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RESEARCH

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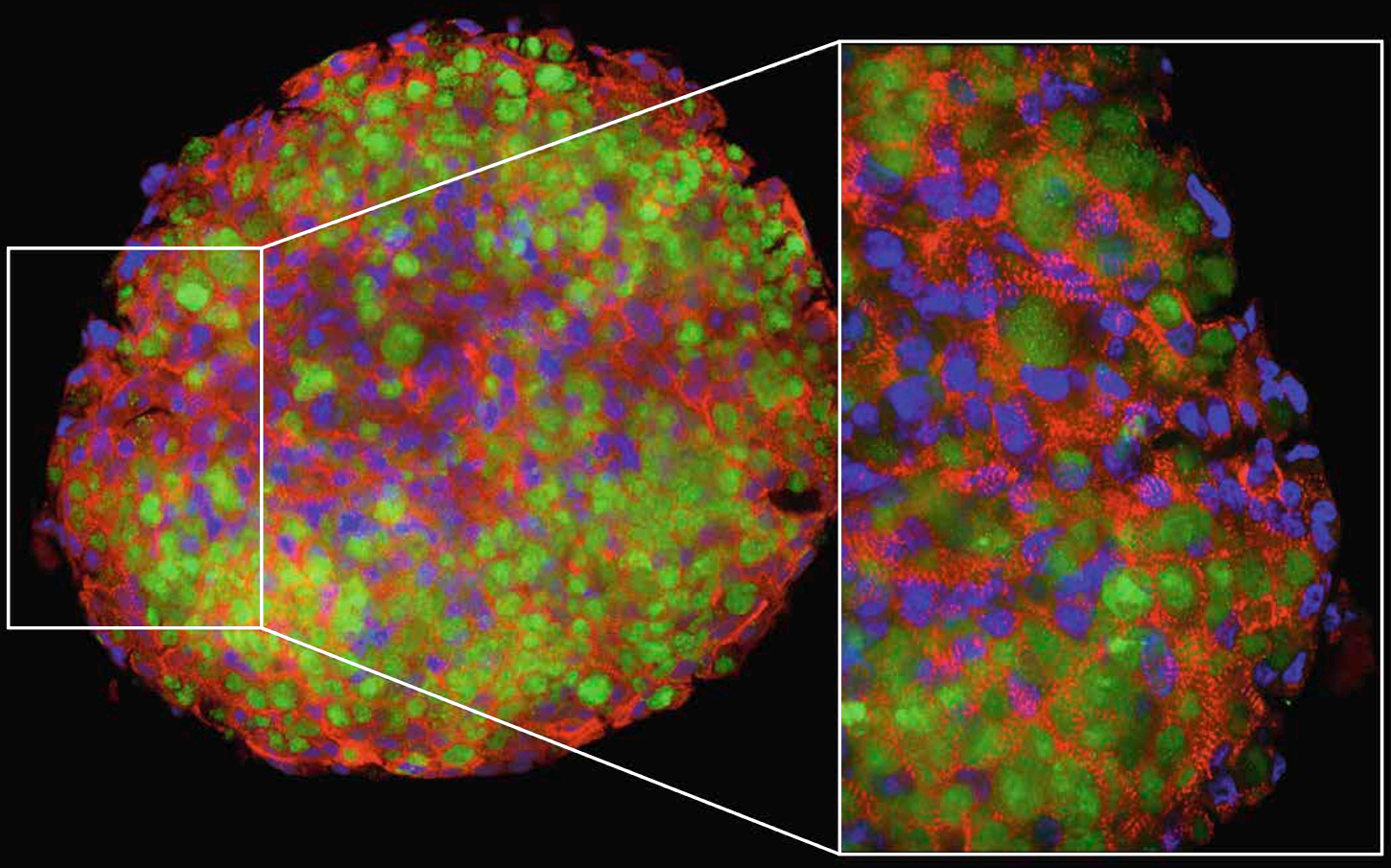
Jahresbericht 2012
Annual Report 2012



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

Cover:
Human cardiomyocytes derived from induced pluripotent stem cells (iPSC) were allowed to self-aggregate in hanging drops. After spontaneously contracting spheroids had formed, the micro-tissue was fixed, immunostained for the muscle protein myomesin (red), connexin-43 (green) and DNA (blue), and images were obtained using confocal microscopy at different magnifications.
Image: Dr. Christian Zuppinger

Contents

The DCR at a Glance

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

Founded in 1994, its mission is to provide the best possible environment and infrastructure to researchers at the Inselspital, Bern University Hospital and at the Faculty of Medicine. In 2012, 51 independent research groups, covering almost all fields of biomedical research, were affiliated with the DCR.

The main goal of the DCR is to establish a bridge between laboratory-based biomedical and patient-oriented clinical research, by offering scientific support to its groups and by operating state-of-the-art technology core facilities and specialised animal core facilities.

Das DKF auf einen Blick

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

Es wurde 1994 mit dem Auftrag gegründet, Forschenden vom Inselspital, Universitätsspital Bern und von der Medizinischen Fakultät eine optimale Infrastruktur zur Verfügung zu stellen. 2012 waren 51 unabhängige Forschungsgruppen dem DKF angeschlossen, die zusammen fast alle Bereiche der biomedizinischen Forschung abdecken.

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

Foreword – Director's Report

Dear readers and colleagues,

Looking back at 2012, we can say that this was a very positive year for the DCR! Many of the achievements of the past year will have a significant impact and improve the breadth of research that can be performed at the DCR.

As you may know, one of the core activities of the DCR is to operate technology core facilities, allowing DCR researchers to perform cutting-edge science. Early in 2012, we created a new core facility, located at the Murtenstrasse 50 division. The "Live Cell Imaging (LCI) Core Facility" is an offshoot of the DCR "Confocal Microscopy Core Facility", which was headed for many years by Prof. Shida Yousefi. We thank her for her commitment in running this former facility and, at the same time, wish Dr. Fabian Blank, who will head the new facility, all the best. One first outstanding accomplishment of the LCI Facility is the approval of an SNSF R'Equip project permitting the purchase of a Zeiss LSM 710, one of the best confocal microscopes available. This microscope will be available to all members of the DCR and will also be part of the Microscopy Imaging Center (MIC) at the University of Bern. Here, we also thank the Fund of the Chefärzte of the Inselspital for providing matching financial support.

The DCR Cytometry Laboratory also obtained an SNSF R'Equip grant. This grant allowed the purchase of a new type of cytometer, ImageStreamX, which combines the speed and power of flow cytometry with high-resolution single-cell microscopy. The newly created "Genomics Core Facility" was likewise able to purchase an Ion Torrent PGM next-generation sequencing machine in 2012. This machine, which allows medium throughput sequencing, is located at Murtenstrasse 31.

Another very positive point that will significantly help many DCR scientists, is the approval given by the Inselspital to fund the development of the bioinformatics support for clinical projects. With this five-year funding, the DCR will be able to hire two bioinformaticians and purchase the needed bioinformatics infrastructure to help develop clinical bioinformatics projects at the Inselspital. This venture will be carried out in close collaboration with the newly created "Interfaculty Bioinformatics Unit" at the University of Bern, headed by Dr. Rémy Bruggmann.

As for the organisation of the DCR, groups of the DCR were given the possibility in 2012 to form "Research Clusters". With these clusters, the DCR aims to support bottom-up initiatives of several DCR research groups to collaborate and organise educational activities together. At the present time, two clusters have formally started their activities: "Regenerative Neuroscience" and "Signal Transduction in Disease". The creation of more research clusters in 2013 is under discussion.

As you know, every year the DCR awards a research prize of CHF 30,000 to support a promising project proposed by a young investigator. In 2012, we had the great luck to reach an agreement with the Johanna Dürmüller-Bol Foundation, who will finance this prize from now on. The award will be re-named "Johanna Dürmüller-Bol DCR Research Award" in 2013 but the aim of the prize will remain unchanged. I take this opportunity to warmly thank the Foundation Board for this very generous support.

On 14 November, the DCR again held a truly remarkable Day of Clinical Research. Particularly unforgettable was the exciting lecture given by Prof. Ada Yonath, Nobel Prize recipient, on ribosomes. Noteworthy also is that during the day, we had the first site visit of the DCR External Advisory Board. Not only were the four scientists able to attend the meeting but they also had the opportunity to listen to presentations by the heads of the DCR Animal and Technology Core Facilities. We received much interesting and constructive feedback from this new board.

Again, as you can see, 2012 was a year full of activities and developments! It is certainly extremely rewarding to be able to head this department. This is also the reason why I would like to warmly thank all the DCR employees for the outstanding spirit and excellent work done for the department and the research community at the University of Bern.

Prof. Dr. Hugues Abriel, MD PhD

Vorwort – Bericht des Direktors

Liebe Leserinnen und Leser
Liebe Kolleginnen und Kollegen

Im Rückblick auf das Jahr 2012 dürfen wir sagen, dass es ein sehr positives Jahr für das DKF war. Viele Errungenschaften des letzten Jahres werden in der nahen Zukunft positive Auswirkungen auf die Möglichkeiten der Forschungsgruppen des DKF entwickeln.

Eine der Kernaufgaben des DKF besteht im Betrieb von Technologie Core Facilities, um den Forschenden im DKF den Zugang zu Spitzentechnologien zu ermöglichen. Anfangs 2012 haben wir im Forschungsbereich Murtenstrasse 50 eine neue Core Facility geschaffen. Die „Live Cell Imaging (LCI) Core Facility" ist die Weiterführung der „Konfokalen Mikroskopie Core Facility" des DKF, welche während vielen Jahren von Prof. Shida Yousefi geleitet wurde. Wir danken Frau Prof. Yousefi für ihr Engagement in der Führung dieser Einheit, und zur gleichen Zeit wünschen wir Dr. Fabian Blank, der die Leitung der neuen LCI übernehmen wird, alles Gute! Eine erste ausserordentliche Leistung konnte die LCI Core Facility bereits verzeichnen. Mit der Genehmigung eines SNF R'Equip Projektes für ein Zeiss LSM 710 Mikroskop, wird die Anschaffung eines der zurzeit besten Konfokalen Mikroskope ermöglicht. Dieses Mikroskop wird den Mitarbeitenden des DKF zur Verfügung stehen und wird auch Teil des Microscopy Imaging Centers (MIC) der Universität Bern sein. An dieser Stelle bedanken wir uns beim Fonds für Infrastruktur der Chefärztinnen und Chefärzte des Inselspitals für die Bereitstellung eines Matching Funds.

Das DKF Zytometrie Labor hat ebenfalls einen SNF R'Equip Förderungsbeitrag zugesprochen erhalten. Dieser ermöglichte den Kauf eines neuen Typs von Zytometer, dem ImageStreamX, der die Geschwindigkeit und die Leistung der Durchflusszytometrie mit der Möglichkeit der hochauflösenden Single-Cell-Mikroskopie kombiniert. Aus fakultären Mitteln konnte die neu geschaffene „Genomics Core Facility" 2012 ein Ion Torrent PGM Next-Generation Sequenziergerät anschaffen. Das Gerät für Sequenzierungen für mittleren Durchsatz befindet sich an der Murtenstrasse 31.

Ein weiterer Punkt, von welchem viele DKF Wissenschaftler profitieren werden, ist die Zustimmung des Inselspitals, die Entwicklung des Bioinformatik-Support für klinische Projekte zu unterstützen. Diese Fünf-Jahres-Finanzierung erlaubt dem DKF die Anstellung von zwei Bioinformatikern und die Anschaffung der nötigen Infrastruktur für Bioinformatik zur Entwicklung von klinischen Bioinformatik-Projekten am Inselspital. Dieses Unternehmen wird in enger Zusammenarbeit mit der neu geschaffenen „Interfaculty Bioinformatics Unit" der Universität Bern, unter der Leitung von Dr. Rémy Bruggmann, durchgeführt werden.

Was die Organisation des DKF betrifft, wird seit 2012 DKF Forschungsgruppen die Möglichkeit geboten sogenannte „Forschungscluster" zu bilden. Das Ziel ist es, mit diesen Clusters bottom-up Initiativen von DKF Forschungsgruppen zu Zusammenarbeiten und zur Organisation gemeinsamer Weiterbildungsaktivitäten zu unterstützen. Aktuell sind zwei Clusters aktiv: „Cluster für Regenerative Neurowissenschaft" und „Cluster Signal Transduction in Disease". Die Schaffung weiterer Clusters im kommenden Jahr wird diskutiert.

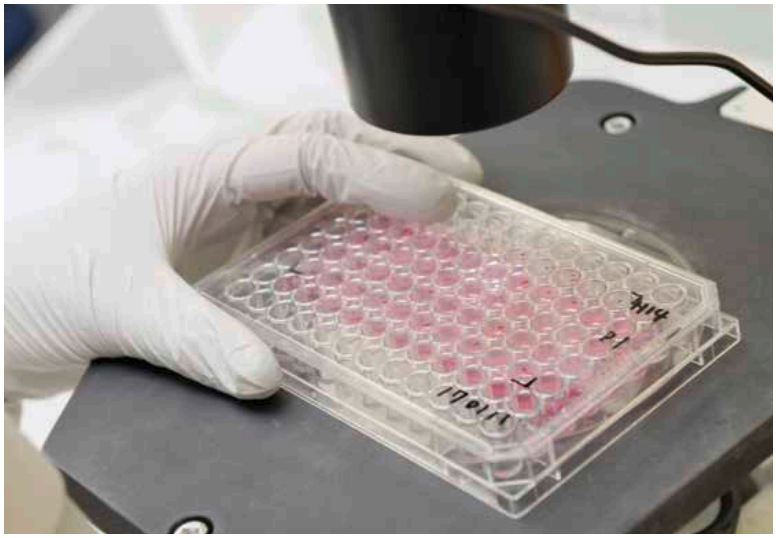
Jährlich verleiht das DKF einen Forschungspreis von CHF 30'000 zur Unterstützung eines vielversprechenden Projektes einer jungen Forscherin/eines jungen Forschers. 2012 konnten wir eine Vereinbarung mit der Fondation Johanna Dürmüller-Bol, die ab 2013 den Preis finanzieren wird, unterzeichnen. Die Auszeichnung wird im 2013 umbenannt in „Johanna Dürmüller-Bol DKF Forschungspreis". Das Ziel des Preises bleibt unverändert. Ich nutze diese Gelegenheit und bedanke mich herzlich beim Stiftungsrat für diese grosszügige Unterstützung.

Am 14. November konnte das DKF wieder den vielbeachteten Tag der Klinischen Forschung durchführen. Besonders in Erinnerung bleiben wird der spannende Vortrag über die Aufklärung der Struktur der Ribosomen der Trägerin des Nobelpreises von 2009, Frau Prof. Ada Yonath (Weitzman Institute, Rehovot, Israel). Erwähnenswert ist ebenfalls, dass am Tag der Klinischen Forschung die erste Site-Visit des External Advisory Boards des DKF stattfand. Die vier Wissenschaftler konnten nicht nur diese Veranstaltung besuchen, sondern hatten auch die Gelegenheit den Präsentationen der Leiter der DKF Tier und Technologie Core Facilities zu folgen. Wir erhielten eine sehr interessante und konstruktive Rückmeldung von diesem neuen Board.

Wie Sie sehen, war auch das Jahr 2012 wieder ein Jahr voller Aktivitäten und Wachstum! Es ist für mich sehr befriedigend, dieses Departement leiten zu dürfen. Aus diesem Grund möchte ich mich ganz herzlich bei allen DKF Mitarbeitenden bedanken für ihren bemerkenswerten Elan und für die exzellente Arbeit, die sie für das Department und die Forschungsgemeinschaft an der Universität Bern geleistet haben.

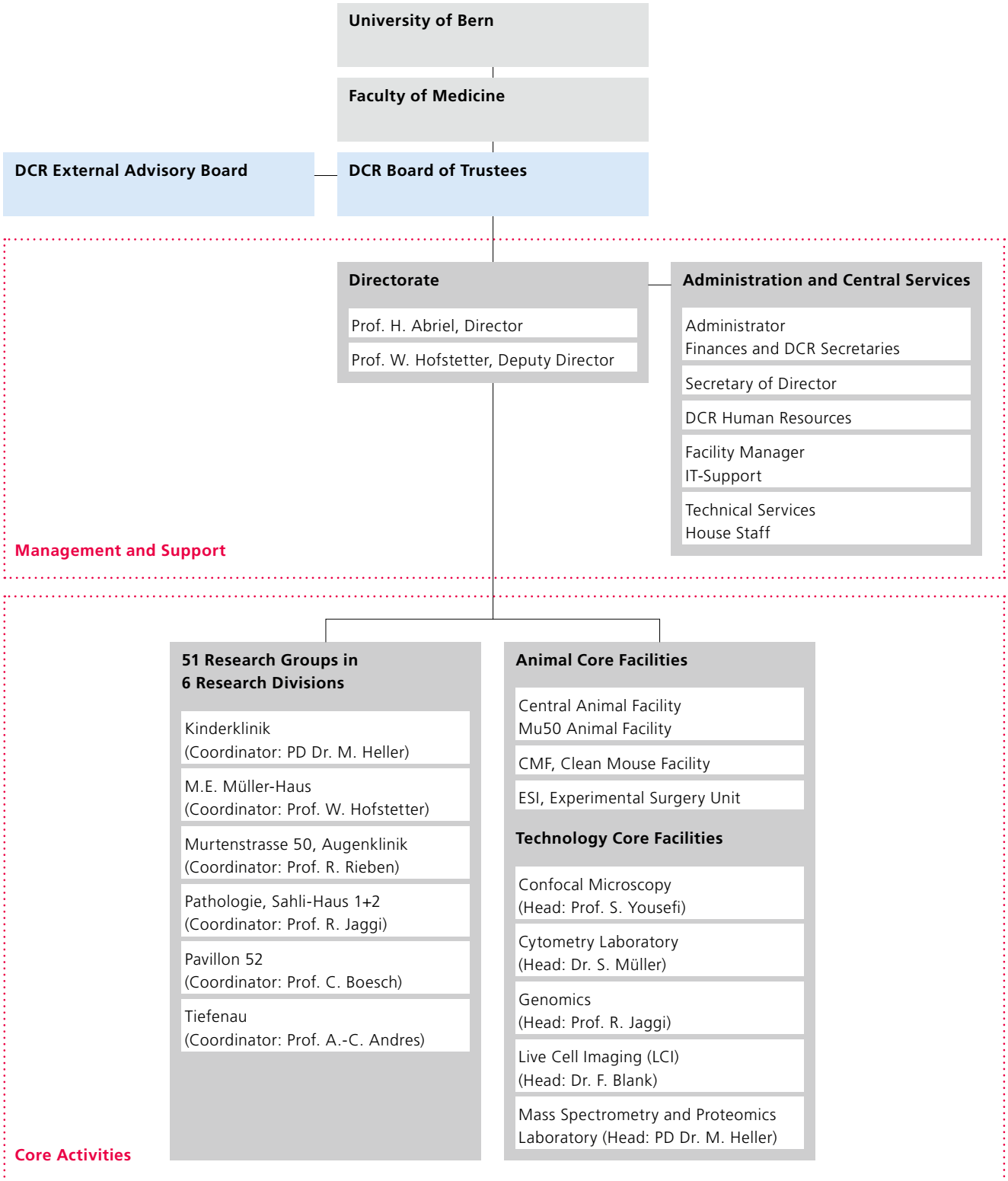
Prof. Dr. Hugues Abriel, MD PhD

Organisation



The role of the DCR is to provide optimal infrastructure and scientific support to its research groups, of which there were 51 at the end of 2012. The vast majority (43) of these groups are from departments of the Inselspital, Bern University Hospital. The remainder (8) are internal DCR groups, involved in the scientific support and coordination of equipment and infrastructure on a daily basis. The 51 groups are divided into 6 Research Divisions. Equally important, the DCR is responsible for operating technology and animal core facilities. Furthermore, the groups of the department are supported by central services responsible for administration, informatics and technical support.

Organigram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51 Research Groups in
6 Research Divisions
Kinderklinik
(Coordinator: PD Dr. M. Heller)
M.E. Müller-Haus
(Coordinator: Prof. W. Hofstetter)
Murtenstrasse 50, Augenklinik
(Coordinator: Prof. R. Rieben)
Pathologie, Sahli-Haus 1+2
(Coordinator: Prof. R. Jaggi)
Pavillon 52
(Coordinator: Prof. C. Boesch)
Tiefenau
(Coordinator: Prof. A.-C. Andres)
Animal Core Facilities
Central Animal Facility
Mu50 Animal Facility
CMF, Clean Mouse Facility
ESI, Experimental Surgery Unit
Technology Core Facilities
Confocal Microscopy
(Head: Prof. S. Yousefi)
Cytometry Laboratory
(Head: Dr. S. Müller)
Genomics
(Head: Prof. R. Jaggi)
Live Cell Imaging (LCI)
(Head: Dr. F. Blank)
Mass Spectrometry and Proteomics
Laboratory (Head: PD Dr. M. Heller)
Core Activities

1

M.E. Müller-Haus
Murtenstrasse 35

2

Murtenstrasse 50

3

Pathologie
Murtenstrasse 31

4

Pavillon 52
Freiburgstrasse 3

5

Kinderklinik
Freiburgstrasse 15

6

Sahli-Haus 1
Freiburgstrasse 14a

7

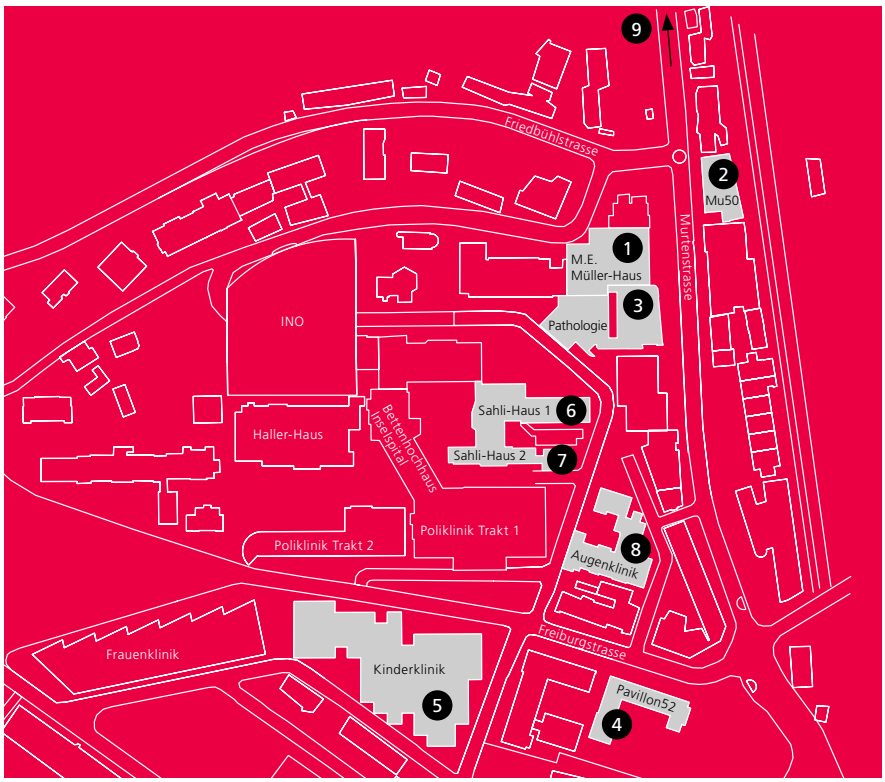
Sahli-Haus 2
Freiburgstrasse 14

8

Augenklinik
Freiburgstrasse 8

9

Tiefenau
Tiefenaustrasse 120c



Key People

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Prof. Dr. Chris Boesch
Pavillon 52

PD Dr. Manfred Heller
Kinderklinik

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

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

Prof. Dr. Robert Rieben
Murtenstrasse 50,
Augenklinik

Heads of Technology Core Facilities

Dr. Fabian Blank
Live Cell Imaging (LCI)

PD Dr. Manfred Heller
Mass Spectrometry and
Proteomics Laboratory

Prof. Dr. Rolf Jaggi
Genomics

Dr. Stefan Müller
Cytometry Laboratory

Prof. Dr. Shida Yousefi
Confocal Microscopy

Confocal Microscopy

www.pki.unibe.ch/content/confocal_microscopy

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

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

Achievements 2012

The service team of the Institute of Pharmacology trained more than 50 scientists from the University of Bern in confocal microscopy and imaging techniques. Training was specifically performed using ongoing research projects of the users. At least five original articles have been published in which the authors used our facility to produce state-of-the-art results. As in previous years, all the activities and services of the facility were coordinated with the Microscopy Imaging Center, University of Bern.

Performance Report 2012

Thirty-one different research groups from the DCR and/or Inselspital departments used the LSM 5 Exciter confocal microscope for a total of 1,373 hours. As in previous years, we organised a biannual two-day practical course for PhD and MD students, and technicians. These courses provided beginners with a basic knowledge of fluorescent staining techniques and subsequent confocal microscopy analysis, including imaging software. Overall, we trained more than 35 scientists. Twenty-four different laboratories received support and licences for Imaris software. Prof. Yousefi was responsible for updating and maintaining the floating licences, as well as providing technical support to users. In terms of personnel resources, Prof. Yousefi was the main person responsible for introducing the confocal microscope and the imaging analysis software (Imaris and Huygens) to new users. Two members of Prof. Hans-Uwe Simon's research group, Dr. Zhaoyue He and Ms. Evelyne Kozlowski, were additionally responsible for training.

