilage, muscle and kidneys. Mice with a targeted deletion of the FgfrL1 gene lack metanephric kidneys and show a malformed diaphragm. Recent experiments indicate that FgfrL1 controls development and survival of muscle fibres. FgfrL1 knockout mice lack slow muscle fibres and die at birth due to respiratory failure.

The **Yerly Group** studied the involvement of drug-reacting T cells in the pathogenesis of drug allergies. Recently, a few HLA alleles have been associated with allergies to specific drugs. The group demonstrated that this HLA association correlates with a particular activation mechanism of T cells. The main focus will now be on the question of whether variable clinical pictures of drug allergy are influenced by the activation pattern of T cells by drugs.

The **Möller Group** was newly established to investigate promonocyte differentiation, with a special focus on common pathways of anaemia of chronic disorder and osteoclastogenesis.



Prof. Dr. Peter Villiger  
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MD (1980) at University of Bern. Postgraduate studies in pathology, surgery, internal medicine, clinical immunology, rheumatology/rehabilitation. Postgraduate research (1989-1991) at Scripps Research Institute and University of California, San Diego (US). Habilitation in rheumatology/immunology (1995) at Faculty of Medicine, University of Zurich. Since 1999, Chair, Department of Rheumatology, Immunology and Allergology, Inselspital.



PD Dr. Frauke Förger  
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Medical studies at Universities of Aachen (DE), Toulouse (F) and Munich (DE); approbation (1995); dissertation (1997) at Technical University Munich; board certification in Internal Medicine (2002) and Rheumatology (2003). Postdoc (2003-2006) at Department of Rheumatology, Immunology and Allergology, Inselspital; since 2008, Physician; venia docendi (2013).



Dr. Stefan Kuchen  
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Medical studies (1990-1997) at University of Bern; postgraduate course in Experimental Medicine and Biology (1998); MD (2001) at University of Zurich; FMH Certification (2006). Research Scientist (2006-2012) at NIAMS, NIH, Bethesda (US). Since 2012, Senior Physician and Scientist, Department of Rheumatology, Immunology and Allergology, Inselspital.



**Prof. Dr. Burkhard Möller**  
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MD (1991) at Hannover Medical School (DE). Postgraduate education in Internal Medicine (1997), Rheumatology (2001) and Haematology/Oncology (2004) at Frankfurt University Hospital (DE). Venia legendi in Frankfurt (DE) (2003) and Bern (2007). Since 2010, Associate Professor of Rheumatology, Department of Rheumatology, Immunology and Allergology, Inselspital.



**Prof. Dr. Michael Seitz**  
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MD (1979) at University of Heidelberg (DE); venia legendi at University of Bern (1991). Since 1988, Deputy Head, Department of Rheumatology, Immunology and Allergology, Inselspital; Associate Professor of Rheumatology (1995).



**Prof. Dr. Beat Trueb**  
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PhD in Biochemistry (1981) at ETH Zurich. Postdoc (1982-1984) at University of Washington, Seattle (US). Venia Legendi (1991) at ETH Zurich. Since 1995, Group Leader, Rheumatology Research Group DCR; venia Docendi (1996); Associate Professor of Biochemistry (2001).



**Dr. Daniel Yerly**  
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MSc in Pharmaceutical Sciences (2000) at ETH Zurich; PhD in Immunology (2007) at University of Bern. Research (2006-2007) at Partners AIDS Research Center, Harvard Medical School, Boston (US); Postdoc in Clinical Immunology/Allergology (2008-2009) at Inselspital. Since 2009, Head Research Laboratory, Drug Allergy Research Group, Department of Rheumatology, Immunology and Allergology, Inselspital.

### Group Members

**Prof. Dr. Peter M. Villiger, Chair**

**PD Dr. Frauke Förger, Group Leader**  
**Manuela Tham, PhD Student (until Jan.)**

**Dr. Stefan Kuchen, Group Leader**  
**Sandra Gsponer, PhD Student (since June)**

**Prof. Dr. Burkhard Möller, Group Leader**  
**Patricia Meyer, PhD Student**

**Prof. Dr. Michael Seitz, Group Leader**  
**Stephanie Uster, PhD Student**

**Prof. Dr. Beat Trueb, Group Leader**  
**Dr. Gilles Bluteau, Postdoctoral Fellow**  
**Dr. Lei Zhuang, Postdoctoral Fellow**  
**Ruth Amann, PhD Student (until July)**

**Dr. Daniel Yerly, Group Leader**  
**Dr. Klara Eriksson, Technician**  
**Dr. Natascha Wuillemin, Postdoctoral Fellow**

