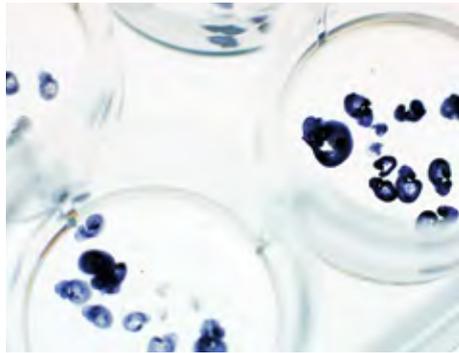
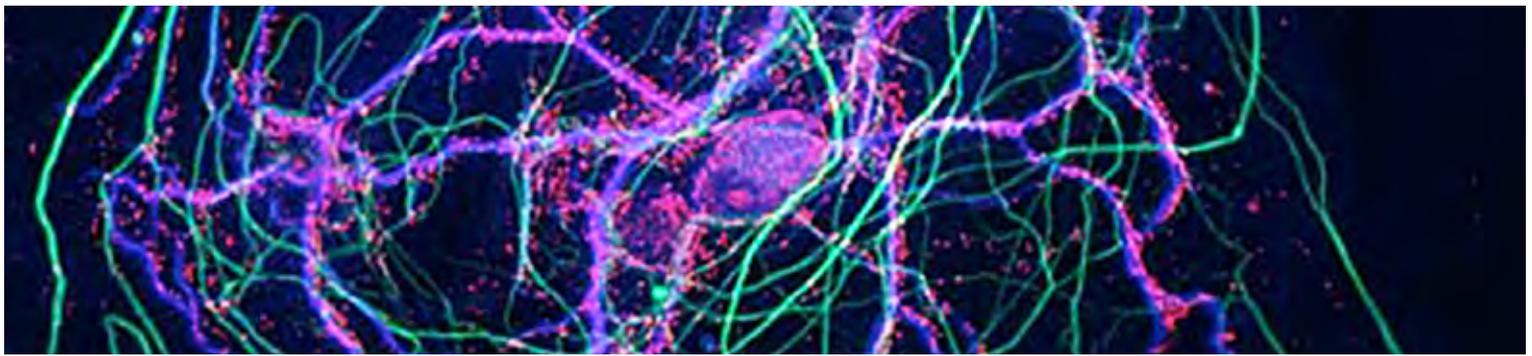


BERLIN INSTITUTE OF HEALTH ANNUAL REPORT 2014



**BERLIN
INSTITUTE
OF HEALTH**

Charité & Max Delbrück Center

Imprint

Publisher

Berlin Institute of Health
Prof. Ernst Th. Rietschel (Chairman of the Board of Directors)
Kapelle-Ufer 2 | 10117 Berlin, Germany
www.bihealth.org/en

Responsible: *Alexandra Hensel (Head of Communications)*

Berlin, May 2015

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Design

Baroneska. Studio für Gestaltung
www.baroneska.de

Printing

Druckteam Berlin
Printed on PEFC-certified paper.
The paper originates from sustainable managed forests and legal sources.



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IMPORTANT EVENTS

2014

FEBRUARY

The Founding Supervisory Board approves the 2014 Research and Budget Plan.

Nobel Prize-Winner in Medicine Thomas Südhof becomes the first visiting scientist.

The Scientific Advisory Board convenes for its constituent meeting in Berlin.

APRIL

First call for the Twinning Research Grants

Launch of the website www.bihealth.org

JULY

Construction commences of interim accommodation for the BIH Omics Core Facilities at Campus Berlin-Buch.

SEPTEMBER

BIH Professorship "Experimental Cardiovascular Research" at Charité: Professor Holger Gerhardt from London is appointed to MDC to a W3 Professorship at Charité and commences his work.

NOVEMBER

BIH Professorship "Cardiology" at Charité: Professor Burkert Pieske from Graz is appointed to a W3 Professorship as Director of the Medical Department, Division of Cardiology at Charité Campus Virchow-Klinikum and commences his work.

DECEMBER

The Berlin Senate approves a draft law stipulating that the Berlin Institute of Health is to become a corporation under public law.

The newly established BIH Bioinformatics Core Unit moves into its accommodation in the Luisenstraße in Berlin-Mitte.

BIH Welcome Symposium "Closing gaps in cardiovascular disease research and therapy" with presentations given by newly appointed Professors Volkmar Falk, Holger Gerhardt, Ulf Landmesser and Burkert Pieske

MARCH

Research funding starts:

The major Collaborative Research Grant projects commence their research activities.

First call for the Translational PhD Project Grants

JUNE

Selection of the first Pathfinder Studies at the Clinical Research Unit at four sites

AUGUST

Construction commences of the BIH Computer Center in the southern campus area at Campus Berlin-Buch.

OCTOBER

BIH Professorship "Cardiology" at Charité: Professor Ulf Landmesser from Zürich is appointed to a W3 Professorship as Director of the Department of Cardiology at Charité Campus Benjamin Franklin and commences his work.

The BIH Omics Core Facilities at the Berlin-Buch site move to the interim building (House 64).

Board Member Walter Rosenthal takes office as President of Friedrich Schiller University Jena and transfers his BIH Board responsibilities to Prof. Thomas Sommer.

Axel Radlach Pries, Professor of Physiology at Campus Charité Mitte, is elected new Dean of Charité, thus becoming a BIH Board Member as of 2015/01/01.

By the end of the year, BIH is supporting 198 individuals doing research at MDC and Charité.

2015

A SHARED RESEARCH SPACE

*Prof. Ernst Th. Rietschel,
Chairman of the Board of Directors*



Dear Readers,

We are often asked about the uniqueness of BIH, a question to which there are a number of answers: its uniqueness in Germany. Its translational and systems medicine approach. How it developed. Its legal basis. But what I find most characteristic is the following aspect: We are establishing a Shared Research Space that very closely integrates research, clinical activities and first-class infrastructure – something that no other comparable institution in Germany can boast of.

The important components of this Research Space are our Clinical Research Unit (CRU) and the core facilities, whose establishment and development made good progress in 2014. The core facilities are vital “organs” supplying the “body”, BIH, with essential substances in the form of data, expertise, information and methods. Last year, BIH spent around 24 million euros on infrastructure, especially on first-class equipment. It has long been put into operation, for in 2014, we already approved seven BIH collaborative projects where Charité and MDC researchers are working together: three large consortia were awarded for the long term with a total of 19 subprojects and four smaller projects with shorter terms and ten subprojects. So the Shared Research Space that we have created with BIH is beginning to thrive.

2014 was an eventful year for the Berlin Institute of Health. Many tasks lay ahead, and today, I can confidently claim that we have mastered them and are ready for further developments. This fills me with pleasure, pride and above all gratitude towards all those who have made these achievements possible – sometimes alongside their regular assignments. Here, highly motivated scientists and clinicians are at work who are convinced of the idea and mission of BIH.

For BIH, it was important right from the onset to launch scientific projects as quickly as possible, this has met with success. The first three research projects, the three major collaborative projects mentioned above, commenced their work in spring, and further calls, also to promote junior scientists, were announced in March and April. We have managed to establish the competitive procedures for these calls and to recruit more than 70 external reviewers for them.

In all, by the end of 2014, BIH had supported 198 scientists and clinicians in a diversity of funding lines, and far more are active in developing the institute. We have been able to appoint the first top-level professors and – with the help of the Private Excellence Initiative Johanna Quandt – attract several renowned researchers from abroad to BIH as visiting scientists, among them a Nobel Prize-Winner. These outstanding experts are contributing not only to establishing a reputation for BIH as an institution of excellent research, but also to developing Berlin into an even more important location for translational and systems medicine-oriented research.

Finally, I would like to express my thanks to two people who have played a central role in the establishment of BIH: Walter Rosenthal, who took office as President of Friedrich Schiller University Jena last fall and passed on his BIH Board activities to Thomas Sommer, and Annette Grütters-Kieslich, who retired from the Board at the end of the year and returned to her clinical pediatric activities. Without their inspiration, their efforts and their empathy, the Berlin Institute of Health would not be where it is now. And there is more news: After two years in office, I will retire from the Board in 2015 and make way for new ideas at BIH.

*Inspired reading,
Yours, Ernst Th. Rietschel*

OUR WAY TOWARDS AN INSTITUTION OF EXCELLENCE

BIH is a new public body, an institution in its own right – and at the same time, it is an integral element of its constituent institutions Charité and MDC. As of 23 April 2015, by virtue of the legislation passed by the Berlin House of Representatives, it will be a corporation under public law. Obviously, this evolution of BIH means new challenges for us in the future, especially in terms of organization, infrastructure, and strategy. If we master these challenges, BIH will make a substantial contribution to health research in Berlin and in Germany as a whole. 2015 is going to be a crucial year in this respect. A look at the future.

Not only philosophers know that the whole is more than the sum of its parts. This also applies to BIH. This new institute combines and enhances the strengths of Charité and MDC, which is accomplished by integrating the founding institutions in the field of translation both scientifically and structurally and by adding the complementary research skills. In this manner, we – Charité and MDC within BIH – jointly seek to become more innovative in the field of systems medicine and translation, to the benefit of people's health.

At the same time, MDC and Charité maintain an independent legal status, from which BIH also benefits enormously. MDC will continue to conduct basic research on the molecular mechanisms of diseases in the context of Helmholtz Association's program-oriented research. It contributes innovative research approaches, cutting-edge technologies and numerous approaches for the development of therapies to BIH. Research at MDC, featuring a broad interdisciplinary base, can benefit from the systems medicine approach of BIH as a reliable structure to boost translational research projects with clinicians.

BIH can build on Charité's integration model in which patient-oriented re-

search and academic teaching are closely linked with high-performance medicine, both scientifically and structurally. Thus, Charité has the scientific and clinical skills regarding common as well as rare diseases at its disposal. At the same time, BIH offers both scientists and physicians at Charité new options for patient-oriented research thanks to state-of-the-art technological approaches in the field of clinical phenotyping and the storage and processing of clinical data. In particular, the development of translational research structures such as the Clinical Research Unit (CRU) provides Charité with excellent prerequisites to contribute its skills in the field of clinical studies to the BIH Shared Research Space.

What is important for us

One central pillar of our research and clinical activities is their excellent quality. Not only should BIH research meet optimum academic standards. At BIH, we seek to develop new quality standards and value concepts for translation against which the institute can be measured. This is going to be one of the central tasks in the coming year. Our research activities have to achieve translational goals. In 2015, we are going to develop the corresponding criteria and

launch accompanying research in order to make the work of BIH even more targeted and make it possible to evaluate it with the aid of these criteria. The important keywords here are access to negative research results and reproducibility despite different methodological approaches.

Scientific-political aspects are also very important for the successful work of BIH. In the long term, BIH is to become a central institution of Berlin health research. Partnerships are to be established with other successful biomedical institutions – both with universities and with non-university institutions. Of course cooperation with industry enterprises are part of BIH's overall objective. We seek to, and are going to, promote new translational transfer potentials.

Raising excellence: inspiration from outside

BIH will only be able to develop new measures in preventive healthcare, diagnostics and therapy to the benefit of humans if it really succeeds in transferring the research results into clinical applications. To this end, BIH needs the expertise of the specialists at MDC and Charité. But inspiration and experiences from outside



Board of Directors (f l t r): Ernst Th. Rietschel, Karl Max Einhäupl, Axel Radlach Pries and Thomas Sommer

are important, too. This means that we are going to increase our efforts to gain an optimum of skills and new ideas via top-level appointments and guest stays for translational and systems medicine-oriented researchers to boost our progress.

Funding and training

A reorientation of the in-service training and professional development system is crucial to a long-term change of culture in the work of biomedical researchers. Here, BIH takes advantage of innovative funding formats to promote knowledge exchange between basic researchers and clinical practitioners and establish integral training programs. Up to 2018, at least 800 BIH researchers are to be active in a diversity of projects. And this innovative potential from Charité and MDC at BIH is going to make our new venture a leading biomedical research institution.

Translation at BIH

At BIH, “translation” stands for a quality-oriented process of transferring knowledge generated in systems medicine-based approaches into medical benefits, as well as observations from clinical practice into basic science. Thus, translation represents an interdisciplinary process encompassing the discovery of mechanisms of action as a basis for the development of new products and procedures for diagnosis, therapy and disease prevention including their testing on patients and volunteers. This process also includes the critical review, further development and revision of established models.

Systems medicine at BIH

Systems medicine at BIH encompasses methods to analyze the dynamic interactions of the molecules, cells, tissues and organs as well as psychosocial factors that form the foundations of life, in an effort to develop a broad understanding of the interrelated systems that constitute a human organism.