Finances 2012

The Confocal Microscopy Core Facility collected CHF 10,525 in user fees. Disbursements included CHF 5,000 for consumables, CHF 1,500 for course expenses and CHF 16,994 for Imaris maintenance, plus CHF 4,320 for an upgrade to Imaris Suite. Many faculties of the University of Bern used the Imaris software. In addition, the DCR paid CHF 6,366 (maintenance flat fee), as well as CHF 28,036 (replacement of UV laser), CHF 1,471 (repair of 100X objective lens) and CHF 1,050 (replacement of lamp) in repairs for the LSM 510 Exciter confocal microscope.

Outlook 2013

In March 2012, the new Live Cell Imaging (LCI) Core Facility, headed by Dr. Fabian Blank, was opened at Murtenstrasse 50. Prof. Yousefi will continue to coordinate the Confocal Microscopy and Image Analysis Facility within the Institute of Pharmacology until March 2013, by which time the LCI Facility will be fully functional. Dr Blank will then also be in charge of the training courses.

Staff Members

Prof. Dr. Shida Yousefi, Head
Dr. Zhaoyue He, Postdoctoral Fellow
Evelyne Kozlowski, Laboratory Technician

Cytometry Laboratory

www.facslab.unibe.ch

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

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

Achievements 2012

By the end of the year, we were able to buy and install an automated, robotic 96-well/384-well sampling device—the HyperCyt-HyperView system. It is now being thoroughly tested. This system allows massively reduced sample volumes and high-throughput, walk-away measurements of extensive screening experiments at a fraction of the time and cost of manual sample acquisition. In addition, our SNF R'Equip application for the ImageStreamX imaging flow cytometer was successful. This instrument will be installed in early 2013. The availability of an imaging flow cytometer will allow our users to take their flow cytometry experiments a step further: in addition to the traditional FACS analyses with plots and histograms, fluorescent microscopic images are taken of each and every cell, allowing morphometry, signalling, (co-)localisation and many more aspects to be assessed in statistically powerful ways and out of complex mixtures of cells.

The server login system is now working. From the beginning of 2013, billing processing and statistical evaluations will be easier to handle and more reliable.

In 2012, we offered two FACS courses and organised a workshop and a seminar, held by company representatives, on topics of wide interest to our FACS users.

Performance Report

We had a very busy year with the state-of-the-art BD LSR II SORP cytometer being almost constantly booked during regular office hours, and often until very late. Altogether, measurements on our analysis instruments increased by 6% compared to 2011. However, sorting decreased by 10.5% compared to 2011, mainly due to an unusually quiet last quarter in 2012.

Finances

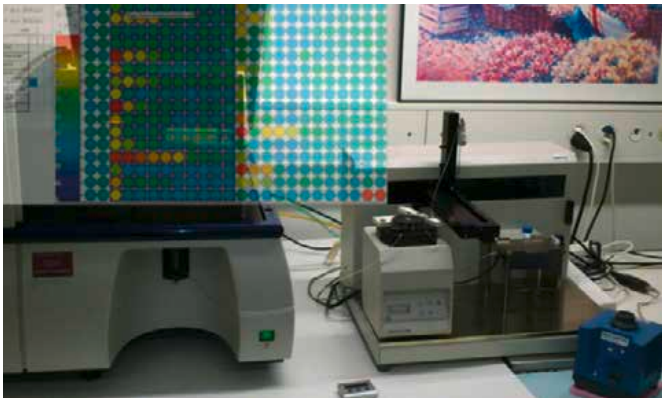
In contrast to 2011, we had to order important service work for our instruments and expenses were CHF 6,200 higher than the revenues. Since 2011 rather than 2012 was the exceptional year with regard to service and repair costs, we have implemented user fee adjustments starting from 2013.

Outlook 2013

- To increase capacity for state-of-the-art 5 lasers/up to 18 colour measurements, we are applying for financial support to upgrade the older BD LSR II cytometer to the "SORP"-level.
- The server login system has been running since 1 January 2013, allowing billing and statistics based on the log files.
- We plan to offer at least two FACS courses. Dates and programme will be posted on our webpage. Course participants from the Graduate School for Cellular and Biomedical Sciences will be entitled to 2 ECTS points.
- The ImageStreamX cytometer will be installed and thoroughly tested. Users will be trained to use the new equipment.

Staff Members

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



Genomics (Core Facility)

www.gcf.dkf.unibe.ch

Molecular Biology (Research Group)

www.molbiol.dkf.unibe.ch

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

Studies in cell biology, PhD (1982). Postdoc (1984-1986) and Group Leader (1986-1988) in Ludwig Institute for Cancer Research, Bern. Research in Institute of Clinical and Experimental Cancer Research, Bern (1988-1996), several research periods in Ireland with Prof. Finian Martin, at University College, Dublin (1989-1992). Habilitation (1990), Professor (1996) at University of Bern. Since 2010, Coordinator in DCR; since 2011, Head of Genomics Core Facility.

Achievements 2012

Steroid hormones are essential regulators of proliferation in oestrogen-dependent breast cancer. Oestrogen binds to the oestrogen receptor (ER) and the complex translocates into the nucleus. There it acts as a transcription factor stimulating or repressing specific genes, some of which regulate or stimulate cell proliferation. It has been known for decades that these tumour cells can be inhibited efficiently by anti-oestrogens like tamoxifen (Tam). Another drug, letrozole (Let), has a similar effect but acts through different mechanisms. Despite extensive research, many aspects of the underlying processes are still not understood. While a majority of ER-positive cancers respond similarly to both drugs, some tumours can only be inhibited by either Tam or Let, and another group are resistant to both drugs or become resistant during treatment. Many patients who develop resistance have a poor prognosis, dying within five years. Moreover, most ER-positive cancers express the ER in only a fraction of tumour cells, while the remaining cells have no ER and cannot respond directly to anti-oestrogens. The mechanism by which these tumours are inhibited is unknown but anti-ER drugs have a significant effect in tumours that contain only a few percent of ER-positive cells.

Our group worked with material from a global trial of more than 8,000 ER-positive breast cancer patients, run by the International Breast Cancer Study Group. They showed that Let for five years or Let for two years followed by Tam for 3 years was superior to any treatment starting with Tam. Although the difference was only about 3%, it was statistically significant. We obtained material from about 300 patients representing two groups (Tam or Let for five years). About half of each group had a recurrence within five years. Gene expression was measured using a NanoString nCounter. We are searching for genes or groups of genes (profiles) whose expression correlates with disease-free survival.

Performance Report

Genomics

In May 2012, we obtained an Ion Torrent PGM instrument (financed by the Faculty of Medicine). After a short introduction, we could run our own experiments using both 314 or 316 chips. Overall, we were very happy with the performance of the machine. We tested DNA from cancer cell lines and partially fragmented DNA isolated from FFPE material for the presence of mutations and deletions using a commercially available cancer panel. Some of the results were directly compared to the results of standard analyses by pyrosequencing. In collaboration with Erik Vassella, we found very good agreements between the two techniques. As a consequence, the Institute of Pathology plans to use the Ion Torrent again in 2013. In December 2012, an independent study from the Vetsuisse Faculty was performed with primers designed in-house and several genomic DNAs derived from horse blood. These results were evaluated by the Bioinformatics Unit and were very valuable. In addition, the Molecular Biology technician made several hundred libraries and started many runs for the Illumina HiSeq 2000 sequencer of the University of Bern Next Generation Sequencing (NGS) Platform.

Finances

Genomics

The Genomics Core Facility had a working credit of CHF 15,000 from the DCR for 2012. Part of the money was used to set up the Ion Torrent instrument and perform initial test runs. We provide reagents and chips for single libraries and single chips so that research groups do not have to build up their own stocks. In addition, we bought a server that can be used for data analysis. It was integrated into the existing infrastructure in the server room of the Bioinformatics Unit. Currently, it is being used for data analysis using the CLC Genomics workbench (license provided by the Bioinformatics Unit).

Outlook 2013

Genomics

In December 2012, the Inselspital decided to support clinical research groups who plan NGS studies. A second laboratory technician could be hired and she will share the work related to high throughput sequencing on the Illumina instrument and the low throughput Ion Torrent instrument. The two technicians will be responsible for the maintenance of the two systems and will provide support and service to clinical groups who want to use the equipment. In addition, we will install new protocols, e.g., for long reads (400 bp) and we will develop novel applications on the Ion Torrent.

Molecular Biology

We will extend our studies on gene expression with ER-positive and ER-negative cells by isolating single cells or small clusters of cells (e.g., by FACS) and analysing gene expression in their RNA. The procedure is currently being tested with cells from cell lines, the RNA is reverse transcribed and amplified by PCR. The PCR products will again be analysed using nCounter. The protocol will then be applied to cells derived from breast cancers stored in the Biobank Bern. The procedure will allow us to characterise ER-positive and ER-negative cells in breast cancer. These and similar techniques may also be of interest for other studies on gene expression from single cells or small groups of cells that are surrounded by other cells.

Staff Members

Prof. Dr. Rolf Jaggi, Group Leader
Dr. Stefan Wyder, Bioinformatician (until Oct.)
Muriel Fragnière, Laboratory Technician
Véronique Vocat, PhD Student

Collaborators

Molecular Biology

Aebi S, Lucerne Cantonal Hospital, Switzerland
Bubendorf L, University of Basel, Switzerland
Cathomas R, Graubünden Cantonal Hospital, Switzerland
Gautschi O, Lucerne Cantonal Hospital, Switzerland
Kammler R, International Breast Cancer Study Group, Switzerland
Kristiansen G, University of Bonn, Germany
Krupp G, AmpTech, Germany
Pestalozzi B, Zurich, Switzerland
Perren A, University of Bern, Switzerland
Regan M, Dana-Farber Cancer Institute, USA
Rothschild S, Basel Cantonal Hospital, Switzerland
Vassella E, University of Bern, Switzerland
Viale G, European Institute of Oncology, Italy
Zlobec I, University of Bern, Switzerland

Grants

Amounts allocated for 2012:

Molecular Biology

- Swiss Cancer League: Molecular profiling from archival human breast cancer samples (R. Jaggi) CHF 43,500
- Swiss Cancer League: Identification of a clinically applicable prognostic RNA signature of prostate cancer (R. Jaggi, G. Kristiansen) CHF 137,700
- W.+H. Berger-Janser Foundation: Characterization of ER-negative cancer cells in ER-positive breast cancer (R. Jaggi) CHF 6,800
- Foundation biobank-suisse: Vergleich von Gewebeproben aus verschiedenen Biobanken der Schweiz: Analyse der Genexpression mit RNA aus gefrorenen und aus fixierten Mammakarzinom-Gewebeproben (R. Jaggi, D. Simeon-Dubach) CHF 12,800

Teaching Activities

- Matthias Schindler: MSc
- Véronique Vocat: PhD Student
- 1st-year medical students: Problem Based Learning
- Omics: Lecture on disease profiling
- Selected topics in molecular pathology: Lecture on molecular processes of disease
- Tumour biology: Lecture on genomics

Publications

Molecular Biology

MicroRNA-29b is involved in the Src-ID1 signaling pathway and is dysregulated in human lung adenocarcinoma. Rothschild, SI; Tschan, MP; Federzoni, EA; Jaggi, R; Fey, MF; Gugger, M; Gautschi, O (2012) in: Oncogene, 31(38), p. 4221-4232.

MicroRNA-381 represses ID1 and is deregulated in lung adenocarcinoma. Rothschild, SI; Tschan, MP; Jaggi, R; Fey, MF; Gugger, M; Gautschi, O (2012) in: J Thorac Oncol, 7(7), p. 1069-1077.

Efficacy of Cetuximab in Metastatic Castration-Resistant Prostate Cancer Might Depend on EGFR and PTEN Expression: Results from a Phase II Trial (SAKK 08/07). Cathomas, R; Rothermundt, C; Klingbiel, D; Bubendorf, L; Jaggi, R; Betticher, DC; Brauchli, P; Cotting, D; Droege, C; Winterhalder, R; Siciliano, D; Berthold, DR; Pless, M; Schiess, R; von, MR; Gillessen, S (2012) in: Clin Cancer Res, 18(21), p. 6049-6057.

Mass Spectrometry and Proteomics Laboratory (Core Facility)

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

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

Achievements 2012

As in the past year, our single instrument LC-MS platform was continuously analysing protein samples, with a few exceptions (breakdowns, maintenance and a lull at the end of summer/beginning of autumn). The steady increase of analytical runs forced us to install a new data interpretation server (6 quad core, 2.7 MHz, 50 GB RAM). We could secure a total of CHF 460,000 from the Faculties of Medicine, Science and Vetsuisse in matching funds for the SNF R'Equip grant. We tested mass spectrometers from two vendors and purchased two new LC-MS systems following WTO guidelines.

We were successful in the spring round of the CRUS SCIEX-NMS^{ch} programme, which fosters training placements in Switzerland for young scientists from new EU states. Marian Petrovic has joined us for one year, after which he will finish his PhD at the Pavol Jozef Šafárik University (SK). He has already run a series of experiments with the goal to improve the algorithm for the theoretical prediction of the isoelectric point of polypeptides (in collaboration with the Proteome Informatics Group at the Swiss Institute of Bioinformatics, Geneva) and define characteristic traits in the proteome of primary endothelial cells of different origins.

Niurka Meneses developed new strategies to characterise the interactome of plasma membrane proteins. Our target was transient receptor potential cation channel subfamily M member 4 protein (TRPM4). Formaldehyde and photoactivable amino acids were employed to cross-link TRPM4 with its nearest interaction partners. The cross-linked complexes were separated by SDS-PAGE and proteins identified by LC-MS/MS. Necessitated by non-specific background, we are developing bioinformatics approaches to distinguish true from false positive interactors.

We tested cell culture conditions that enable the in-vivo labelling of primary endothelial cells with stable-isotope marked amino acids (SILAC). We intend to perform quantitative proteome studies of these delicate cells using this method. Furthermore, we have improved our protocol for microparticle isolation and proteomic analysis.

Performance Report

Mass Spectrometry and Proteomics

The lab had to be moved to a temporary facility within the Children's Hospital in April. We took the chance to do some preventive maintenance on all instruments. This caused some problems on one of the HPLCs that took several weeks to fix. Furthermore, a malfunction in a power supply board on the mass spectrometer caused unexpected shutdowns of the system. Despite the down times, we will break last year's sample throughput record anew (666 in 2011, >>1000 in 2012).

Finances

Mass Spectrometry and Proteomics
In April, we changed our billing structure from a charge based on type of analysis to one based on actual machine time and other resources used. The Faculty of Medicine Resources Committee granted CHF 8,000 to cover some of the running costs. The Core Facility budget covered seven months' salary for Sophie Braga-Lagache. Thanks to the accumulation of funds in the last years and this year's revenue, we were able to roughly break even.

Outlook 2013

The year 2013 will be a milestone for our facility. In calendar week 7, we can move back to the refurbished laboratories, which can hold up to four LC-MS instruments, featuring uninterrupted power supply and air conditioning. Two new LC-MS instruments will be installed, giving us more freedom in working on more complicated proteomics projects and developing new methods, such as an in-depth discovery proteome analysis within 24 hours, targeted quantification for clinical samples, and lipidomics. We will receive professional bioinformatics support thanks to new bioinformatics positions funded by the Faculty of Science and Inselspital funds. This support is essential for our ambitious goals.

Staff Members

PD Dr. Manfred Heller, Head
Dr. Niurka Meneses Moreno, Postdoctoral Fellow (Research Group)
Sophie Braga-Lagache, Laboratory Technician (Core Facility)
Natasha Buchs Tetkovic, Laboratory Technician (Core Facility & Research Group)
Marian Petrovic, visiting PhD Student (SCIEX program, Research Group & Core Facility)

Collaborators

Müller M, Swiss Institute of Bioinformatics, Switzerland
Wittwer M, Labor Spiez, Switzerland

Grants

Amounts allocated for 2012:
Protein and Cell Biology
- SNF: NCCR TransCure sub-project: Physiology, pharmacology and pathophysiology of the calcium-activated non-selective cation TRPM4 channel (M. Hediger, H. Abriel, M. Heller) CHF 111,300
- Sciex-NMS^{ch}: Quantification of new protein synthesis by endothelial cells under shear stress using SILAC method (M. Petrovic, M. Heller) CHF 15,500

Teaching Activities

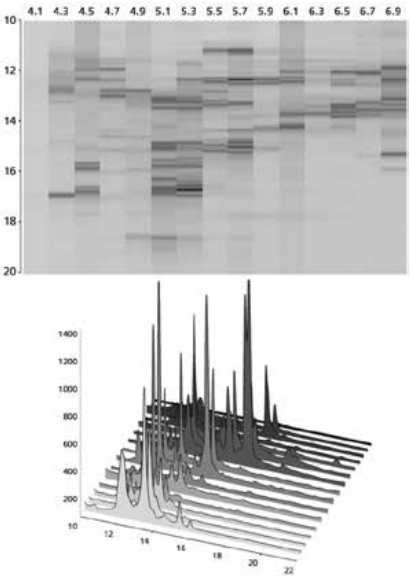
- 1st-year medical students: Problem Based Learning, Tutor block 1
- Proteomics lectures: Tumour biology (Faculty of Medicine, Biomedical Engineering), Omics (Faculty of Science)

Publications

Cause or Effect of Arteriogenesis: Compositional Alterations of Microparticles from CAD Patients Undergoing External Counterpulsation Therapy. Al, KA; Traupe, T; Stutz, M; Buchs, N; Heller, M (2012) in: PLoS One, 7(10), p. e46822.

Eukaryotic translation elongation factor 1A (eEF1A) domain I from S. cerevisiae is required but not sufficient for inter-species complementation. Eltschinger, S; Greganova, E; Heller, M; Butikofer, P; Altmann, M (2012) in: PLoS One, 7(7), p. e42338.

Proteome remodelling during development from blood to insect-form Trypanosoma brucei quantified by SILAC and mass spectrometry. Gunasekera, K; Wuthrich, D; Braga-Lagache, S; Heller, M; Ochsenreiter, T (2012) in: BMC Genomics, 13(1), p. 556.



Bone Biology & Orthopaedic Research

www.bonebiology.dkf.unibe.ch

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

Research Highlights 2012 / Outlook 2013

Bone Biology & Orthopaedic Research Group

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

- During Prof. Hofstetter's sabbatical at the Matsumoto Dental University, Japan, a new osteoclast resorption assay was developed, which will be modified to be used as a medium-throughput assay.
- The transporter repertoire of osteoblast and osteoclast lineage cells was analysed using low-density arrays. Functional tests will be performed to assess the roles of specific molecular transporters in bone metabolism. Glutamate was found to be an osteogenic compound. Inhibition of glutamate transporters in osteoblasts caused an increase in extracellular glutamate and a stimulation of osteoblast differentiation (W. Xie).
- The bone phenotypes of TRPV6, NCX1 and MK2 knockout mice were characterised on cell and tissue levels.
- IL17 was found to inhibit osteoclast development by inducing the release of GM-CSF by osteoblast lineage cells. Since the effect was dependent on the presence of monocyte/macrophage lineage cells, the respective mechanisms need to be further investigated (D. Balani).
- Antagonists of osteogenic signalling pathways were found to be upregulated in delayed fracture healing in mice. This suggests that an excess of inhibitors rather than a lack of growth factors is responsible for the delay in healing.
- A genetically engineered inhibitor of BMP antagonists was found to increase the efficacy of BMP2 in vivo. A critical size defect model in rats was used to investigate bone healing and biomaterial turnover.
- The first experiments were performed using a bioreactor that allows the application of complex mechanical loading protocols on osteochondral grafts. Dedifferentiation and redifferentiation of chondrocyte lineage cells of bovine origin were investigated in vitro (R. Egli, A. Tekari).

Osteo-Articular Research Group

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

- The regulated expression of S100A1 and S100B proteins in primary human articular chondrocytes in culture was demonstrated by combining FACS, Western blot, cellular ELISA and qRT-PCR.
- The precise measurements of cartilage thickness within the intact joint (normal versus arthritic) were performed by combining contrasting agents with microCT. A strong correlation with histology was shown in rat, rabbit and goat animal models.
- A study of growth factor release between leukocyte- and platelet-rich fibrin (L-PRF), plasma and blood clot showed the superiority of L-PRF for potential use in clinical treatments of tears in the red-white zone of the meniscus (M. Schär).
- Testing collagen-derived sponges for neochondrogenesis was performed with human chondrocytes in vitro (D. Herz).

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
Deepak Balani, PhD Student (until May)
John Choy, PhD Student
Adel Tekari, PhD Student
Wenjie Xie, PhD Student

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

Clinicians with projects in the group
Dr. Frank Klenke, Consultant, Department of Orthopaedic Surgery, Inselspital

Collaborators

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

Grants 2012

Amounts allocated for 2012:

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

Osteo-Articular Research
- AO Foundation: Start-up grant S-11-96N – S100 as a cellular marker for chondrogenicity of human aritcular chondrocytes (D. Nesic, M. Zumstein) CHF 60,000
- Geistlich Pharma: Testing collagen derived matrices in vitro (D. Nesic) CHF 50,000
- KTI 9853.1 PFLS-LS: Comprehensive morphological characterization of arthritis in animal models by microCT – innovative biomarkers for assessment of arthritic cartilage and bone (D. Nesic, R. Mueller, B. Koller) CHF 45,828
- RMS and Biomet International: The effect of Leukocyte- and Platelet-Rich Fibrin, Leukocyte- and Platelet-Rich Plasma and blood clot on the migration of fibroblast and endothelial cells: an in vitro study (M. Zumstein, M. Schär, D. Nesic) CHF 24,600

Teaching Activities

- Masters course in Biomedical Engineering: Tissue Engineering (Nesic)
- Masters course in Biomedical Engineering: Osteology (Hofstetter)
- 3rd-year dentistry students: Pathophysiology – Skeleton (Hofstetter)
- 1st-year medical students: Molecular biology practical courses (Hofstetter)
- 2nd-year medical students: Kidney block – calcium and phosphate metabolism (Hofstetter)

Publications

L51P – a BMP2 variant with osteoinductive activity via inhibition of Noggin. Albers, CE et al. (2012) in: Bone, 51(3), p. 401-406.

IL-17A stimulates GM-CSF release in the presence of 1,25(OH)(2) D(3) by osteoblasts and inhibits osteoclast development in vitro. Balani, D et al. (2012) in: Arthritis Rheum.

Mitogen-activated protein kinase 2 (MK2) regulates physiological and pathological bone turnover. Braun, T et al. (2012) in: J Bone Miner Res.

Comparison of cartilage histopathology assessment systems on human knee joints at all stages of osteoarthritis development. Pauli, C et al. (2012) in: Osteoarthritis Cartilage, 20(6), p. 476-485.

Blockade of the hedgehog pathway inhibits osteophyte formation in arthritis. Ruiz-Heiland, G et al. (2012) in: Ann Rheum Dis, 71(3), p. 400-407.

Inhibition of endogenous antagonists with an engineered BMP-2 variant increases BMP-2 efficacy in rat femoral defect healing. Sebald, HJ et al. (2012) in: Acta Biomater, 8(10), p. 3816-3820.

Modulation of human osteoblasts by metal surface chemistry. Hofstetter, W et al. (2012) in J Biomed Mat Res (in press).

Expression of antagonists of WNT and BMP signaling after non-rigid fixation of osteotomies. Montjovent; MO et al. (2012) in Bone (in press).

Cardiovascular Research

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

Research Highlights 2012 / Outlook 2013

Vascular endothelial cells and their role in ischemia/reperfusion (I/R) injury as well as in transplant rejection were the focus of our research in 2012.

We continued a project on the use of plasma products to attenuate I/R injury in a rat hind limb ischemia model. For our experiments, we used C1-inhibitor (C1-INH), an enzyme isolated from human plasma known to block the complement-, coagulation- and kallikrein/kinin-pathways. The rats were treated systemically by C1-INH shortly before induction of ischemia in a hind limb. This experimental setup was chosen in order to mimic the clinical situation of elective surgery on extremities. We observed a significant reduction of the tissue oedema that occurs after reperfusion of the hind limb, by the use of C1-INH. This finding may have a rather immediate impact on clinical practice because C1-INH is already registered for clinical use and there is as yet no other treatment available to prevent I/R injury in skeletal muscle. Currently, we are analysing tissue and plasma samples from these experiments in order to describe the mechanism by which C1-INH prevents I/R injury in this model. All of the cascade systems seem indeed to be involved but the sequence of events by which the innate immune system causes the inflammatory reaction leading to reperfusion injury remains to be elucidated in detail.