### Selected Collaborators

**Engelhardt B, Stein J, University of Bern, Switzerland**

**Häuptl T, Charité – University Medicine Berlin, Germany**

**Krähenbühl S, University of Basel, Switzerland**

**Potbilewicz B, Technion – Israel Institute of Technology, Israel**

**Rey F, Pasteur Institute, France**

### Selected Grants

**Amounts allocated for 2014:**

- SNF: Role of the receptor FGFR1 in FGF signaling and cell-cell fusion (B. Trueb) CHF 130,000
- SNF: Osteoclastogenesis and chronic inflammatory rheumatic disorders (M. Seitz) CHF 85,000
- Swiss Society of Rheumatology: Warnery Research Prize 2014 (B. Möller) CHF 60,000
- Allergy Foundation Ulrich Mueller-Gierok: Hypersensitivity to amoxicillin, does the T cell recognition pattern influence the clinical picture? (D. Yerly, N. Wuillemin) CHF 65,000
- Helmut Horten Foundation: Role of the receptor FGFR1 in the development of the retina (B. Trueb) CHF 78,500

### Selected Publications

The Fgfr1 receptor is required for development of slow muscle fibers. Amann, R; Wyder, S; Slavotinek, AM; Trueb, B (2014) in: Dev Biol, 394(2), p. 228-241.

Targeted disruption of the intracellular domain of receptor Fgfr1 in mice. Bluteau, G; Zhuang, L; Amann, R; Trueb, B (2014) in: PLoS One, 9(8), p. e105210.

Anaemia may add information to standardised disease activity assessment to predict radiographic damage in rheumatoid arthritis: a prospective cohort study. Moller, B; Scherer, A; Forger, F; Villiger, PM; Finckh, A (2014) in: Ann Rheum Dis, 73(4), p. 691-696.

T cells infiltrate the liver and kill hepatocytes in HLA-B(\*):57:01-associated floxacillin-induced liver injury. Wuillemin, N; Terracciano, L; Beltraminelli, H; Schlapbach, C; Fontana, S; Krahenbuhl, S; Pichler, WJ; Yerly, D (2014) in: Am J Pathol, 184(6), p. 1677-1682.

Oxypurinol directly and immediately activates the drug-specific T cells via the preferential use of HLA-B\*58:01. Yun, J; Marcaida, MJ; Eriksson, KK; Jamin, H; Fontana, S; Pichler, WJ; Yerly, D (2014) in: J Immunol, 192(7), p. 2984-2993.

# Visceral and Transplantation Surgery

[www.dkf.unibe.ch/research-group/27/](http://www.dkf.unibe.ch/research-group/27/)

## Research Highlights 2014 / Outlook 2015

### Liver regeneration

Our research focuses on improving liver regeneration after injury or resection following several lines of investigation:

- A gene therapy approach using in vivo siRNAs targeting proteins of the Hippo signalling pathway (Stroka/Candinas).
- Isolating liver-derived Lgr5+ stem cells for reconstitution of diseased liver tissue (Stroka/Keogh/Candinas).
- Modulating effector cell function by extracellular purines on hepatic lymphoid cells, e.g., 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 explored the impact of IL-22 on liver regeneration (Beldi).
- The impact of gut bacteria on liver regeneration. Regeneration is independent of the presence of bacteria, as hepatocellular proliferation remains unchanged in germ-free mice compared to colonised mice (Beldi/Candinas).
- Extending our models of liver regeneration to the *Danio rerio* (zebrafish) (Stroka/Institute of Anatomy).

### Stem cell approach in skeletal (sphincter) muscle regeneration

Adipocyte-derived stem cells were injected into injured muscle where they were successfully incorporated and a functional improvement of muscle contraction was observed. The exact mechanism for this improved muscular healing will continue to be investigated in 2015 (Brügger).

### Gastrointestinal tumours

New targets for the treatment of gastrointestinal cancers were investigated, e.g., targeting YAP1 of the Hippo Pathway in models of hepatocellular carcinoma (Banz). Radiation-induced liver disease, a limiting factor for the use of ionising radiation to treat liver tumours is being studied (Stroka/Radiation Oncology Group).

### On-going studies bridging clinical and basic research

- A prospective randomised trial exploring the impact of Terlipressin on post-operative morbidity after major hepatic resection (Beldi).
- A large SNF-funded prospective multicentre trial to improve intraoperative communication will start in 2015 (Beldi).
- The development of prototype devices based on novel technologies to treat patients with severe fecal incontinence. In 2015, we are planning an observational pilot study to assess anatomical, physiological and biomechanical characteristics of the pelvic floor (Brügger/Institute for Surgical Technology and Biomechanics/Biomaterials Science Center, Basel/EMPA/Cantonal Hospital of Schaffhausen).
- The feasibility of intraoperative radiation therapy for GI 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).
- The applicability and feasibility of computer-assisted, navigated liver surgery in patients undergoing open or laparoscopic hepatic interventions as well as percutaneous CT-guided navigated ablation (Banz).



