

# NewsLetter DKF

Dezember 2010

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Dachterrasse MEM 01.12.2010

**Schöne Festtage und alles Gute im 2011!**

# The NCCR TransCure network: new perspectives towards the treatment of human diseases

*Transport proteins and ion channels play a critical role for proper functioning of the human body. Embedded in the membranes of cells and organelles, they control the flow of sugars, vitamins, trace elements, among other substances vital for the body. Many of these membrane proteins are implicated in major chronic diseases. The objectives of the new NCCR "TransCure" are to investigate the pathophysiological roles of selected membrane proteins and to correct dysfunction with specific chemical compounds.*

Cancer, osteoporosis, neurodegenerative disorders and heart diseases impact modern society in that they cause immense human suffering at immeasurable costs. Such chronic diseases are of complex nature and their understanding remains a supreme effort of the millennium. Progresses in biomedical research have revealed that such diseases are often the consequence of dysfunctional membrane transport proteins and ion channels. As gatekeepers, they are controlling the flow of vital substances across the cell membrane. The National Center of Competence in Research (NCCR) TransCure - a joint research project that was recently funded by the Swiss National Science Foundation (SNSF) – wishes to validate medically relevant transport proteins as potential drug targets and to develop novel medications that cure diseases, prevent their progression, or alleviate their symptoms.

## **From genes to drugs**

The aim of the NCCR TransCure is two-fold: (1) to develop new insights into the pathological effects caused by functionally impaired transport proteins and ion channels, and (2) to generate novel medications that target these membrane proteins. To achieve these goals, clinicians, biologists and chemists from 20 national laboratories located in Basel, Bern, Lausanne and Zurich commit themselves to work together. The leading house is the Institute of Biochemistry and Molecular Medicine at the University of Bern with Matthias A. Hediger as the director, and Jean-Louis Reymond, Department of Chemistry and Biochemistry, University of Bern, as the deputy director.

The elucidation of the molecular structure and the biological function of strategically important transport proteins are milestones on the TransCure-avenue. This is primarily the task of physiologists and structural biologists. The chemists, on the other hand, are spearheading the search for chemical compounds that modulate functionally impaired transporters in a favorable way. Finally, pharmacologists are concerned about the evaluation of newly discovered compounds *in vitro* and *in vivo* with respect to their potential as therapeutic drugs. Identified compounds will also prove helpful in providing more detailed insights into the pathophysiological role of transport proteins. Once chemical compounds are found that exhibit a therapeutic effect, NCCR TransCure seeks collaborations with industry partners to further develop and facilitate the commercialization of therapeutic "lead compounds". Thus, the NCCR TransCure brings together scientists with different expertise, a prerequisite for moving all the way "from genes to drugs".

## **Why are transport proteins so important?**

Membrane transporters and ion channels control the uptake and efflux of vital substances such as sugars, vitamins, trace elements, signal molecules and drugs. They make up about 10% of the human genome and can be categorized according to their diverse mechanisms of transport: ion coupled transporters (co-transporters), facilitated transporters, exchangers, ion channels, water channels, pumps, ABC transporters, gap junction proteins, and others. For example, ion channels are critical for the heart's function, as they control the electrical excitations that are responsible for the heart beating. Blocked ion channels are also responsible for the Long QT syndrome, an abnormality of the heart's electrical system. While the mechanical function of the heart is entirely normal, this condition may cause sudden cardiac death. Another condition, preeclampsia, in which hypertension arises in pregnancy, may be triggered by dysfunctional placental transport systems. Neurological diseases, such as epilepsy, schizophrenia, Alzheimer's, Parkinson's, and Huntington's disease, are all linked to an imbalance in the uptake of neurotransmitters into cells and synaptic vesicles. This imbalance is known to be, at least in part, caused by the dysfunction of transport proteins specific for neurotransmitters. Thus, membrane transporters and channels represent an immense pharmaceutical wealth. Targeting these proteins has been rather ignored, thus far, by the pharmaceutical industry due to their structural complexity and hydrophobic nature. This is in contrast to the still prevailing pharmaceutical focus on kinases, G-protein coupled receptors (GPCRs) and other elements of signal transduction. Many of these regulatory proteins are by now well characterized and established targets for which drugs have been developed. For example, up to 50% of currently marketed drugs target GPCRs.

### Next generation biomedical scientists

In addition to the multifaceted research focus of the NCCR TransCure, this network is committed to promoting young scientists and to supporting them in their scientific career. The goal is to enable the efficient training of translational and interdisciplinary-oriented young researchers – the next generation of biomedical scientists. All PhD students and post-doctoral fellows who are involved in the different TransCure projects will join an educational training program (“summer school”) which is being organized by the NCCR TransCure. The training will offer theoretical and practical expertise in translational research. The focus lies on (1) methodologies for the study of the role of membrane proteins in human diseases, and (2) the application of modern drug discovery technologies to identify new medications. Moreover, the NCCR TransCure is organizing courses and scientific events dealing with the interdisciplinary research activities of the network, in order to give young scientists the opportunity to get in contact with researchers from related disciplines.