Similar to I/R injury, vascular endothelial cells are also activated in models of xenotransplantation. We use both in vitro and ex vivo perfusion models of pig-to-human xenotransplantation in order to study mechanisms of endothelial cell activation/vascular rejection and therapeutic strategies to prevent them. An in vitro model in which whole, non-anticoagulated human blood is incubated with porcine endothelial cells grown on microspheres was used to study the effect of human transgenes on xenorejection mechanisms. As a simple readout, time to coagulation can be used in this system, which is dependent on activation of the porcine endothelial cells and thus loss of their natural anticoagulation properties. We found that human thrombomodulin, a membrane protein regulating the coagulation cascade, significantly prolonged time to coagulation in our model, suggesting that this gene should indeed be included in multi-transgenic pigs to be bred as organ donors for human patients. In addition, the role of the lectin pathway of complement was demonstrated for the first time in a pig-to-human xenotransplantation model. In 2013, ex vivo perfusions of pig legs with whole human blood will be performed, using donor pigs expressing different human transgenes. These experiments are being carried out in collaboration with the Department of Plastic and Hand Surgery, Inselspital and the Ludwig-Maximilian University of Munich (DE).

Group Members

Prof. Dr. Robert Rieben, Group Leader
Dr. Yara Banz, Research Associate (Pathology)
Dr. Jana Ortmann, Research Associate (Tiefenau Hospital)
Dr. Pranitha Kamat, Postdoctoral Fellow (until Nov.)
Julie Denoyelle, Laboratory Technician
Anjan Bongoni, PhD Student
Claudia Dührkop, PhD Student
Shengye Zhang, PhD Student
Uyen Schmutz, Web Designer, BNF Program (Sep.-Nov.)
Franziska Wiedmer, Webmaster, BNF Program (since Oct.)

Collaborators

Bovin N, Institute of Bioorganic Chemistry, Russia
Constantinescu MA, Inselspital, Switzerland
Gorantla V, University of Pittsburgh Medical Center, USA
Hani R, EMPA Dübendorf, Switzerland
Heier J, EMPA Dübendorf, Switzerland
Jenni HJ, Inselspital, Switzerland
Khattab A, Inselspital, Switzerland
Klymiuk N, University of Munich, Germany
Korchagina E, Institute of Bioorganic Chemistry, Russia
Ruder T, University of Zurich, Switzerland
Seebach J, Geneva University Hospital, Switzerland
Spirig R, CSL Behring AG, Switzerland
Stringer S, University of Manchester, UK
Vemula P, Massachusetts Institute of Technology, USA
Vögelin E, Inselspital, Switzerland
Wolf E, University of Munich, Germany

Grants

Amounts allocated for 2012:

- SNF: Endothelial cell protection – The role of heparan sulfate proteoglycans and complement in pathophysiology and prevention of ischemia / reperfusion injury (R. Rieben) CHF 130,000
- SNF: Composite tissue preservation by extracorporeal blood perfusion and vascular cytoprotection to extend the time limit to replantation or transplantation (E. Vögelin, M.A. Constantinescu, R. Rieben) CHF 75,000
- CSL Behring: Effects and mechanisms of anti-inflammatory treatment by plasma products to attenuate ischemia/reperfusion injury (R. Rieben) CHF 85,000
- American Society for the Surgery of the Hand: A Novel Therapeutic Method Targeting Local Immunosuppression in Composite Tissue Allotransplantation (E. Vögelin, R. Rieben, T. Gajanayake) USD 20,000

Teaching Activities

- Elective module in the Master of Biomedical Sciences curriculum: Induction of transplantation tolerance in composite tissue allotransplantation
- Elective course 5034 for medical students: Ihr Partner im Labor – Forschung auf den Gebieten Organtransplantation, Chirurgie und Herzinfarkt
- 3rd-year medical students: Problem Based Learning tutorial – Störungen der Auseinandersetzung zwischen körpereigen und fremd
- Graduate School for Cellular and Biomedical Sciences PhD students: Immunology tutorial
- Four high-school students: Patenschaften für Maturaarbeiten (2-week lab stay each)

Publications

Evaluation of multimeric tyrosine-O-sulfate as a cytoprotectant in an in vivo model of acute myocardial infarction in pigs. Banz, Y; Hess, OM; Meier, P; Korchagina, EY; Gordeeva, EA; Robson, SC; Gajanayake, T; Csizmadia, E; Mettler, D; Haeberli, A; Bovin, NV; Rieben, R (2012) in: Cardiology, 121(1), p. 59-70.

Assessment of endothelium and inflammatory response at the onset of reperfusion injury in hand surgery. Kamat, P; Juon, B; Jossen, B; Gajanayake, T; Rieben, R; Vogelin, E (2012) in: J Inflamm (Lond), 9(1), p. 18.

Ischemia/reperfusion injury of porcine limbs after extracorporeal perfusion. Muller, S; Constantinescu, MA; Kiermeir, DM; Gajanayake, T; Bongoni, AK; Vollbach, FH; Meoli, M; Plock, J; Jenni, H; Banic, A; Rieben, R; Vogelin, E (2012) in: J Surg Res.

Pancuronium dose refinement in experimental pigs used in cardiovascular research. Veres-Nyéki, O; Rieben, R; Spadavecchia, C; Bergadano, A (2012) in: Vet Anaesth Analg, e-pub ahead of print, doi:10.1111/j.1467-2995.2012.00732.x.

Ion Channels and Channelopathies

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

Training both as a biologist at ETH Zurich and physician at University of Lausanne. After two years at Lausanne University Hospital, post-doc at Columbia University (US). In 2002, Swiss National Science Foundation Professor and start of independent research studying the role of ion channels in human disorders. Since 2009, Professor of Pathophysiology, University of Bern and DCR Director. Since 2012 member of the research council of the SNF.

Research Highlights 2012 / Outlook 2013

Our group's research focuses on the role of ion channels in human diseases, so-called channelopathies. In the past years, we have been mainly investigating voltage-gated channels involved in the generation of the cardiac action potential and their roles in cardiac arrhythmias.

In 2012, several members of the group studied the cardiac sodium channel Nav1.5. Diana Shy and Ludovic Gillet investigated a new genetically modified mouse model in which the Nav1.5 channel is truncated and, as a consequence, cannot interact with important regulatory proteins. A manuscript is ready for submission. Valentin Sottas studied several genetic variants of Nav1.5 found in patients with cardiac arrhythmias. This study was carried out within the frame of the SNF-funded SCOPES collaboration with Russian and Ukrainian scientists.

In parallel, we continued our work on another cardiac channel called TRPM4. Ninda Syam, Valentin Sottas and Yassine Amarouch performed biochemical and functional investigations of genetic variants of the TRPM4 gene found in patients with cardiac arrhythmias. A first article on patients with Brugada syndrome was accepted in 2012, and we will submit another one on patients with cardiac conduction defect during 2013.

In these different projects, both Jean-Sébastien Rougier, Senior Teaching and Research Assistant since July 2012, and Maria Essers, Laboratory Manager, have played an essential role in coaching the younger scientists of the group.

In collaboration with Isabelle Decosterd's group (Pain Center, University Hospital of Lausanne), we also demonstrated the role of the drug rufinamide in blocking the voltage-gated sodium channel Nav1.7 and its effect in a mouse model of neuropathic pain. Using the same model but in rats, we could also show that the ubiquitin ligase Nedd4-2, which is known to regulate sodium channels, is decreased in dorsal root ganglion cells.

On another note, we had the great fortune to organise the general assembly of the EUTrigTreat consortium, of which we are part. This meeting entitled "Identification and therapeutic targeting of common arrhythmia trigger mechanisms" was organised in Beatenberg (CH) in June 2012.

As for the main perspectives for 2013, we will continue our investigations on the molecular determinants underlying the distribution of the different pools of Nav1.5 in cardiac cells, and will also pursue our research on the roles of TRPM4 in physiology and disease. In addition, in the framework of the NCCR TransCure, and in collaboration with the groups of Jean-Louis Reymond and Matthias Hediger (University of Bern), we will focus on screening pharmacological compounds targeting TRPM4. This study will be performed by Yassine Amarouch, who was awarded a TransCure International Fellowship from January 2013.

Group Members

Prof. Dr. Hugues Abriel, Group Leader
Dr. M. Yassine Amarouch, Postdoctoral Fellow
Dr. Ludovic Gillet, Postdoctoral Fellow
Dr. Jean-Sébastien Rougier, Research Assistant, Senior Teaching Assistant
Maria Essers, Laboratory Technician
Louis Amport, Secretary (since Aug.)
Verena Frazao, Secretary
Cédric Laedermann, PhD Student
Markus Mühlemann, PhD Student (since Aug.)
Diana A. Shy, PhD Student
Valentin Sottas, PhD Student
Ninda Syam, PhD Student

Collaborators

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

Grants

Amounts allocated for 2012:

- SNF: In vivo relevance of the PY and PDZ-domain binding motifs of the cardiac sodium channel Nav1.5 (H. Abriel) CHF 230,000
- SNF: Roles of ion channel-interacting proteins in cardiac channelopathies (H. Abriel, E.V. Zaklyazminskaya, O.S. Sychov) CHF 27,500
- SNF: NCCR TransCure subproject – Physiology, pharmacology and pathophysiology of the calcium-activated non-selective cation TRPM4 channel (M. Hediger, H. Abriel, M. Heller) CHF 185,200
- SNF: Force-controlled patch clamp (pc-FluidFM) (T. Zambelli, H. Abriel) CHF 111,400
- European Commission: EUTrigTreat – Identification and therapeutic targeting of common arrhythmia trigger mechanisms (S. Lehnart, H. Abriel) CHF 114,000

Teaching Activities

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

Publications

Cardiac sodium channel Na(v)1.5 mechanosensitivity is inhibited by ranolazine. Abriel, H (2012) in: Circulation, 125(22), p. 2681-2683.

TRPM4 channels in the cardiovascular system: physiology, pathophysiology, and pharmacology. Abriel, H; Syam, N; Sottas, V; Amarouch, MY; Rougier, JS (2012) in: Biochem Pharmacol, 84(7), p. 873-881.

A modern approach to classify missense mutations in cardiac channelopathy genes. Abriel, H and Zaklyazminskaya, EV (2012) in: Circ Cardiovasc Genet, 5(5), p. 487-489.

Dynamic of ion channel expression at the plasma membrane of cardiomyocytes. Balse, E; Steele, DF; Abriel, H; Coulombe, A; Fedida, D; Hatem, SN (2012) in: Physiol Rev, 92(3), p. 1317-1358.

Neuronal expression of the ubiquitin ligase Nedd4-2 in rat dorsal root ganglia: Modulation in the spared nerve injury model of neuropathic pain. Cachemaille, M; Laedermann, CJ; Pertin, M; Abriel, H; Gosselin, RD; Decosterd, I (2012) in: Neuroscience, 227, p. 370-380.

Mapping genetic variants associated with beta-adrenergic responses in inbred mice. Hersch, M; Peter, B; Kang, HM; Schupfer, F; Abriel, H; Pedrazzini, T; Eskin, E; Beckmann, JS; Bergmann, S; Maurer, F (2012) in: PLoS One, 7(7), p. e41032.

Deubiquitylating enzyme USP2 counteracts Nedd4-2-mediated downregulation of KCNQ1 potassium channels. Krzystanek, K; Rasmussen, HB; Grunnet, M; Staub, O; Olesen, SP; Abriel, H; Jespersen, T (2012) in: Heart Rhythm, 9(3), p. 440-448.

Role of "non-cardiac" voltage-gated sodium channels in cardiac cells. Rougier, JS and Abriel, H (2012) in: J Mol Cell Cardiol, 53(5), p. 589-590.

Unexpected dominance: Brugada syndrome SCN5A variants exert negative dominance via alpha-subunit interaction. Rougier, JS and Abriel, H (2012) in: Cardiovasc Res, 96(1), p. 1-3.

Cardiac sodium channel Na(V)1.5 distribution in myocytes via interacting proteins: The multiple pool model. Shy, D; Gillet, L; Abriel, H (2012) in: Biochim Biophys Acta.

Rufinamide Attenuates Mechanical Allodynia in a Model of Neuropathic Pain in the Mouse and Stabilizes Voltage-gated Sodium Channel Inactivated State. Suter, MR; Kirschmann, G; Laedermann, CJ; Abriel, H; Decosterd, I (2012) in: Anesthesiology.

Prevalence of Significant Genetic Variants in Congenital Long QT Syndrome is Largely Underestimated. Zaklyazminskaya, EV and Abriel, H (2012) in: Front Pharmacol, 3, p. 72.

Mammary Gland Biology and Carcinogenesis

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

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

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

Research Highlights 2012 / Outlook 2013

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

This transgenic model serves as a tool to investigate the role of EphB4/ephrin-B2 signalling in the control of the mammary stem cell niche. We have shown that over-expression of the native ephrin-B2 gene leads to an augmentation of the luminal and bi-potent precursor cell fractions. Overexpression of EphB4 resulted in a comparable phenotype. In contrast, mammary glands of truncated ephrin-B2 transgenic mice contained significantly more stem cells and alveolar ER-positive progenitor cells. Thus, ephrin-B2-derived signalling is involved in the control of the stem cell niche and in the regulation of cell fate decisions.

We intend to characterise signal transduction pathways involved in the ephrin-B2-induced phenotypes by microarray analyses on RNA from different transgenic mammary epithelial subpopulations. In these analyses, we will concentrate on the expression of genes involved in either the TGF-beta or the wnt signalling pathway, since preliminary results have indicated that these pathways might be the primary targets of the attenuated ephrin-B2 expression.

In addition, we have joined a collaborative project with the Department of Gynaecology and Obstetrics, Inselspital and the Institute of Pathology, University of Bern aiming at the comparative analysis of the epithelial cell hierarchy in distinct groups of human breast cancers.

Group Members

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

Collaborators

Djonov V, University of Bern, Switzerland
Günthert A, Inselspital, Switzerland
Stute P, University of Bern, Switzerland
Tapia C, University of Bern, Switzerland

Grants

Amounts allocated for 2012:

- SNF: The role of EphB4 and ephrin-B2 in the control of the mammary gland stem/progenitor cell population (A.-C. Andres) CHF 64,000
- Swiss Cancer League: The molecular mechanisms provoking the ephrin-B2 induced deregulation of the mammary stem cell niche and leading to metastatic tumour growth. (A.-C. Andres) CHF 100,000
- Schweizerische Stiftung für Klinisch-Experimentelle Tumorforschung: Transgenic mouse models to study the molecular mechanisms leading to the invasive phenotype of mammary tumors (A.-C. Andres) CHF 40,000

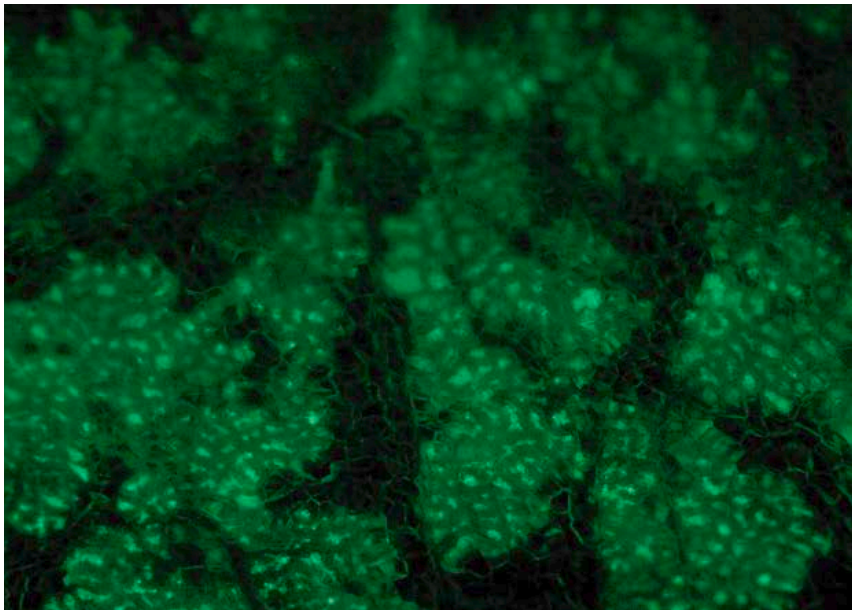
Teaching Activities

- Member, Graduate School Commission Biological Systems
- Member, Commission for the Master Studies Curriculum in Biomedical Sciences
- Bachelor and Master studies in biomedical sciences: Organiser and teacher, Tumour biology programme
- 1st-year medical students: Organiser and teacher, Developmental biology programme; Transgenic seminar: Lecture on cell death of multicellular organisms
- 1st-year veterinary medicine students: Lecture on transgenic animals
- Graduate School: Molecular biological methods in clinical diagnosis practical course
- Master in Bioengineering: Molecular biology practical course
- 1st-year medical students elective module: Genetic mutations – cyto- and molecular genetics

Publications

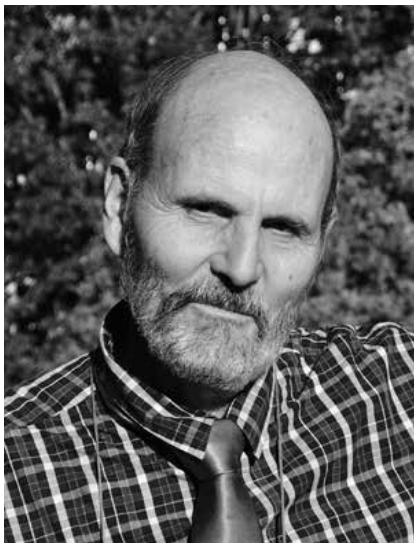
Deregulated ephrin-B2 signaling in mammary epithelial cells alters the stem cell compartment and interferes with the epithelial differentiation pathway. Kaenel, P; Antonijevic, M; Richter, S; Kuchler, S; Sutter, N; Wotzkow, C; Strange, R; Andres, AC (2012) in: Int J Oncol, 40(2), p. 357-369.

The multifaceted roles of Eph/ephrin signaling in breast cancer. Kaenel, P; Mosimann, M; Andres, AC (2012) in: Cell Adh Migr, 6(2), p. 138-147.



Phytopharmacology, Bioanalytics and Pharmacokinetics

www.phytopharm.dkf.unibe.ch



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

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

Research Highlights 2012 / Outlook 2013

Highlights of our research include:

- All the constituents of a *Bryophyllum pinnatum* leaf extract, its press juice used to prevent premature delivery, could be identified. Flavonoids were shown to be the main active compounds. Using in vitro and clinical studies, we could also demonstrate the inhibiting effects of the leaf press juice on the overactive bladder. A pilot study on children with Attention Deficit Hyperactivity Disorder has been started, showing positive preliminary effects.

- A study of the plasma of patients with alcoholic liver fibrosis or hepatitis C vs. healthy volunteers showed increased anandamide levels. This confirms the impact of liver diseases on the endocannabinoid system.

- In vitro validation studies with vaporiser devices showed that non-pyrolytic inhalation is an efficient and significantly less harmful application mode for cannabinoids.

In 2013, we will continue the endocannabinoid profiling on plasma samples collected from patients suffering from non-alcoholic fatty liver disease.

Group Members

Prof. Dr. Rudolf Brenneisen, Group Leader
Dr. Christian Lanz, Laboratory Supervisor, Research Assistant
Karin Fürer, PhD Student
Dr. Johan Mattsson, Postdoctoral Fellow, BNF Program (Mar-Sep)

Collaborators

Doblin R, Multidisciplinary Association of Psychedelic Studies, USA
Dufour J-F, Inselspital, Switzerland
Freeman D, University of Oxford, UK
Gasser P, Solothurn, Switzerland
Hamburger M, University of Basel, Switzerland
Morrison P, King's College London, UK
Schnelle M, Weleda AG, Switzerland
Skendaj R, University Hospital Basel, Switzerland
Stickel F, Inselspital, Switzerland
Von Mandach U, University Hospital Zurich, Switzerland
Wüest A, Paracelsus Hospital Richterswil, Switzerland

Grants

Amounts allocated for 2012:

- Department of Visceral Surgery and Medicine, Hepatology Inselspital, Prof. J.-F. Dufour (R. Brenneisen) CHF 30,000
- Weleda AG Arlesheim: Clinical efficacy, pharmacology and analytics of Bryophyllum (U. von Mandach) CHF 50,000
- Additional funding: Neuropharmacology of iv THC (D. Freeman, P. Morrison) CHF 10,000

Teaching Activities

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

Publications

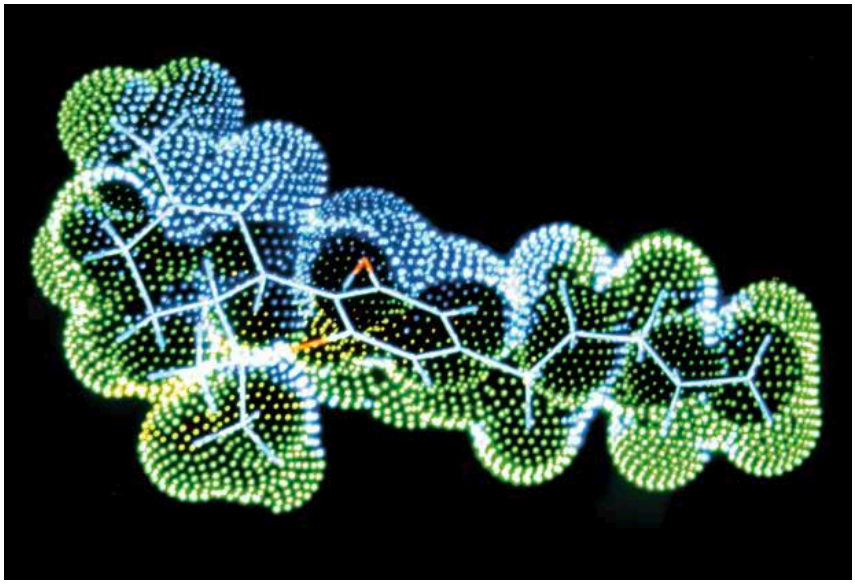
Cannabidiol inhibits THC-elicited paranoid symptoms and hippocampal-dependent memory impairment. Englund, A; Morrison, PD; Nottage, J; Hague, D; Kane, F; Bonaccorso, S; Stone, JM; Reichenberg, A; Brenneisen, R; Holt, D; Feilding, A; Walker, L; Murray, RM; Kapur, S (2012) in: J Psychopharmacol.

Single-dose Pharmacokinetics and Tolerability of Oral Delta-9-Tetrahydrocannabinol in Patients with Amyotrophic Lateral Sclerosis. Joerger, M; Wilkins, J; Fagagnini, S; Baldinger, R; Brenneisen, R; Schneider, U; Goldman, B; Weber, M (2012) in: Drug Metab Lett.

Bryophyllum pinnatum inhibits detrusor contractility in porcine bladder strips–a pharmacological study towards a new treatment option of overactive bladder. Schuler, V; Suter, K; Furer, K; Eberli, D; Horst, M; Betschart, C; Brenneisen, R; Hamburger, M; Mennet, M; Schnelle, M; Simoes-Wust, AP; von, MU (2012) in: Phytomedicine, 19(10), p. 947-951.

Communication breakdown: delta-9 tetrahydrocannabinol effects on pre-speech neural coherence. Stone, JM; Morrison, PD; Brugger, S; Nottage, J; Bhattacharyya, S; Sumich, A; Wilson, D; Tunstall, N; Feilding, A; Brenneisen, R; McGuire, P; Murray, RM; Ffytche, DH (2012) in: Mol Psychiatry, 17(6), p. 568-569.

Acute effects of intravenous heroin on the hypothalamic-pituitary-adrenal axis response: A controlled trial. Walter, M; Gerber, H; Kuhl, HC; Schmid, O; Joechle, W; Lanz, C; Brenneisen, R; Schächinger, H; Riecher-Rössler, A; Wiesbeck, GA; Borgwardt, SJ in: J Clin Psychopharmacol (in press).



Vasoactive Peptide

www.dkf.unibe.ch/research-group/22/

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

Research Highlights 2012 / Outlook 2013

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

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

This year, Dr. Shaw was Executive Guest Editor of a *Cardiology Research & Practice* special issue on "Cell Signalling Pathways Leading to Novel Therapeutic Strategies in Cardiovascular Disease". In terms of events, Dr. Shaw was Co-organiser and Chairman of the 4th UCL-Royal Free International Cardiovascular Diseases Workshop, which took place on 12 September. This workshop is held each year at the Royal Free Hospital campus of University College London, UK. He was also a member of the organizing committee and Co-chairman of the International Society for Applied Cardiovascular Biology meeting, held from 12-15 September at University College London, UK.

Group Members

Dr. Sidney G. Shaw, Group Leader
Jane Shaw, Laboratory Technician

Collaborators

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

Grants

Amounts allocated for 2012:

- Royal Society Joint International Research Grant: The role of Toll like receptor signalling in Peripheral Arterial Disease (J. Tsui, S. Shaw) CHF 30,000
- UK Medical Research Council: Importance of 11-beta-hydroxysteroid dehydrogenase (HSD-1) in the consequences of chronic alcohol consumption (H. Little, S. Shaw) CHF 50,000
- European Foundation for the Study of Diabetes: The role of toll like receptor signalling in diabetes related cardiovascular disease (S. Shaw) CHF 50,000

Teaching activities

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

Publications

Toll-like receptors in ischaemia and its potential role in the pathophysiology of muscle damage in critical limb ischaemia. Patel, H; Shaw, SG; Shi-Wen, X; Abraham, D; Baker, DM; Tsui, JC (2012) in: Cardiol Res Pract, 2012, p. 121237.