**Prof. Dr. Daniel Candinas**  
daniel.candinas@insel.ch

Board examination (1987); 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); Studied 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).



**Dr. Vanessa Banz**  
vanessa.banz@insel.ch

Board examination (2001); MD at University of Basel (2005). Fellowship at HPB and Liver Transplant Unit, Queen Elizabeth Hospital and Centre for Liver Research, IBR, Birmingham (UK) (2008-2010). FMH certification in Surgery (2008). Since 2010, Staff Surgeon, Department of Visceral and Transplantation Surgery, Inselspital.



**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, Boston (US) (2006-2007). FMH certification in Surgery (2005). Since 2008, Staff Surgeon, Department of Visceral and Transplantation Surgery, Inselspital. Venia docendi (2009); Associate Professor (2012).



**Dr. med. Lukas Brügger**  
lukas.bruegger@insel.ch

MD (1992) at University of Bern; FMH certification in Surgery (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  
**Dr. Vanessa Banz**, Group Leader  
**Prof. Dr. Guido Beldi**, Group Leader  
**Dr. Lukas Brügger**, Group Leader

**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. Andreas Kohler**, Staff Surgeon  
**Dr. Thomas Malinka**, Staff Surgeon  
**Dr. Peter Studer**, Staff Surgeon

**Andreas Furer**, Laboratory Technician  
**Cynthia Furer**, Laboratory Technician  
**Anita Born**, Laboratory Technician  
**Sarah Overney**, Laboratory Technician  
**Lilian Smith**, Secretary

**Felix Baier**, PhD Student (since Apr.)  
**Michel Dosch**, MD-PhD Student  
**Jacopo Gavini**, PhD Student (since May)  
**Agata Gorecka**, PhD Student  
**Ramesh Kudira**, PhD Student  
**Giulio Loforese**, PhD Student  
**Nicolas Melin**, PhD student (since Apr.)

### Selected Collaborators

**Eberli D**, University Hospital of Zurich, Switzerland  
**Halazonetis T**, University of Geneva, Switzerland  
**Kanse S**, University of Oslo, Norway  
**Starlinger P, Brostjan C**, Vienna General Hospital, Austria  
**Tschan F**, University of Neuchatel, Switzerland

### Selected Grants

#### Amounts allocated for 2014:

- SNF: NTPDase1/CD39 and innate lymphoid cells in liver injury and repair (G. Beldi) CHF 112,493
- Forschungs-Grant des Inselspitals für Nachwuchsforschende: Targeting YAP1 of Hippo pathway to control the growth of hepatocellular carcinoma (V. Banz) CHF 80,000

- Johnson & Johnson: Hepato-Pancreato-Biliary Fellowships (B. Gloor) CHF 100,000
- Nano-Tera.ch: Smart Muscle for Incontinence Treatment (L. Brügger) CHF 215,000
- Novartis Foundation for Medical-Biological Research: Mechanism and consequences of ATP secretion in endotoxemia (G. Beldi) CHF 60,000
- 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

### Selected Publications

Computer planned, image-guided combined resection and ablation for bilobar colorectal liver metastases. Banz, VM; Baechtold, M; Weber, S; Peterhans, M; Inderbitzin, D; Candinas, D (2014) in: World J Gastroenterol, 20(40), p. 14992-14996.

A novel animal model for external anal sphincter insufficiency. Brugger, L; Inglin, R; Candinas, D; Sulser, T; Eberli, D (2014) in: Int J Colorectal Dis, 29(11), p. 1385-1392.

Elevated liver regeneration in response to pharmacological reduction of elevated portal venous pressure by terlipressin after partial hepatectomy. Fahrner, R; Patsenker, E; de, GA; Stickel, F; Montani, M; Stroka, D; Candinas, D; Beldi, G (2014) in: Transplantation, 97(9), p. 892-900.

Tumor necrosis factor-related apoptosis-inducing ligand on NK cells protects from hepatic ischemia-reperfusion injury. Fahrner, R; Trochsler, M; Corazza, N; Graubardt, N; Keogh, A; Candinas, D; Brunner, T; Stroka, D; Beldi, G (2014) in: Transplantation, 97(11), p. 1102-1109.

In vitro rescue of FGA deletion by lentiviral transduction of an afibrinogenemic patient's hepatocytes. Stroka, D; Keogh, A; Vu, D; Fort, A; Stoffel, MH; Kuhni-Boghenbor, K; Furer, C; Banz, V; Demarmels, BF; Lammle, B; Candinas, D; Neerman-Arbez, M (2014) in: J Thromb Haemost, 12(11), p. 1874-1879.