THE FIRST MAJOR INTEGRATED PROJECTS GAIN MOMENTUM

BIH coordinates research, supports research, and conducts research. Two central instruments for translational and systems medicine-oriented medicine are provided, interlinking basic researchers with clinical practitioners of MDC and Charité: the larger consortia, the Collaborative Research Grants (CRGs), and the smaller Twinning Projects (Twinning Research Grants, TRGs). Three CRGs commenced their activities involving 50 scientists and clinicians in spring 2014.

The first CRG projects started in March. One consortium each, consisting of five to seven teams with staff from MDC and Charité, is conducting research on T cell therapy in cancer, on proteostasis network in Alzheimer's disease and on molecular mechanisms and diagnosis of congenital diseases in children.

For the three projects with a total of 19 subprojects, a total of around 17 million euros is available for the period 2014–2018. In 2014, 50 researchers and clinicians and 11 science supporting employees worked for the CRGs.

A second CRG call was launched in fall 2014. A fourth CRG consortium is to be selected in July 2015, and is to commence its activities from August 2015 onwards.

In the following, the principal investigators present their activities and the most important milestones in the three projects in 2014:

Genomic analysis of inherited pediatric diseases

Prof. Christian Rosenmund and **Prof. Carmen Birchmeier** on their research into improving the understanding and diagnosis of congenital diseases:

Our goal

We study congenital, genetically determined diseases, which are extremely complex, diverse and difficult to quickly and reliably

diagnose. Our research consortium is addressing the latter in particular. Swift diagnosis mitigates the suffering of patients and their families by helping them to gain clarity and cope more easily with the conditions surrounding the disease. Reliable monitoring of disease progression and beginning therapeutic measures as soon as possible are also important. In summary, we seek to introduce state-of-the-art technologies in clinical diagnostics and gain a better understanding of the mechanisms underlying diseases in order to pave the way for new therapeutic approaches.

Milestones in 2014

- In order to analyze the mechanisms of mental retardation and microcephaly, we have begun investigating the first mouse model for congenital microcephaly (MCPH3) in terms of neuronal differentiation and network formation.
- We have recruited patients and conducted preliminary whole-exome sequencing for the identification and characterization of new disease-associated genes and non-coded sequences.
- With the aid of a laboratory animal model, we have demonstrated that the mutation of the zinc finger factor *Insm1* in adult β cells results in severe alterations in insulin discharge. The mutant cells lose their mature character and resemble immature β cells found in newborn animals.
- With genome-wide association studies, we have identified sequence polymorphisms in the human genome that coincide with alterations in sugar metabolism.
- We have established two protocols for mapping open chromatin: firstly, a version of the widely established DNase-Seq,

(f l t r) Carmen Birchmeier and
Christian Rosenmund



in which open chromatin areas are identified by enzymatic splitting of the DNA by DNaseI and, secondly, ATAC-seq, a novel approach in which sequencing primers are inserted into open chromatin regions using transposase. We have adapted our existing analysis programs to the ATAC-seq protocol and modified the procedure so that little experimental effort is required for results of a quality comparable to those of DNase-seq.

- We have established the chromatin status of regulatory sections in the genome of patient-specific induced pluripotent stem cells (ps-iPSCs) and examined the influence on gene expression during the differentiation of heart muscle cells among patients with Fallot tetralogy (ToF).
- In order to obtain expression profiles from patients with clinically well-characterized chronic heart diseases, we have conducted RNA-seq on tissue from the right heart chamber of ToF patients and healthy individuals.
- We have begun compiling gene expression profiles of patients with deficiency of the heart septa.
- We have established general biochemical analysis protocols and have developed a bioinformatics pipeline for processing the gathered data.

Subprojects and Principal Investigators

- Common pathways and transcription network control in intellectual disability and microcephaly
Angela Kaindl (Charité), **Christian Rosenmund** (Charité)
- Towards a better understanding of congenital endocrine diseases
Carmen Birchmeier (MDC), **Heiko Krude** (Charité)
- Mis-regulated chromatin folding as a cause of congenital disease
Stefan Mundlos (Charité), **Ana Pombo** (MDC)
- Integrative omics-based dissection of molecular mechanisms underlying congenital abnormalities of the kidney and the urinary tract
Wei Chen (MDC), **Dominik Müller** (Charité)
- Transcription network controlling heart development and congenital heart disease
Uwe Ohler (MDC), **Silke Rickert-Sperling** (Charité)



(f l t r) Thomas Blankenstein and Peter-M. Kloetzel

T Cell Therapy in Cancer

Coordinators **Prof. Thomas Blankenstein** and **Prof. Peter-M. Kloetzel** on their research on “Targeting somatic mutations in human cancer by T cell receptor gene therapy”:

Our goal

We are developing a new form of cancer therapy, T cell receptor gene therapy. This therapy consists of genetically altering T cells of cancer patients so that they can recognize and destroy the cancer cells. The procedure is simplified by the T cells highly specifically recognizing an individual structure (a small peptide from a protein; called an antigen) and by this specificity being mediated by the T cell receptor. The challenge of efficiently producing patient-specific T cells through T cell receptor transfer in a cell culture for a subsequent reinfusion into patients has virtually been solved already. The decisive issues that we are dealing with are: Which somatic mutations of the cancer cell should be selected as the target structure? How can suitable T cell receptors be acquired? Can a mutation-specific T cell receptor gene therapy be implemented clinically?

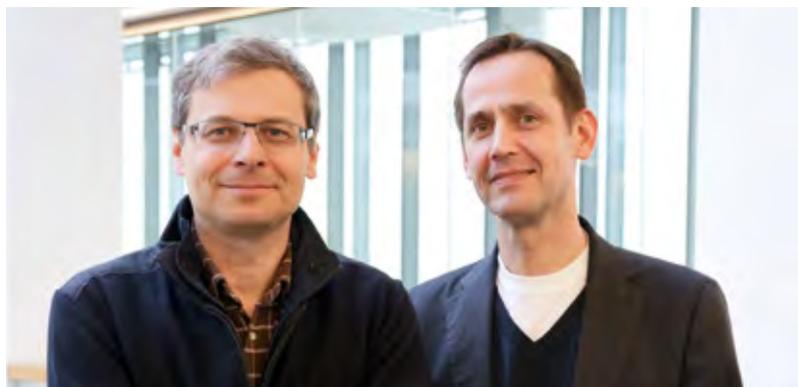
Milestones in 2014

- We established a humanized mouse model to isolate mutation-specific T cell receptors and generated the first of the T cell receptors. (Analysis in early 2015)
- We established methods to identify the generation of mutant peptides.
- We demonstrated that somatic mutations are a suitable target structure for the rejection of large established tumors through T cell receptor gene therapy.

- An in vivo model was established for the analysis of the suitability of human T cell receptors and human antigens.
- The expression of T cell receptors in primary human T cells was optimized.
- We determined the logistics for sequencing the cancer genome of patients.
- The preparation of the GMP Laboratory for clinical studies was started.

Subprojects and Principal Investigators

- Identifying immunogenic mutant epitopes
Peter Kloetzel (Charité)
- Mutation-specific T cell receptors
Thomas Blankenstein (MDC)
- Targeting unique tumor-specific antigens
Hans Schreiber (Charité)
- Tumor rejection capacity of mutant-specific TCRs
Wolfgang Uckert (MDC)
- A transposon-based TCR gene transfer for clinical use
Zsuzsanna Izsvák (MDC)
- Identification of cancer-specific immunogenic mutations and their expression
Michael Hummel (Charité)
- Moving mutation-specific TCR gene therapy into the clinic and preclinical efficacy comparison to lymphoma lineage-specific TCRs
Antonio Pezzutto (Charité)



(f l t r) Erich E. Wanker and Frank L. Heppner

Alzheimer's Research

Coordinators **Prof. Erich E. Wanker** and **Prof. Frank L. Heppner** on their activities in the project “Elucidating the proteostasis network to control Alzheimer's disease”:

Our goal

Alzheimer's disease continues to be a phenomenon that can only be treated at the level of the symptoms. The currently available drugs can only postpone the progression of dementia for a limited time. Our consortium brings together experts in the molecular and pathological processes that play an important role in Alzheimer's disease and neurodegeneration. Several teams are analyzing the highly complex interplay of proteins in the nerve cells affected by Alzheimer's disease. Together we are examining which functional connections are disturbed in neurons and how we can interfere in disease patterns at the molecular level in order to develop new therapeutic approaches. In a nutshell, we want to develop new diagnostic tools and test therapeutic agents for Alzheimer's.

Milestones in 2014

- We successfully developed a cellular assay for the identification of therapeutic agents that disassemble disease-relevant aggregates of beta-amyloid-polypeptide. With an in vitro assay, we were also able to demonstrate the inhibition of beta-amyloid aggregation through chemical agents. In addition, we carried out an initial screening using the assays.
- We succeeded in developing a new humanized (genetically engineered to incorporate human genes) mouse model for Alzheimer's in order to examine the influence of genetic risk factors on the metabolism of the disease-relevant beta-amyloid polypeptide.
- We were able to demonstrate that the induction of age-dependent inflammatory proteasomes is enhanced in a mouse model for Alzheimer. This bears out our hypothesis that the production of type 1 interferon triggers neuroinflammation, induces the formation of immune proteasome, and thus plays a role in causing the onset of Alzheimer's disease. In order to test proteasome inhibitor agents, we established a model for the simulation of neuroinflammation that is based on organotypic brain sections.
- We collected samples from patients suffering from Alzheimer's and control test persons who visited the Charité memory clinic because of memory complaints. We added

those samples to our biomaterial bank. With the aid of the samples, we started to develop protocols to establish new biomarkers.

- We carried out preparatory work on the design and organization of the clinical study of a drug candidate for Alzheimer's.
- We characterized the expression of circular RNA molecules in the nervous system and established methods for their isolation and quantification from biological samples of Alzheimer's patients and mouse models. The “circBase” data bank was established at → www.circbase.org, which provides the research community with extensive data sets on circular RNAs.

Subprojects and Principal Investigators

- Repurposing, validating and mechanistically understanding IL-12/23 and NALP3 inhibitors as novel preclinical and clinical Alzheimer's disease modifiers
Frank Heppner (Charité)
- APOE receptors as targets for prevention of Aβ oligomerization and neurotoxicity in Alzheimer's disease
Thomas Willnow (MDC)
- Effects of small molecule modulators of proteostasis and protein aggregation on dysfunction and neurotoxicity in Alzheimer's disease
Erich Wanker (MDC)
- Perturbations of proteostasis networks in Alzheimer's Disease: focus on the ubiquitin proteasome system
Elke Krüger (Charité)
- Proteostasis and long-term disease progression in Alzheimer's dementia
Oliver Peters (Charité)
- Repurposing of approved drugs impacting on proteostasis for the treatment of Alzheimer's disease
Josef Priller (Charité)
- Expression and function of circular RNAs and micropeptides in Alzheimer's disease
Nikolaus Rajewsky (MDC)

INNOVATIVE: “TWINNING RESEARCH” AT BIH

The first four Twinning Research Grants (TRGs) were awarded in November 2014. Funding of TRGs will be granted for two years, aim to support small-scale cooperative, interdisciplinary projects carried out by basic scientists, computational researchers and clinicians at Charité and MDC and explicitly address early-career scientists. Each TRG ideally comprises two subprojects. The four projects that are now being funded commence in 2015. We interviewed the principal investigators:



Simon Jacob (top)
and James Poulet (bottom)

The role of corollary discharge and the dopamine system in controlling sensory processing

- Dr. James Poulet (MDC and Charité)
- Dr. Simon Jacob (Charité)

What is the central idea of your project?

We are concentrating on a fundamental neurobiological mechanism that may give rise to symptoms which are common to severe mental disorders. We are particularly interested in those neuronal processes that predict sensory consequences of one's own action (sensory inference). In individuals suffering from psychosis, e.g. schizophrenia patients, sensory inference is thought to be altered such that new sensory signals are not properly integrated with learned predictions. The neurobiological basis of this is still unknown.