### NCCR TransCure Network

The NCCR “TransCure – From Transport Physiology to Identification of Therapeutic Targets” seeks to integrate the disciplines of medicine, biology and chemistry to develop new therapeutic strategies for treating major human diseases.

**Leading House:** University of Bern, Institute of Biochemistry and Molecular Medicine (IBMM)

**Finances:** 14'155'000 CHF (Contribution SNF 2010 – 2013)

**Start Date:** November 1, 2010

**Director:** Prof. Matthias A. Hediger, Institute of Biochemistry and Molecular Medicine, University of Bern

**Deputy Director:** Jean-Louis Reymond, Department of Chemistry and Biochemistry, University of Bern

**Number of Principal Investigators:** 23

**Number of Projects:** 20

### NCCR TransCure Directorate

#### Prof. Matthias A. Hediger, Director

Matthias Hediger has identified and characterized various transport proteins, including transporters of metal ions, vitamins, amino acids and neurotransmitters, and has investigated their physiological implications in human diseases. He has obtained patent protection on several commercially important transporters and has completed numerous corporate-sponsored research projects with international pharmaceutical companies. His premise is that integration of medicine, biology and chemistry is necessary in order to accelerate the translational avenue “from genes to drugs”. The name “TransCure” is composed of two terms: “Cure” which stands for curing diseases, and “Trans” which describes three important aspects of the network; transport proteins, translational science and transfer of knowledge.

#### Prof. Jean-Louis Reymond, Deputy Director

During his scientific career, Jean-Louis Reymond has designed fluorescent probes for enzymes to serve research in biocatalysis, which concerns the use of enzymes as clean and environmentally friendly catalysts for chemical manufacturing. His group developed assay systems for important enzyme classes such as lipases and proteases addressing selectivity problems. Many of Reymond’s assays have become part of the standard arsenal of enzyme screening methods. Since 2002 his group has entered the field of combinatorial peptide chemistry. For the NCCR TransCure, Reymond and his coworkers are pursuing a number of small molecule drug discovery projects by exploiting virtual screening schemes for searching very large compound databases.

## TransCure Principal Investigators and Projects

| Principal Investigator(s)   | Project Title  |
|---|--|
| Matthias Hediger (IBMM, University of Bern)   | Structure, Function and Pharmacology of the Epithelial Calcium Channel TRPV6                                       |
| Ernst Niggli (Physiology, University of Bern)   | Function, Pharmacology and Pathophysiology of TRPC1 Channels   |
| Hugues Abriel and Manfred Heller (DKF, University of Bern)  | Physiology, Pharmacology and Pathophysiology of the Calcium-Activated Non-Selective Cation TRPM4 Channel           |
| Willy Hofstetter (DKF, University of Bern)  | Role of Ion Transporter TRPV6 and Other Transporters in Bone Homeostasis   |
| Henning Stahlberg (Biozentrum Basel)  | Structural Biology of Transporters and Channels of Therapeutic Interest  |
| Daniel Fuster (Division of Nephrology and Hypertension, Inselspital Bern)                           | Sodium/Hydrogen Exchangers and their Involvement in the Pathogenesis of Hypertension and Diabetes Mellitus         |
| Daniel Ackermann (Division of Nephrology and Hypertension, Inselspital Bern)                        | Immunohistochemical Studies of Transporter of Therapeutic Interest   |
| Raimund Dutzler (Biochemistry Institute, University of Zurich)                                      | Structure, Function and Pharmacology of Chloride Channels Metal Ion Transporters                                   |
| Pascale Anderle (IBMM, University of Bern)  | Transporters and Channels in Cancer Therapy  |
| Andrea Volterra and Paola Bezzi (Department of Cell Biology and Morphology, University of Lausanne) | Vesicular Transporters in the Treatment of Neurological Diseases   |
| Dimitrios Fotiadis (IBMM, University of Bern)   | Structure and Pharmacology of Molecular Transport Mechanisms of Vitamin C and Nucleobase Transporters              |
| Bernard Thorens (Center for Integrative Genomics, University of Lausanne)                           | Glucose, Myo-Inositol and Urate Transporters: From Heart Metabolism to Gout and Mood Disorders                     |
| Daniel Surbek and Marc Baumann (Department of Obstetrics and Gynecology, Inselspital Bern)          | Placental Nutrient Transporters and Their Role in Pregnancy-Related Disorders                                      |
| Jean-Louis Reymond (Department of Chemistry and Biochemistry, University of Bern)                   | Rational Drug Design for Transporters and Channels   |
| Karl-Heinz Altmann (Institute of Pharmaceutical Sciences, ETH Zurich)                               | Ligand Development for Vesicular Monoamine Transporters  |
| Martin Lochner (Department of Chemistry and Biochemistry, University of Bern)                       | Development of Selective Fluorescence- and Photoaffinity - Labeled Ligands for Glutamate Transporters and Channels |
| Jürg Gertsch (IBMM, University of Bern)   | Screening Assay Development and Screening of Natural Product Libraries   |
| Kaspar Locher (Department of Biology, ETH Zurich)   | Structural and Mechanistic Studies of Lipid/Drug Transporters and Their Therapeutic Relevance                      |
| Bruno Stieger (Division of Clinical Pharmacology and Toxicology, University of Zurich)              | Role of Canalicular Lipid Secretion in Acquired Forms of Cholestasis   |
| Christiane Albrecht (IBMM, University of Bern)  | Novel Transport Routes for Nutrients in the Mammary Gland  |