## Key Events

**Swiss Youth in Science:  
"Biology and Medicine" Study Week  
16-22 Mar.**

**Welcome Event 2014**

**21 May**

Around 70 interested DCR newcomers attended this event, which will take place again on 27 May 2015.

**"Nacht der Forschung" of the  
University of Bern**

**6 Sep.**

For the first time, the DCR participated with a series of lectures in the "Nacht der Forschung". They covered such diverse topics as high-tech surgery and rheumatoid arthritis, as well as questions such as what cardiac arrhythmia, pain and migraine have in common.

**Day of Clinical Research 2014**

**4-5 Nov.**

As usual, a large and interested audience followed the presentations of **Suzan G. LeVine** (U.S. Ambassador to Switzerland and Liechtenstein) entitled "U.S. and Switzerland: Partnering for Medical Innovation" and **Prof. Dr. Thomas Eschenhagen** (Chairman of the Board, German Centre for Cardiovascular Research; Director, Department of Experimental Pharmacology and Toxicology, University Medical Center, Hamburg-Eppendorf, Germany) entitled "The German Centre for Cardiovascular Research (DZHK) – a New Structure for Promoting Translation in Cardiology".

Eight candidates applied for the Johanna Dürmüller-Bol DCR Research Prize 2014 (funded by the Johanna Dürmüller-Bol Foundation) and 192 abstracts were submitted for the Poster Prizes of the DCR and the Research Prize Alumni MedBern. The winners were (left to right in photo below):

*Research Prize Alumni MedBern*

**Dr. Tim Vanbellingen**

Perception and Eye Movement Laboratory, Department of Neurology, Inselspital and Neurology, DCR; Centre for Neurology and Neurorehabilitation, Lucerne Cantonal Hospital)

*Johanna Dürmüller-Boll DCR*

*Research Prize*

**Dr. Ramanjaneyulu Allam**

Department of Hematology and Central Hematology Laboratory, Inselspital and Hematology (Adults), DCR

*Poster prizes of the DCR for*

– *best clinical project*

**Sophie Braga Lagache**

Protein and Cell Biology, DCR

– *best project by a medical student*

**Sebastian Sahli**

Department of Neurosurgery, Inselspital and Cluster for Regenerative Neuroscience, DCR

– *best preclinical project*

**Giulio Loforese**

Visceral and Transplantation Surgery, DCR



The next Day of Clinical Research will be held 3-4 November 2015.

**DCR Open House**

**6 Nov.**

Around 250 visitors joined guided tours of the DCR (Maurice E. Müller and Murtenstrasse 50 buildings) and of the ARTORG (Murtenstrasse 21 and 50).

**"Clinical Research" symposium  
for Biomedical Sciences students of  
the University of Fribourg**

**6 Nov.**



**DKF Research Conferences 2014**

With an average of 60 visitors each month, the DKF Research Conferences continue to be very successful. In 2014, we were pleased to present the following speakers:

**3 Feb.** – Prof. Dr. Johannes Loffing  
University of Zürich, Switzerland  
*Cooperation needed – integrative control of potassium homeostasis*

**3 Mar.** – Prof. Dr. Patrick Most  
Heidelberg University Hospital, Germany  
*S100A1 – a versatile molecular regulator of cardiac and vascular function*

**7 Apr.** – Prof. Dr. Daniel Ricklin  
University of Pennsylvania School of Medicine, USA  
*A “complementary” path towards treating immune and inflammatory diseases: advances in the therapeutic modulation of the complement system*

**5 May** – Prof. Dr. Viola Vogel  
ETH Zurich, Switzerland  
*Nanomechanics by which cells explore their environments and pick up their prey*

**2 June** – Dr. Laura Audí  
Vall d’Hebron Research Institute (VHIR), Barcelona, Spain  
*Disorders/Differences of Sex Development (DSD): clinical, molecular and sociocultural evolution*