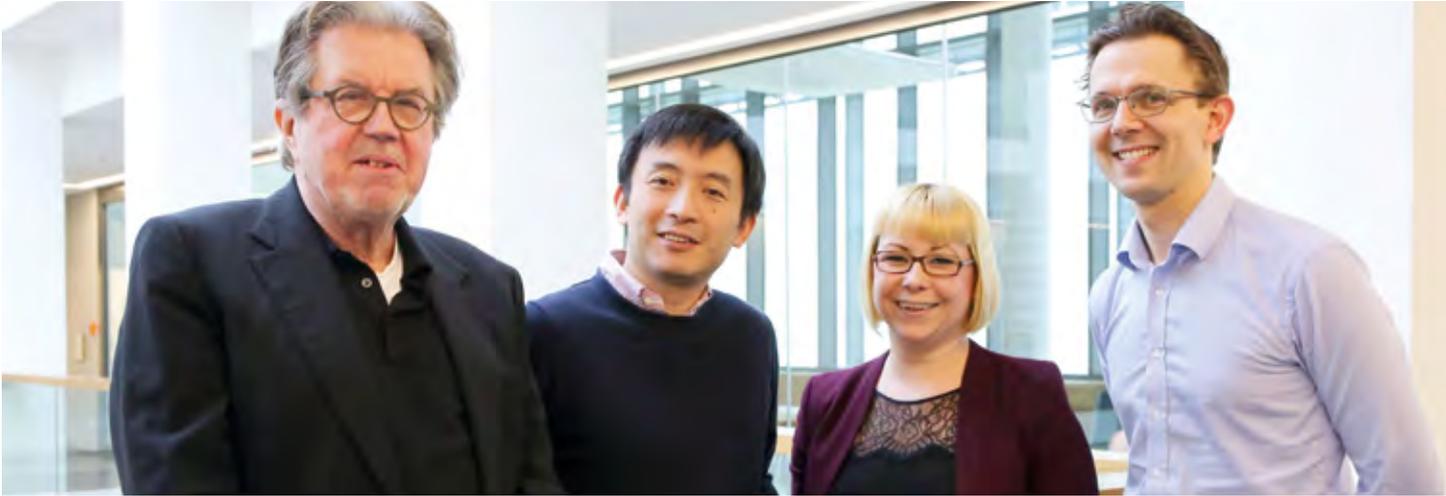
How does your project benefit from BIH?

We will provide an in-depth mechanistic description of sensory inference at multiple levels, ranging from single neurons through circuits of neurons to whole cortical regions in mouse models and human patients. Our collaboration is unique in that no other institution in Germany is able to match our expertise in single neu-

ron recordings in awake humans (Charité) and among behaving rodents (MDC).

How are your results going to help patients one day?

Psychiatric disorders represent an immense burden for the individuals affected and for their environment. In many fields of medicine, there has been significant diagnostic and therapeutic progress over the last few years because specific physiological and biochemical changes have been discovered. However, there have been hardly any improvements for patients suffering from psychiatric diseases. The overarching goal of our project is to gain a better understanding of how characteristic symptoms of schizophrenia (delusions and hallucinations) are generated, and for this purpose, we are trying to understand the basic disease mechanisms at the level of neuronal circuits. By focusing on this objective, our work can make a sustainable contribution to the pathophysiology of psychotic disorders. Our results could help in developing innovative methods for diagnosis and treatment.



(f l t r) Walter Birchmeier, Wei Chen, Annika Fendler and Jonas Busch

Systems medicine in kidney cancer: towards cancer stem cell-directed therapy

- Prof. Walter Birchmeier (MDC)
- Dr. Wei Chen (MDC)
- Dr. Jonas Busch (Charité)

What is the central idea of your project?

We are working on Clear Cell Renal Cell Carcinoma (ccRCC). Renal cell carcinomas of this cell type are by far the most frequently occurring ones. Cancer stem cells control the growth of tumors and play a crucial role in metastasis as well as in how the tumors respond to drug therapy approaches. We have observed that cancer stem cells respond differently among individual patients to drugs already employed and those under development. Whereas the cancer stem cells of some patients show a very good response to a treatment, those of other patients do not, or do so only weakly. Our project aims to develop novel therapy strategies that specifically target cancer stem cells in Clear Cell Renal Cell Carcinoma and to identify molecular markers that can predict therapeutic responses. For this purpose, we analyze the genome, the transcriptome (all genes transcribed, i.e. rewritten as RNA by DNA, in a cell at a given point), and the epigenetic signature

of the tumor cells, which shows us which regulators influence the development of the cell and its succeeding generations. Ultimately, these results are to be used in the development of new therapies. We are also using the results to derive new, non-invasive markers from the molecular signature of cancer stem cells circulating in the blood of patients with metastasized kidney carcinomas.

How does your project benefit from BIH?

Jonas Busch and Klaus Jung of the Department of Urology are providing clinical expertise on the kidney cell carcinoma and its treatment, especially on therapy involving tyrosine-kinase inhibitors. Tyrosine kinases are a group of enzymes that play a role in signal transmission between proteins and make an important contribution to cellular signal transmission as part of receptor systems. The research groups of Walter Birchmeier with Annika Fendler and Wei Chen of MDC have several years of experience in research on cancer stem cells and in the development and application of next-generation sequencing. The combination of this expertise enables us to integrate data from the genomic profiles of circulating cancer stem cells and from the molecular characterization of therapy responses to establish novel biomarkers

that can be used in treatment decisions and disease monitoring.

How will kidney cancer patients one day benefit from your results?

As yet, metastasized Renal cell carcinomas only show a restricted response for a limited period of time to the therapies that are currently applied. Moreover, opting for a therapy is based solely on clinical parameters (such as the size of the tumor or the number of metastases). And at the moment, imaging techniques remain the option to measure tumor recurrence after tumor extirpation or therapy surveillance, and few molecular markers have been proposed for that purpose. We want to use our research results to develop more effective therapies for metastasized kidney cell carcinomas. In parallel, we seek to identify molecular markers that enable individualized therapy decisions and therapy surveillance. The long-term goal is to employ novel treatment methods that have proved successful in preclinical studies in compassionate use or in early clinical trials.

Systems medicine of BRAF-driven tumors

- Prof. Nils Blüthgen (Charité)
- Dr. Markus Landthaler (MDC)

What is the central idea of your project?

Over the last few years, genomic research has developed rapidly. This has enabled the analysis of recurrent mutations in the genomes of tumors, resulting in novel targeted therapies. Some mutations occur at high frequencies across multiple tumor entities. One example of such mutations is a mutation in the BRAF gene that occurs among 40 per cent of the melanoma patients but also in colorectal cancer. This inhibitor shows high response in patients with malignant melanoma that carry this BRAF mutation. In contrast, 10 per cent of the patients with colorectal cancer that carry the same mutation show no response. We will investigate the posttranscriptional regulatory networks that relay BRAF signals in order to understand the mechanisms responsible for intrinsic resistance to BRAF inhibitors. Moreover, we want to identify novel biomarkers of the BRAF-associated networks for therapy stratification of BRAF tumors.

How does your project benefit from BIH?

At MDC, in Markus Landthaler's research group, we developed novel methods to investigate the regulation of RNAs by RNA-binding proteins. Here, these methods, which have been used mainly in basic research so far, are to be applied to a clinically relevant issue. This has been made possible by working together with Charité research groups in tumor biology (Christine Sers/Reinhold Schäfer), pathology (Hendrik Bläker) and mathematical and bioinformatics analysis (Nils Blüthgen).

How will patients with malign tumors benefit from your results?

Of course there is still a long way to go. Posttranscriptional regulatory interactions which turn the cell into a tumor cell can be specifically manipulated by antisense oligonucleotide molecules. Influencing these mechanisms could lead to the development of novel therapies to cure cancer diseases by blocking molecular interactions that are essential for tumors. Also, a precise understanding of the networks involved in oncogenesis and oncogenesis can unveil targetable vulnerabilities and new therapeutic opportunities.

Muscular organ failure in critically ill intensive care patients – molecular mechanisms and preventive therapy strategies

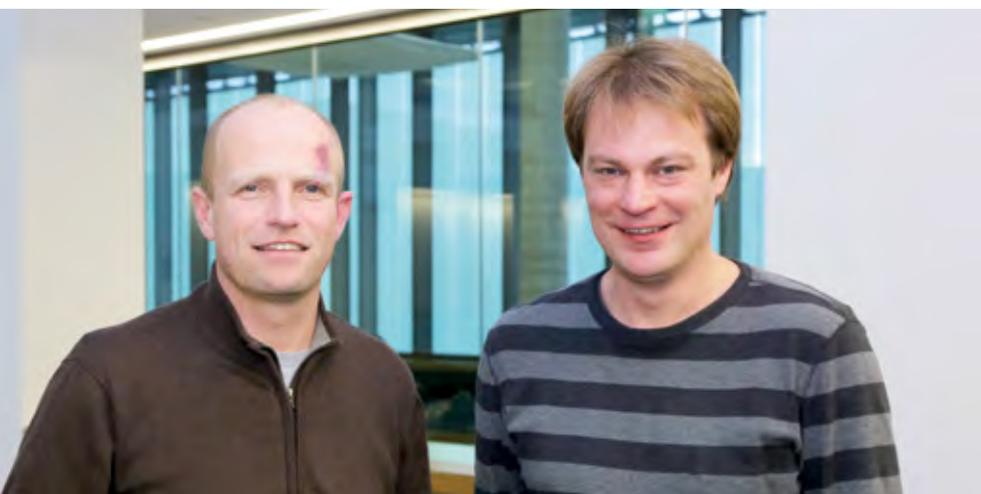
- Prof. Carmen Birchmeier (MDC)
- PD Dr. Steffen Weber-Carstens (Charité)
- PD Dr. Jens Fielitz (ECRC & Charité)

What is the central idea of your project?

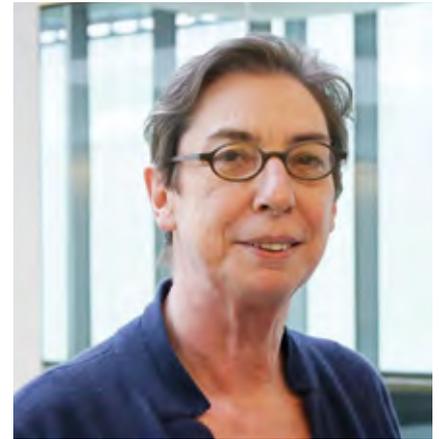
ICU-acquired weakness is a major sequela of critical illness. It is the clinical consequence of an acquired neuromuscular organ failure that is characterized by a reduced force capacity per cross sectional muscle area with significant loss of myosin heavy chain (MyHC), and an impaired excitability of nerve and muscle membranes. ICU-acquired weakness aggravates intensive care treatment, delays weaning of mechanical ventilation, prolongs rehabilitation, and results in a sustained limitation of physical independency even years after discharge from intensive care unit. As yet, preventive therapies or uniform therapy programs are not known.

Almost all of the papers published on the topic describe phenotypes and mechanisms at the terminal point of the disease. Our previous work indicated that mechanisms resulting in muscle pathology are already activated very early at the onset of a critical illness. We are therefore applying a novel approach in this project. We investigate the early stages of inflammation-induced muscle failure in both an experimental and a clinical setting.

In the experimental part of our project, we concentrate on the role of the satellite cells, the stem cells of the muscle, and



(f l t r) Markus Landthaler and Nils Blüthgen



(f l t r) Steffen Weber-Carstens, Jens Fielitz and Carmen Birchmeier

in the development of ICU-acquired weakness. As yet, it is not known whether these cells are activated in inflammation-induced muscle atrophy, and whether satellite cell-mediated mechanisms can ameliorate the outcome of the disease.

In an investigator-initiated trial, we will investigate the usefulness, effectiveness and safeness of preventive measures like muscle activation and physiotherapy.

How does your project benefit from BIH?

We examine the medical condition of patients with ICU-acquired muscular organ failure from the various perspectives – at molecular level, in acute critical care, and in chronic/rehabilitation care. For this purpose, we gain muscle biopsy specimens from critically ill patients during defined clinical situations of early critical illness. It is usually difficult to gain muscle biopsy samples in defined clinical situations. Here, we benefit from the opportunity to conduct a clinical study at Charité that is tailored to our specific research objectives. MDC expertise enables us to gain comprehensive insights into molecular disease mechanisms from the valuable muscle biopsy specimens of these patients. In addition, we will be able to evaluate the ef-

fect of a preventive therapeutic approach at clinical and molecular level.

For ethical and logistical reasons, it is almost impossible to obtain muscle biopsy samples at frequent consecutive intervals from critically ill patients. We will use the expertise of the group in performing proteomic and pathway analyses at the MDC and ECRC to address the molecular pathway at defined stages of inflammatory myopathy in an established mouse model of inflammation-induced muscle failure and in transgenic animals. In addition, we will make use of MDC expertise to assess the role of adult muscle stem cells in inflammatory myopathy. Comparing the data of patients, mice and muscle cells will help to describe the phenotype of inflammatory muscle atrophy in greater detail, uncover pathways involved in the disease process, and open avenues to ameliorate the disease by activating stem cell-mediated repair.