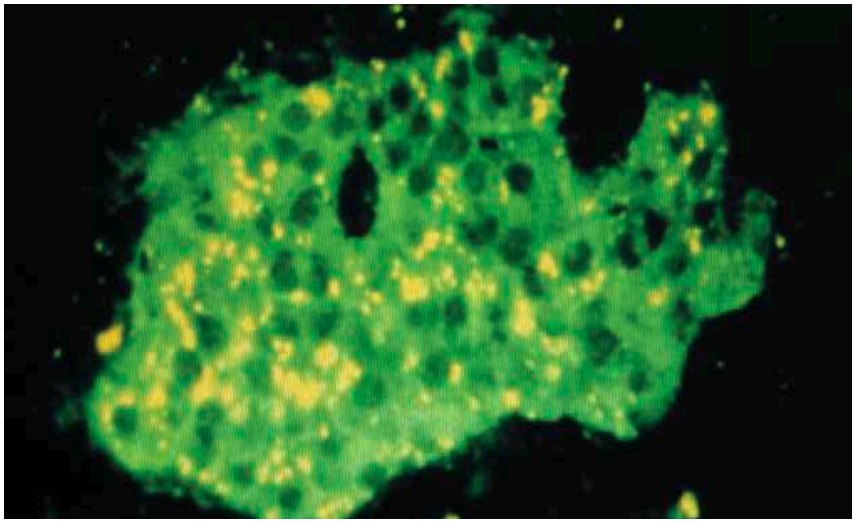
Torcetrapib impairs endothelial function in hypertension. Simic, B; Hermann, M; Shaw, SG; Bigler, L; Stalder, U; Dorries, C; Besler, C; Luscher, TF; Ruschitzka, F (2012) in: Eur Heart J, 33(13), p. 1615-1624.

Additive effect of homocysteine- and cholesterol-lowering therapy on endothelium-dependent vasodilation in patients with cardiovascular disease. Wustmann, K; Klaey, M; Burow, A; Shaw, SG; Hess, OM; Allemann, Y (2012) in: Cardiovasc Ther, 30(5), p. 277-286.

Therapeutic role of toll-like receptor modification in cardiovascular dysfunction. Navi, A; Patel, H; Shaw, S; Baker, D; Tsui, J (2012) in: Vascul Pharmacol.

The Emerging Role of TLR and Innate Immunity in Cardiovascular Disease. Spirig, R; Tsui, J; Shaw, S (2012) in: Cardiol Res Pract, 2012, p. 181394.

Cell signaling pathways leading to novel therapeutic strategies in cardiovascular disease. Shaw, S; Baker, D; Abraham, D; Tsui J (2012) in: Cardiology Research and Practice (in press).



DCR Research Groups from the Inselspital

Forty-three research groups from departments of the Inselspital were affiliated with the DCR at the end of 2012. Below is a list of the groups and the names of the Chairs of Departments and/or Group Leaders. Fifteen of the groups are featured on the following pages. Other groups will be featured in future annual reports.

Anaesthesiology: Prof. Dr. Frank Stüber, Dr. Rolf Lauber, PD Dr. Martin Luginbühl

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

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

Cardiology: Prof. Dr. Bernhard Meier, Prof. Dr. Yves Allemann, Prof. Dr. Etienne Delacrétaz, Prof. Dr. Paul Mohacsi, PD Dr. Claudio Sartori, Prof. Dr. Urs Scherrer, Prof. Dr. Christian Seiler, Prof. Dr. Thomas Suter, Prof. Dr. Stephan Windecker

Cardiovascular Surgery: Prof. Dr. Thierry Carrel, Prof. Dr. Hendrik Tevaearai, Dr. Henriette Brinks, Prof. Dr. Martin Czerny, PD Dr. Florian Dick, Dr. Sarah Longnus

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

Dental Research: Prof. Dr. Anton Sculean, Prof. Dr. Adrian Lussi, PD Dr. Dieter Bosshardt, Prof. Dr. Matthias Chiquet, Prof. Dr. Reinhard Gruber, PD Dr. Sigrun Eick

Dermatology: Prof. Dr. Luca Borradori, Dr. Bertrand Favre, PD Dr. Robert Hunger, Prof. 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

Endometrium & Ovary: Prof. Dr. Michael von Wolff

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

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

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

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

Hand Surgery: Prof. Dr. Esther Vögelin, Prof. Dr. Robert Rieben

Hepatology: Prof. Dr. Jean-François Dufour, PD Dr. Andrea de Gottardi, Prof. Dr. Jeff Idle, PD Dr. Nasser Semmo, Prof. Dr. Marc Solioz, Prof. Dr. Felix Stickel

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

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

Internal Medicine: Prof. Dr. Karin Fattinger, Prof. Dr. Beatrice U. Müller

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

Nephrology and Hypertension: Prof. Dr. Bruno Vogt, Prof. Dr. Brigitte Frey

Neurology: Prof. Dr. Claudio L. Bassetti, Prof. Dr. Alain Kaelin, Prof. Dr. Heinrich Mattle, Prof. Dr. René Müri

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

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

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

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

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

Perception and Eye Movement: Prof. Dr. Claudio L. Bassetti, PD Dr. Stephan Bohlhalter, Prof. Dr. René Müri, PD Dr. Thomas Nyffeler

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

Prenatal Medicine: Prof. Dr. Daniel Surbek

Psychosomatic Medicine: Prof. Dr. Roland von Känel

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

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

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

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

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

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

Tumor-Immunology: Prof. Dr. Adrian Ochsenbein

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

Visceral and Transplantation Surgery: Prof. Dr. Daniel Candinas, Dr. Deborah Stroka

Audiology

www.artorg.unibe.ch/content/research_units/artificial_hearing_research

Research Highlights 2012 / Outlook 2013

2012 was a year of transition for the Audiology group: Prof. Stieger joined Harvard Medical School (US) as a Research Fellow, a number of projects were successfully finished and the results published in high-ranking journals, and new projects, along with an additional PhD-thesis, were started.

Two new, large-scale EU-projects, HEAR-EU (www.hear-eu.org) and NAONOCI (www.nanoci.org) started this year. Both investigate novel methods to improve hearing and speech understanding in deaf patients.

Members of our group received several awards for their work, including best scientific paper for "Development of an auditory implant manipulator" by Stieger et al. in the *Journal of Laryngology and Otology*, and best poster award for "Novel Body Access for Hemodialysis" by Guignard et al. at the KTI Medtech Event.

Among the successfully finalised projects in 2012 was a multi-centre Swiss study on tinnitus in cochlear implant patients, which was received with considerable interest at several international conferences. Another long-term project on acoustic trauma in the Swiss army was finalised and published. Anja Kurz, a PhD student who started in 2011, finished her first sub-project, a comparison of two bone-anchored hearing aids in different acoustic settings.

In 2013, work on the EU-projects will gain momentum and we expect to see the very first results. Among other projects that will continue, is a new cooperation with Kosice University (SK). A first project involving adults with single-sided sensorineural deafness has already started and the first measurements have been performed. A project using a completely new bone conduction hearing aid, the Bonebridge, was initiated in late 2012. First implantations have already been performed successfully in Bern by Prof. Caversaccio. Wilhelm Wimmer, a new PhD student, joined our team in August to work on this project. Furthermore, we expect Jéremie Guigniard to successfully finish his PhD work next year.

Prof. Dr. Marco Caversaccio
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MD from University of Geneva. Research fellowship at Imperial College London (UK). Broad research focus with special interest in technical assistance systems (NCCR CO-ME). Since 2009, Chair, Department of Ear, Nose and Throat Diseases, Head and Neck Surgery, Inselspital. Since 2010, also Vice-Director, ARTORG Center for Biomedical Engineering, University of Bern.

Prof. Dr. Martin Kompis
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MD from University of Zurich. PhD in electrical engineering from ETH Zurich. Postdoc at Purdue University (US). Since 1997, Head of Audiology, Department of Ear, Nose and Throat Diseases, Head and Neck Surgery, Inselspital. Associate Professor of Biomedical Engineering and Acoustics, University of Bern.

Prof. Dr. Christof Stieger
christof.stieger@artorg.unibe.ch

Studies in electrical engineering and medical physics at EPF Lausanne and ETH Zurich, and at University of Louvain la Neuve (BE). PhD from University of Neuchâtel. Since 2008, Assistant Professor of Artificial Hearing, Department of Ear, Nose and Throat Diseases, Head and Neck Surgery, Inselspital. Currently Research Fellow at Eaton-Peabody Laboratory, Harvard Medical School (US).

PD Dr. Pascal Senn
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MD from University of Bern. Board-certified otolaryngologist, head and neck surgeon. Research fellowship on inner ear stem cells at Harvard and Stanford University Medical Schools (US). Since 2008, Head Cochlear Implant Division, Inselspital. Coordinator of the EU-funded NANOCI project.

Group Members

Prof. Dr. Marco Caversaccio, Chair, Group Leader
Prof. Dr. Martin Kompis, Group Leader
PD Dr. Pascal Senn, Group Leader
Prof. Dr. Christof Stieger, Group Leader (until Nov.)
Dr. Marta Roccio, Postdoctoral Fellow (since Sep.)
Simona Wiedmer, Research Assistant
Ruth Birrer, MD Student
Nicolas Gerber, PhD Student
Jéremie Guignard, PhD Student
Stefan Hahnewald, PhD Student (since Sep.)
Anja Kurz, PhD Student
Wilhelm Wimmer, PhD Student (since Aug.)

Collaborators

Koval J, Krempaska S, University of Kosice, Slovakia
Labadie R, Vanderbilt University, USA
Lenarz T, Hannover Medical School, Germany
Merchant S, Rosowski J, Mylanus E, Snik AD, Radboud University, The Netherlands
Nakajima H, Harvard Medical School, Massachusetts Eye and Ear Infirmary, Boston, USA
Vetter R, University of Applied Sciences, Burgdorf, Switzerland

Grants

Amounts allocated for 2012:

- European Commission: HEAR-EU (M.A. Gonzalez Ballester, M. Caversaccio, S. Weber, in collaboration with ARTORG) CHF 280,000
- European Commission: NANOCI (P. Senn) CHF 120,000
- Cochlear Inc.: Optimized bone anchored stimulation (M. Kompis, M. Caversaccio) CHF 46,556
- Cochlear Inc.: Comparative study Baha Intenso/BP110 (M. Kompis) CHF 29,160

Five Selected Publications

Extended frequency range hearing thresholds and otoacoustic emissions in acute acoustic trauma. Buchler, M; Kompis, M; Hotz, MA (2012) in: Otol Neurotol, 33(8), p. 1315-1322.

Tinnitus before and 6 months after cochlear implantation. Kompis, M; Pelizzone, M; Dillier, N; Allum, J; DeMin, N; Senn, P (2012) in: Audiol Neurootol, 17(3), p. 161-168.

A multilingual audiometer simulator software for training purposes. Kompis, M; Steffen, P; Caversaccio, M; Brugger, U; Oesch, I (2012) in: Acta Otolaryngol, 132(4), p. 428-433.

Retrograde cochlear implantation in postmeningitic basal turn ossification. Senn, P; Rostetter, C; Arnold, A; Kompis, M; Vischer, M; Hausler, R; Ozdoba, C; Mantokoudis, G; Caversaccio, M (2012) in: Laryngoscope, 122(9), p. 2043-2050.

Laser Doppler vibrometric assessment of middle ear motion in Thiel-embalmed heads. Stieger, C; Candreia, C; Kompis, M; Herrmann, G; Pfiffner, F; Widmer, D; Arnold, A (2012) in: Otol Neurotol, 33(3), p. 311-318.

Cardiology

www.cvrc.dkf.unibe.ch

Prof. Dr. Bernhard Meier
bernhard.meier@insel.ch

Studied medicine at University of Zurich (1975); board certified: internal medicine (1980), cardiology (1983). Cardiology training at Emory University (US). Head of invasive cardiology, University Hospital, Geneva (1983-1992). Chair and Professor of Cardiology (1992), rotating Chair (2001), Inselspital. Involved in coronary angioplasty since the first case in 1977. Currently Chair of Cardiology, Inselspital.

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

Prof. Dr. Etienne Delacrétaz
etienne.delacretaz@insel.ch

MD at University of Lausanne (1987), Resident in internal medicine in Aigle, Morges, Geneva (HUG); Chief Resident and Cardiovascular Research Fellow in Lausanne (CHUV); Cardiology Fellow in Bern (1994-1996), Fellow in electrophysiology in USA at Brigham and Women's Hospital (1997-1999). Staff in electrophysiology: Lausanne (1999-2000), Bern (2000). PD (2002), Assistant Professor (2002), Associate Professor (2006) at University of Bern.

Research Highlights 2012 / Outlook 2013

Allemann/Scherrer/Sartori Groups

In 2012, we published the very first report demonstrating that assisted reproductive technology (ART) induces vascular dysfunction in young, apparently healthy children. This vascular dysfunction is of similar magnitude to that which we recently reported in offspring of preeclampsia, a condition known to be associated with a markedly increased risk of premature stroke. Our ongoing studies demonstrate that ART induces vascular dysfunction and arterial hypertension in in vitro fertilised mice, and suggests that epigenetic mechanisms may play a role.

In a collaborative effort with a group in Bolivia, we provided evidence that exaggerated chronic hypoxia in patients suffering from chronic mountain disease not only induces pulmonary but also systemic vascular dysfunction. This dysfunction appears to be related to exaggerated oxidative stress, causing alveolar fluid accumulation in the pulmonary circulation during moderate physical activity.

Delacrétaz Group

One main objective of our group is to improve the detection of atrial fibrillation (AF) and the prevention of AF-related stroke. The last decade has witnessed intense developments in AF treatment, especially in ablative therapy, and management of AF will remain a key cardiology field in the coming years. A second objective is to improve the management of patients with heart disease and complex arrhythmias, including patients who have grown-up with congenital heart disease and patients with scar-related ventricular arrhythmias. Preliminary data show that management with catheter ablation at an earlier stage of the disease may improve the quality of life and long-term prognosis.

Mohacsi Group

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

Suter Group

We seek to prevent cardiovascular side effects associated with cancer therapies, as well as to improve clinical management strategies. It is a worrisome fact that ischemia and cardiotoxic compounds can lead to cellular damage and irreversible decline of cardiac function. Thus, it is critically important to understand these complications in order to provide better diagnostics and therapy. We investigate mechanisms of cardiotoxicity of old and new anti-cancer therapies and cardiac-specific survival pathways that show potential as cardiovascular treatments.

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MD at University of Zurich. Postdoc in USA at Stanford University Medical Center (1991-1993). Since 1993, Medical Director, Heart Failure and Cardiac Transplantation, and Head of Research, Department of Cardiology, Inselspital. Konsiliarus in Transplantation Immunology, University of Freiburg (DE) (2008-2012). Visiting Professor in Canada at University of British Columbia (2008, 2011). eMBA from University of Zurich (2009).

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Group Members

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Prof. Dr. Stephan Windecker, Head of Research

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PD Dr. Claudio Sartori, Group Leader
Prof. Dr. Urs Scherrer, Group Leader
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Dr. Jens Seiler, Research Associate
PD Dr. Hildegard Tanner, Research Associate

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

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

Prof. Dr. Thomas M. Suter, Group Leader
Dr. Christian Zuppinger, Research Associate
Dr. Philippe Beauchamp, Postdoctoral Fellow (since Aug.)

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Raio L, Inselspital, Switzerland
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Sawyer, DB, Vanderbilt University Medical Center, USA
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Grants

Amounts allocated for 2012:

- SNF: Coronary Collateral Circulation of the Human Heart (C. Seiler) CHF 237,000
- SNF: Systemic vascular function in young healthy offspring of preeclampsia (Y. Allemann, Y. Vial, S. Rimoldi, D. Hutter, L. Raio) CHF 103,000
- SNF: Insulin-resistance in offspring of assisted reproductive technologies (C. Sartori, S. Rimoldi, Y. Allemann) CHF 140,000
- Swiss Society of Hypertension Astra-Zeneca Scholarship: Vascular dysfunction in offspring of assisted reproductive technologies: role of epigenetic mechanisms (E. Rexhaj, U. Scherrer, Y. Allemann) CHF 40,000
- CTI: Body-on-the-Plate – An Integrated Ready-To-Use Platform For Investigating Multi Organ Toxicity (C. Zuppinger) CHF 110,000
- Swiss Heart Foundation: The Effect of Acute Afterload Reduction on Coronary Collateral Function (S. Glökler, C. Seiler) CHF 44,000
- Swiss Transplant Cohort Study: Evaluation of genomic and proteomic blood biomarkers for diagnosis of heart/kidney allograft rejection (P. Mohacsi) CHF 30,000

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

Prof. Dr. Thomas M. Suter
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MD at University of Zurich (1986), Cardiology and CCU/ICU Fellowship in internal medicine at Zurich University School of Medicine. In USA, Research Fellowship in Cardiovascular Physiology at Boston University School of Medicine; Cardiology Fellowship at Boston University (1992-1998); Internship at Brigham and Women's Hospital (1998). Since 2005, Associate Professor, University of Bern.

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MD Degree at University of Heidelberg (DE) (1992). FMH certification in cardiology. Currently, Professor of Invasive Cardiology at University of Bern and Chief of Cardiology, Inselspital. President-Elect, European Association of Percutaneous Cardiovascular Interventions.

Five Selected Publications

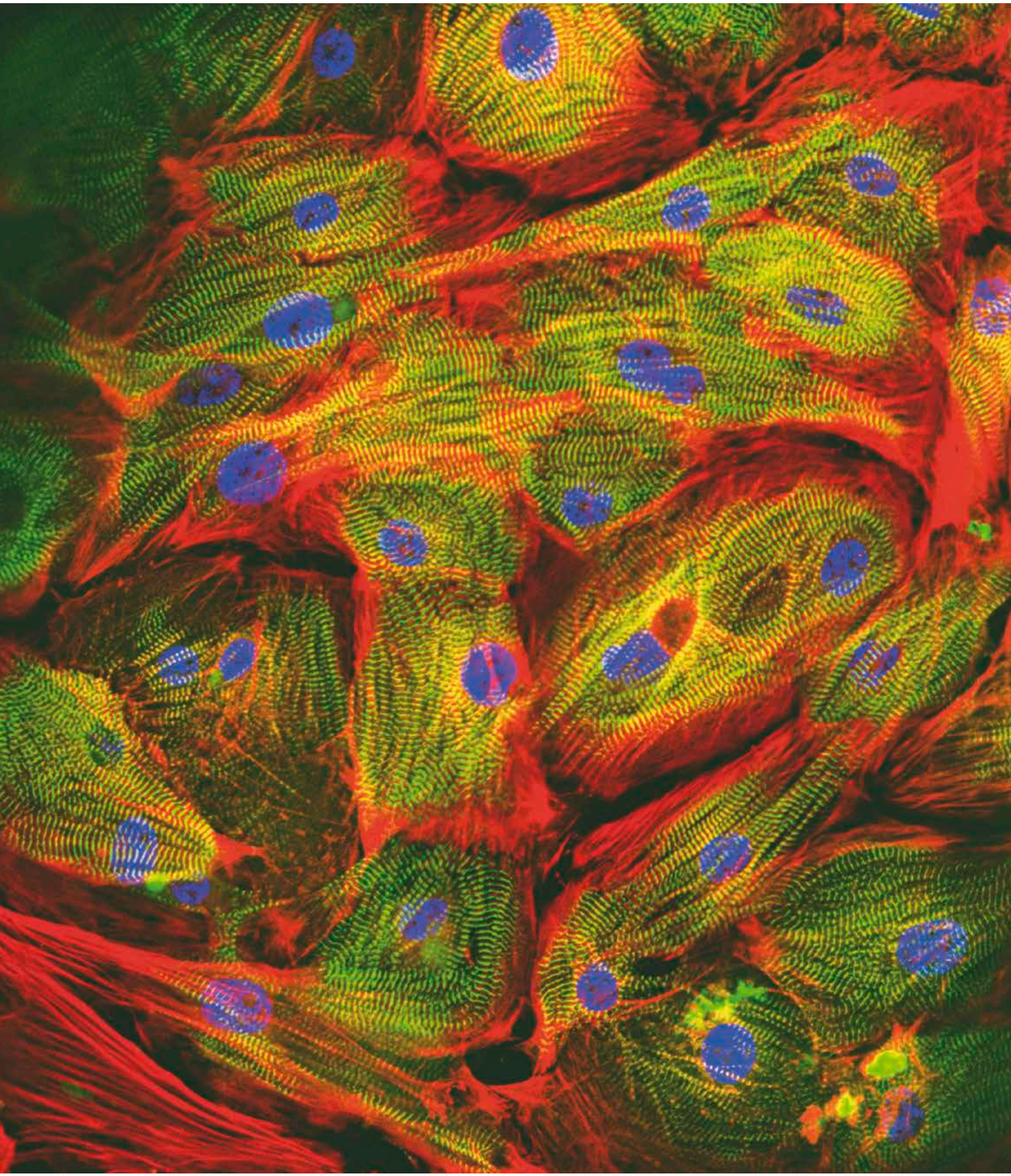
Cancer therapy modulates VEGF signaling and viability in adult rat cardiac microvascular endothelial cells and cardiomyocytes. Chiusa, M; Hool, SL; Truetsch, P; Djafarzadeh, S; Jakob, SM; Seifriz, F; Scherer, SJ; Suter, TM; Zuppinger, C; Zbinden, S (2012) in: J Mol Cell Cardiol, 52(5), p. 1164-1175.

Long-term outcome of ablative therapy of post-operative atrial tachyarrhythmias in patients with tetralogy of Fallot: a European multi-centre study. de Groot, NM; Lukac, P; Schalij, MJ; Makowski, K; Szili-Torok, T; Jordaens, L; Nielsen, JC; Jensen, HK; Gerdes, JC; Delacretaz, E (2012) in: Europace, 14(4), p. 522-527.

Editorial Comment: The clinical relevance of antibody-mediated rejection: a new era of heart transplantation. Mohacsi, P; Martinelli, M; Banz, Y; Boesch, C (2012) in: Eur J Cardiothorac Surg, 42(6), p. 1047-1049.

Systemic vascular dysfunction in patients with chronic mountain sickness. Rimoldi, SF; Rexhaj, E; Pratali, L; Bailey, DM; Hutter, D; Faita, F; Salmon, CS; Villena, M; Nicod, P; Allemann, Y; Scherrer, U; Sartori, C (2012) in: Chest, 141(1), p. 139-146.

Systemic and pulmonary vascular dysfunction in children conceived by assisted reproductive technologies. Scherrer, U; Rimoldi, SF; Rexhaj, E; Stuber, T; Duplain, H; Garcin, S; de Marchi, SF; Nicod, P; Germond, M; Allemann, Y; Sartori, C (2012) in: Circulation, 125(15), p. 1890-1896.



Cardiovascular Surgery

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Studied medicine at University of Bern; clinical training in general surgery, FMH (1990); cardiovascular surgery FMH (1993) in Basel and Bern. Habilitation in Zurich (1993), followed by fellowships at clinics in Paris (FR), Hannover (DE) and Helsinki (FI). Joined Clinic for Thoracic and Cardiovascular Surgery, Inselspital as Senior Attending (1995). Since 1999, Chair, Department of Cardiovascular Surgery, Inselspital.

Research Highlights 2012 / Outlook 2013

Our research focuses on the following projects:

Myocardial Tissue Engineering

Engineering of contractile bio-artificial tissues for myocardial repair. This SNF-funded project was initiated in 2003 and expanded to include collaborations with EMPA, St. Gallen and the Department of Cardiology, University of Fribourg.

Non-Heart Beating Donors

Since its formation in 2009, this group aims to evaluate reperfusion strategies to promote the use of hearts obtained from donors after cardiac death. 2012 has seen further consolidation and expansion, making this a central research group of the Department of Cardiovascular Surgery.

Myocardial Recovery

This project focusing on evaluation of mechanisms leading to reverse remodelling of failing hearts has progressed from incubation to a fully operational research group in 2012. Thanks to the generous support of both the Swiss Heart Foundation and the DCR, the outlook for this group in 2013 is strong.

Limb Ischemia/Reperfusion

This project evaluates the molecular pathways underpinning muscle cell death of skeletal muscle and future pathways to protect ischemic muscle against reperfusion injury. The gathered data bolster the strategic value of the approach to develop new translational approaches.

Clinical Research: Cardiac

Clinical research in cardiac surgery continued to focus on aortic projects, including the elucidation of a new mechanism of propagation in type B aortic dissection. Several clinical papers were published in this field of research. 2013 will start with the publication of a very promising project on a new biomarker in patients with asymptomatic thoracic aortic disease.

Clinical Research: Vascular

Research focused on optimised management strategies for ruptured abdominal aortic aneurysm and on the general improvement of follow-up surveys in the context of observational research. In an award-winning (USGG 2012) randomised experiment, a strategy was identified that allowed achievement of close to 100% follow-up information of retrospective series. This method will be used to follow a larger vascular patient sample in 2013, to validate a novel scoring system for postoperative complications.

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Studied medicine at University of Lausanne, followed by clinical training in general surgery, FMH (1995) and cardiovascular surgery FMH (2002). Research fellowship at Duke University (US) (1999-2001). Since 2003, Senior Attending and since 2005, Head of Research and Development, Department of Cardiovascular Surgery, Inselspital.