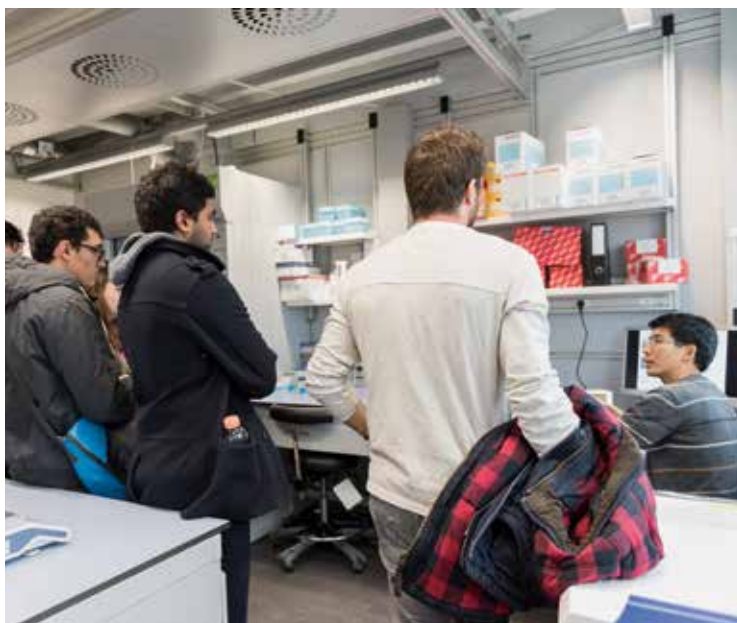
**7 July** – Prof. Dr. Yosef Shiloh  
Tel Aviv University, Israel  
*The ATM protein kinase: a busy intersection*

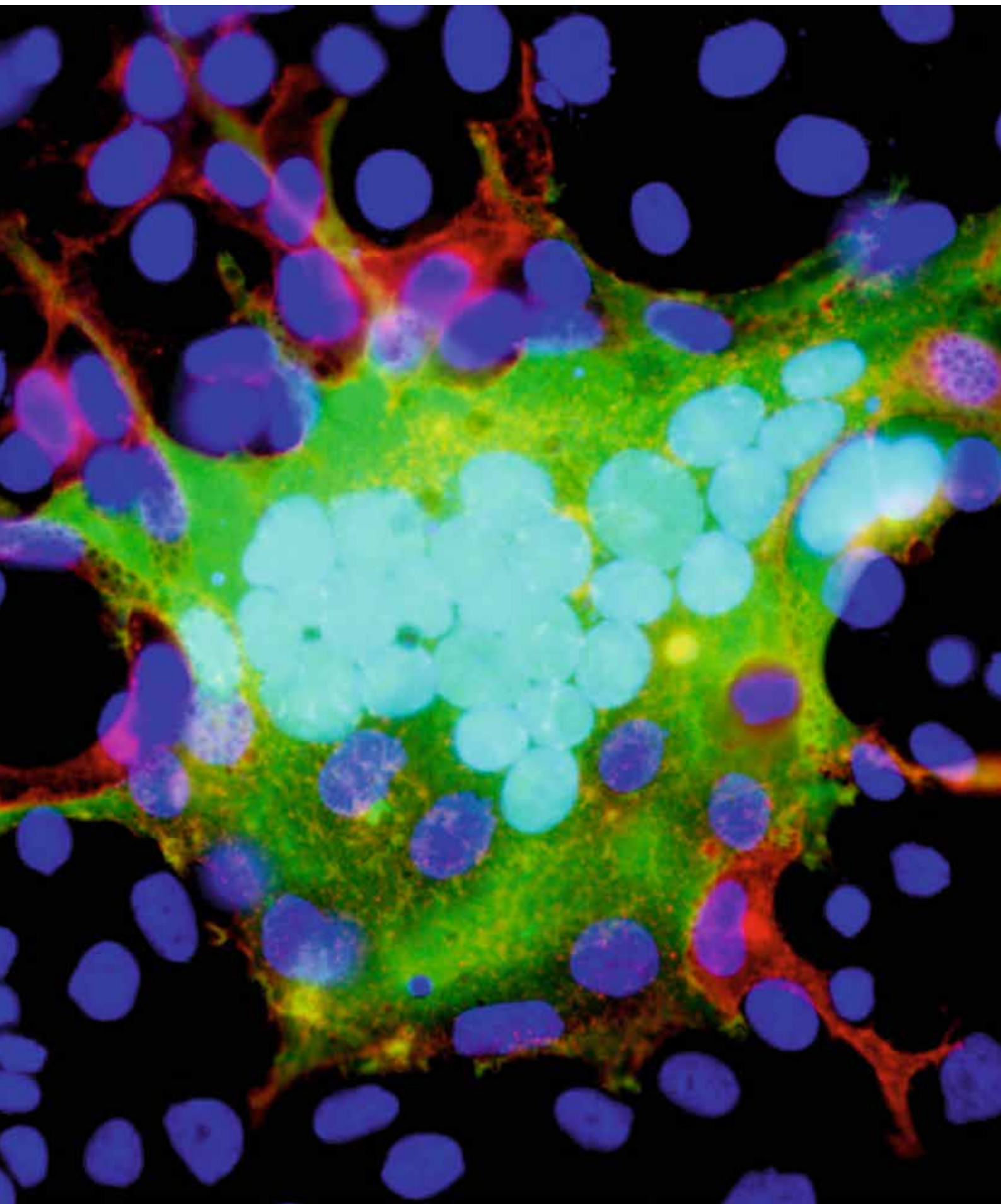
**1 Sep.** – Prof. Dr. Mariusz Z. Ratajczak  
University of Louisville, USA  
*Quo Vadis Regenerative Medicine? – of Stem Cells, Regeneration, Aging and Cancer*