How are your results going to help patients one day?

We still know too little about therapeutic measures that already prevent muscle wasting and weakness in the early stages of critical illnesses. There is some evidence that early physical and occupational

therapy improves physical functioning and independence among patients discharged from intensive care.

Our translational scientific approach has the potential to improve treatment strategies preventing ICU-acquired muscular organ failure of critically ill patients during acute care and will help to define the optimal care regarding protocol-based physiotherapeutic treatment as well as electrical muscle stimulation early after the onset of critical illness. Our examinations will help to evaluate possible therapies that are based on adult stem cells. All in all, our examinations aim at shortening the time of intensive care treatment and improving long-term recovery and physical functioning of patients after ICU treatment.

NEW PROFESSORS TO BOOST TRANSLATIONAL SYSTEMS MEDICINE RESEARCH

Three aces for Berlin: In 2014, three outstanding experts working abroad in the field of translational cardiovascular research accepted calls to Berlin. These appointments are important for BIH, for they support our strategic goal – that of achieving better exchange between top-level research and top-level medicine.

The physicians and scientists Burkert Pieske, Ulf Landmesser and Holger Gerhardt are working together at a cross-institutional level and are going to contribute to progress in translational research in their specialties over the next few years. It has been possible to fill the three professorships thanks to close cooperation between Charité, MDC, German Center for Cardiovascular Research (DZHK), German Heart Institute Berlin

(DZHB) and BIH. At the same time, the three experts are working together with Volkmar Falk, the Medical Director of the German Heart Institute Berlin, who was also won over to Berlin in 2014, and are thus intensifying cooperation between Charité and the German Heart Institute Berlin. This cross-institutional collaboration creates a broader basis for cardiovascular medicine as a whole in Berlin, and

in particular, it strengthens translational medicine in Berlin.

The appointments of Holger Gerhardt, Ulf Landmesser and Burkert Pieske coincided with the creation of the first three BIH Professorships. The BIH-funded researchers bear their titles for the duration of their activities in Berlin.

Profiles of the three specialists



Holger Gerhardt
(*1969)

Holger Gerhardt has been head of a research group at MDC and a W3 Professor of Experimental Cardiovascular Research at Charité since 2014/09/01. Furthermore, he is a DZHK Professor. He aims to uncover the fundamental principles and mechanisms driving functional blood vessel network formation, as well as their adaptation and plasticity in disease and regeneration. Previously, he had been at the London Research Institute, at the Vesalius Research Center of the Flemish Institute for Biotechnology (VIB), and at the Catholic University of Leuven in Belgium.

→ BIH Professorship “**Experimental Cardiovascular Research**” at Charité



Ulf Landmesser
(*1970)

Ulf Landmesser assumed the position of Director of the Department of Cardiology at Charité Campus Benjamin Franklin on 2014/10/01. Previously, he had been Deputy Director of the Clinic for Cardiology at the University Hospital of Zurich. Ulf Landmesser plans among other things to integrate new, interventional techniques of cardiovascular treatment in Berlin. Furthermore, he wants to promote research on causes of myocardial infarction with systems medicine approaches.

→ BIH Professorship “**Interventional Cardiology**” at Charité



Burkert Pieske
(*1961)

Burkert Pieske took office as Director of the Medical Department, Division of Cardiology at Charité Campus Virchow-Klinikum on 2014/11/01. He is also the new Director of Cardiology at the German Heart Institute Berlin. Latterly, Burkert Pieske was Director of the Clinical Department for Cardiology at the Medical University of Graz in Austria. One of his goals in Berlin is to identify new biomarkers that are suitable to improve the adjustment of patients to certain therapeutic procedures.

→ BIH Professorship “**Cardiology**” at Charité

WELCOME AND BIENVENUE IN BERLIN

Nothing is as enriching as external impulses. This applies to many areas of life and work, and also to translational and systems medicine research. In order to maintain its international competitiveness, BIH has opted for internationally experienced top-level scientists. In 2014, three renowned researchers were selected as BIH Einstein Visiting Fellows. They are strengthening BIH research in several important disciplines.

The Mediterranean or the Spree? For **Michael Sieweke**, it's going to be both during the next three years. The expert on stem cells is a MDC group head as well as a Research Director at the Centre d'Immunologie de Marseille-Luminy and at the Centre National de la Recherche Scientifique (CNRS). He was chosen as one of the first BIH Einstein Visiting Fellows in October 2014. Sieweke now takes leave from his workplace in the French port several times a year in order to establish and support a working group in Berlin together with his colleague Klaus Rajewsky of MDC. Sieweke and his Berlin team are looking at the role of macrophages and examining how they influence various degenerative disease patterns of the lungs, the heart and the central nervous system. Macrophages are a type of white blood cell that play a critical role in immunity and tissue regeneration. Michael Sieweke's Fellowship is above all giving the areas of hematology and immunology important impulses.

Florian Sennlaub was also chosen as an Einstein BIH Visiting Fellow in October. He is currently conducting research at the Institut de la Vision in Paris. Sennlaub is a specialist in the fields of ophthalmology and immunobiology. Together with Olaf Strauß of Charité's Department of Ophthalmology, Sennlaub will be investigating the role of mononuclear phagocytes in hypertension induced vascular remodeling and their interactions with the retinal pigment epithelium. With his expertise he is strengthening translational research

on hypertonia and the causes of critical retina diseases. Like Michael Sieweke, Florian Sennlaub commences his work for BIH in 2015.

With **Thomas Südhof**, we were already able to recruit a Nobel Prize-Winner in Medicine as a visiting scientist in the spring. Together with Südhof, who teaches and does research at Stanford University in California, the research group headed by Christian Rosenmund of Charité is examining how nerve cells interact during diseases. The Nobel Prize-Winner came to BIH for an initial work stay in November. In America, he has started to investigate the role of mutant proteins in the synaptic transmission of information. In cooperation with Rosenmund's research group, these investigations are being intensified in order to gain a better understanding of how these protein modifications contribute to the genesis and development of various disease patterns in humans. Based on this work, it will be possible in future to gain a more holistic view of neurological mechanisms that are also of relevance to other BIH projects.

In the context of Thomas Südhof's Fellowship, several academic researchers of the Charité research group headed by Christian Rosenmund will be trained in stem cell technology in Stanford. Thus research at BIH is benefiting from the knowhow of the American experts in more than one way.



Thomas Südhof: first working visit at BIH

The Einstein BIH Visiting Fellow Program is a cooperative venture by Stiftung Charité and the Einstein Foundation Berlin.



Einstein Stiftung Berlin
Einstein Foundation Berlin

STIFTUNG CHARITÉ

The Einstein BIH Visiting Fellowships are awarded to internationally distinguished researchers. Funding is up to 150,000 euros per year per fellow, and is initially approved for a period of three years.

WHERE WORLDS OF RESEARCH COME TOGETHER

It all starts with a convincing idea: that translational research can only meet with success if basic researchers and clinical practitioners are working together hand in hand under one roof. It was this notion that led us to the establishment of the new Clinical Research Unit (CRU) of BIH. Developments have been in progress at four sites in Berlin since early 2014 – with the first clinical studies, construction plans and, above all, the purchase of equipment.



CRU is all about interdisciplinary research. Boundaries between the different research worlds disappear as joint activities get underway. The CRU unites workspaces in the lab with ambulatory research at the Charité and MDC campuses. This includes the three Charité sites with inpatient wards of Campus Benjamin Franklin in Steglitz, Campus Virchow-Klinikum in Wedding and Campus Mitte as well as the common MDC-Charité site Campus Buch with its outpatient and inpatient facilities. Our planning and organization of the CRU is based on the knowhow and experience gained in translational research at Charité and MDC, for example from clinical studies in oncology, or from the already established joint Experimental and Clinical Research Center (ECRC) in Buch. In addition to these sites of the CRU, a cross-locational CRU will be developed for intensive care research before, during and after operations. Knowhow, services and

infrastructure currently being established at the CRU will be available to all BIH sites and users in the future.

Interdisciplinary and quality-assured research – the example of the CRU

Systems medicine research at BIH above all means one thing: joint studies in cooperation with various clinical departments. Our goal is that study patients can be examined independently of their clinical care and on an interdisciplinary basis, that the overarching and central services can be made use of. Moreover, we want to generate new cohorts of systems medicine patients in the medium term. Avoiding the duplication of structures and ensuring efficiency through synergies and quality assurance are paramount in this context.

Developing a structure through clinical studies

Our Pathfinder Studies are key to establishing an effective CRU research infrastructure. The Pathfinder Studies started in fall 2014, and 25 are in progress. These studies help identify the details of BIH-specific requirements and then optimize processes and modules involved in the study. Examples here include the bio-sample management system and an electronic data capture system for study data.

The CRU of the ECRC at Campus Buch, which has already been operating since 2002, has also been integrated in the plans for a cross-locational CRU research structure since 2014 and is contributing its experience and suitable Pathfinder Studies.

In late 2015, an internal evaluation is proposed to examine the role of the Pathfinder Studies e.g. in establishing a general infrastructure and personnel structure.

Investments, construction planning, staff

“Establishing” refers both to purchasing equipment and rooms and to human resources. Since 2014, inpatient and outpatient study teams have been working at the individual CRU. These study teams consist of two study physicians and one to three study nurses and medical technical assistants, who are supporting ongoing studies. Here, the CRU is also responsible for the training of staff. This includes both the transfer of basic knowhow for conducting clinical studies in general (working in accordance with Good Clinical Practice) and professional development relating to individual studies incorporating methods for specific projects. Two site coordinators are heading, coordinating and developing study teams and structures at local level. There is a further coordinator for the cross-locational peri-operative and intensive care unit that was also established in 2014.

In addition, central service units were set up at the CRU that provide services for all CRU sites, and contacts have been established with the BIH core facilities to ensure long-term access to the BIH technologies for all CRU users.

The Pathfinder Studies have been selected both by their potential for establishing the CRU structure and the compatibility to the site. Investments at Campus Charité

Mitte last year focused on extended phenotyping (sonography equipment with automated IMT measuring, LZ-RR equipment with parallel pulse wave analysis, Body Plethysmography [BOD POD], bio-impedance z-analysis). In this context, a software prototype for the automatic detection of visceral fat tissue with MRT imaging has been developed that enters the test phase in 2015. In addition, study nurses were trained with a special focus on neuro-cognition and cardio-neurovascular and metabolic clinical research.

At **Campus Virchow-Klinikum**, an S1 lab was set up for pre-analytics in 2014, entering operation in January 2015. Work has been in progress since late 2014 on establishing the “Labvantage” facility, a cross-locational laboratory information and management system for automated sample management and tracking. Furthermore, the establishment of a cross-locational data register for the peri-operative and intensive care CRU has commenced.

In addition to staff training and construction planning, the exchange of knowledge with the existing networks has been a focal area of activity at **Campus Benjamin Franklin**. Since late 2014, construction measures have been carried out at this site – CRU’s own examination and treatment areas are scheduled to enter operation in the second half of 2015.

Planning details will be developed in 2015 for a new building that is to be set up at **Campus Charité Mitte** in the long term. Accommodation in temporary facilities is scheduled for late 2015. Also in 2015, CRU facilities are to be created at **Campus Virchow-Klinikum**.

All campuses with inpatient wards have been set up with equipment such as centrifuges, freezers, refrigerated storage cabinets for medication, infusomates, perfusors, precision scales, ECG equipment, blood pressure equipment, and

The Pathfinder Studies are externally funded clinical studies. The systems medicine focus of these studies is being developed with BIH support (infrastructure or staff).



THE CROSS-LOCATIONAL CENTRAL SERVICES:

- Bio-sample management
- Biostatistics
- Quality management
- Data management
- IT services
- Neuropsychology

The CRU is a unit for patient-oriented and volunteers research.

The CRU of BIH is a research unit that operates separately from regular outpatient and inpatient care.

The CRU enables the establishment of and access to well characterized, stratified groups of patients or healthy volunteers. They are the basis of Investigator Initiated Trials [IIT].

personal scales. In 2014, the RedCap – an open-source system – was chosen as electronic data capture system and adapted to CRU requirements.

The CRU at **Campus Buch** already has a respiration chamber that enables the detection of metabolic changes at five-minute intervals as well as a normobar hypoxia chamber. Plans are currently being drawn up for a modernization of the Robert-Rössle-Institut, which accommodates CRU Buch and the ECRC. The construction activity, which is to take several years, centers on a new building for the BIH omics core facilities and space for BIH research projects at Berlin-Buch.