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

Prof. Dr. Martin Czerny
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Studied medicine in Vienna (AT); worked at Clinic for Cardiothoracic Surgery, Medical University of Vienna (1998-2009). General Surgery (2004) and Vascular Surgery (2005) qualifications, as well as MBA (2008). In 2009, joined Department of Cardiovascular Surgery, Inselspital as an Attending, becoming Head of Cardiac Surgery Research in 2010.

PD Dr. Florian Dick
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Studied medicine at University of Basel; FMH (2005) including a vascular surgery specialisation. Joined Department of Cardiovascular Surgery, Inselspital as a Resident (2004); Attending (2006). Spent a year in Vascular Surgery Research Group, Imperial College London (GB). Since returning, Head of Vascular Surgery Research (2010) and Senior Attending (2012).

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

Group Members

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Prof. Dr. Martin Czerny, Senior Attending, Group Leader
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Bettina Kohler, Data Manager
Monika Sperisen, Data Manager
Sorin Ciocan, Laboratory Technician (since Nov.)
Céline Fouassier, Laboratory Technician (until Nov.)
Céline Giroud, Laboratory Technician
Veronika Mathys, Laboratory Technician (since Dec.)
Adrian Segiser, Laboratory Technician (since May)
Joevin Sourdon, Laboratory Technician (until Aug.)
Barbara Schweizer, Secretary (Apr.-Sep.), Data Manager (Oct.-Dec.)
Laura Seidel, Secretary
Monika Dornbierer, MD-PhD Student
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Collaborators

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Grants

Amounts allocated for 2012:

- Ruth und Arthur Scherbarth Foundation: Cardioprotection: Physical and molecular interventions for limiting reperfusion injury to the heart (S. Longnus, H. Brinks, H. Tevaearai) CHF 40,000
- Research Prize 2012: Ventricular unloading combined with inotropic gene therapy in the failing heart (H. Brinks) CHF 30,000
- University of Bern, Faculty of Medicine Resource Committee: Blood Gas Analyzer for Ischemia/Reperfusion Injury (T. Carrel, H. Tevaearai, S. Longnus) CHF 17,780
- University of Bern, Faculty of Medicine Resource Committee: Isolated, perfused rat heart system for Ischemia/Reperfusion Injury (T. Carrel, H. Tevaearai, S. Longnus) CHF 41,518
- Swiss Heart Foundation: Towards myocardial recovery: Enhanced adrenergic response via ßARKTct gene therapy in the unloaded heart (H. Brinks) CHF 68,000

Five Selected Publications

Endovascular suitability and outcome after open surgery for ruptured abdominal aortic aneurysm. Dick, F et al. (2012) in: Br J Surg, 99(7), p. 940-947.

Early reperfusion hemodynamics predict recovery in rat hearts: a potential approach towards evaluating cardiac grafts from non-heart-beating donors. Dornbierer, M et al. (2012) in: PLoS One, 7(8), p. e43642.

Fine-tuning of substrate architecture and surface chemistry promotes muscle tissue development. Guex, AG et al. (2012) in: Acta Biomater, 8(4), p. 1481-1489.

Controlled angiogenesis in the heart by cell-based expression of specific vascular endothelial growth factor levels. Melly, LF et al. (2012) in: Hum Gene Ther Methods, 23(5), p. 346-356.

Mild hypothermia during global cardiac ischemia opens a window of opportunity to develop heart donation after cardiac death (DCD). Stadelmann, M et al. in: Transplant International (in press).

Cranio-Maxillofacial Surgery

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

Prof. Dr. Tateyuki Iizuka
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MD and DDS in Germany; PhD in Medicine (1992). Since 1996, Associate Professor at Helsinki University (FI). Since 2000, Professor of Cranio-Maxillofacial Surgery, University of Bern; Chair of Department since 2006. Lecturer at Helsinki University, External Professor at Osaka Dental University (JP) and National University of Singapore. Director of postgraduate programmes in oral and maxillofacial surgery in Switzerland, Germany, Finland and European Association for Cranio-Maxillofacial Surgery.

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Studies in dental medicine and MSc from University of Belgrade (RS). European PhD (2005) at University of Santiago de Compostela (ES). Research and Teaching Associate at University of Geneva (2006-2007). Since 2007, Research Associate, University of Bern. Since 2012, Group Leader, Cranio-Maxillofacial Surgery, DCR.

Research Highlights 2012 / Outlook 2013

Clinical Studies

Paediatric patients with fractures of the anterior skull base frequently present with associated injuries, many with multiple associated injuries, including polytrauma. The analysis of occurrence, sites, and types of associated injuries indicated the need for multidisciplinary trauma units.

We studied whether a daily course of antibiotics affects the incidence of postoperative infection after displaced fractures. Patients with orbital blow-out fractures were randomly assigned to two groups, both of which were given amoxicillin/clavulanic acid intravenously from the time of admission to 24h postoperatively. The 5-day group were then given amoxicillin/clavulanic acid orally for 4 further days and the 1-day group a placebo orally at the same time intervals. Results showed that a postoperative 1-day course of antibiotics may be as effective in preventing infective complications in patients with displaced orbital fractures as a 5-day regimen.

Assessment of peri-implant bone changes is considered one of the critical components for long-term success of dental implants. Peri-implant bone changes, frequently assessed by reporting on bone height, might actually neglect the process of bone remodelling. Hard and soft tissue parameters around implants supporting fixed prostheses were analysed over a period of 5 years. An increase in bone density indicated a regain of the crestal bone level after initial bone loss around implants.

Preclinical Studies

We previously demonstrated in vivo that the application of a collagen barrier membrane in periosteal distraction osteogenesis was beneficial to bone formation. An in vitro study performed at the School of Dental Medicine, University of Bern demonstrated that bone morphogenic protein-2 and transforming growth factor β1 soak-loaded membranes increased osteoblast proliferation when compared to control collagen membranes. Administration of bone morphogenic protein-2 increased osteoblast differentiation markers such as osterix, collagen I, and osteocalcin, as well as mineralisation of primary osteoblasts. The ongoing in vivo study evaluates the contribution of the barrier membrane soaked with growth factors to bone formation in periosteal distraction osteogenesis in rats and assessment of new bone formation using two rates of periosteal distraction in rabbits.

The collaboration with the School of Dental Medicine includes in vivo studies performed at the Clinic for Oral Surgery. These evaluated impact of harvesting techniques on cell viability and release of molecules affecting bone formation and the use of new materials (TiZr) on osseointegration of dental implants.

Group Members

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Grants

Amounts allocated for 2012:
None

Five Selected Publications

Low-profile titanium mesh in the use of orbital reconstruction: A pilot study. Lieger, O; Schaller, B; Kellner, F; Messmer-Schai, B; Iizuka, T (2012) in: Laryngoscope, 122(5), p. 982-991.

Osteoblast proliferation and differentiation on a barrier membrane in combination with BMP2 and TGFbeta1. Miron, RJ; Saulacic, N; Buser, D; Iizuka, T; Sculean, A (2012) in: Clin Oral Investig.

Clinical and radiographic outcome of dental implants supporting fixed prostheses: the relevance of cortical bone formation. Saulacic, N; Abboud, M; Pohl, Y; Wahl, G (2012) in: Implant Dent, 21(4), p. 323-329.

Occurrence, types and severity of associated injuries of paediatric patients with fractures of the frontal skull base. Schaller, B; Hosokawa, S; Buttner, M; Iizuka, T; Thoren, H (2012) in: J Craniomaxillofac Surg, 40(7), p. e218-e221.

The role of postoperative prophylactic antibiotics in the treatment of facial fractures: a randomised, double-blind, placebo-controlled pilot clinical study. Part 1: orbital fractures in 62 patients. Zix, J; Schaller, B; Iizuka, T; Lieger, O (2012) in: Br J Oral Maxillofac Surg.

Dermatology

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

Research Highlights 2012 / Outlook 2013

Allergies

Thymic stromal lymphopoietin (TSLP) is a cytokine released by epithelial cells upon stimulation by various environmental stresses (e.g., viruses, bacteria, allergens) and one of the major culprits in the allergic inflammatory diseases asthma, allergic rhinitis, and atopic dermatitis. In collaboration with the research groups of H.-U. Simon and S. Yousefi (Institute of Pharmacology), we demonstrated that TSLP triggers the release by eosinophils of extracellular DNA in association with eosinophilic cationic protein, termed eosinophil extracellular traps (EETs). This release of EETs was dependent on integrin-mediated adhesion or production of reactive oxygen species, and exhibited antimicrobial activity against *Staphylococcus aureus* and *S. epidermidis*. This mechanism provides a link between the injury to an epithelial barrier and increased TSLP expression, with subsequent pathogen defense response by eosinophils and eosinophilic inflammation.

Psoriasis

Innate immune responses play a central role in psoriasis. Our investigations showed that a new retinoid named alitretinion leads to clinical amelioration and abrogates innate inflammation in palmoplantar pustular psoriasis. Heat shock proteins may play an important part in plaque psoriasis. The expression of these proteins in psoriasis and their regulation through proinflammatory cytokines is currently been investigated.

Hidradenitis Suppurativa (HS)

Antimicrobial peptide cathelicidin expression was found to be significantly increased in lesional HS skin at the mRNA and protein level. Using immunofluorescence double staining we could demonstrate that neutrophils and dendritic cells expressing cathelicidin are present in the lesions. By analysing freshly isolated cells from lesional skin by flow cytometry, we could further confirm the expression of cathelicidine on CD15-positive neutrophils and CDD4+CD3-infiltrating cells.

Malignant Melanoma

We investigated the role of various immunohistochemical markers in predicting disease progression and showed that high expression of the T cell marker FoxP3 is associated with bad prognosis in melanoma patients.

Plakins

Plectin is a cytolinker of the plakin family with intermediate filaments (IFs) that is important for cell cytoarchitecture, and for cell and tissue resilience to mechanical stress, especially in the skin and skeletal muscle. Investigation of the interaction of plectin with IFs revealed much more complex binding than previously published, thanks to a new method to test and quantify protein-protein interactions. Moreover, we found that phosphorylation of a serine residue in the carboxyl tail of plectin inhibits its interaction with IFs, and identified two protein kinases catalysing this phosphorylation in vivo. Our data provide insights into the molecular basis of plectin- and IF-related human diseases associated with pathogenic mutations affecting functionally relevant sites within these molecules.

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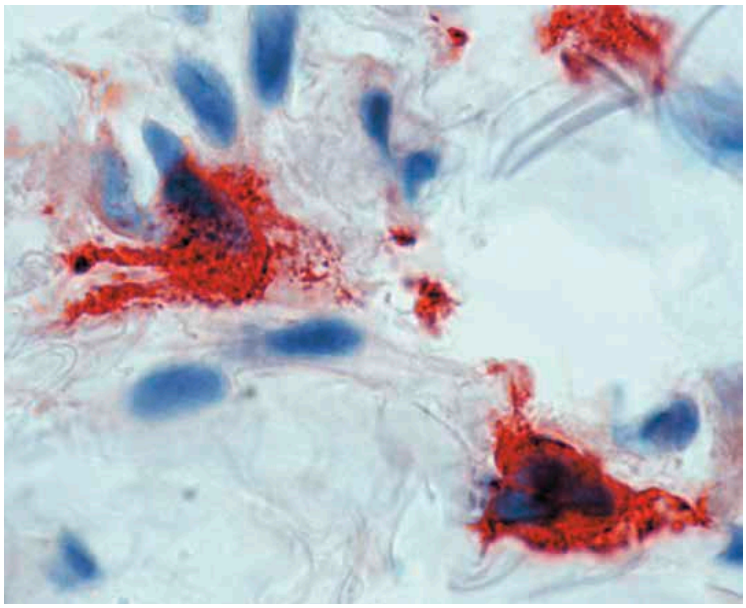
MD at University of Basel (1988). Board certifications: Dermatology (1995), Allergy and Clinical Immunology (1998) at University of Bern. Postdocs in USA at University of California, San Francisco (1995) and Harvard Skin Disease Research Center (2000-2002). Since 2006, Associate Professor, Department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



Group Members

Prof. Dr. Luca Borradori, Chair, Group Leader
Prof. Dr. Robert Hunger, Group Leader
Prof. Dr. Dagmar Simon, Group Leader
Prof. Dr. Nikhil Yawalkar, Group Leader
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Ursula Läderach, Laboratory Technician
Evelyne Seger, Laboratory Technician
Prakash Lingasamy, Research Associate (until Aug.)
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Grants

Amounts allocated for 2012:

- SNF: Analysis of molecular and cellular mechanisms in immune-mediated tissue damage of the skin: Hidradenitis suppurativa as a model disease (R. Hunger, N. Yawalkar) CHF 70,000
- OPO Foundation, Zurich: The effects of thymic stromal lymphopoietin (TSLP) on eosinophil extracellular DNA release (D. Simon) CHF 32,000

Five Selected Publications

Endemic pemphigus foliaceus: towards understanding autoimmune mechanisms of disease development. Di, ZG; Zambruno, G; Borradori, L (2012) in: J Invest Dermatol, 132(11), p. 2499-2502.

Alitretinoin abrogates innate inflammation in palmoplantar pustular psoriasis. Irla, N; Navarini, AA; Yawalkar, N (2012) in: Br J Dermatol, 167(5), p. 1170-1174.

Thymic stromal lymphopoietin stimulates the formation of eosinophil extracellular traps. Morshed, M; Yousefi, S; Stockle, C; Simon, HU; Simon, D (2012) in: Allergy, 67(9), p. 1127-1137.

The role of androgens on hypoxia-inducible factor (HIF)-1alpha-induced angiogenesis and on the survival of ischemically challenged skin flaps in a rat model. Shafighi, M; Olariu, R; Brun, C; Fathi, AR; Djafarzadeh, S; Jakob, SM; Hunger, RE; Banic, A; Constantinescu, MA (2012) in: Microsurgery, 32(6), p. 475-481.

Eosinophil extracellular DNA traps: molecular mechanisms and potential roles in disease. Yousefi, S; Simon, D; Simon, HU (2012) in: Curr Opin Immunol, 24(6), p. 736-739.

Gastroenterology / Mucosal Immunology

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Studied biochemistry (PhD, 1983) and Medicine (MB, 1985) at University of Cambridge (UK). Research Group Leader and senior medical staff at University Hospital Zurich (1998-2004), Professor of Medicine at McMaster University (CA) (2004-2008). Since 2008, Chief of Gastroenterology and Co-Chair, Department of Visceral Surgery and Medicine, Inselspital.

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Research Highlights 2012 / Outlook 2013

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

Macpherson Group

IgA is the dominant antibody isotype secreted at mucus membranes, yet the precise immunological functions of IgA are only partially understood. Using metabolic labelling of bacteria or plasmid-based systems to assess bacterial proliferation, we are performing experiments to address whether mucosal antibodies (and IgA in particular) have an impact on the dynamics of intestinal commensal bacteria, such as bacterial proliferation, retention of bacteria in different niches, and shedding of bacteria. We are investigating the stratification of bacteria within the gut and determining the dynamics of bacteria within the different mucus layers lining the gut epithelium. Although under homeostatic conditions live bacteria are compartmentalised to mucosal sites, bacterial products can penetrate to systemic sites. We are actively studying the consequences of these products on the systemic immune system. In this context, we also investigate the role of natural antibodies at systemic sites in handling these penetrating bacterial products. We are also investigating the impact of exposure to intestinal microbes on the innate lymphoid system at intestinal and extra-intestinal sites at different time points during immune development.

McCoy Group

We have observed that the pathways that normally repress the production of IgE antibodies are disrupted in the absence of microbes, resulting in extremely elevated serum IgE levels in germ-free mice, which reflects immune dysregulation. We have now elucidated that the complexity of the microbiota present early in life is instrumental in instructing a normal immune regulatory status. A critical threshold of microbial complexity has to be reached early during colonisation to ensure proper induction of immune regulation. This is the first experimental demonstration of a mechanism that could be an underlying cause of the observations described in the 'hygiene hypothesis'. We are now investigating the role of the innate immune system in sensing this microbial complexity and what signals are involved in instructing regulation of the adaptive immune system.

Geuking Group

In 2011, we published results showing that intestinal bacterial colonisation induces strong regulatory T cell and interleukin-10 responses to ensure immune homeostasis following colonisation. Based on these findings, we are now investigating the antigen-specificity requirements for efficient regulatory T cell induction using genetically modified *E. coli* strains expressing a particular T cell epitope that is recognised by a transgenic T cell receptor. In addition, we are investigating the cooperation between regulatory T cell and IgA responses in controlling mutualism with the intestinal microbiota.

Group Members

Prof. Dr. Andrew Macpherson
Chief of Gastroenterology, Co-Chair
Prof. Dr. Kathy McCoy, Group Leader
Dr. Markus Geuking, Group Leader
Dr. Julia Cahenzli, Postdoctoral Fellow
Dr. Mercedes Gomez de Aguero, Postdoctoral Fellow
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Dr. Melissa Lawson, Postdoctoral Fellow
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Santamaria P, University of Calgary, Canada
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Stecher B, Ludwig Maximilian University, Germany

Grants

Amounts allocated for 2012:

- SNF: Compartmentalisation of commensal intestinal microbes and host IgA immunity in maintaining host-microbial mutualism (A. Macpherson) CHF 335,000
- SNF: The role of antigen-specific and Toll-like receptor-dependent de novo generation of inducible regulatory T cells in the induction of intestinal immune homeostasis (M. Geuking) CHF 176,741
- SNF: Shaping of the innate immune system during neonatal exposure to commensal intestinal microbes (A. Macpherson) CHF 137,500
- SNF: Investigation into the impact of environmental microbes on regulation of IgE and allergic disease (K. McCoy) CHF 100,000
- European Research Council: Mechanisms of hygiene-mediated immune dysregulation and impact on the susceptibility to allergic and autoimmune diseases (K. McCoy) CHF 300,000
- Juvenile Diabetes Research Foundation: Type 1 diabetes protection through commensal intestinal bacterial exposure (A. Macpherson, K. McCoy) CHF 101,000

Five Selected Publications

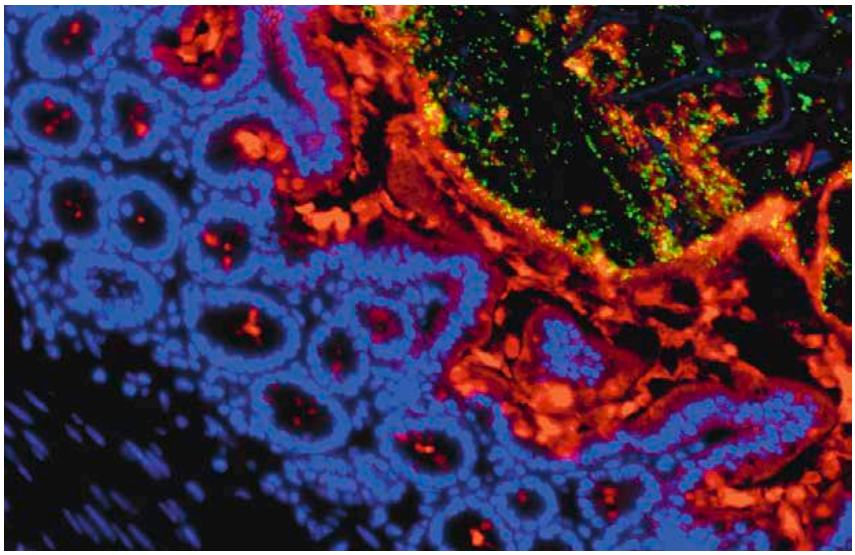
Microbial-immune cross-talk and regulation of the immune system. Cahenzli, J; Balmer, ML; McCoy, KD (2012) in: Immunology.

The function of secretory IgA in the context of the intestinal continuum of adaptive immune responses in host-microbial mutualism. Geuking, MB; McCoy, KD; Macpherson, AJ (2012) in: Semin Immunol, 24(1), p. 36-42.

Homeland security: IgA immunity at the frontiers of the body. Macpherson, AJ; Geuking, MB; McCoy, KD (2012) in: Trends Immunol, 33(4), p. 160-167.

The habitat, double life, citizenship, and forgetfulness of IgA. Macpherson, AJ; Geuking, MB; Slack, E; Hapfelmeier, S; McCoy, KD (2012) in: Immunol Rev, 245(1), p. 132-146.

Interactions between the microbiota and the immune system. Hooper, LV; Littman, DR; Macpherson, AJ (2012) in: Science, 336(6086), p. 1268-1273.



Haematology / Oncology (Paediatrics)

www.dkf.unibe.ch/research-group/16/

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

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

Research Highlights 2012 / Outlook 2013

We are involved in several projects aiming to identify molecular targets for the development of novel therapies for childhood cancer, with an emphasis on embryonal tumours (medulloblastoma, neuroblastoma) and leukaemia (ALL and AML). We are also involved in several clinical studies in paediatric cancer patients. A summary of the main studies of 2012 is presented below.

Laboratory Studies

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

We evaluated R1507, a humanised neutralising antibody against the insulin-like growth factor-1 receptor (IGF-1R), as an anti-proliferative agent in medulloblastoma and neuroblastoma. This study revealed that R1507 had single agent activity in only a limited number of medulloblastomas and neuroblastomas. However, R1507 could be combined with standard chemotherapeutic drugs such as cisplatin.

We evaluated novel pharmacological inhibitors of the class II phosphoinositide 3-kinase C2β (PI3KC2β), as anti-proliferative agents in acute leukaemia, glioblastoma, medulloblastoma and neuroblastoma. Over-expression of PI3KC2β could be documented in primary tumours at the mRNA and protein level. In addition, pharmacological inhibitors of PI3KC2β inhibited the proliferation and survival of cell lines from the above-mentioned cancers.

We identified a novel role for PI3KC2β in the regulation of the actin cytoskeleton and the activation of Rho family GTPases. A multi-protein complex involving the guanine nucleotide exchange factor Dbl, Grb2 and PI3KC2β was identified in various cell lines. This complex was shown to control several Rho-dependent processes, including actin stress fibre formation and protection from detachment-induced cell death (anoikis).

Clinical Studies

We prospectively investigate and monitor cognitive abilities in children with brain tumours and in children with malignancies that do not involve the CNS. Neuropsychological assessments are performed before and after medical intervention, as well as yearly follow-up exams. The studies also include implementation and evaluation of a cognitive training programme for affected children.

With the aim to improve supportive car in children with chemotherapy-induced fever in neutropaenia, a variety of prospective and retrospective clinical studies are being performed.

Group Members

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Paulina Cwiek, PhD Student
Valeriya Dimitrova, PhD Student
Katrin Höland, PhD Student (until Mar.)
Zaira Leni, PhD Student
Geetha Parakkal, PhD Student
Fabiana Salm, PhD Student (until May)
Anna Wojtalla, PhD Student (until May)

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Grants

Amounts allocated for 2012:

- European Commission: ASSET (A. Arcaro) CHF 240,000
- Beatrice Borer-Stiftung: Neuropsychologische Evaluation von Kindern mit Malignomen (K. Leibundgut) CHF 130,000
- Berner Stiftung für krebskranke Kinder und Jugendliche: (K. Leibundgut) CHF 238,340
- Novartis Foundation for medical-biological research: Identification of synthetic lethal interaction partners of Myc genes in medulloblastoma (A. Arcaro) CHF 60,000
- Stiftung für klinisch-experimentelle Tumorforschung: Identification and characterization of leukemia stem cells in pediatric acute lymphoblastic leukemia using a novel in vivo model (A. Arcaro, K. Leibundgut) CHF 67,000
- Stiftung zur Krebsbekämpfung: Novel molecular targets for medullo-blastoma in relation to c-Myc (A. Arcaro) CHF 10,000
- Swiss Paediatric Oncology Group: Klinische Forschung, Multizenterstudien (K. Leibundgut) CHF 41,086

Five Selected Publications

Phosphoinositide 3-kinase C2beta regulates RhoA and the actin cytoskeleton through an interaction with Dbl. Blajecka, K; Marinov, M; Leitner, L; Uth, K; Posern, G; Arcaro, A (2012) in: PLoS One, 7(9), p. e44945.

Targeting PI3KC2beta impairs proliferation and survival in acute leukemia, brain tumours and neuroendocrine tumours. Boller, D; Doepfner, KT; De, LA; Guerreiro, AS; Marinov, M; Shalaby, T; Depledge, P; Robson, A; Saghir, N; Hayakawa, M; Kaizawa, H; Koizumi, T; Ohishi, T; Fattet, S; Delattre, O; Schweri-Olac, A; Holand, K; Grotzer, MA; Frei, K; Spertini, O; Waterfield, MD; Arcaro, A (2012) in: Anticancer Res, 32(8), p. 3015-3027.

RNA interference screening identifies a novel role for autocrine fibroblast growth factor signaling in neuroblastoma chemoresistance. Salm, F; Cwiek, P; Ghosal, A; Lucia, BA; Largey, F; Wotzkow, C; Holand, K; Styp-Rekowska, B; Djonov, V; Zlobec, I; Bodmer, N; Gross, N; Westermann, F; Schafer, SC; Arcaro, A (2012) in: Oncogene.