**6 Oct.** – Prof. Dr. Tom Eirik Mollnes  
University of Oslo, Norway  
*Bride and groom in systemic inflammation: The bells ring for complement and toll-like receptors in cooperation*

**1 Dec.** – Prof. Dr. Antonio Lanzavecchia  
Università della Svizzera italiana, Switzerland  
*Dissecting the Antibody Response to Pathogens and Self Antigens*

In 2015, the DKF Research Conferences will take place as usual every first Monday of the month from 5-6 pm, followed by an apéro.





# Personnel Update

## Academic Degrees

The following academic degrees were awarded to DCR group members:

### Professor

**Prof. Dr. Nils Kucher**  
Angiology

### Associate Professor

**Prof. Dr. Urs M. Fischer**  
Neurology

**Prof. Dr. Katia Monastyrskaya-Stäuber**  
Urology

**Prof. Dr. Luigi Raio**  
Prenatal Medicine

**Prof. Dr. Andreas Schoenenberger**  
Geriatrics / Medicine of Ageing

**Prof. Dr. Hildegard Tanner**  
Cardiology

### Titular Professor

**Prof. Dr. Yves Allemann**  
Cardiology

**Prof. Dr. Stephan Bohlhalter**  
Neurology

**Prof. Dr. Alain Kaelin**  
Neurology

**Prof. Dr. Thomas Nyffeler**  
Neurology

### Lecturer (Privatdozent)

**PD Dr. Steffen Glökler**  
Cardiology

**PD Dr. Simon Jung**  
Neurology

**PD Dr. Johannes Lemke**  
Human Genetics

**PD Dr. Urban Novak**  
Oncology

**PD Dr. Stefano Rimoldi**  
Cardiology

**PD Dr. Michael Schüpbach**  
Neurology

**PD Dr. Andreas Vogt**  
Anaesthesiology

**PD Dr. Kathrin Zaugg**  
Radiation Oncology

**PhD**  
(supervisors in brackets)

**Ruth Claire Diana Amann**  
(Prof. Dr. Beat Trueb)  
Role of fibroblast growth factor receptor like1 (FGFRL1) during muscle development

**Jasmin Balmer**  
(PD Dr. Volker Enzmann)  
Cell death pathways in sodium iodate-induced retinal degeneration in vivo and in vitro

**Paulina Cwiek**  
(PD Dr. Alexandre Arcaro)  
Identification of new targeted therapies for cancers of the nervous system

**Dirk de Beer**  
(Prof. Dr. Gabriela Baerlocher)  
Telomere biology in normal and pathological haematopoiesis

**Janine Hensel**  
(Prof. Dr. George Thalmann)  
The stroma response in bone metastasis

**Victor Johann Raul Jeger**  
(Prof. Dr. Stephan Jakob)  
Angiotensin and mitochondrial function in septic shock

**Kei Mikami**  
(PD Dr. Yitzhak Zimmer)  
Impact of p53 status on radiosensitization of tumor cells by MET inhibition-associated checkpoint abrogation

**Maria Consolata Miletta**  
(Dr. Vibor Petkovic, Prof. Dr. Primus Mullis)  
Variable effects of Butyrate on GH secretion

**Sheida Moghadamrad**  
(PD Dr. Andrea de Gottardi)  
Investigations on the development of portal hypertension in the absence of microbial intestinal flora in mice

**Ramesh Periasamy**  
(Prof. Dr. Daniel Surbek, Dr. Andreina Schoeberlein)  
Preconditioning of chorion-derived mesenchymal stem cells for subsequent neural differentiation

**Kseniia Poliakova**  
(Prof. Dr. Luca Borradori, Dr. Bertrand Favre)  
Localization and function of bullous pemphigoid antigen 1 in C2.7 myoblasts

**Emilie Seydoux**  
(PD Dr. Christophe von Garnier, Prof. Dr. Barbara Rothen-Ruthishauser)  
Biomedical nanoparticles as immune modulators – In vitro and in vivo investigation of intrinsic immunomodulatory properties of polystyrene and gold nanoparticles

**Ninda Syam**  
(Prof. Dr. Hugues Abriel)  
Biochemical analyses of ion channels regulation and their role in channelopathies

**Adel Tekari**

(Prof. Dr. Willy Hofstetter, Dr. Rainer Egli)  
Roles of collagen type II and transforming growth factor-beta in the formation of cartilage-like tissues