*Thomas Schnyder on behalf of the NCCR TransCure*

## ***Forschungsbereich Murtenstrasse 50***

Die folgenden Forschungsgruppen DKF sind neu in die Murtenstrasse 50 eingezogen:

### **3. Geschoss**

- Pneumologie (Erwachsene)
- Pneumologie (Pädiatrie)
- Thoraxchirurgie

### **4. Geschoss**

- Herz- und Gefässe
- Plastische Chirurgie
- Handchirurgie
- Angiologie

Auf dem Intranet Inselspital sind ein Faktenblatt und die Medienmitteilung [http://www.kommunikation.unibe.ch/content/medien/medienmitteilungen/news/2010/einweihung\\_murtenstrasse\\_50/](http://www.kommunikation.unibe.ch/content/medien/medienmitteilungen/news/2010/einweihung_murtenstrasse_50/) zur Murtenstrasse 50 aufgeschaltet.

Wenn Sie am Uniserver sind, gelangen Sie wie folgt ins Intranet:

<http://iwwext.insel.ch/> >Login >Access wählen

Intranet Inselspital >News Forschung & Medizin >26.11. Forschungs-Neubau

Prof. Dr. Robert Rieben, Koordinator Forschungsbereich Murtenstrasse 50

## ***Wir gratulieren!***

### **Ernennungen**

**PD Dr. sc.nat. Nick A. Bersinger**, Forschung Endometriose und Reproduktionsmedizin DKF, wurde der Titel eines Assoziierten Professors verliehen.

**PD Dr. med. Burkhard Möller**, Forschung Rheumatologie DKF, wurde der Titel eines Assoziierten Professors verliehen.

## ***Weiterbildung/Veranstaltung/Ausschreibungen***

There will be a new lecture course in the spring semester, which may be of interest to graduate students and/or post docs:

### **Stem Cells and Regenerative Medicine**

#### **Course Description**

This course will cover a broad range of topics relevant to stem cell biology in reference to regenerative medicine. This fast-moving field brings together many aspects of basic and applied biology and medicine including development, regeneration/repair, and cancer. The course will cover the following concepts and themes: Types of stem cells (including adult, embryonic, germline stem cells, and induced pluripotent stem cells); Stem cell biology relevant to specific organ systems; Stem cells and cancer; Therapeutical approaches using stem cells in regenerative medicine, and Ethics.

Further information:

[http://www.gcb.unibe.ch/content/curriculum/course\\_information/index\\_eng.html](http://www.gcb.unibe.ch/content/curriculum/course_information/index_eng.html)

## CAS Forschungsmanagement

Mit der eigenen Forschungsarbeit herausragende Ergebnisse erzielen – das ist das Ziel jedes Forschers und jeder Forscherin. Dabei unterstützt sie der neue, in der Schweiz einmalige Studiengang „CAS Forschungsmanagement“ der Universität Bern.

[http://www.zuw.unibe.ch/content/wbzuw/forschungsmanagement/index\\_ger.html](http://www.zuw.unibe.ch/content/wbzuw/forschungsmanagement/index_ger.html)

Der Studiengang richtet sich an Personen, die in einer mittleren Führungsebene in der Wissenschaft, in Unternehmen oder der öffentlichen Verwaltung als „Research Manager“ tätig sind und komplexere Forschungsprojekte leiten.