Novel Agents Targeting the IGF-1R/PI3K Pathway Impair Cell Proliferation and Survival in Subsets of Medulloblastoma and Neuroblastoma. Wojtalla, A; Salm, F; Christiansen, DG; Cremona, T; Cwiek, P; Shalaby, T; Gross, N; Grotzer, MA; Arcaro, A (2012) in: PLoS One, 7(10), p. e47109.

Serious medical complications in children with cancer and fever in chemotherapy-induced neutropenia: results of the prospective multicenter SPOG 2003 FN study. Luthi, F; Leibundgut, K; Niggli, FK; Nadal, D; Aebi, C; Bodmer, N; Ammann, RA (2012) in: Pediatr Blood Cancer, 59(1), p. 90-95.

Hand Surgery

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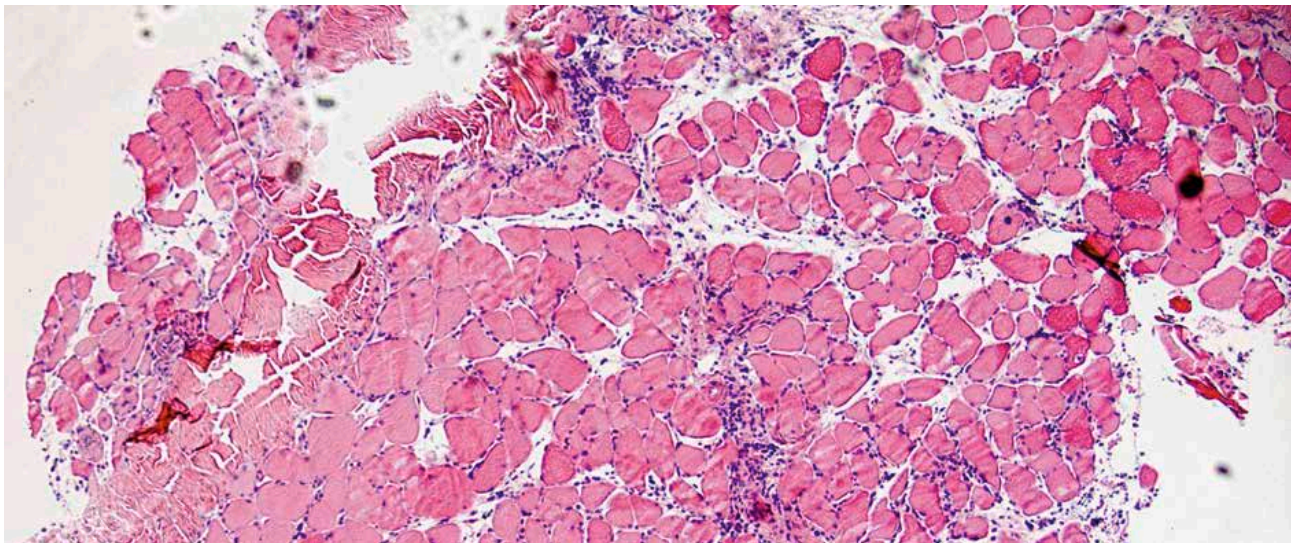
Studied medicine at University of Basel. Clinical training in plastic/reconstructive surgery at Mount Vernon Hospital, Northwood (UK) and The Wellington Hospital, London (UK). Research Fellow in hand and microsurgery at University of California, Los Angeles, (US). Since 2007, Physician-in-Chief and Co-Chair, Department of Plastic and Hand Surgery, Inselspital.

Research Highlights 2012 / Outlook 2013

The highly promising use of composite tissue allotransplantation (CTA), for example hand transplantation, as a reconstructive treatment has become a clinical reality. However, the major obstacle hindering the progress of CTA is the need for chronic immunosuppression. Thus, our current research focus is on discovery of novel strategies that can be used as a replacement for current immunosuppressive protocols. We aim at developing a local immunosuppressive drug delivery system. This might reduce concomitant systemic exposure of drugs, which may eventually curb drug-specific adverse effects, as well as increase bioavailability of the drugs in the allograft.

In collaboration with MIT in Boston (US), we have successfully developed a novel, biocompatible hydrogel system that allows for encapsulation of the immunosuppressive drug FK506 in therapeutic concentrations. Enzymes that are produced in the tissue during inflammatory conditions degrade the hydrogel and release FK506 in an on-demand manner to prevent rejection. In 2012, rat hind limb allotransplantations in a Brown Norway to Lewis model were performed to evaluate the therapeutic potential of FK506-laden hydrogel. These experiments showed that local, subcutaneous injection of the gel on day 1 post transplantation alone is sufficient to prevent rejection for at least 100 days. In 2013, these experiments will be continued and analyses performed with respect to drug release, immune responses, graft rejection and relevant molecular mechanisms. Furthermore, we are investigating other potential drug delivery systems/local immunosuppression that can be used in CTA.

Recently, an ex vivo system to perfuse amputated extremities with whole, anticoagulated blood was set up in collaboration with the Plastic Surgery group and the perfusionist's team/Cardiovascular Surgery group. This system was tested experimentally with pigs and is ready for clinical use to prolong the time to replantation for traumatically amputated extremities. In 2012, the system was used to perform experiments in the context of xenotransplantation, i.e., porcine limbs were perfused with human blood. This project is being carried out in collaboration with the Ludwig-Maximilian University of Munich (DE), Revivicor, Inc., Blacksburg (US), and the Department of Immunology and Allergology, Geneva University Hospital. Limbs of alpha-gal knockout pigs, which were further genetically modified by introduction of the human complement regulator CD46 and human HLA-E, were ex vivo perfused with human blood in order to test the effect of the different transgenes on xenorejection mediated by human preformed anti-pig antibodies, the complement system, and natural killer cells. So far, our data have revealed that, in contrast to solid organ perfusions, no hyperacute rejection occurs during leg perfusion. This is quite surprising and allows us to use this perfusion system to assess delayed rejection mechanisms, which are still a major barrier for pig-to-human xenotransplantation. In 2013, the experiments will be continued and further transgenes will be tested, with emphasis on the role of the coagulation system (human thrombomodulin transgene).



Group Members

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Prof. Dr. Robert Rieben, Head of Research
Dr. Bettina Juon, Consultant
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Dr. Thusitha Gajanayake, Postdoctoral Fellow

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Klymiuk N, Wolf E, Ludwig-Maximilian University of Munich, Germany
Seebach J, Geneva University Hospital, Switzerland
Vemula P, Harvard University, USA

Grants

Amounts allocated for 2012:

- SNF: Composite tissue preservation by extracorporeal blood perfusion and vascular cytoprotection to extend the time limit to replantation or transplantation (E. Vögelin, M. Constantinescu, R. Rieben) CHF 75,000
- American Foundation for Surgery of the Hand: A clinically relevant therapeutic approach to induce tolerance in composite tissue allotransplantation (E. Vögelin, T. Gajanayake, R. Rieben) USD 20,000
- Olga Mayenfisch Foundation: Implication of local immunosuppression in induction of donor-specific tolerance in composite tissue allotransplantation (T. Gajanayake, E. Vögelin, R. Rieben) CHF 20,000

Five Selected Publications

Assessment of endothelium and inflammatory response at the onset of reperfusion injury in hand surgery. Kamat, P; Juon, B; Jossen, B; Gajanayake, T; Rieben, R; Vogelin, E (2012) in: J Inflamm (Lond), 9(1), p. 18.

Evaluation of a porcine whole-limb heterotopic autotransplantation model. Kiermeir, DM; Meoli, M; Muller, S; Abderhalden, S; Vogelin, E; Constantinescu, MA (2012) in: Microsurgery.

Nonanimal stabilized hyaluronic Acid for tissue augmentation of the dorsal hands: a prospective study on 38 patients. Leclere, FM; Vogelin, E; Mordon, S; Alcolea, J; Urdiales, F; Unglaub, F; Trelles, M (2012) in: Aesthetic Plast Surg, 36(6), p. 1367-1375.

Ischemia/reperfusion injury of porcine limbs after extracorporeal perfusion. Muller, S; Constantinescu, MA; Kiermeir, DM; Gajanayake, T; Bongoni, AK; Vollbach, FH; Meoli, M; Plock, J; Jenni, H; Banic, A; Rieben, R; Vogelin, E (2012) in: J Surg Res.

Early versus delayed surgical treatment in open hand injuries: a paradigm revisited. Angly, B; Constantinescu, MA; Kreutziger, J; Juon, BH; Vogelin, E (2012) in: World J Surg, 36(4), p. 826-829.

Human Genetics

www.dkf.unibe.ch/research-group/12/human-genetics

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PhD in human genetics at University of Bern. Postdocs at Hammersmith Hospital and St. Mary's Hospital, London (UK), Boston Children's Hospital and FBI-Academy, Quantico (US). Specialist in Medical and Genetic Analysis (FAMH). Since 1994, DCR Group Leader. Associate Professor (1997). Since 2003, Head and Extraordinary Professor of Human Genetics, Department of Paediatrics, Inselspital.

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Medical studies at University of Jena (DE); MD (2005). Since 2010, Consultant in Human Genetics Department of Paediatrics, Inselspital.

Dr. André Schaller
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Studied biology at University of Bern; PhD (1999). Postdocs at Institute of Cell Biology, University of Bern, Infectious Disease and Oncology, University of Zurich Children's Hospital. Assistant at Division of Human Genetics, Inselspital. Research Fellow at Institute for Molecular and Cellular, CNRS (FR) (2006-2007). Since 2007, Senior Assistant, Division of Human Genetics, Department of Paediatrics, Inselspital.

Research Highlights 2012 / Outlook 2013

Cystic Fibrosis (CF)

One difficulty in diagnosis and therapy of CF, the most common lethal autosomal-recessive hereditary disorder in Caucasians, is the huge phenotypic variability observed, even in patients carrying the same CF transmembrane conductance regulator (CFTR) genotype. We aim to elucidate mechanisms for this phenotypic heterogeneity at the genomic and proteomic level. We were able to identify six sequence variants (SNPs) in four genes of the CFTR interactome that may modify disease severity. Moreover, generating proteome profiles from CF and non-CF primary nasal epithelial cell cultures, we detected differentially expressed proteins involved in oxidative stress, cytoskeletal organisation, polarisation, CFTR turnover and epithelial-to-mesenchymal transition. Thus, diverse pathways may modulate the phenotypic manifestation of CF. Future steps include investigation of influences of candidate gene variants on expression level, as well as confirmation of our proteomics findings by Western blot analyses and functional studies.

Epilepsy

Understanding the underlying molecular pathomechanisms of epilepsy, one of the most common disorders, affecting 2-4% of the general population, may have an impact on the choice of pharmacologic therapies. We introduced a targeted next generation sequencing (NGS) approach for molecular genetic diagnostics of epilepsy disorders and successfully applied this method in several dozen cases. In so doing, we revealed various, apparently rare, genetic diseases, which led to the suggestion that many orphan epilepsy entities might actually not be as rare as suggested in the literature. As a result of a broad international collaboration, we furthermore identified a main genetic predisposition factor for focal childhood epilepsy (e.g., Rolandic epilepsy). As part of the EuroEPINOMICS consortium, we collect and genotype patients with rare epilepsy syndromes. Ideally, our results will give insight into the genetic bases of many rare epilepsy disorders and even enable the development of novel therapeutic approaches.

Mitochondrial Diseases

A gene-panel for NGS was developed, allowing the simultaneous mutational analysis of approx. 1450 nuclear-encoded mitochondrial genes in patients with a mitochondrial disorder. After process optimisation and quality assurance, this analytical approach will be translated into routine diagnostics. In addition, we established a serial qPCR assay based on increasing amplicon size to measure degradation status of mtDNA samples. Using this approach, we can exclude erroneous mtDNA quantification due to degraded samples (e.g., long post-excision time, autolytic processes, freeze-thaw cycles) and ensure abnormal DNA content measurements (e.g., depletion) in non-degraded patient material. The third mitoNET Congress on Mitochondrial Medicine was successfully organised in Bern in July.

Group Members

Prof. Dr. Sabina Gallati, Head, Group Leader
Dr. Johannes Lemke, Group Leader
Dr. André Schaller, Group Leader
Dr. Franziska Joncourt, Research Assistant
Dr. Claudine Rieubland, Consultant
Daniela Dumke, Laboratory Technician (since July)
Ludmilla Lieder, Laboratory Technician (until Apr.)
Nadia Cassani, Secretary
Franziska Gisler, PhD Student
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Collaborators

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Prokisch H, University of Technology, Munich, Germany
Stanke F, Hannover Medical School, Germany, Swiss CF Screening Group, Switzerland
Syrbe S, University of Leipzig, Germany
Weckhuysen S, University of Antwerp, Belgium

Grants

Amounts allocated for 2012:

- SNF: Genetics of the Rare Epilepsies (J. Lemke) CHF 103,742
- Vinetum Foundation: Molecular diagnostic in children with mitochondrial disorders (A. Schaller) CHF 70,000
- Gottfried und Julia Bangerter-Rhyner Foundation: Mitochondriopathies; characterisation of molecular mechanisms (S. Gallati) CHF 80,000

Five Selected Publications

Retrospective analysis of stored dried blood spots from children with cystic fibrosis and matched controls to assess the performance of a proposed newborn screening protocol in Switzerland. Barben, J; Gallati, S; Fingerhut, R; Schoeni, MH; Baumgartner, MR; Torresani, T (2012) in: J Cyst Fibros, 11(4), p. 332-336.

Identification of SNPs in the cystic fibrosis interactome influencing pulmonary progression in cystic fibrosis. Gisler, FM; von, KT; Kraemer, R; Schaller, A; Gallati, S (2012) in: Eur J Hum Genet.

Duplication of the sodium channel gene cluster on 2q24 in children with early onset epilepsy. Goeggel, SB; Rieubland, C; Courage, C; Strozzi, S; Tschumi, S; Gallati, S; Lemke, JR (2012) in: Epilepsia, 53(12), p. 2128-2134.

qPCR-based mitochondrial DNA quantification: influence of template DNA fragmentation on accuracy. Jackson, CB; Gallati, S; Schaller, A (2012) in: Biochem Biophys Res Commun, 423(3), p. 441-447.

Targeted next generation sequencing as a diagnostic tool in epileptic disorders. Lemke, JR; Riesch, E; Scheurenbrand, T; Schubach, M; Wilhelm, C; Steiner, I; Hansen, J; Courage, C; Gallati, S; Burki, S; Strozzi, S; Simonetti, BG; Grunt, S; Steinlin, M; Alber, M; Wolff, M; Klopstock, T; Prott, EC; Lorenz, R; Spaich, C; Rona, S; Lakshminarasimhan, M; Kroll, J; Dorn, T; Kramer, G; Synofzik, M; Becker, F; Weber, YG; Lerche, H; Bohm, D; Biskup, S (2012) in: Epilepsia, 53(8), p. 1387-1398.

Magnetic Resonance Spectroscopy and Methodology, AMSM

www.amsm.dkf.unibe.ch

Research Highlights 2012 / Outlook 2013

Our research is based on methodological developments and applications of magnetic resonance imaging (MRI) and/or spectroscopy (MRS) in humans. The non-invasive observation of morphology and metabolism of the human body allows us to study physiology and pathology, together with the underlying mechanisms, in situ. Three SNF grants with PIs in our group and five SNF grants in collaboration with other groups define the direction of our research.

Insulin resistance is one major area, which is also the "glue" for many collaborations with internal (endocrinology, diabetology, hepatology) and external (Lausanne (CH), Pittsburgh (US), Lyon (FR), Tübingen (DE)) groups. Since insulin resistance is a major cause of cardiovascular diseases such as stroke and myocardial infarction, better understanding of this phenomenon will help us to prevent these acute diseases. We study effects of chronic or acute exercise and different kinds of carbohydrates, lipids, and amino acids on muscle and liver metabolism. In addition, volumes of body compartments, in particular visceral lipids, have been determined. One PhD student and an MD student finished their theses on these topics in 2012.

"Magnetic Resonance Techniques to Investigate Human Brain Physiology" is a second SNF grant that aims at the development of MR methods that are tailored to the observation of brain metabolism, yet are also transferable to other organs. In collaboration with the University of Zurich, exchange processes between amide protons and water were first observed in human brain and were then extended to skeletal muscle. One PhD student defended her thesis on this topic in 2012.

A third SNF project deals with the application of MRI and MRS to investigate native and transplanted kidneys. Transplanted kidneys were studied in the donors and recipients using multiple MR techniques such as diffusion-weighted and oxygen-dependent MRI. In collaborations with ARTORG groups, image post processing was developed to deal with motion-related problems of the MR acquisition.

Since MR spectra in vivo have a limited spectral resolution, high-resolution magic angle spinning (HR-MAS) techniques are currently being developed in order to correlate spectra of tissue in vivo and vitro.

A large multi-centre study on whiplash-patients was completed some years ago and is now leading to a series of publications. One major paper reports the difficulty of four experienced readers to find objective MRI-signs within 48 hours after a whiplash trauma.

In 2013, three PhD students will defend their theses and will be, or have already been, replaced by a new generation of students, including one in a co-authored European project starting in 2013. Our intervention studies with exercise and diet require flexible booking of MR systems. Fortunately, the Inselspital has increased the number of MR systems such that the growing number of studies, as well as increasing demands for training new PhD students, can be accommodated.

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

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

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Studied chemistry at University of Münster (DE); PhD in physical chemistry with Prof. Müller-Warmuth. Postdoc (1995-1996), DFG Fellow (1996-1998), Assistant Specialist at University of California, San Francisco (US) (1998-2000). At University of Bern since 1999, Habilitation (2008).

Group Members

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Karin Zwygart-Brügger, Technician
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Andreas Boss, PhD Student
Vaclav Brandejsky, PhD Student
Tania Buehler, PhD Student (until Apr.)
Gaëlle Diserens, PhD Student (since Aug.)
Sila Dokumaci, PhD Student (since Mar.)
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Scheurer E, Ludwig Boltzmann Institute, Austria
Schick F, Machann J, University of Tübingen, Germany
Stellingwerff T, Canadian Sport Centre Pacific, Canada
Strik W, Dierks T, University Hospital of Psychiatry, Bern, Switzerland
Sturzenegger M, Inselspital, Switzerland
Tappy L, Amati F, University of Lausanne, Switzerland
Zimmermann H, Inselspital, Switzerland
Zysset P, Reyes M, University of Bern, Switzerland

Grants

Amounts allocated for 2012:

- SNF: Multi-nuclear magnetic resonance spectroscopy (MRS) and imaging (MRI) on a clinical whole-body MR-system: insulin resistance, ageing, and physical activity (C. Boesch) CHF 103,860
- SNF: Magnetic Resonance Techniques to Investigate Human Brain Physiology: Acquisition and Post-processing Tools to Advance Spectroscopy at Clinical and High Magnetic Fields (R. Kreis) CHF 90,174
- SNF: Advanced multi-modal MR Imaging and Spectroscopy for Comprehensive Characterization of Renal Function in Native and Transplanted Kidneys (P. Vermathen) CHF 60,240

Five Selected Publications

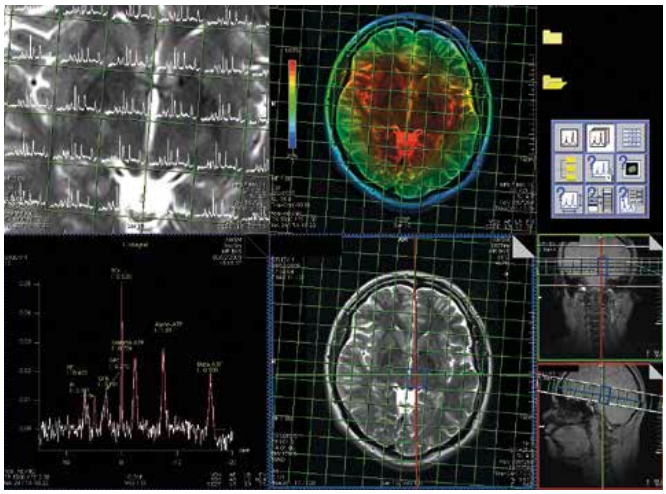
Skeletal muscle (1)H MRSI before and after prolonged exercise. II. visibility of free carnitine. Boss, A; Kreis, R; Saillen, P; Zehnder, M; Boesch, C; Vermathen, P (2012) in: Magn Reson Med, 68(5), p. 1368-1375.

Restricted or severely hindered diffusion of intramyocellular lipids in human skeletal muscle shown by in vivo proton MR spectroscopy. Brandejsky, V; Kreis, R; Boesch, C (2012) in: Magn Reson Med, 67(2), p. 310-316.

Magnetic resonance imaging based determination of body compartments with the versatile, interactive sparse sampling (VISS) method. Buehler, T; Ramseier, N; Machann, J; Schwenzer, NF; Boesch, C (2012) in: J Magn Reson Imaging, 36(4), p. 951-960.

Effect of two beta-alanine dosing protocols on muscle carnosine synthesis and washout. Stellingwerff, T; Anwander, H; Egger, A; Buehler, T; Kreis, R; Decombaz, J; Boesch, C (2012) in: Amino Acids, 42(6), p. 2461-2472.

Skeletal muscle (1)H MRSI before and after prolonged exercise. I. muscle specific depletion of intramyocellular lipids. Vermathen, P; Saillen, P; Boss, A; Zehnder, M; Boesch, C (2012) in: Magn Reson Med, 68(5), p. 1357-1367.



Neurology

www.neuro-bern.ch

Research Highlights 2012 / Outlook 2013

The Department of Neurology has a long-standing research tradition, and with the election of Prof. Bassetti as the new head of the department in 2012, clinical and translational research were both strengthened.

Our groups focus on the following main research areas:
- Bassetti Group – sleep and stroke in humans and animals
- Kaelin Group – movement and motor disorders in humans and animals
- Mattle Group – stroke and multiple sclerosis in humans
- Müri Group – cognitive neurology, neurorehabilitation, eye perception/ neuro-ophthalmology, gerontechnology and rehabilitation in humans

In 2012, a total of 12 SNF projects were running in our department and the following research positions were financed: 500% MD, 1,200% PhD (two-thirds in clinical and one-third in animal research), 800% study nurses, and 50% study coordinator/biostatistician.

Current developmental efforts (2012-2013) include the creation of:
- a new laboratory for animal research (Zentrum für experimentelle Neurologie; ZEN)
- a platform for conducting clinical studies (Neuroklinisches Studienzentrum; NKSZ)
- a multidisciplinary, multicenter research group on the topic of epilepsy, sleep and consciousness
- new positions for residents interested in research (50% clinical-50% research appointments)

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

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

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

Prof. Dr. René Müri
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MD at University of Bern (1984); 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; Head, Unit of Cognitive and Restorative Neurology, Department of Neurology, Inselspital. Associate Professor of Neurology (2008).

Group Members

Prof. Dr. Claudio L. Bassetti, Chair, Group Leader
Prof. Dr. Johannes Mathis, Senior Consultant
Dr. Heidemarie Gast, Consultant
PD Dr. Arto Nirko, Consultant
PD Dr. Kaspar Schindler, Consultant
Dr. Corinne Roth, Research Associate
Dr. Thomas Horvath, Research Assistant
Dr. Sarah Schroth, Research Assistant
Dr. Francesca Baracchi, Postdoctoral Fellow
Dr. Ertugrul Cam, Postdoctoral Fellow
Dr. Bo Gao, Postdoctoral Fellow
Dr. Svitlana Palchykova, Postdoctoral Fellow
Dr. Frédéric Zubler, Postdoctoral Fellow
Aleksandra Hodor, PhD Student
Maria Pace, PhD Student

Prof. Dr. Alain Kaelin, Group Leader
Prof. Dr. Kai Rösler, Senior Consultant
Prof. Dr. Matthias Sturzenegger, Senior Consultant
Dr. Niklaus Meier, Consultant
Dr. Michael Schüpbach, Consultant
Prof. Dr. Jean-Marc Burgunder, External Consultant
Dr. Christine Capper-Loup, Postdoctoral Fellow
Susanne Sgroi, PhD Student

Prof. Dr. Heinrich Mattle, Vice-Chair, Group Leader
Prof. Dr. Marcel Arnold, Senior Consultant
Prof. Dr. Werner Z'Graggen, Senior Consultant
Dr. Oliver Findling, Consultant
PD Dr. Urs Fischer, Consultant
Dr. Aikaterini Galimanis, Consultant
Dr. Simon Jung, Consultant
Dr. Christian Kamm, Consultant
Dr. Marie-Louise Mono, Consultant

Prof. Dr. René Müri, Group Leader
PD Dr. Klemens Gutbrod, Senior Researcher
Dr. Manuel Bertschi, Postdoctoral Fellow
Tobia Brusa, Dipl. Ing.
Diego De Leon Rodriguez, PhD Student
Noëmi Eggenberger, PhD Student
Susanna Hopfner, PhD Student
Matthias Lüthy, PhD Student
Basil Preisig, PhD Student
Rahel Schumacher, PhD Student
Tim Vanbellingen, PhD Student

Selected Collaborators

Annoni J-M, University of Fribourg, Switzerland
Baumann C, Luft A, University Hospital Zurich, Switzerland
Bloch J, CHUV Lausanne, Switzerland
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Mormannn F, University Clinic of Epileptology Bonn, Germany
Mosimann UP, Nef T, University of Bern, Switzerland
Nedeltchev K, Remonda L, Khatami R, Cantonal Hospital Aarau, Switzerland
Nobili L, Niguarda Hospital Ca' Granda, Italy
Nyffeler T, Bohlhalter S, Lucerne Cantonal Hospital, Switzerland
Ptak R, University of Geneva, Switzerland
Raabe A, Beck J, Pollo C, Inselspital, Switzerland
Schroth G, Gralla J, Wiest R, Inselspital, Switzerland
Thaler D, Kent D, Tufts Medical Center, USA

Grants

Amounts allocated for 2012:
SNF-financed projects only

- Sleep apnea and stroke, human (C. Bassetti) CHF 100,000
- Restless leg and cardiovascular risk, human/animal (M. Manconi, C. Bassetti) CHF 50,000
- Fatigue in autommune diseases, animal (A. Fontana, H. Gast) CHF 50,000
- Imaging large scale neuronal networks in epilepsy, human (M. Seeck, K. Schindler) CHF 115,000
- PFO Konsortium, human (M. Mono) CHF 17,000
- Cerebral perfusion, vasospasm, subarachnoid hemorrhage, human (J. Beck, W. Z'Graggen) CHF 120,000
- Aphasia and co-speech gestures, human (R. Müri) CHF 146,000
- Bilingualism, human (J.-M. Annoni, R. Müri) CHF 100,000
- Motion and spatial neglect, human (T. Nyffeler, R. Müri) CHF 108,000
- Neural basis of praxis production, human (S. Bohlhalter, R. Müri) CHF 110,000
- Enhancement of sensory processing by attention, human (R. Ptak, R. Müri) CHF 110,000
- Etiology, diagnosis, treatment of cervicocerebral artery dissections, human (M. Arnold) CHF 650,000 (special programme university medicine)

Five Selected Publications

Theta burst stimulation reduces disability during the activities of daily living in spatial neglect. Cazzoli, D et al. (2012) in: Brain, 135, p. 3426-3439.