**Sameer Sopanrao Udhane**

(Prof. Dr. Christa E. Flück)  
Regulation of human adrenal androgen production

**Xianghong Zhang**

(Prof. Dr. Frank Stüber)  
8p23 beta-defensin copy number variation in severe sepsis

**Line Cristel Kim Zurkinder**

(PD Dr. Geneviève Escher)  
Role of sterol 27-hydroxylase in reverse cholesterol transport and atherosclerosis: Regulation by bile acids

**Awards**

The following DCR group members received awards in 2014:

**Dr. Christoph Albers, Prof. Dr. Willy Hofstetter, Prof. Dr. Klaus-Arno Siebenrock, Prof. Dr. Regine Landmann, PD Dr. Frank Klenke**

Orthopaedic Surgery; Bone Biology & Orthopaedic Research  
Venel Prize, Swiss Orthopaedics: "In vitro cytotoxicity of silver nanoparticles on osteoblasts and osteoclasts at antibacterial concentrations"

**Dr. Ramanjaneyulu Allam**

Hematology (Adults)  
Johanna Dürmüller-Bol DCR Research Award: "The role of ribonuclease inhibitor (RNH1) in hematopoiesis and ribosomopathies"

**Dr. Ramanjaneyulu Allam**

Hematology (Adults)  
Abstract Achievement Award, American Society of Hematology: "An Unexpected role for ribonuclease inhibitor (RNH1) in erythropoiesis"

**Dr. Regula von Allmen**

Cardiovascular Surgery  
Award for Best Presentation in Clinical Research, Swiss Surgical Society (SGC) Annual Meeting

**Dr. Deepak Balani, PD Dr. Daniel Aebersold, Prof. Dr. Willy Hofstetter, Prof. Dr. Michael Seitz**

Bone Biology & Orthopaedic Research; Rheumatology  
Basic Research Award, Swiss Bone and Mineral Society (SBMS): "Interleukin-17A stimulates granulocyte-macrophage colony-Stimulating factor release by murine osteoblasts in the presence of 1,25-Dihydroxyvitamin D3 and inhibits murine osteoclast development in vitro"

**Dr. Vanessa Banz**

Visceral and Transplantation Surgery  
Award for Best Oral Presentation, Swiss Surgical Society Annual Meeting: "In vitro and in vivo correction of afibrinogenemia"

**Dr. Maris Bartkevics**

Cardiovascular Surgery  
Young Investigator Award, European Association for Cardio-Thoracic Surgery: "Efficacy of mechanical postconditioning following warm, global ischemia depends on circulating fatty acid levels in an isolated, working rat heart model"

**Dr. Andreas Boss**

Magnetic Resonance Spectroscopy and Methodology (AMSM)  
Benoît Pochon Prize: "Application of multinuclear magnetic resonance spectroscopy for the non-invasive investigation of skeletal muscle and liver metabolism"

**Dr. Andreas Boss**

Magnetic Resonance Spectroscopy and Methodology (AMSM)  
Best PhD Thesis 2013, Graduate School for Cellular and Biomedical Sciences: "Application of multinuclear magnetic resonance spectroscopy for the non-invasive investigation of skeletal muscle and liver metabolism"

**Sophie Braga Lagache**

Protein and Cell Biology  
Poster Prize of the DCR for the Best Clinical Project: "Quantitative protein measurement of circulating plasma microparticles by data-independent nanoLC-MS2"

**Dr. Julia Cahenzli, Yasmin Köller**

Gastroenterology / Mucosal Immunology  
Pfizer Research Prize 2014, Honoured for excellent work in infectious diseases, rheumatology and immunology: "Intestinal microbial diversity during early-life colonisation shapes long term IgE"

**Paola Francica**

Radiation Oncology  
Best Young Investigator Presentation 2014, Scientific Association of Swiss Radiation Oncology (SASRO): "Met targeting in combination with ionizing radiation induces senescence in gastric cancer tumor models"

**Dr. Monika Haubitz, PD Dr. Elisabeth Oppliger Leibundgut, Ingrid Helsen, Heidi Baumgartner, Dr. Naomi A. Porret, Prof. Dr. Gabriela M. Baerlocher**

Hematology (Adults)  
Prize for Clinical Hematology, Swiss Society of Hematology (SGH): "Mutational analysis in genes of the telomere complex in patients screened for telomeropathies"

**Ramesh Kudira**

Visceral and Transplantation Surgery  
Ethicon Travel Award, SGG-SGVC-SASL Annual Meeting 2014: "Extracellular nucleotides and CD39 modulate the secretion of IL-22 by hepatic lymphocytes"

**Giulio Lofrese**

Visceral and Transplantation Surgery  
Poster Prize of the DCR for the Best Preclinical Project: "Regulation of hippo pathway during liver regeneration"