January 20/21, 2011, University of Fribourg

## 7th Swiss Experimental Surgery Symposium

Information and registration under: [www.sess.ch](http://www.sess.ch)

Das **Welcome Center der Universität Bern** koordiniert auch im 2011 2 Projekte zur Unterstützung von akademischen Doppelkarrierepaaren (sogenannte „Dual Career Couples“ (DCC). Infos und Antragsbedingungen unter [www.welcomecenter.unibe.ch](http://www.welcomecenter.unibe.ch)

1. Bundesprogramm Chancengleichheit (CRUS) „Dual Career Couples“  
[http://www.int.unibe.ch/content/welcome/dual\\_career\\_couples/finanzierungspool\\_dcc\\_crus/index\\_ger.html](http://www.int.unibe.ch/content/welcome/dual_career_couples/finanzierungspool_dcc_crus/index_ger.html)
2. DCC Projekt „Familienexterne Kinderbetreuung“ für Neuestellte NachwuchswissenschaftlerInnen  
[http://www.int.unibe.ch/content/welcome/dual\\_career\\_couples/dcc\\_massnahme\\_fuer\\_nachwuchsforschende/index\\_ger.html](http://www.int.unibe.ch/content/welcome/dual_career_couples/dcc_massnahme_fuer_nachwuchsforschende/index_ger.html)

*Information and registration forms in English:*

[http://www.int.unibe.ch/content/welcome/index\\_eng.html](http://www.int.unibe.ch/content/welcome/index_eng.html)

## For Women in Science

Förderprogramm von L'Oréal Schweiz in Kooperation mit der Schweizerischen UNESCO-Kommission und den Akademien der Wissenschaften Schweiz. Das Programm richtet sich an Nachwuchsforscherinnen in der Schweiz.

Postdoktorandinnen sind eingeladen ihre Bewerbung ab dem 1. Dezember 2010 bis **1. März 2011** einzureichen.

Informationen unter: [www.unesco.ch](http://www.unesco.ch) und [www.akademien-schweiz.ch](http://www.akademien-schweiz.ch)

Bewerbungsbogen und Statuten unter [www.loreal-akademien-schweiz.ch](http://www.loreal-akademien-schweiz.ch)

## The Berrow Foundation Scholarships

Auch diesen Herbst hat die am Oxford Lincoln College angesiedelte Berrow Foundation sechs Stipendien für Schweizer Studierende und Doktoranden aller Fachrichtungen ausgeschrieben, die es erlauben, bis zu drei Jahre in Oxford zu studieren.

**Deadline** für die Bewerbung auf die „The Berrow Foundation Scholarships“ und die sich an MedizinerInnen, ChemikerInnen und BiochemikerInnen richtenden „The Berrow Foundations Lord Florey Scholarships“ **ist der 21. Januar 2011**.

Infos: [www.lincoln.ox.ac.uk/berrow](http://www.lincoln.ox.ac.uk/berrow)

## Gesunde Versuchspersonen für einen kurzen Test gesucht – wir messen Ihre Augenbewegungen

### **Worum geht es?**

Das Studium und die Analyse der Augenbewegungen können in der Neurologie zur Diagnostik von Krankheiten verwendet werden. Dazu werden die Werte der Patienten mit einer altersentsprechenden Kontrollgruppe verglichen. In unserem Test wollen wir untersuchen, wie sich Geschwindigkeiten von Augenbewegungen bei gesunden Versuchspersonen verhalten.

### **Welche Versuchspersonen werden gesucht?**

Wir suchen gesunde Versuchspersonen, welche zwischen 30 und 60 Jahre alt sind.

### **Wie sieht der Test aus?**

Während der Messung der Augenbewegungen wird Ihnen eine Reihe von Bildern auf einem Bildschirm gezeigt. Ihre Aufgabe ist es lediglich, die Bilder anzuschauen. Der Messung ist einmalig und dauert zirka 20 Minuten. Computererfahrung ist nicht notwendig.

### ***Wir starten im Januar 2011 mit den Messungen***

### ***Besteht ein Nutzen für Sie?***

Neben Ihrem persönlichen Beitrag im Bereich der eminent wichtigen Frühdiagnostik zum Beispiel der Parkinsonschen Krankheit, offerieren wir Ihnen als kleines Dankeschön ein Gutschein für die Berner Stadt Kinos.

### ***Wer führt den Versuch durch?***

Das Labor für Perzeption und Okulomotorik des Inselspitals (Neurologie, DKF).

Kontakt: Tobia Brusa, Dipl Ing  
Labor für Perzeption und Okulomotorik  
Inselspital Bern  
[tobia.brusa@dkf.unibe.ch](mailto:tobia.brusa@dkf.unibe.ch)  
Tel. 031-632-0189 (jeweils Mittwochs und Freitags)

Eine Anmeldung ist jetzt schon möglich. Für Ihre Mithilfe bedanken wir uns im Voraus!