Regular meetings to foster progress

All site coordinators meet once a week to discuss the progress at CRU and exchange knowledge, experiences and ideas. They are responsible for strategic on-site developments, including staff recruitment, purchase of equipment, and organization of day-to-day routines. Also, a steering committee has been appointed consisting of clinic directors of all Charité campuses and MDC representatives. The steering committee is to accompany and monitor on-site developments and has appointed working groups to deal with specific topics such as governance, user regulations and calls for clinical research projects.

Outlook 2015: improving services, developing infrastructure, establishing cooperation

Our most important goal for 2015 is to make the CRU fully operational. Above all, this means providing a sufficient number of adequate facilities at all sites: examination and treatment areas, service rooms and “special facilities” such as labs, archive rooms and rooms for refrigerating equipment. Also, we will focus not only on CRU

expertise, rooms and services benefiting BIH-funded studies in the long term but on offering this to other excellent researchers as well.

Furthermore

- cooperation with the coordinators of the BIH Core Facilities is being intensified,
- governance structures are being developed, regular access for Charité and MDC researchers to CRU services is being created, and terms of use and quality assurance activities are being established,
- infrastructure is being optimized; for example, the sample management system is being employed in further studies and adapted to the requirements of the users,
- a patient identification system is being established on the basis of the legal data protection guidelines,
- long-term cooperation concepts with already existing study facilities at Charité are being developed.

CRU SITE COORDINATORS	
Campus Charité Mitte	PD Dr. Knut Mai and Dr. Jens Steinbrink
Campus Benjamin Franklin	PD Dr. Denis Poddubnyy and Dr. Joachim Weber
Campus Virchow-Klinikum	Prof. Nina Babel and Dr. Anne Flörcken
Campus Buch	Dr. Michael Boschmann and PD Dr. Robert Preissner

DECENTRALIZED COORDINATORS	
Peri-operative and intensive care unit	PD Dr. Steffen Weber-Carstens
Quality management	Dr. Kerstin Bollweg
Interface with the omics technologies	Prof. Uwe Kornak
Biostatistics	Alexander Krannich
IT	Peter Brunecker
Cognition and neuropsychology	Dr. Antje Kraft

CRU Steering committee

NAME	ORGANIZATION	AS REPRESENTATION FOR ...
Prof. Joachim Spranger (Speaker)	Charité	Charité Campus Mitte
Prof. Britta Siegmund (Deputy speaker)	Charité	Charité Campus Benjamin Franklin
Prof. Angelika Eggert	Charité	Charité Campus Virchow-Klinikum
Prof. Matthias Endres	Charité	Charité Campus Mitte
Prof. Ulrich Frei	Charité	Clinical Center Management Charité
Prof. Michael Gotthardt	MDC	MDC
Prof. Ulrich Kintscher	Charité	Clinical Trial Management Unit
Prof. Young-Ae Lee	MDC/ECRC	Experimental and Clinical Research Center
Prof. Friedrich C. Luft	MDC/ECRC	Experimental and Clinical Research Center
Prof. Dominik Müller	MDC	Experimental and Clinical Research Center
Prof. Antonio Pezzutto	Charité	Charité Campus Benjamin Franklin
Prof. Burkert Pieske	Charité	Charité Campus Virchow-Klinikum
Prof. Kai Schmidt-Ott	MDC	MDC
Prof. Simone Spuler	ECRC	Experimental and Clinical Research Center
Prof. Dieter Volk	Charité	Charité Campus Virchow-Klinikum
PD Dr. Frank-Dietrich Wagner	Charité	Charité Research Organisation

Pathfinder Studies at the four sites



CAMPUS	STUDY	TOPIC
Campus Benjamin Franklin	GESPIC	Spondylarthritis
	Painful Knee	Inflammation
	INSPIRE	Stroke
	CRG "T cell receptor gene therapy"	Cancer, genetics
	Neuropathic Pain	Neurology
Campus Mitte + Peri-operative and intensive care unit	Capsys	Lung, inflammation
Campus Mitte	TAVAP	Rheumatism, neurology
	OA Treat	Inflammation
	Berlin Lifetime Observation of Vascular Events – BeLOVE	Metabolic diseases
	RepDiet	Endocrinology
	CRG "Proteostasis for treatment of Alzheimer"	Alzheimer's disease
Campus Virchow-Klinikum	CRG "Congenital Disease"	Rare diseases, pediatrics, mutation of genes
	BlDRIM	Immunosuppression in patients who underwent kidney transplantation
	ImbruVeRCHOP	Oncology, lymphoma
	IntReALL SR/HR-Studies	Paediatric leukaemia
Peri-operative and intensive care unit	BioCog	Gerontological research, postoperative cognitive dysfunction
	EPJIC	Implant, infection
	Rejection/Transplant	Rejection/Transplant
	TRG-Inflammation	Anaesthesiology, intensive care
	SAFE-T	General surgery, nephrology
Campus Buch	Seeing Sodium	Sodium and cell and organ functions
	Hypoximet	Metabolic diseases
	Circular RNA	Characterization of circular RNAs in human diseases
	MyoPain	Neuromuscular diseases
	Metab	Metabolic diseases

HIGH-PERFORMANCE TECHNOLOGIES

Biomedical research needs structures. We want to provide our researchers with the best technological platforms, which is why the establishment and development of scientific infrastructure and core facilities with high-performance equipment is one of our central objectives. We can only be successful in systems medicine-oriented translation if we have first-class equipment and methods at our disposal. In all, we invested around 24 million euros in BIH Core Facilities in 2014: omics technologies, bioinformatics and IT, stem cells and transgenic technologies, biobank and medical imaging, and chemical biology.*

Last year, over forty scientific and technical positions were created in the individual BIH Core Facilities. We want to provide the best technologies and aim at the perfect integration of and cooperation between the facilities themselves, with research projects, and with the CRU.

The BIH Omics Core Facility

The BIH Omics Core Facility integrates three independent core facilities for genomics, proteomics and metabolomics, thus linking all three levels of high-throughput data generation. It is central to the success of the systems medicine approach that all three omics core facilities work hand in hand, being actively involved in the development and optimization of the methodological expertise, in close exchange with associated research groups, bioinformatics and the clinic. This kind of integrated omics infrastructure focusing on clinical issues is unique in Germany and represents one unique feature of BIH. The BIH Omics Core Facility is located in a new “interim” BIH building on the MDC Campus in Buch. After the refurbishment of lab and office spaces, the core facilities set up their technical equipment in December 2014. In future, the BIH Omics Core Facility will be located at the



refurbished Robert-Rössle-Institut on Campus Buch.

1. Genomics

The goal of genomics is the systematic analysis of the genome, i.e. all genes expressed in a cell, a tissue, an organ or an entire organism. It is based on methods to extract, multiply and sequence DNA. The BIH Core Facility Genomics was set up in 2014 and equipped with state-of-the-art technologies for next generation sequencing. The core facility has already been supporting a wide range of projects conducted by BIH, MDC and Charité groups. The facility possesses four sequencers (2 HiSeq4000, 1 Illumina NextSeq 500, 1 Fluidigm C1) for a broad spectrum of applications (e.g. de novo genome sequencing, genome re-sequencing, transcriptome sequencing,

total-RNA/mRNA sequencing, single cell mRNA sequencing).

In order to meet the considerable sequencing demand of the systems medicine projects, new methods that are particularly suitable for clinical applications are being developed. In addition, the entire sequencing process for human material is to be optimized and standardized in order to fulfill clinical quality standards.

→ Contact:
Dr. Wei Chen (MDC)

2. Metabolomics

The comprehensive analysis of primary and secondary metabolites in cell lysates and other samples is the core task of the BIH Core Facility Metabolomics. It combines metabolomics analysis with mathematical tools like flux balance analysis, which predicts the behavior of metabolic networks in different environmental conditions, and with bioenergetic measurements. Metabolomics provides important information on the mechanisms of diseases like cancer, neurodegenerative diseases, asthma or diabetes.

The technological focal point of this core facility is the analysis of human samples

* in cooperation with the Leibniz Institute for Molecular Pharmacology (FMP)



*“Eppendorf epMotion 7075”:
an automated liquid handling system
for the preparation of RNA libraries.*

with absolute quantitative metabolomics methods. The basic service of the core facility (which is equipped with three mass spectrometers: GcXGc-TOF, LC-QQQ and nLC-LTQ-Orbitrap, coupled with several chromatographic systems) comprises the analysis of around 100 polar compounds (metabolites of glycolysis, citric acid cycle, amino acids, organic acids and amines). Depending on the sample material, an additional several hundred higher molecular polar compounds and lipids can be analyzed. Thanks to the rapid developments in metabolomics, the core facility portfolio will be extended by further analytical techniques. The Core Facility Metabolomics was already supporting BIH research projects and various research groups at Charité and MDC in 2014.

→ Contact:
Dr. Stefan Kempa (MDC)

3. Proteomics

Each of the body's cells consists of more than one hundred thousand proteins. Qualitative proteomics enables a quantification and identification of thousands of proteins from cell samples. The BIH Core Facility Proteomics assists BIH-supported research groups with these analyses, using state-of-the-art mass spectrometers (GCxGC-EI-ToF; QQQ-LC-MS; Q-Exactive [Orbitrap]). These data can be applied in analyzing the cellular response to stimuli

or disease-related alterations or in defining and decoding alterations in the interactome of a certain protein. In order to guarantee an efficient implementation and the long-term excellence of the core facility and to maximize synergies, integration with the core facilities for metabolomics and genomics and linking up with the MDC Proteomics Service Unit is essential.

→ Contact:
Dr. Gunnar Dittmar (MDC)

The Bioinformatics Core Unit

The Bioinformatics Core Unit was established in 2014 as a central service facility offering expertise for bioinformatics and analysis of biological data generated in clinical research. The Bioinformatics Core Unit closely cooperates with the other core facilities, especially with the BIH Omics Facility and IT.

The establishment of this new service-oriented unit started in 2014. Teams of bioinformatics experts, covering different areas of knowledge, as well as a core unit leader were recruited. The teams are cooperating with other BIH Core Facilities both with regard to computational methods and to the analysis and evaluation of biological data. In October 2014, the BIH Steering Committee Bioinformatics organized a best-practice workshop on the topic of translational bioinformatics with internationally renowned experts from Europe and the USA. More than 100 scientists from the Berlin area participated in the workshop. In December, the core unit moved to a new location in the Luisenstraße in Berlin Mitte.

→ Contact:
Dr. Dieter Beule (BIH)

BIH Core Facility IT

IT activities focused on measures to create a BIH-wide network infrastructure. For this purpose, the BIH Core Facility IT established W-LAN in areas with inpatient wards, a preparatory activity to achieve better, and mobile clinical documentation. The core components for the yet to be created BIH network environment and integration in the high-performance computer center at MDC Campus Buch have been set up. The core facility has been extended by additional storage capacities for archiving data from BIH projects. Adapting and extending IT applications in clinical areas was a further measure.



The most important construction project for the core facility last year was the BIH high-performance computer center. The building was completed in 2014. This computer center provides sufficient space for scientific computing at BIH. It consists of approx. 90 computer nodes and 1.5 PB mass memories, all of which communicate with one another via a very fast network. The energy efficiency and therefore cost efficiency is a unique feature of the computer center. Its power usage effectiveness (PUE) is at around ≤ 1.06 . PUE defines the ratio of entire electric energy consumption at the computer center (IT equipment plus infrastructure components) to electric energy consumption of the IT equipment alone; a PUE value of 1.0 implies 100 per cent efficiency. In comparison, the computer center set up by a major American search engine enterprise in 2008 has a PUE of 1.21. Also, initial earthworks demonstrate that

the fast, redundant connection of Campus Buch with Charité started in 2014.

→ Contact:
Dr. Michael Mallach, Martin Peuker
 (Charité), **Dr. Alf Wachsmann** (MDC)

BIH Core Facility Stem Cells

Based on the existing excellent expertise at Charité and MDC, a multidisciplinary BIH Core Facility Stem Cells has been established at two different locations. The service unit at Charité Virchow-Klinikum site focuses on generating disease-specific iPS cell lines for basic research and clinical applications in the fields of rare diseases, muscular-skeletal systems, nephrology, cardiology, and cancer. The service unit at Campus Buch concentrates on generating patient-specific iPS cell lines with disease-specific mutations, including isogenic controls, quality control and the establishment of specific differentiation protocols. In 2014, the facility leaders of the two sites were recruited, and at both sites units were established replacing S1 and S2 cell culture labs. Also, specialized equipment that is necessary to provide all BIH scientists with the latest cutting-edge stem cell technologies was purchased. This includes a comprehensive range of cell culture and molecular biology accessories to derive, maintain, characterize and differentiate human-induced pluripotent stem cells (hiPS). The cell culture labs of the core facility were equipped with S2 safety cabinets that have a build-in (fluorescence-)stereo microscope.