**Prof. Dr. Bernhard Meier**

Cardiology  
Legend in Cardiology Award 2014, Anniversary Meeting Complex Cardiovascular Catheter Therapeutics

**Prof. Dr. Bernhard Meier**

Cardiology  
The Greats of Cardiology Award 2014, University of Freiburg, Germany

**Byron Oppliger, Dr. Marianne Joerger-Messerli, U. Reinhard, Dr. Andreina Schoeberlein, Prof. Dr. Daniel Surbek**

Prenatal Medicine  
Poster Prize, Swiss Society of Gynaecology and Obstetrics: "Transnasal approach to deliver stem cells in a model of hypoxic-ischemic brain injury in rat pups"

**Mary Princip**

Psychosomatic Medicine  
Poster Prize, German Congress of Psychosomatic Medicine and Psychotherapy (DKPM): "Speaking in images – was uns Herzezeichnungen über das subjektive Stressempfinden von Herzinfarktpatienten sagen"



**Dr. Emrush Rexhaj**

Cardiology  
Cardiovascular Research Prize 2014, Swiss Society of Cardiology: "Mice generated by in vitro fertilization exhibit vascular dysfunction and shortened life span"

**Sebastian Sahli**

Cluster for Regenerative Neuroscience  
Poster Prize of the DCR for the Best Project by a Medical Student: "Increased yield of dopaminergic neurons by chronic minocycline treatment and HIF-1 alpha stabilization"

**Dr. Monica Schaller, Irmela Sulzer, Magdalena Skowronska, Dr. Monique Vogel, Dr. Karim Kentouche, Prof. Dr. Bernhard Lämmle, PD Dr. Johanna Anna Kremer Hovinga Strebler**  
Hematology (Adults)  
Roche Hemostasis Award 2014: "Anti-idiotypic DARPins neutralize anti-ADAMTS13 autoantibodies in acquired Thrombotic Thrombocytopenic Purpura (aTTP) in a concentration dependent manner"

**PD Dr. Petra Stute**

Endocrinology of the Breast  
Bionorica Global Research Initiative:  
"Impact of black cohosh on hippocampal and hypothalamic gene expression profiles in ovariectomized rats"

**Dr. Tim Vanbellingen**

Neurology  
Research Prize Alumni MedBern: "Home-based training to improve manual dexterity in patients with multiple sclerosis: a randomized controlled trial"

**Dr. Tingting Wen, Maxime Schmutz, Dr. Christoph Lippuner, Marcel Schiff, Prof. Dr. Frank Stüber, Prof. Dr. Ulrike Stamer**

Anaesthesiology  
Free Communication (2nd prize) 2014, Annual Meeting of the Swiss Society of Anaesthesiology and Resuscitation: "Postoperative nausea and vomiting: do genetics variants contribute?"

**Staff Changes****New Staff****Michael Ackermann**

IT-Support (70%), Administration (since July)

**Alain Despont**

Laboratory Technician (100%), Cardiovascular Research (since Feb.)

**Michel Hauser**

Doctoral Student (100%), Bone Biology & Orthopaedic Research (since July)

**Sabine Noemi Nafzger**

Laboratory Technician (40%), Ion Channels and Channelopathies (since Jan.)

**Claudia Quarroz**

Laboratory Technician (100%), Hematology (Adults) (since Oct.)

**David Schär**

IT-Support (50%), Administration (since Nov.)

**Beatrice Stalder**

DCR Secretary (70%), Administration (since Mar.)

**Retirements****Prof. Dr. Anne-Catherine Andres**

Group Leader / Coordinator (100%), Mammary Gland Biology and Carcinogenesis / Research Division Tiefenau (until Jan.)

**Prof. Dr. Rudolf Brenneisen**

Group Leader (100%), Phytopharmacology, Bioanalytics and Pharmacokinetics (until July)

**Ruth Scheuter**

DCR Secretary (50%), Administration (until Mar.)

**Internal Reallocations****François Achermann**

Laboratory Technician (100%), Mass Spectrometry and Proteomics Laboratory (since Feb.)

**Carlos Wotzkow**

Laboratory Technician (90%), Live Cell Imaging (LCI) (since Feb.)

**Dr. Eva-Maria Hau-Grosch**

Research Assistant (50%), Pediatric Surgery (until Aug.)

**Dr. Christian Lanz**

Research Assistant (50%), Phytopharmacology, Bioanalytics and Pharmacokinetics (until July)

**Marta Pace**

Research Assistant (100%), Neurology (until Dec.)

**Dr. Mina Rezaei**

Postdoctoral Fellow (100%), Nephrology and Hypertension (until May)

**Oliver Schweizer**

IT-Support (60%), Administration (until June)