Sleep deprivation prior to stroke increases sleep rebound and attenuated brain lesions in the rat. Cam, E et al. in: Exp Neurol (in press).

On seeing the trees and the forest: single-signal and multisignal analysis of periictal intracranial EEG. Schindler, K et al. (2012) in: Epilepsia, 53, p. 1658-1668.

Adverse effect of early epileptic seizures in patients receiving endovascular therapy for acute stroke. Jung, S et al. (2012) in: Stroke, 43, p. 1584-1590.

Adaptive gene expression changes on the healthy side of parkinsonian rats. Capper-Loup, C et al. in: Neuroscience 2012 (in press).

Perception and Eye Movement

www.eyelab.dkf.unibe.ch

Research Highlights 2012 / Outlook 2013

In 2012, we obtained a new SNF grant (PhD student: S. Hopfner) for a project that aims to study the conditions under which motion may modulate visual hemineglect. Motion is omnipresent in daily live, and from clinical observations we know that moving objects may improve or deteriorate neglect. One goal is to find out the characteristics of the patients who improve by motion stimuli. We hope this will be a new approach for the rehabilitation of neglect.

We have an SNF project (PhD student: D. de León Rodríguez) concerning bilingualism and reading strategies in collaboration with the University of Fribourg. It investigates linguistic and individual factors in bilingual language processing, since reading strategies are dependent not only on reading proficiency but also on language characteristics. We especially aim to test whether there are different patterns of reading between the first (L1) and second (L2) languages. Specifically, we will test equally proficient, as well as low proficient, bilingual subjects mastering an opaque language (like French or English) and a transparent one (like German and Italian).

The SNF project (PhD students: N. Eggenberger, B. Preisig) concerning aphasia and co-speech gestures started well. One goal of the project is to study the close interaction between language and co-speech gestures in healthy subjects and patients with aphasia, with special focus on the perception of co-speech gestures. It is not clear whether aphasic patients are able to use such additional non-verbal information. To this end, we perform complex behavioural analysis by coding speech and gestures in time during conversations between two people (facing page, left image). In addition, we analyse fixation behaviour (facing page, right image: circles represent fixations; the diameter indicates fixation duration). For 2013, we plan to extend this project by studying cultural influences on the perception of co-speech gestures (financed by a CCLM grant). In this project, we will examine the influence of different L1 on gesture production and gesture perception.

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MD at University of Basel (1985); neurology residency in Bern/Lausanne, FMH certification (1992). Research fellowships in neurophysiology, Institute of Physiology, Basel and sleep medicine, University of Michigan, Ann Arbor (US). Venia docendi (1997). Professor, 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.

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

MD at University of Zurich (1994). Chief, Division for Restorative and Behavioral Neurology, Lucerne Cantonal Hospital; PD in neurology at University of Bern. President, Swiss Parkinson Association Research Committee and Advisory Panel.

Prof. Dr. René Müri
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MD at University of Bern (1984); 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; Head, Unit of Cognitive and Restorative Neurology, Department of Neurology, Inselspital. Associate Professor of Neurology (2008).

PD Dr. Thomas Nyffeler
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MD at University of Bern (1995); neurology residency in Geneva, Zurich, Bern, and Paris (FR). PD at University of Bern (2009). Joined Perception and Eye Movement Laboratory in 2002. Senior Consultant, Division for Cognitive and Restorative Neurology, Inselspital (2007). Since summer 2012, Co-Chief, Division for Restorative and Behavioral Neurology, Lucerne Cantonal Hospital.

Group Members

Prof. Dr. Claudio L. Bassetti, Chair, Group Leader
PD Dr. Stephan Bohlhalter, Group Leader
Prof. Dr. René Müri, Group Leader
PD Dr. Thomas Nyffeler, Group Leader
Dr. Manuel Bertschi, Postdoctoral Fellow
Tobia Brusa, Dipl. Ing.
Diego de León Rodríguez, PhD Student
Noëmi Eggenberger, PhD Student
Simone Hopfner, PhD Student
Mathias Lüthi, PhD Student
Basil Preisig, PhD Student (since June)
Rahel Schumacher, PhD Student
Tim Vanbellingen, PhD Student

Collaborators

Annoni J-M, University of Fribourg, Switzerland
Mosimann UP, University of Bern, Switzerland
Nef T, University of Bern, Switzerland
Ptak R, University of Geneva, Switzerland

Grants

Amounts allocated for 2012:

- SNF: Neural basis of praxis production – From higher-order processing to fine motor control (S. Bohlhalter) CHF 110,000
- SNF: Aphasia and co-speech gestures (R. Müri) CHF 146,000
- SNF: Bilingualism (J.-M. Annoni) CHF 100,000
- SNF: Motion and spatial neglect (T. Nyffeler) CHF 108,000
- SNF: Enhancement of sensory processing by attention: cognitive, electrophysiological, and neuropsychological studies (R. Ptak) CHF 110,000
- Ernst Göhner Foundation: Transcranial Magnetic Stimulation in Neurorehabilitation (R. Müri) CHF 80,000
- Center for Cognition, Learning, and Memory, University of Bern: Gesture and Culture – transcultural differences in co-speech gesture perception (R. Müri) CHF 50,000

Five Selected Publications

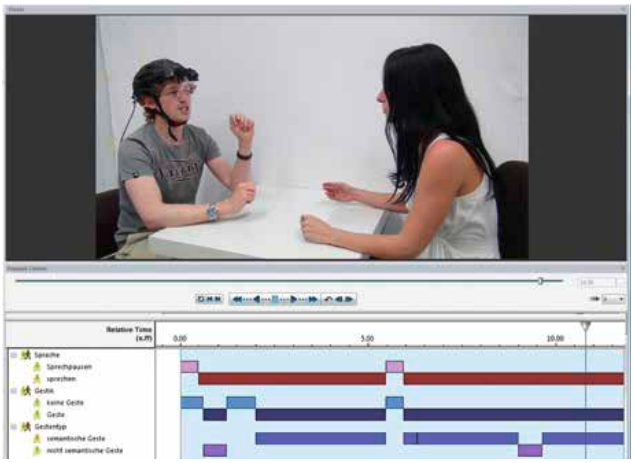
Theta burst stimulation reduces disability during the activities of daily living in spatial neglect. Cazzoli, D; Muri, RM; Schumacher, R; von, AS; Chaves, S; Gutbrod, K; Bohlhalter, S; Bauer, D; Vanbellingen, T; Bertschi, M; Kipfer, S; Rosenthal, CR; Kennard, C; Bassetti, CL; Nyffeler, T (2012) in: Brain, 135(Pt 11), p. 3426-3439.

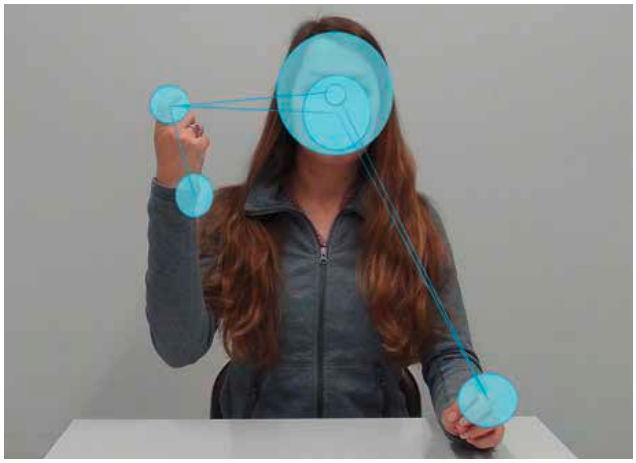
Theta burst stimulation over the right Broca's homologue induces improvement of naming in aphasic patients. Kindler, J; Schumacher, R; Cazzoli, D; Gutbrod, K; Koenig, M; Nyffeler, T; Dierks, T; Muri, RM (2012) in: Stroke, 43(8), p. 2175-2179.

Dancing eyes and uvula after brain tumour extirpation—a sign of tumour progression? Kipfer, S; Pirovino, C; El-Koussy, M; Nyffeler, T; Lukes, A; Muri, RM (2012) in: Lancet, 379(9830), p. 1983.

Unmasking the contribution of low-level features to the guidance of attention. Ossandon, JP; Onat, S; Cazzoli, D; Nyffeler, T; Muri, R; Konig, P (2012) in: Neuropsychologia, 50(14), p. 3478-3487.

Impaired pantomime in schizophrenia: Association with frontal lobe function. Walther, S; Vanbellingen, T; Muri, R; Strik, W; Bohlhalter, S (2012) in: Cortex.





Prenatal Medicine

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

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

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

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

Research Highlights 2012 / Outlook 2013

Our research focuses on two major translational research fields:

Stem Cell Research

Premature birth is a major cause of neonatal morbidity and mortality. Cerebral palsy with its severe, lifelong disability typically arises from oligodendrocyte damage leading to periventricular leukomalacia. Our major research focus is on the development of stem cell transplantation strategies for neuroregeneration in peripartum brain damage due to hypoxia or preterm birth. We assessed the developmental plasticity of umbilical cord tissue-derived mesenchymal stem cells (MSC), and were recently able to show that differentiation of these cells into neural cell lines, including oligodendrocyte precursors is feasible. This property, together with their immunomodulatory effects, makes these cells the ideal candidate for stem cell grafts in peripartum brain damage. To determine the effect and the mechanism of stem cell-mediated neuroregeneration, we use a rat model of peripartum brain damage. Subcutaneous administration of *E. coli*-derived lipopolysaccharides followed by left carotid artery defined hypoxia (8% O_2, 40 min) was performed on early postnatal rats. Different therapeutic approaches were chosen, including MSC transplantation with or without neurotrophic growth factors. In brain sections, the induced damage and the transplant are identified and evaluated by immunohistochemistry. Functional outcome was evaluated by different tests such as footprint and walking pattern test. Donor cells were detected in the brain post transplantation. Morphologic assessment of the induced brain damage indicated periventricular leukomalacia. Administration of stem cells alone and in combination with erythropoietin reduced the extent of the damage. Functional tests indicate a significant reduction of spastic paresis.

Preeclampsia Research

This research project is part of the large NCCR TransCure in Bern (PI: Prof. Matthias Hediger). Foetal programming in preeclampsia leads to cardiovascular and metabolic diseases in offsprings later in life. This phenomenon and its prevention is a major focus of our project. We aim to determine the role of specific transmembrane transporters (Glut1/3, Glut9, OAT4, TRPV6, SVCT2 and DMT1) in the placenta and in the pathway of preeclampsia. In particular, we make use of vesicle and transwell experiments, in vitro placental perfusion experiments and transgenic mouse models to validate target transporters. In further experiments in collaboration with chemists and structural biologists, we are testing potential compounds and their effects on preeclampsia pathogenesis and foetal programming.

Group Members

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

Collaborators

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NCCR TransCure, Research groups, Universities of Bern and Lausanne, ETH Zurich, Switzerland
Paidas M, Yale University, USA
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Platform for Stem Cell Research and Regenerative Medicine, University of Bern and VetSuisse, Switzerland
Villiger P, Förger F, University of Bern, Switzerland
Widmer HR, University of Bern, Switzerland

Grants

Amounts allocated for 2012:

- SNF: NCCR TransCure (D. Surbek, M. Baumann) CHF 204,000
- SNF: Systemic vascular function in offsprings of preeclampsia (Y. Allemann, L. Raio) CHF 120,000
- Cryo-Save: Umbilical cord stem cells for neuroregeneration (D. Surbek, M. Messerli) CHF 50,000
- Eagle Foundation: Perinatal stem cell transplantation for brain injury (D. Surbek, A. Schoeberlein) CHF 100,000
- Ruth & Arthur Scherbarth Stiftung: Perinatal stem cell transplantation (A. Schoeberlein) CHF 20,000

Five Selected Publications

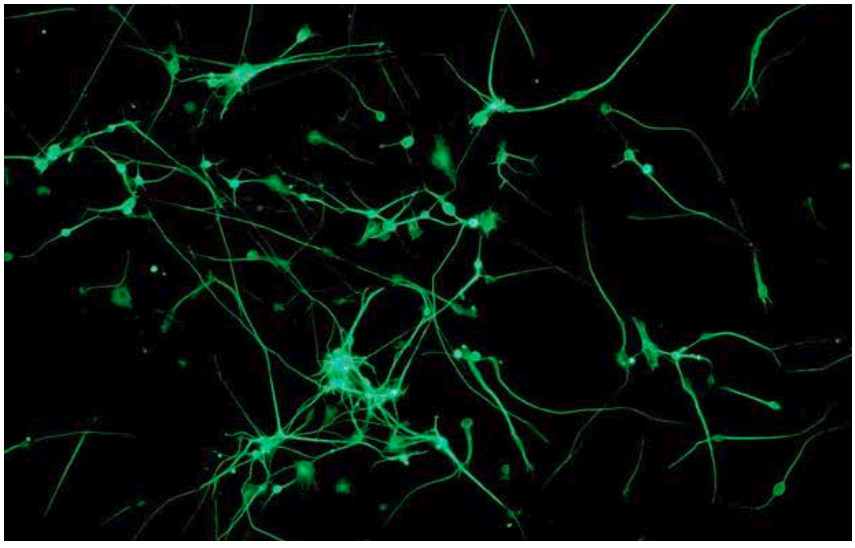
17beta-Estradiol Protects 7-Day Old Rats From Acute Brain Injury and Reduces the Number of Apoptotic Cells. Mueller, MM; Middelanis, J; Meier, C; Surbek, D; Berger, R (2012) in: Reprod Sci. (Aug 8 e-pub ahead of print)

Homing of placenta-derived mesenchymal stem cells after perinatal intracerebral transplantation in a rat model. Schoeberlein, A; Mueller, M; Reinhart, U; Sager, R; Messerli, M; Surbek, DV (2011) in: Am J Obstet Gynecol, 205(3), p. 277 e1-6.

Stress and pain response of neonates after spontaneous birth and vacuum-assisted and cesarean delivery. Schuller, C; Kanel, N; Muller, O; Kind, AB; Tinner, EM; Hosli, I; Zimmermann, R; Surbek, D (2012) in: Am J Obstet Gynecol, 207(5), 416 e1-6.

High acceptance rate of hybrid allogeneic-autologous umbilical cord blood banking among actual and potential Swiss donors. Wagner, AM; Krenger, W; Suter, E; Ben, HD; Surbek, DV (2012) in: Transfusion (Oct 15 ahead of print).

Stem cells from umbilical cord Wharton's jelly from preterm birth have neuroglial differentiation potential. Messerli, M; Wagner, A; Sager, R; Mueller, M; Baumann, M; Surbek, DV; Schoeberlein, A. in: Reprod Sci 2012 (in press)



Thoracic Surgery

www.dkf.unibe.ch/research-group/50/thoracic-surgery/

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

Research Highlights 2012 / Outlook 2013

Frese Group

We are interested in how lung cancer cells can be sensitised for receptor-mediated apoptosis. We found different pathways for sensitisation and are currently working on elucidating mechanisms. We are also investigating how immune cells and cytokines of the tumour necrosis factor family influence the growth of chemically induced lung cancer. By coincidence, we recently discovered that the topoisomerase I inhibitor irinotecan (known for its use in chemotherapy of metastatic cancer) is able to efficiently suppress the autoimmune disease systemic lupus erythematosus in mice. Further studies revealed that doses necessary for the suppression are much lower than doses used for chemotherapy. These observations led to the planning of a pilot study in collaboration with the Departments of Nephrology and Hypertension, and Medical Oncology (Inselspital), using low-dose irinotecan in patients with active lupus nephritis refractory to conventional treatment. If financial support can be secured, initiation of the study is planned for the beginning of 2013.

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

Marti and Peng Group

We investigate endogenous lung stem cells in health and disease. In healthy lung, we have identified resident lung stromal stem cells, which can potentially be used as a therapeutic cell source for end-stage lung disease such as emphysema. In collaboration with the Theodor Kocher Institute (University of Bern), we will extend this project to elucidate the role of stem cells in resolving or promoting lung repair. In diseased lung, e.g., lung adenocarcinoma and pleural mesothelioma, we identified cancer stem cells and showed that lung cancer stem cells are resistant to conventional chemotherapeutic drugs. Paradoxically, a common feature of cancer stem cells is the dysregulation of the DNA damage response pathway, which orchestrates DNA damage repair/tolerance, cell cycle progression and DNA replication. We are currently evaluating DNA damage levels and the status of the DNA damage response machinery in putative lung cancer stem cells. Our aim is to target these cells based on their specific alterations of the DNA damage response pathway. In addition, we investigate the dysfunction of the endocytic trafficking machinery, which is linked to asymmetric cell division, a known feature of cancer stem cells.

Dr. Thomas M. Marti
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PhD in biology at University of Bern. Postdoc at UCSF Comprehensive Cancer Center (US) (2003-2006). Principal investigator at Laboratory of Molecular Oncology, University Hospital Zurich (2006-2012). Since 2012, Group Leader, Department of Thoracic Surgery, DCR.

Dr. Renwang Peng
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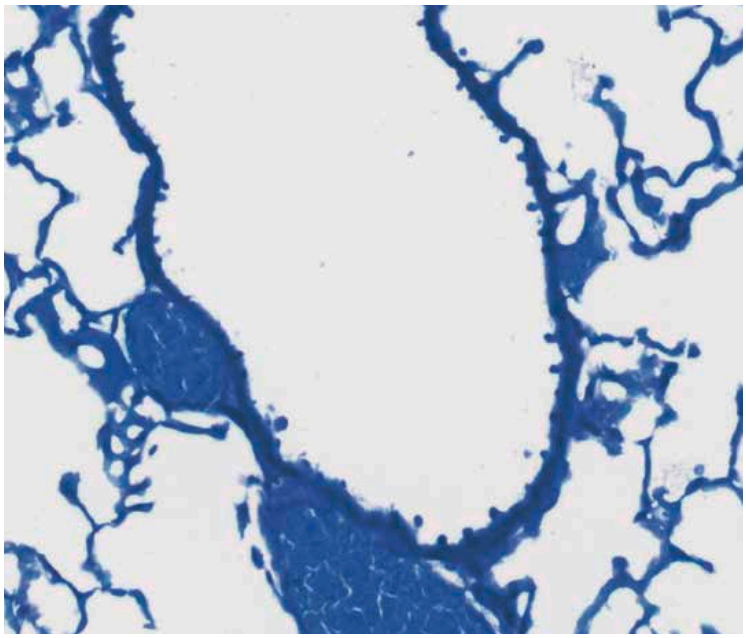
PhD in biochemistry at Chinese Academy of Sciences, Beijing (CN). Scholarship from Max Planck Society (DE) and visiting scholar at Dartmouth Medical School (US). Group Leader at ETH Zurich (2006-2010). Since 2012, Group Leader, Department of Thoracic Surgery, DCR.



Group Members

Prof. Dr. Ralph A. Schmid, Chair
PD Dr. Steffen Frese, Group Leader
Dr. Thomas M. Marti, Group Leader
Dr. Renwang Peng, Group Leader
Dr. Manuela Frese-Schaper, Postdoctoral Fellow
Laurent Fromment, Laboratory Technician
Selina Steiner, Laboratory Technician
Dr. med. Gregor Kocher, Clinical Fellow
Andreas Keil, PhD Student (since Aug.)

Collaborators

Benarafa C, University of Bern, Switzerland
Galetta D, European Institute of Oncology, Italy
Guenat O, University of Bern, Switzerland
Gugger M, University of Bern, Switzerland
Hideo Y, Juntendo University School of Medicine, Japan
Huynh-Do U, Inselspital, Switzerland
Diamond B, Feinstein Institute for Medical Research, USA
Ochsenbein A, Inselspital, Switzerland

Grants

Amounts allocated for 2012:

- SNF: Inhibition of topoisomerase I: a new strategy for the treatment of systemic lupus erythematosus (S. Frese) CHF 104,265
- Albert Böni Foundation: Inhibition of topoisomerase I: a new strategy for the treatment of systemic lupus erythematosus (S. Frese), CHF 13,300
- Bernese Foundation for Clinical and Experimental Cancer Research: Zelluläre Mechanismen der Sensitivierung von Lungenkrebszellen für Rezeptor (TRAIL) vermittelten programmierten Zelltod (S. Frese) CHF 104,742

Five Selected Publications

High expression of octamer-binding transcription factor 4A, prominin-1 and aldehyde dehydrogenase strongly indicates involvement in the initiation of lung adenocarcinoma resulting in shorter disease-free intervals. Cortes-Dericks, L; Galetta, D; Spaggiari, L; Schmid, RA; Karoubi, G (2012) in: Eur J Cardiothorac Surg, 41(6), p. e173-e181.

Long term survival after trimodal therapy in malignant pleural mesothelioma. Fahrner, R; Ochsenbein, A; Schmid, RA; Carboni, GL (2012) in: Swiss Med Wkly, 142, p. w13686.

Diffuse descending necrotizing mediastinitis: surgical therapy and outcome in a single-centre series. Kocher, GJ; Hoksch, B; Caversaccio, M; Wiegand, J; Schmid, RA (2012) in: Eur J Cardiothorac Surg, 42(4), p. e66-e72.

1,25-Dihydroxycholecalciferol with low-calcium diet reduces acute rejection in rat lung allotransplantation. Kubisa, B; Stammberger, U; Gugger, M; Uduehi, AN; Grodzki, T; Schmid, RA (2012) in: Eur J Cardiothorac Surg, 42(5), p. 871-877.

Weight gain after lung reduction surgery is related to improved lung function and ventilatory efficiency. Kim, V; Kretschman, DM; Sternberg, AL; DeCamp, MM, Jr.; Criner, GJ (2012) in: Am J Respir Crit Care Med, 186(11), p. 1109-1116.

Urology

www.dkf.unibe.ch/research-group/26/urology

Prof. Dr. George N. Thalmann
george.thalmann@insel.ch

MD (1984), trained in surgery and urology. Postdoc in USA at MD Anderson Cancer Center (1994-1996). Urology Consultant (1996), Fellow of European Board of Urology (1997), Habilitation (2000). Senior Physician (1996-2000), Senior Attending and Deputy Physician-in-Chief (2000-2005), Physician-in-Chief "ad personam" (2005-2010). Since 2010, Chair, Department of Urology, Inselspital.

Dr. Marco G. Cecchini
marco.cecchini@dkf.unibe.ch

MD (1979); physician in internal medicine/endocrinology at Padua University (IT) (1979-1982). Postdoc at Wander Research Institute, Bern (1982-1983). Research Associate at Institute of Pathophysiology, University of Bern (1984-1993, 1994-1997). Associate Professor at Beth Israel Hospital, Boston (US) (1993-1994). Head, Gene Therapy Laboratory, DCR (1997-2001). Since 2002, Head, Urology Research Laboratory, DCR.

PD Dr. Katia Monastyrskaya
katia.monastyrskaia@dkf.unibe.ch

BSc and MSc in molecular biology, Moscow State University (RU). DPhil in Biochemistry, Wadham College, University of Oxford (UK). Postdoc at NERC Institute of Virology, Oxford (UK). Senior Scientist at Hoffmann-La Roche/Givaudan, Switzerland. Since 2001, Senior Research Associate, Habilitation (2007) at University of Bern. Since 2011, Group Leader, Urology Research Laboratory, DCR.