In addition, two training programs were offered to the BIH scientists in 2014 (“Training on handling and maintenance of human pluripotent stem cells”).

Together with the German Stem Cell Network (GSCN), the BIH Core Facility Stem Cells is in the process of initiating a network of core facilities for iPS derivation in Germany.

The aim of this network is to establish common standards by sharing cell lines, tools and protocols, which leads to a greater degree of efficiency and comparability.

→ Contact:
Dr. Sebastian Diecke (MDC),
Dr. Harald Stachelscheid (Charité)

Core Facility Transgenic Technologies

The Core Facility Transgenic Technologies is developing an engineering, differentiation and phenotyping facility for iPS cell-based modeling of diseases. The core facility can be used by scientists in BIH projects to gain new insights into human genetics and disease mechanisms. In the context of the core facility, a research group at MDC began to establish CRISPR/Cas-based gene editing in close cooperation with the BIH Core Facility Stem Cells. This enables single gene or allele knockouts to be generated, an application that is applied e.g. in the investigation of Parkinson's disease at genome level.

→ Contact:
Dr. Ralf Kühn (MDC)





BIH Core Facility Biobank

In order to meet the requirements of systems medicine research at BIH, the BIH Core Facility Biobank has been established at two locations, at Charité Campus Virchow-Klinikum and at MDC. The MDC site in Berlin-Buch provides for the long-term storage of liquid bio-samples from large cohorts, in particular in epidemiological studies. The biobank facilities at the Charité Campus Virchow-Klinikum site are suited for the storage of liquid and tissue samples from clinical routine diagnostics and disease-oriented clinical studies and from model organisms. The capacities of the existing biobank units are being expanded for the BIH requirements. The biobank stores various types of specimens under standardized conditions with the employment of automated storage systems at very low temperatures. Here, the emphasis is on the high quality of the samples, reliability, swift identification and the accessibility of samples to be used for examinations.

In addition to the storage of samples, various services such as histology and immunohistochemistry, DNA or RNA extraction are to be provided in the future.

Planning of the new BIH Biobank buildings at Campus Virchow-Klinikum and at Campus Buch took place in 2014, and construction is to commence in 2015. Since the work of the BIH Core Facility Biobank does not consist solely of storing single bio-specimens but also comprises services for the evaluation, preparation and analysis of biosamples, a range of equipment has been purchased to improve the service capacities of the biobank. The establishment of ethical and legal frameworks for the use of single specimens from patients and related clinical data in BIH research projects has commenced. In addition, the acquisition of patient samples for the first BIH projects has started.

➔ Contact:
Prof. Dr. Michael Hummel (Charité),
Prof. Dr. Tobias Pischon (MDC)

Chemical Biology

In order to identify new pharmaceutical agents, BIH is participating in the Chemical Biology Unit of Leibniz Institute for Molecular Pharmacology (FMP) on Berlin-Buch Campus. The unit was established in 2003 and has since then been steadily expanded. This FMP unit offers support in the development and adaptation of tests for high-throughput screening, and screening and validating of the hits. The substance library containing around 60,000 substances is an intelligently designed library derived from the World Drug Index. In addition, access is provided to non-commercial substances with unique structures that come from academic donors. This unique library presents a rationally designed screening collection with maximal and efficient coverage of the chemical space providing highly diverse structures and high hit rates.

Each year, several successful screenings have been processed at the Medical Chemistry Unit of the FMP through chemical optimization and/or derivatization of the compounds with the aim of obtaining a proof-of-concept compound/early lead substance.

In addition to the services provided starting from May 2014, the technical equipment of the Chemical Biology Unit was further extended to support the systems medicine – i.e. personalized and risk-adapted – and translational approach of BIH. 2,300 FDA-authorized agents (authorized drugs and substances undergoing clinical tests enabling swift translation to the clinic: drug repurposing) were identified and integrated in the substance library, as well as 20,000 natural substances from Analyticon Discovery. In addition,

new substance were synthesized, a new fragment concept for the identification of lead structures was developed, a new high performance liquid chromatography (HPLC) was integrated, and the data bank was updated with the new substances (structure, amount, profiling data). In the area of screening, new technologies were integrated: high-throughput screening with flow cytometry (FACS, MacsQuant, Miltenyi) and high content screening with modernized automatic microscopes (3 ArrayScan microscopes).

Through cooperation with EU-OPEN-SCREEN, ChemBioNet and Helmholtz Drug Research, the Chemical Biology Unit enables BIH researchers to benefit from Open-Access Technologies.

→ Contact:

Dr. Jens Peter von Kries,
Dr. Marc Nazaré

(Leibniz-Institut für Molekulare
Pharmakologie)

Medical Imaging

Medical Imaging is of relevance to research at BIH. On the one hand, phenotyping of test persons and patients can be achieved with high-end imaging technologies. On the other hand, medical imaging signatures are increasingly being used as the conclusions of proof-of-concept studies and in clinical studies of phases II and III. Thus, the expertise and development of non- or minimally invasive imaging technologies are essential for translational research.

In 2014, a children's MRT (magnetic resonance tomography) was purchased for BIH to be located at Campus Virchow-Klinikum, and an angiography workplace was established at Campus Charité Mitte. A cross-locational concept for imaging techniques at BIH is to be implemented in 2015.

→ Contact:

Prof. Dr. Bernd Hamm,
Prof. Dr. Winfried Brenner (Charité)



Milestones in 2015

- Development of **Standard Operation Procedures** (SOPs) and rules for users
- Establishment of a **Laboratory Information and Management System** (LIMS)
- Extension of the range of training programs
- Introduction and coordination of **data protection guidelines** for the integration of biological data from diverse sources
- Start of operations of the **BIH Computer Center** (computer clusters and archive systems)
- Construction and opening of the new **Biobank building** at Charité Campus Virchow-Klinikum
- Definition and development of interfaces between different core facilities

NEW APPROACHES IN TRAINING AND PROFESSIONAL DEVELOPMENT

All BIH training and educational offers are accommodated under the roof of the BIH Biomedical Academy. Our aim is to train a new generation of translation-minded scientists and clinicians. We focus on the improvement of specialist training and career prospects for early-career scientists in biomedical research.

We have established a number of closely coordinated training and funding programs. The mission of the BIH Biomedical Academy includes the integration and development of existing program curricula and educational offers at MDC and Charité that hold relevance for BIH research. The integration of clinical and basic research activities at an early stage ensures greater competencies in translational research.

In 2014, we supported a total of 39 junior scientists through the BIH Biomedical Academy. Our funding instruments in detail:

BIH Translational PhD Project Grants

- require “twinning”, i.e. cooperation between Charité and MDC.
- must represent new developments and encourage knowledge exchange between basic research and clinical application.
- first call in March 2014, ten projects were chosen (read more about this on page 30)
- second call in March 2015

BIH Junior Clinical Scientists in cooperation with the Charité Clinical Scientist Program

- supports physicians who take an interest in scientific research at the beginning of their clinical training; 20 per cent of working hours are protected for research time.
- first call in August 2014, ten candidates were chosen for funding
- Two further rounds of calls are planned for 2015 for up to 20 further Junior Clinical Scientists.

BIH Clinical Scientists in cooperation with the Charité Clinical Scientist Program

- Physicians taking an interest in research during the second half of their clinical training are supported by a structured, scientifically and clinically profiled training program.
- first rounds of calls for the program in May and August 2014, co-financed together with Stiftung Charité and the Charité Medical Faculty, a total of 18 candidates were selected for funding
- A further round of calls for up to ten Clinical Scientists was announced in early March 2015. They are to be funded half via BIH and half by the Charité Medical Faculty.

Doctoral scholarships for dentistry and medicine students (MD Student Research Stipends)

- for doctoral candidates pursuing a Dr. med. or Dr. med. dent. degree
- Students taking an interest in research can already concentrate on translational research activities at the beginning of their career.
- first call for this funding instrument in October 2014, eleven candidates were selected for funding
- A further call is planned for Fall 2015.

BIH Translational Postdoc Grants

There will be a first call for translational postdoc project grants in 2015.

"It's quite a challenge for a physician to be a researcher as well. This program creates ideal conditions for high-quality research."

Agustin Liotta (Clinical Scientist)



Mirjam Karber*

"It's much easier for a Clinical Scientist to engage in academic health science."

Michaela Golic (Clinical Scientist)



Christian Lucht*

"I'm convinced that significant progress in medicine can only be achieved through integrated thinking and working."

Simon Jacob (Clinical Scientist)



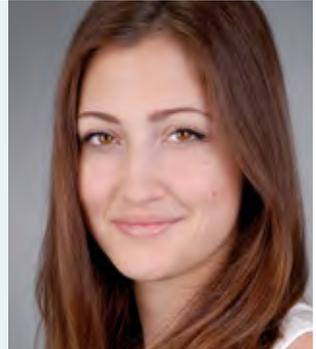
Julia Loeffler*



Henrike Lisa Sczakiel**

"Working with patients in the clinic always shows me what our research projects are really about."

Julian Hellmann-Regen (Clinical Scientist)



Rebeka Major**

"The Clinical Scientist career track is an excellent way to combine clinical and research activities."

Wolfgang Böhmerle (Clinical Scientist)



Julian Pholan**

"Combining clinical and research careers helps us offer tomorrow's patients better treatment."

Florian Kurth (Clinical Scientist)



Carmen Lorenz*

"Physicians engaging in science are key to translational research."

Philipp Enghard (Clinical Scientist)



Carl Goetzke**

DISSERTATION IN TRANSLATION

One of our overarching goals is to provide in-service training and educational offers for translational and systems medicine-oriented early-career scientists – this includes supporting doctoral candidates in various disciplines who are working at the interface between basic research and clinical research. BIH Translational PhD Project Grants require “twinning”, i.e. a project initiated jointly by Charité and MDC. They should tackle new research questions and encourage knowledge exchange between basic research and clinical application. In 2014, the first ten translational PhD projects were awarded and PhD students were recruited to them.

With the BIH Translational PhD Project Grants, the BIH Biomedical Academy offers qualified early-career scientists the opportunity to choose a translational-systems medicine focus for their doctoral degree. The first step is the selection of ten suitable research projects. The projects are assessed by an internal panel of experts. In a second step, students are recruited to one of these projects. In addition to funding for their position, selected doctoral candidates are provided with a small budget for laboratory expenses and/or travel costs for a three-year period and are supervised by two scientists from different research fields, e.g. a combination of clinical basic science and systems medicine group leaders.

Eight female and two male early-career researchers are being funded in the context of the projects selected in 2014:

Divisha Bhatia is examining immigration and hiding mechanisms of leukemia cells in the testicles in childhood acute lymphatic leukemia.

Supervisors Uta E. Höpken, Cornelia Eckert

Program Helmholtz Graduate School “Molecular Cell Biology”, MDC

Project title Dissecting the cellular and molecular mechanisms of leukemia cell migration and localization to and within the testis in childhood ALL

Amanda Luisa de Andrade Costa seeks to characterize interactions between human microglia cells with glioma cells. Microglia cells play the chief role in active immune defense in the central nervous system; as yet, it is unclear how they affect the growth of gliomas and brain tumors.

Supervisors Helmut Kettenmann, Michael Synowitz

Program International Graduate Program Medical Neurosciences, Charité

Project title The role of human microglia for glioma progression

In the project of **Mirjam Karber**, data from Charité patients with a rare liver disease as a result of artificial feeding are to be established in a novel approach and be analyzed at clinical and molecular level. In future, preventive therapy approaches are to be derived from this for these patients and patients suffering from chronic failure of the intestine and other chronic liver diseases.

Supervisors Karsten Henrich Weylandt, Ulrich F. Pape, Wolf-Hagen Schunck

Program International Helmholtz Research School, MDC

Project title Regulation of pro- and anti-inflammatory mechanisms mediated by fatty acid metabolites in metabolic liver damage – a role for omega-3 fatty acids in prevention?

Larissa Kraus is concentrating on RNA editing, a biochemical cellular process that only recently turned out to be a key mechanism in certain harmful neuronal alterations in epilepsy. The team seeks to identify specific RNA GlyR antagonists and validate the therapeutic potential of these substances.

Supervisors Martin Holtkamp, Jochen Meier

Program International Graduate Program Medical Neurosciences, Charité

Project title RNA-edited glycine receptor as marker and therapeutic target in intractable epilepsy

Julia Löffler is looking at immune responses during the regeneration of bones. Specifically, she is examining links between the energy metabolism and immune cell activation within the hematoma micro-milieu.