Research Highlights 2012 / Outlook 2013

The highlights of our research in 2012 concern our projects on:

Metastatic Disease in Prostate Cancer (PCa)

We demonstrated that growth of human PCa can be driven by multiple, stem-like progenitor cells with a differentiated phenotype rather than by a single, stem-like cell with undifferentiated phenotype. We identified aldehyde dehydrogenase 1A1 (ALDH1A1) and NANOG as markers of these stem-like cells, which may be potentially useful as prognostic markers in PCa patients.

A circulating tumour cell (CTC)-capture microfluidic chip was developed and validated. This device allows immunoaffinity-capture and subsequent direct in situ culture of CTCs in a 3D biomimetic hydrogel matrix for assaying their clonal, spheroid growth potential.

We defined the whole transcriptome associated with the stromal reaction in mouse models of either osteoblastic or osteolytic bone metastases. We also identified a family of proteins, induced in the stroma of osteolytic bone metastasis, with an unprecedented activity in stimulating osteoclast generation and consequent bone resorption.

For 2013, we plan to investigate the value of ALDH1A1 and NANOG as prognostic markers in a large cohort of PCa tissue samples. Within the frame of the "Global Prostate Cancer Biomarker Initiative", recently initiated by the Movember Foundation, expression of a stem cell marker set in CTCs from blood samples of early PCa patients will be validated as a method to stratify patients as "indolent" or "aggressive" PCa. The bioinformatics analysis of differentially regulated genes in the stroma of osteoblastic and osteolytic bone metastases will be further refined, and the functional role of highly regulated, novel genes from these lists will be investigated.

Bladder Pain Syndrome (BPS)

BPS is a painful and debilitating condition characterised by urgency, frequency and incomplete emptying. Its aetiology is not yet known, but impairment of the mucinous layer and epithelial damage has often been invoked.

In earlier studies, we demonstrated that BPS is accompanied by a significant alteration of the mRNA and protein levels of several signalling and structural proteins involved in pain perception, regulation of urothelial integrity and neurogenic inflammation.

Our group was the first to implicate miRNAs in bladder remodelling during lower urinary tract diseases. Last year, we started a comparative investigation of mRNAs and miRNAs altered in BPS and overactive and acontractile bladders, addressing the role of differentially expressed miRNAs in the regulation of genes important for bladder function. Our experimental approach combines analysis of human biopsy material with in vitro models. The clinical part of this project is in collaboration with Fiona Burkhard (Department of Urology).

We validated some of the differentially expressed miRNAs as regulators of tachykinin receptors. Using cell-based models, we have recently established the role of miR-199a-5p in the regulation of urothelial permeability.

For 2013, we plan to characterise additional disease-induced miRNAs, validate their target genes and silence their expression levels.

Group Members

Prof. Dr. George N. Thalmann, Chair, Group Leader
Dr. Marco G. Cecchini, Head of Laboratory, Group Leader
PD Dr. Katia Monastyrskaya, Group Leader
Ursula Gerber, Laboratory Technician
Irena Klima, Laboratory Technician
Ali Hashemi Gheinani, PhD Student
Janine Hensel, PhD Student

Collaborators

Bubendorf L, University Hospital Basel, Switzerland
Draeger A, University of Bern, Switzerland
Grewal T, University of Sydney, Australia
Kellenberger S, University of Lausanne, Switzerland
Lutolf MP, EPF Lausanne, Switzerland
Mills I, University of Oslo, Norway
Sanchez-Freire V, Stanford University, USA
Temanni M-R, University of Maryland, USA
Van der Plujm G, Leiden University Medical Centre, The Netherlands
Williams ED, Monash University, Australia

Grants

Amounts allocated for 2012:

- SNF: The role of microRNAs in organ remodelling in lower urinary tract dysfunction (K. Monastyrskaya) CHF 120,960
- SNF: Detection and targeting of lymph node metastases in prostate cancer (G. Thalmann) CHF 105,000
- European Commission: Prostate Research Organizations-Network of Early Stage Training (Pro-Nest) (G. Thalmann) EUR 80,000
- Amgen Switzerland: Dual targeting of the BMP antagonist noggin and RANK/RANKL axis in osteolytic bone metastasis by solid cancers (M. Cecchini) CHF 23,000
- Bernese Cancer League: Electro-physiological assessment of the male canine pelvic autonomic neural anatomy and translation to the perioperative human setting in the context of nerve-sparing radical cystectomy (P. Zehnder) CHF 40,000
- Bernese Cancer League: Molecular profiling of treatment naïve primary urothelial bladder cancers and correlation with response to neoadjuvant chemotherapy (R. Seiler) CHF 50,000

Five Selected Publications

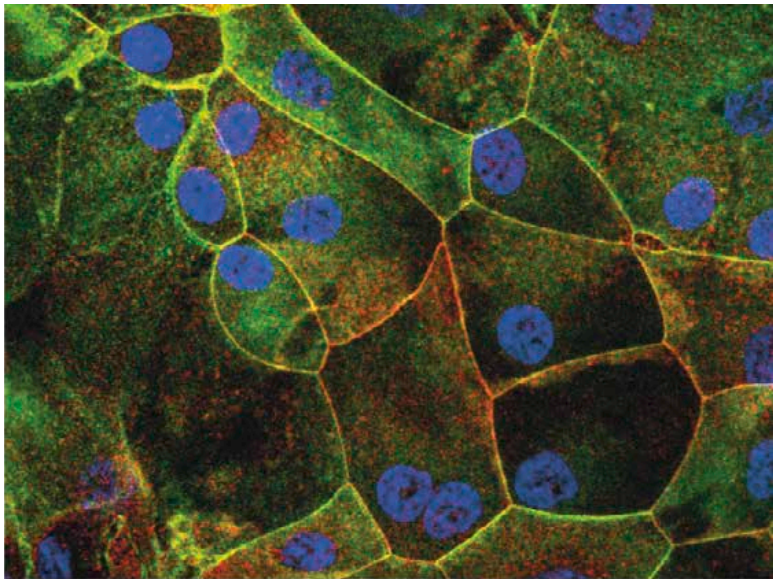
Diagnostic microchip to assay 3D colony-growth potential of captured circulating tumor cells. Bichsel, CA; Gobaa, S; Kobel, S; Secondini, C; Thalmann, GN; Cecchini, MG; Lutolf, MP (2012) in: Lab Chip, 12(13), p. 2313-2316.

Increased expression of putative cancer stem cell markers in primary prostate cancer is associated with progression of bone metastases. Colombel, M; Eaton, CL; Hamdy, F; Ricci, E; van der Pluijm, G; Cecchini, M; Mege-Lechevallier, F; Clezardin, P; Thalmann, G (2012) in: Prostate, 72(7), p. 713-720.

Stem-like cells with luminal progenitor phenotype survive castration in human prostate cancer. Germann, M; Wetterwald, A; Guzman-Ramirez, N; van der Pluijm, G; Culig, Z; Cecchini, MG; Williams, ED; Thalmann, GN (2012) in: Stem Cells, 30(6), p. 1076-1086.

Annexin A6 is a scaffold for PKCalpha to promote EGFR inactivation. Koese, M; Rentero, C; Kota, BP; Hoque, M; Cairns, R; Wood, P; Vila de, MS; Reverter, M; Alvarez-Guaita, A; Monastyrskaya, K; Hughes, WE; Swarbrick, A; Tebar, F; Daly, RJ; Enrich, C; Grewal, T (2012) in: Oncogene.

miR-199a-5p Regulates Urothelial Permeability and May Play a Role in Bladder Pain Syndrome. Monastyrskaya, K; Sanchez-Freire, V; Gheinani, AH; Klumpp, DJ; Babiychuk, EB; Draeger, A; Burkhard, FC (2012) in: Am J Pathol.



Key Events

Welcome Event 2012
30 May

Around 60 interested DCR newcomers attended this event, which in the future will take place yearly. The Welcome Event for 2013 will be held 29 May (4-6 pm).

Day of Clinical Research 2012
13-14 Nov. 2012

A large and interested audience followed the presentations of **Prof. Dr. Ada Yonath** (Structural Biology Department, Weizmann Institute of Science, Rehovot, Israel) entitled "Can structures lead to better antibiotics?" and **Prof. Dr. William Pralong** (Life Sciences and Technologies Teaching Section, EPF Lausanne) entitled "Can the ETH domain take an active role in the training of physician scientists?"

Six candidates applied for the Research Prize 2012 (funded by the DCR and the Johanna Dürmüller-Bol Foundation) and 170 abstracts were submitted for DKF Poster Prizes and the Alumni MedBern Prize. The winners were (left to right in photo below): Alumni MedBern Prize – **Janine Ruppen** (ARTORG Center); best patient-oriented project – **Dr. Spyridon Arampatzis** (Department of Nephrology and Hypertension and Department of Emergency Medicine, Inselspital); Research Prize – **Dr. Henriette Brinks** (Department of Cardiovascular Surgery, Inselspital and Cardiovascular Surgery, DCR); best laboratory-oriented project – **Christopher Jackson** (Human Genetics, DCR); best project by a medical student – **Anna Lena Fuchs** (Department of Neurosurgery, Inselspital).

The next Day of Clinical Research will be held 5-6 November 2013.

DKF Research Conferences 2012

With an average of 60 visitors each month, the DKF Research Conferences continue to be very successful. In 2012, we were pleased to present the following speakers:

6 Feb. – Prof. Dr. Yoshihiro Fujimura
Nara Medical University, Kashihara City, Japan
ADAMTS13: Clinical relevance in chronic liver disease and novel insights into the localization in the brain.

5 Mar. – Prof. Dr. Vincent Mooser
CHUV, Lausanne, Switzerland
Genetics in pharmaceutical sciences: Human as the next animal model.

2 Apr. – Prof. Dr. Marguerite Neerman-Arbez
University of Geneva, Switzerland
Modelling fibrinogen deficiency in the zebra fish.

7 May – Prof. Dr. Joseph D. Brain
Harvard School of Public Health, Boston, USA
When are metals essential nutrients? When therapeutic? When toxic?

4 June – Dr. Dusko Ilic
King's College London, UK
Human embryonic stem cell research – where are we now?

2 July – Prof. Dr. Benjamin Podbilewicz
Technion – Israel Institute of Technology, Haifa, Israel
Mechanisms of neuronal tree generation and regeneration following nano-surgery.

3 Sep. – Prof. Dr. Tim Arnett
University College London, UK
Bone cell regulation – don't forget the fundamentals.

1 Oct. – Prof. Dr. Tea Lanišnik Rižner
University of Ljubljana, Slovenia
Progesterone in proliferative diseases: a friend or a foe?

5. Nov. – Prof. Dr. David R. Goodlett
University of Washington, Seattle, USA
The conundrum of proteomic technology development: approaches to a 24 hour proteome for clinical investigations.

3. Dec. – Prof. Dr. Rudi GJ Westendorp
Leiden University Medical Centre and Leyden Academy on Vitality and Ageing, Leiden, The Netherlands
Control of human lifespan.

In 2013, DKF Research Conferences will take place as usual every first Monday of the month from 5-6 pm, followed by an apéro.

Personnel Update

Academic Degrees

The following academic degrees where awarded to DCR group members:

Full Professor

Prof. Dr. Claudio L. Bassetti
Neurology, and Perception and Eye Movement

Prof. Dr. Bruno Vogt
Nephrology and Hypertension

Prof. Dr. Roland von Känel
Psychosomatic Medicine

Professor

Prof. Dr. Nicolas Regamey
Pulmonary Medicine (Paediatrics)

Associate Professor

Prof. Dr. Nicolas Alexander Diehm
Angiology

Prof. Dr. Daniel Inderbitzin
Visceral and Transplantation Surgery

Prof. Dr. Alain Kaelin
Neurology

Assistant Professor

Prof. Dr. Kathy McCoy
Gastroenterology / Mucosal Immunology

Lecturer (Privatdozent)

PD Dr. Daniel Aeberli
Rheumatology

PD Dr. Malte Book
Anaesthesiology

PD Dr. Florian Michael Dick
Cardiovascular Surgery

PD Dr. Siamak Djafarzadeh
Intensive Medicine

PD Dr. Philipp Latzin
Pulmonary Medicine (Paediatrics)

PD Dr. Semmo Nasser
Hepatology

PD Dr. Jean-Marc Nuoffer
Endocrinology / Diabetology / Metabolism (Paediatrics)

PD Dr. Andreas Pasch
Nephrology and Hypertension

PD Dr. Tobias Traupe
Cardiology

PhD

(supervisors in brackets)

Deepak Haresh Balani
(Prof. Dr. Michael Seitz, Prof. Dr. Willy Hofstetter)
Role of inflammatory cytokines in osteoclast development

Pomme Boissier
(Prof. Dr. Uyen Huynh-Do)
Endocytic regulation and targeting of EphA2 in pancreatic cancer

Tania Buehler
(Prof. Dr. Chris Boesch)
Development and application of magnetic resonance spectroscopy methods in studies on insulin resistance and metabolism of human liver and skeletal muscle

Polychronis Dimitrakis
(Dr. Christian Zuppinger)
Potential cardiotoxicity of targeted cancer therapy

Elena Alessandra Federzoni
(PD Dr. Mario P. Tschan)
Novel transcriptional targets of PU.1 involved in myeloid differentiation and cell survival

Nadine Graubardt
(Prof. Dr. Guido Beldi)
Impact of extracellular nucleotides on NK cell function and differentiation during liver regeneration

Anne Géraldine Guex
(PD Dr. Marie-Noëlle Giraud-Flück)
Design and functionalization of electrospun substrates for muscle repair

Magali Humbert
(PD Dr. Mario P. Tschan)
Role and Regulation of Krüppel-like factor 5 (KLF5) and death-associated protein kinase 2 (DAPK2) in differentiation of acute myeloid leukemia blasts

Melissa Agnes Eve Lawson
(Prof. Dr. Andrew J. Macpherson, Prof. Dr. Kathy McCoy)
The two-way interactions between commensal intestinal bacteria and the mammalian host

Daniel Lienhard
(Prof. Dr. Brigitte Frey)
High salt intake down-regulates colonic 11b-HSD2, mineralocorticoid receptors and epithelial sodium channels

Erin Leigh MacMillan
(Prof. Dr. Roland Kreis)
Application of metabolite cycled non-water-suppressed magnetic resonance spectroscopy, and measurement of magnetization transfer between water and

metabolites, in the human brain, spinal cord, and skeletal muscles at 3 T and 7 T

Sarah Mans
(Prof. Dr. Thomas Pabst)
The role of extracellular calreticulin in acute myeloid leukemia (AML)

Stéphane Rodriguez
(Prof. Dr. Uyen Huynh-Do)
Eph receptors in health and disease states

Madhusudanarao Vuda
(Prof. Dr. Stephan Jakob)
Mitochondrial function in sepsis: Effects of vasoactive support and analgo-sedation

MD

(supervisor in brackets)

Florian Aelle
(Prof. Dr. Anne-Catherine Andres)
Immunhistochemische Untersuchung von Lokalisierung und Differenzierungsgrad der Brustepithel-Stammzellen während der Entwicklung

Samuel Jakob Küchler
(Prof. Dr. Anne-Catherine Andres)
Immunhistochemische Strukturanalyse der murinen Brustdrüsen-Outgrowths von Ephrin-B2 und EphB4-modifizierten Zellen

Mischa Mosimann
(Prof. Dr. Anne-Catherine Andres)
Die Gefässdichte in experimentellen metastasierenden und nicht-metastasierenden Brustkarzinomen

Angelica Ramseier
(PD Dr. Gian-Marco Sarra)
Characterisation of retinal stem cells and evidence of C-Met expression

MD PhD

(supervisors in brackets)

Maria Luisa Balmer
(Prof. Dr. Andrew J. Macpherson)
Immune pathology and physiology of commensal bacterial containment

Vanessa Banz Wüthrich
(PD Dr. Deborah Stroka)
CXCR3 and CCR6 mediate recruitment and positioning of Th17 cells in the inflamed liver

Oliver Peter Fuchs
(Prof. Dr. Urs Frey, Prof. Dr. Claudia Kuehni)
The impact of genes and environment on respiratory disease in infants and children

Elisabeth Kieninger
(Prof. Dr. Nicolas Regamey)
Clinical impact and pathophysiology of viral inflections and early lung disease in cystic fibrosis

Berna Özdemir
(Prof. Dr. George Thalmann)
The stroma reaction in osteoblastic bone metastases of prostate cancer – Cancer cells reinvent the wheel

Christoph Schlapbach
(PD Dr. Robert Hunger)
Telomerase-specific GV1001 peptide vaccination in patients with cutaneous T cell lymphoma

Christian Martijn Schürch
(Prof. Dr. Adrian Ochsenbein)
Immune surveillance of cancer stem cells in chronic myeloid leukemia

Awards

The following DCR group members received awards in 2012:

Dr. Chiara Abbas
Pulmonary Medicine (Paediatrics)
Award of the Young Researchers in Paediatrics, Swiss Society of Paediatrics Annual Meeting: "A new lung function test to assess early lung disease and treatment effects in CF"

Dr. Mohamed Yassine Amarouch
Ion Channels and Channelopathies
Poster Award of the European Society of Cardiology Working Group on Cardiac Cellular Electrophysiology

Dr. Henriette Brinks
Cardiovascular Surgery
Research Prize 2012: "Ventricular unloading combined with inotropic gene therapy in the failing heart"

Claudia Dührkop
Cardiovascular Research
Poster Award (3rd prize), Pharmaceutical Society of Zurich: "C1 esterase inhibitor treatment in skeletal muscle ischemia/reperfusion injury"

PD Dr. Volker Enzmann
Ophthalmology
Euretina Poster Competition 2012 (1st Prize), 2nd Euretina Winter Meeting: "Bone marrow-derived stem cell transplantation in a Mouse Model of retinal degeneration"

Dr. Markus Geuking
Gastroenterology / Mucosal Immunology
Dr. Lutz Zwillenberg Prize 2012: "Intestinal bacterial colonization induces mutualistic regulatory T cell responses"

Anne Géraldine Guex
Cardiovascular Surgery
CSF-Award for best contribution, 7th International Ascona Workshop on Cardiomyocyte Biology: "Functionalised Scaffolds for myocardial VEGF delivery"

Prof. Dr. Ernst B. Hunziker
Orthopaedic Surgery
Marshall R. Urist Award for Excellence in Tissue Regeneration Research

Christopher Jackson
Human Genetics
DKF Poster Prize for best laboratory-oriented project

Prof. Dr. Stephan Jakob, Prof. Dr. Jukka Takala
Intensive Medicine
Prize for best clinical publication, Swiss Society of Intensive Care Medicine: "Dexmedetomidine vs midazolam or propofol for sedation during prolonged mechanical ventilation: two randomized controlled trials."

Prof. Dr. Roland Kreis
Magnetic Resonance Spectroscopy and Methodology, AMSM
Fellow of the European Society of Magnetic Resonance in Medicine and Biology

Cédric Laedermann
Ion Channels and Channelopathies
Young Investigator Award (2nd prize),

Oetliker Foundation for Physiology: "Ubiquitin ligase Nedd4-2 modulates peripheral sensory voltage-gated sodium channels and contributes to neuropathic pain"

Prof. Dr. Kathy McCoy
Gastroenterology / Mucosal Immunology
European Research Council Starting Grant Award

Dr. Martin Müller
Prenatal Medicine
Bayer-Schering Prize for best scientific work in gynaecology: "Early intracranial mesenchymal stem cell therapy after perinatal rat brain damage"

Dr. Emrush Rexhaj
Cardiology
Postdoctoral Novel Disease Model Award, American Physiological Society Experimental Biology 2012 Meeting; 2012 Faculty Prize for doctoral thesis, Faculty of Biology and Medicine, University of Lausanne

PD Dr. Andreas Schoenenberger
Geriatrics / Medicine of Ageing
Best Abstract Prize, Swiss Society of Cardiology: Risk factors, hypertension, rehabilitation, thromboembolism: "Invasive findings in patients with angina equivalent symptoms but no coronary artery disease; results from the heart quest cohort study"

Prof. Dr. Anton Sculean
Dental Research
IADR-/Straumann Award in Regenerative Periodontal Medicine 2012

Diana Shy
Ion Channels and Channelopathies
Poster Prize, 2012 EUTrigTreat General Assembly

Dr. Florian Singer
Pulmonary Medicine (Paediatrics)
Poster Prize, German Society for Paediatric Pneumology Annual Meeting: "Ist eine effiziente Messung des Lung Clearence Index in der Routine CF Ambulanz möglich?"

Christian Tinner, Dr. Regula von Allmen, PD Dr. Florian Dick, Prof. Dr. Jürg Schmidli, Prof. Dr. Hendrik Tevaearai
Cardiovascular Surgery
Best Communication SSVS, 13th Annual Meeting, Union of Vascular Societies of Switzerland: "Improved assessment of follow-up in the context of observation studies efficacy results of a randomised controlled investigation"

PD Dr. Martin A. Walter
Nuclear Medicine
EANM Eckert & Ziegler Abstract Award, European Society of Nuclear Medicine Annual Meeting

Staff Changes

New Staff

Dr. Marco Alves
PhD (100%), Pulmonary Medicine (Paediatrics) (since May)

Louis Amport
DCR Secretary (10%), Administration (since Aug.)

Dr. Fabian Blank
Head (40%), Live Cell Imaging (LCI) (since Mar.)

Dr. Julia Cahenzli
Research Assistant (100%), Gastroenterology / Mucosal Immunology (since Sep.)

Basak Ginsbourger
DCR Administrator (100%), Administration (since Nov.)

Michael Jäger
Doctoral Student (100%), Psychiatry (since Jan.)

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

Dr. Melissa Lawson
Research Assistant (100%), Gastroenterology / Mucosal Immunology (since Apr.)

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

Thomas Späti
IT-Support (60%), Administration (since July)

Resignations

Steven Balestra
IT-Support (30%), Administration (until Mar.)

Larissa Bettler
Laboratory Technician (30%), Osteoporosis Densitometry DOPH (until Mar.)

Dr. Christine Capper Loup
Research Assistant (15%), Neurology (until Mar.); transfer to Inselspital

Franziska Gisler
Doctoral Student (50%), Human Genetics (until Dec.); transfer to Inselspital

Monika Graf
Laboratory Technician (50%), Pulmonary Medicine (Paediatrics) (until Dec.); transfer to Inselspital

Gaby Hofer
Laboratory Technician (80%), Endocrinology / Diabetology / Metabolism (Paediatrics) (until Dec.); transfer to Inselspital

Irena Klima
Laboratory Technician (60%), Urology (until Feb.); transfer to Inselspital

Véronique Kretschmer
DCR Administrator (80%), Administration (until Feb.)

Therese Lauterburg
Laboratory Technician (80%), Neurology (until Mar.)

Hai Li
PhD (100%), Gastroenterology / Mucosal Immunology (until Dec.)

Ludmilla Lieder
Laboratory Technician (80%), Human Genetics (until Apr.)

Ida Schiess
Laboratory Technician (80%), Osteoporosis Densitometry DOPH (until Dec.); transfer to Inselspital

Sabine Schneider
Laboratory Technician (50%), Cytometry Laboratory / FACSlab (until Mar.)

Jan Stohler
IT-Support (40%), Administration (until June)

Dr. Stefan Wyder
Research Assistant (90%), Molecular Biology, and Genomics (until Oct.)

Short Employment (<12 months)

Dr. Francesca Baracchi
Research Assistant (50%), Neurology (Apr.-Oct.)

Dr. Reto Bertolini
PhD (60%), Nephrology and Hypertension (Jan.-Dec.)

Gaby Bloem
DCR Administrator (90%), Administration (Mar.-Sep.)

Anjan Bongoni
Doctoral Student (100%), Cardiovascular Research (Aug.-Dec.)

Pomme Boissier
Doctoral Student (100%), Nephrology and Hypertension (June-Sep.)

Dr. Bo Gao Brunner
Research Assistant (50%), Neurology (Feb.-May)

Julie Denojelle
Laboratory Technician (80%), Cardiovascular Research (July-Dec.)

Claudia Dürkop
Doctoral Student (100%), Cardiovascular Research (July-Dec.)

Janine Hensel
Doctoral Student (100%), Urology (Dec.)

Aleksandra Hodor
Doctoral Student (100%), Neurology (July-Dec.)

Anne-Laure Huguenin
Laboratory Technician (60%), Oncology / Haematology (Adults) (Sep.-Dec.)

Kwet Choy Kwong Chung Cheong
Doctoral Student (100%), Gastroenterology / Mucosal Immunology (Dec.)

Berna Oezdemir
Doctoral Student (100%), Urology (July-Sep.)

Dr. Carsten Riether
PhD (100%), Tumor-Immunology (Jan.-Mar.)

Jennifer Leona Scheffler
Laboratory Technician (20%) Tumour-Immunology (Feb.-Aug.)

Dr. Martina Schobesberger
Laboratory Technician (40%), Neurology (May-Dec.)

Dr. Nahoko Shintani
Research Assistant (75%), Osteoporosis Densitometry DOPH (Dec.)

Nathalie Vielle
Doctoral Student (100%), Pulmonary Medicine (Paediatrics) (Apr.-June)

Véronique Vocat
Doctoral Student (100%), Molecular Biology (Oct.-Dec.)

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