Supervisors Stefan Kempa, Georg Duda, Anke Dienelt
Program Berlin-Brandenburg School for Regenerative Therapies
Project title Impact of energy metabolism on bone regeneration

Carmen Lorenz is examining Leigh Syndrome (LS), a so far incurable congenital disease incorporating a mitochondrial metabolism disorder. Research is aimed at understanding the LS mechanisms causing the disease.

Supervisors Alessandro Prigione, Markus Schülke-Gerstenfeld
Program Helmholtz Graduate School “Molecular Cell Biology”, MDC
Project title Investigation of the energy expenditure of human iPSC-derived basal ganglia neurons from patients with Leigh Syndrome

The project of **João Miguel Parente Fernandes** examines new approaches in cancer therapy. The focus is on protein synthesis via the internal ribosome entry site (IRES), which tumor cells use to maintain their oncogene expression.

Supervisors Matthias Selbach, Patrick Hundsdoerfer
Program Helmholtz Graduate School “Molecular Cell Biology”, MDC
Project title Targeting alternative translational initiation of oncogenes in cancer cells

After heart attacks, the level of the trans-membrane protein rises in humans. The diagnostic or therapeutic use of the protein for this disease is being examined by **Bernadette Nickl**.

Supervisors Michael Bader, Karl Stangl
Program International Helmholtz Research School, MDC
Project title Functional characterization of osteoactivin/Gpnmb in myocardial infarction



Markus Petermann is examining how anti-depressive agents affect mice lacking brain serotonin. The long-term goal is to identify anti-depressant mechanisms and alternative methods to treat depressions or age-conditioned retardation of learning and memory capabilities.

Supervisors Golo Kronenberg, Michael Bader
Program International Graduate Program Medical Neurosciences, Charité
Project title Identifying the mechanisms of antidepressant drug action in mice lacking brain serotonin

Laura Moreno Velásquez is examining the activity and maturing of the cerebral cortex shortly after birth. The goal here is to learn more about the link between malfunctioning in the development of neuronal networks in this phase and their later impacts.

Supervisors Friedrich Jochenning, James Poulet
Program International Graduate Program Medical Neurosciences, Charité
Project title Modulation of neonatal olfactory cortex spontaneous synchronized activity in the GLUK2 KO model of mental retardation

A new call for up to ten further research grants was announced in March 2015 and will be decided in May 2015.

EXCHANGE AND NETWORKING: BIH YOUNG SCIENCE

The BIH Young Science initiative has been in existence since the founding of BIH. Its founding meeting was held in January 2014. Prof. Britta Siegmund, Prof. Max Löhning and Prof. Alexander Loewer are the initiators and spokespersons of BIH Young Science – and thus form the spearhead of particularly engaged junior scientists among translation-minded basic and clinical researchers at BIH.



(f l t r) Roman Marek (Coordinator), Max Löhning, Britta Siegmund and Alexander Loewer

How did this initiative come about?

The first meetings and preliminary talks on launching our initiative already took place in February 2013. Our role model was the “Junge Charité” initiative for physicians and junior scientists, which had been started in 2006 and has promoted closer links between clinic, research and teaching. In addition, we wished to create a network for the junior scientists at Charité and MDC and give them a voice at BIH. By cooperating, we benefit from experience gathered so far by MDC and Charité, such as the jointly operated Experimental Clinical Research Center (ECRC) on Buch Campus. Stiftung Charité and Humboldt Universität zu Berlin have also supported our network activities right from the onset.

BIH Young Science already had more than 50 members in late 2014. What have the most important topics been so far?

Basically, our aim is that all those at Charité and MDC get to know each other better and join forces in identifying new research interests, so that via this exchange, new cooperation ventures can develop under the roof of BIH. This is why two or three of our members at Charité and MDC present themselves with their research foci and methods at each meeting. Furthermore, BIH Young Science has succeeded in establishing itself as a communication platform concerning BIH issues. In the context of our colloquia, we discuss BIH activities such as the Clinical Research Unit at the various campuses or the latest BIH calls for project proposals. In order

to achieve optimal networking among our members, we are developing a database providing a fast overview of the individual groups and fields of research.

Which goals have you set yourselves for 2015?

Our most important goal remains that of promoting communication and cooperation between MDC and Charité scientists through regular meetings. Also, we want to continue providing information on the latest structural developments within BIH in order to make the institute more transparent for insiders and outsiders. One key event in 2015 will be the BIH Young Science Symposium, taking place from 8–9 October, and involving international speakers and scientists from Charité and MDC. Three of our members are seeing to the scientific organization of the Symposium: Michael Hinz, Uta Höpken and Michael Schumann. Furthermore, we are planning a workshop retreat for our members so that we can develop proposals together and provide new ideas for BIH.

OUTLOOK

**BIH Young Science Symposium:
Translating basic research into
clinical application**
8–9 October 2015

TAILORED FUNDING

Offering optimum working conditions and attracting international top-level researchers and junior scientists to BIH: These are the central goals of the “Private Excellence Initiative Johanna Quandt” of Stiftung Charité. In 2014, calls were announced for nine out of a total of twelve programs with which scientists distinguished by a clear translational and systems medicine profile are being promoted.

The Private Excellence Initiative Johanna Quandt primarily supports individuals and individual projects. Thus it is an important supplement to the project-oriented funding lines of BIH. A total of 40 million euros is available for developing BIH in the framework of the Private Excellence Initiative. A top-class scientific advisory council maintains quality assurance of the programs and the funding decisions.

Promoting translational research at BIH

Stiftung Charité’s programs **BIH Clinical Fellows** and **BIH Clinical Scientists** support scientists working in the clinical area. Outstanding senior physicians at Charité wishing to engage in translational research benefit from the BIH Clinical Fellowships. The first four BIH Clinical Fellows – senior physicians – were selected in September.

The **Clinical Scientists Program** provides physicians with support giving them time for their own research during the second half of their clinical training, for after-duty research is no longer in keeping with the times. After a successful pilot phase initiated by Stiftung Charité, Charité has adopted the program. Stiftung Charité continues to fund some of the positions.

The **BIH Delbrück Fellows** and **BIH Short Term Fellows** are concepts for particular junior scientists. Via the former, postdoc

positions plus allowances for research costs are funded for a period longer than average of up to five years; the second program supports qualified researchers from abroad who receive monthly incomes for the duration of their stay. Both programs were announced in 2014 for the first time. Funding commences in spring 2015.

Supporting students and enabling investments

In order to promote students who have demonstrated outstanding performance and engagement, in a further program, Stiftung Charité has also participated in funding up to 40 **Deutschlandstipendien** a year since 2012.

However, Stiftung Charité does not only support individuals. In addition, via the

STIFTUNG CHARITÉ

In 2014, a total of nine Clinical Scientists were funded supported at all sites with support of Stiftung Charité (page 51).

*BIH Clinical Fellows: PD Dr. Kaven Baebler, PD Dr. Christian Bamberg; Prof. Dr. Daniel Baumgart; Dr. Christiane Montag; PD Dr. Stefan Röpke; PD Dr. Michael Synowitz
BIH Delbrück Fellow: Dr. Prateep Beed.*

“I want to contribute to our offering the best conditions to the best brains. Students, physicians and top-level scientists from abroad are to have the opportunity to engage in outstanding and internationally visible health research at BIH. This will push forward not only biomedical research in Germany, but also Berlin as a scientific location.”

JOHANNA QUANDT, FOUNDER OF STIFTUNG CHARITÉ



MEMBERS OF THE SCIENTIFIC ADVISORY BOARD

Prof. Matthias Kleiner**Chairman**

President of the Leibniz Association

Prof. Leena Bruckner-Tuderman**Deputy Chair**

Medical Director and consulting physician in dermatology and venerology at the University Skin Clinic in Freiburg; Vice-President of the German Research Foundation

Prof. Peter Gruss

Academic member of the Max Planck Society

Prof. Thomas Klingebiel

Director of the Clinic for Childhood and Adolescent Medicine of Johann Wolfgang Goethe University Frankfurt and Vice-Dean of the Medical Department

Prof. Babette Simon

Executive Board Chair and Medical Chair of University Medicine in Mainz and Senator of the Helmholtz Association for the research area of "Health"

Prof. Günter Stock

President of the Berlin-Brandenburg Academy of Sciences and Humanities

Meetings of the Scientific Advisory Board in 2014: 4 April | 17 September



Alexander von Humboldt
Stiftung/Foundation



Einstein Stiftung Berlin
Einstein Foundation Berlin

BIH Investment Fund, construction projects and the procurement of large-scale equipment that cannot or cannot fully be paid for with the means of the parties involved or third-party funding and that are of strategic importance to the BIH can be funded.

A total of up to three million euro is provided for the program which is to be spent in two funding rounds. The first call was opened in November 2014. Selection is to be scheduled for spring 2015.

Funding programs with strong partners

In cooperation with the Alexander von Humboldt Foundation, Stiftung Charité awards **Humboldt Research Fellowships at the Berlin Institute of Health**. These fellowships are there to enable international scientists to have a long-term research stay at BIH. The first fellow to be chosen for support was Keisuke Sehara from Japan in May 2014. She is conducting research in the NeuroCure Cluster of Excellence at Charité.

The Einstein BIH Visiting Fellow Program

is a collaborative program with the Einstein Foundation Berlin. The program exclusively addresses international top-level scientists seeking to support BIH with their expertise. The visiting scientists establish a working group of their own with their hosts for which they come to Berlin several times a year for work stays.

Already in February 2014, we were able to announce that we had won over Nobel Prize-Winner in Medicine Thomas Südhof as a BIH Visiting Fellow. In September, with Florian Sennlaub and Michael Sieweke, further Einstein BIH Visiting Fellows were supported with the additional funds. The Einstein Foundation Berlin performs the expert assessment process and assures the program's academic quality with a tried-and-tested multiphase program. A new call started in October. You can find more information on the research projects of the three Visiting Fellows on page 17.

Stiftung Charité seeks to consistently elaborate its program funding in 2015 in order to also support and provide impulses for BIH in the future – in particular thanks to the considerable effort of **Professor Jürgen Zöllner**, who above all supports the establishment of BIH in Berlin's health research and health-care industry with verve.

www.stiftung-charite.de/en

EQUAL OPPORTUNITIES



“Realizing the equal participation of women and men in their diversity” is an important objective of the BIH. In order to achieve this goal, we wish to eliminate mechanisms creating disadvantages for women scientists, raise the share of women at all career levels at which they are under-represented, create family-friendly working conditions and develop an organizational culture featuring gender and diversity competence. We can achieve such a culture by being sensitive to structural and interactional disadvantages, questioning traditional role models and gender stereotypes and accepting modern work models and ways of life.

In this manner, the potential of both sexes, different age levels, and social and cultural backgrounds is to be put to the use of developing BIH and the legally prescribed mission of equality is to be fulfilled.

As an initial step, an equal opportunities coordinator was appointed at the end of 2014. First, an equal opportunities strategy will be developed for BIH, and initial measures to promote equal opportunities, e.g. in the funding lines, will be implemented.

CONTACT PERSON

Caren Kunze

Coordinator Equal Opportunity

Phone: + 49 (0) 30 450 54302

E-Mail: kunze@bihealth.de



FROM RESEARCH TO APPLICATION

In order to successfully use new medical products and methods to the benefit of people, scientific results have to be transferred to new products and innovations. We promote transfer processes and accompany and support these technology transfer processes with various measures.



For example, two BIH Technology Transfer Scouts were employed in 2014 who support MDC and Charité technology transfer units. The scouts are there to advise researchers in BIH projects on identifying utilizable inventions, the commercial development of research results and cooperation with industry or the founding of spin-offs. Furthermore, in cooperation with Charité, we plan to take stock of the existing technology transfer structures in 2015 in order to compile recommendations for their development. In addition, we support transfer processes with seminars, coachings and the following programs.

Technology Transfer Fund

This fund supports projects that bear a commercial or clinical innovation potential the economic exploitation of which yet has to be validated. The funding approved is to be used for validation. Twice a year, there are calls with varying foci for the

BIH Technology Transfer Fund. Funds from the BIH Technology Transfer Fund – Pharma can be used by Charité and MDC researchers for projects aimed at developing new agents or new diagnostics. Project proposals in the fields of medical engineering and Health IT can be funded in the context of the BIH Technology Transfer Fund – Medical Devices.

In addition to the opportunity to receive financial support, the fund provides applicants with expert advice in the context of the review process. The special aspect here is that this qualified counseling will be provided regardless of whether or not the applications are selected for funding. The chosen projects are supported with up to 50,000 euros over a maximum period of nine months.

Four project funding schemes in 2014

In the first call, which was launched in July 2014, 14 proposals were submitted, and funding was approved for four projects. The topics are: novel substances for prostate cancer therapy (**Ulrich Gohlke, MDC**), a quick test for the non-invasive, prenatal diagnostics of trisomy 21 (**Julian Kamhieh-Milz, Charité**), a web-based service platform for diagnostics in single photon emission computed tomography (**Ralph Buchert, Charité**), and a core facility for the manufacture of therapeutics in the treatment of tumors (**Hendrik Fuchs, Charité**).

The funding decisions for the second call (period from 2014/10/31 to 2015/01/31) will be taken in April. The third call of the BIH Technology Transfer Fund on the topic of medical engineering and IT was launched in March 2015.

SPARK BIH Berlin

With SPARK BIH, we have succeeded in launching a program that follows the example of California's Stanford University in bringing discoveries in the field of pharmacology to applications in patients. To implement the SPARK BIH Berlin program, with Professor Craig Garner from Stanford, we have won over an internationally experienced partner who has already successfully participated in SPARK Stanford. The program is to be jointly implemented with the Co-Directors of SPARK, Professor Ulrich Dirnagl (Charité) and Dr. Frank-Roman Lauter.

The first call for SPARK BIH will be launched in May 2015. The aim is to fund three to five projects in the first year with up to 50,000 euros and choose mentors to provide the researchers supported with knowhow from the field of technology transfer.

INFORMATION AND DIALOG

BIH public relations activities started in January 2014. Our key task was initially that of creating the communication strategy foundations in terms of structures and contents in order to provide information about BIH internally and externally. There were a number of occasions for public relations activities to focus on – as reported in the previous chapters. A summary of our public relations activities for BIH.

The first step was to create visibility of BIH: a word mark that would also reflect cooperation between Charité and MDC in a logo. The basic guidelines for its use are defined in a style guide for the word mark. In a comprehensive communications concept, we subsequently defined the goals, target groups and measures with which BIH is to become visible to the public. Here, the focus is above all on clearly presenting the special features of BIH and providing information internally on all activities and steps.

Present in the Net

BIH has been online since April 2014. The bilingual website bihealth.org provides information on the institute, research, funding programs and the latest developments. The BIH Young Science initiative presents itself, and a calendar gives details of the latest BIH events or MDC and Charité events addressing relevant topics. Continuous editing and the elaboration and development of contents is a key objective in our communication.

Integrated communication

Media activities, events and publications represent further communication channels in external communication. Two leaflets contain general information about BIH (“BIH at a Glance”) and about funding opportunities at the BIH Biomedical Academy (“Funding Opportunities”). Both leaflets went to print in the summer of 2014.

Internal communication is also of key significance. Here, it is important to bring BIH together with involved and interested individuals at MDC and Charité. Who is doing what where? Which projects are in progress there? What does interdisciplinary work actually look like? Which services do the BIH Core Facilities offer? This and much more was discussed at the internal BIH-Meeting 2014 in November. More than 220 interested individuals from MDC and Charité came to this event held in Berlin-Mitte and discussed topics with the Board, BIH activists and Head Office staff. In the context of the accompanying poster exhibition, grantees and those responsible for the development and expansion of infrastructure and translational organizational units gave details of concrete projects and plans. In 2015, further information and network events are to follow at the various locations in Berlin.

Scientific events

In December, BIH presented the new cardiovascular specialists for Berlin to the public with a “Welcome Symposium”. In a joint effort with Charité, MDC, German Centre for Cardiovascular Research (DZHK) and German Heart Institute Berlin (DZHB), BIH has succeeded in winning over top-level scientists to Berlin and establishing the first three BIH professorships. In the joint symposium, the newly appointed specialists presented their focal areas of research and work. With around



WWW.BIHEALTH.ORG/EN

Berlin Institute of Health online

170 participants, the symposium was a great success – despite its taking place at the height of the academic event season.

Speaking at congresses and conferences

Above all Chair of the Board of Directors Professor Ernst Th. Rietschel presented BIH at numerous congresses, conferences and meetings. Examples include the Medical Faculties Congress, The Innovation Congress of German University Medicine, the World Health Summit and the European Students' Conference.

First presentation abroad

In terms of international visibility, our participation in the GAIN (German Academic Network) Conference in Boston/USA in September was an important step. Here, more than 400 scientists working in the USA meet each year. The Chair of the Board of Directors presented BIH in various panel rounds and workshops and discussed new approaches in translational research with the scientists. General information about BIH was presented at the Talent Fair. Delegations from Japan and Thailand visiting Charité were also interested in BIH.

The first BIH Visiting Fellow Thomas Südhof was a special highlight from a communications perspective. BIH's having recruited a Nobel Prize-Winner with him was worth a broad media coverage. We already look forward to announcing the first exciting research results to the public.

OUTLOOK

In 2015, BIH is to further extend internal communication and create a digital platform for information, communication and transparency.

The further development of online communication enabling the continuous provision of information on activities in and from BIH is just as relevant. Last but not least, scientific events and workshops will be important elements in establishing systems medicine-oriented research at BIH next year.



BIH Welcome Symposium
in December 2014



**BERLIN INSTITUTE
OF HEALTH
FACTS AND FIGURES 2014**

Objective and Legal Framework of BIH

Charité - Universitätsmedizin Berlin and Max Delbrück Center for Molecular Medicine (MDC) combine their expertise in Berlin Institute of Health (BIH). The aim is to establish a Shared Research Space for interdisciplinary, systems medicine-oriented research projects. This will accelerate the translation of basic research findings into benefits for patients and enable clinical observations to be transferred to new, basic research issues.

The legal framework for the work of BIH in 2014 was provided by the founding agreement signed in 2013 for an internal GbR ("Innen-GbR"), a partnership under civil law, and the administrative agreement signed by the Federal Government and the State Government of Berlin.

The Innen-GbR was transformed into a **corporation under public law** in its own right with the legislation for the formation of the Berlin Institute of Health (Gesetz über das Berliner Institut für Gesundheitsforschung) coming into effect on 23 April 2015. The law for the establishment of BIH was passed by the Berlin House of Representatives (Berliner Abgeordnetenhaus) on 26 March 2015.

The following financial and personnel numbers give an overview of the financial year 2014, subject to the pending annual audits. (Status February 2015)

All financial numbers refer to full costs, i.e. the sum of direct costs and overheads. The overhead rates for the BIH Innen-GbR were externally certified in 2013.

Funding

The Berlin Institute of Health is funded by the Federal Government and, from 2015 on, jointly by the Federal Government and the State of Berlin (90:10 ratio). For 2013/2014, funding was provided via the Federal Government through the funds pledged by Helmholtz Association. In addition, entrepreneur and founder of Stiftung Charité Johanna Quandt is supporting the development of BIH until 2022 with a "Private Excellence Initiative" providing a total of up to 40 million euros. The funds are administrated by Stiftung Charité. (Details of these funding decisions are not the object of this report.)

Funding lines 2014

Systems medicine

Funding of research projects; Collaborative Research Grants and Twinning Research Grants

Translation

Clinical Research Unit, Knowledge Management, Technology Transfer

Core Facilities

Omics technologies, IT, Bioinformatics, Biobank, Stem Cells, Medical Imaging, Transgenic techniques, Chemical Biology

Education

BIH Biomedical Academy with the funding programs Clinical Scientist and Junior Clinical Scientist, Translational PhD, Translational Postdoc and Medical Student Research Stipends, BIH Young Science

Recruitment

Appointments of leading scientists and recruitment of excellent researchers

Individual Budgets

Construction measures

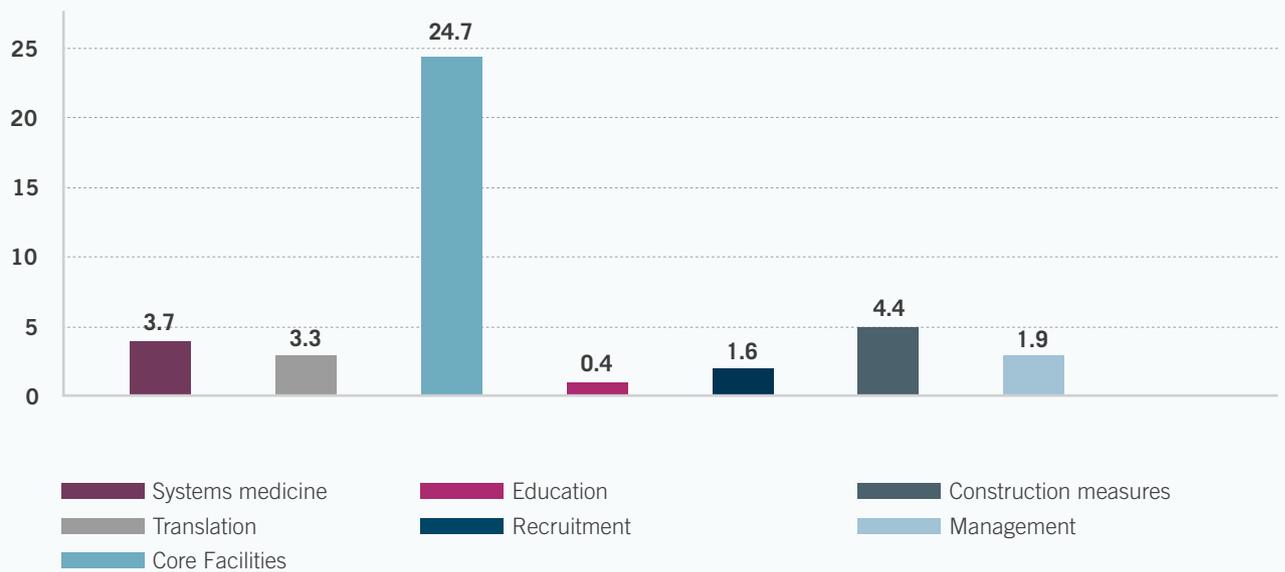
Management

Finance and Personnel

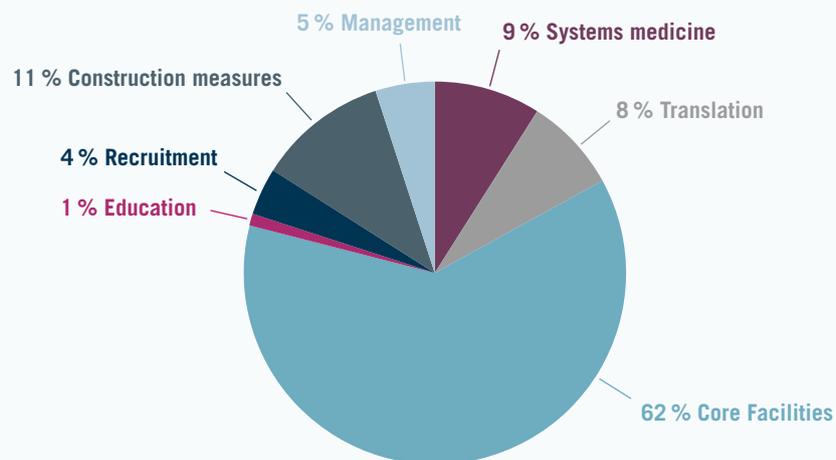
(Status: February 2015)

For the year 2014, federal grants were made available to BIH for the amount of approx. 37 million euros. All funds available to BIH were spent by 31 December 2014. Funding was concentrated in 2014 on establishing and developing existing infrastructure and core facilities.

Allocation of funding according to funding lines (in million euros)*

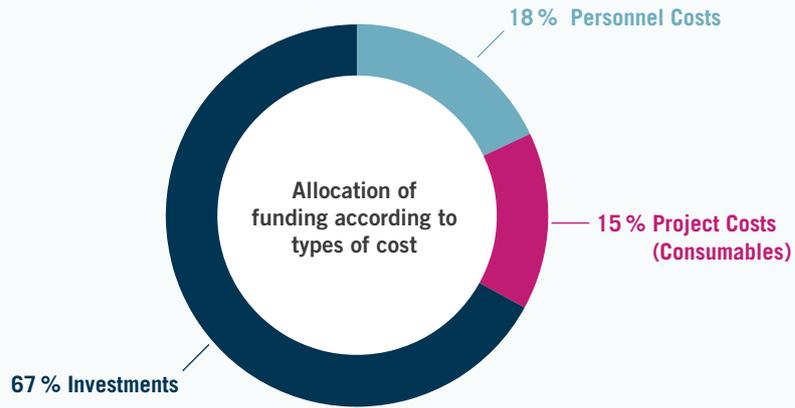


Allocation of funding according to funding lines (percentual)

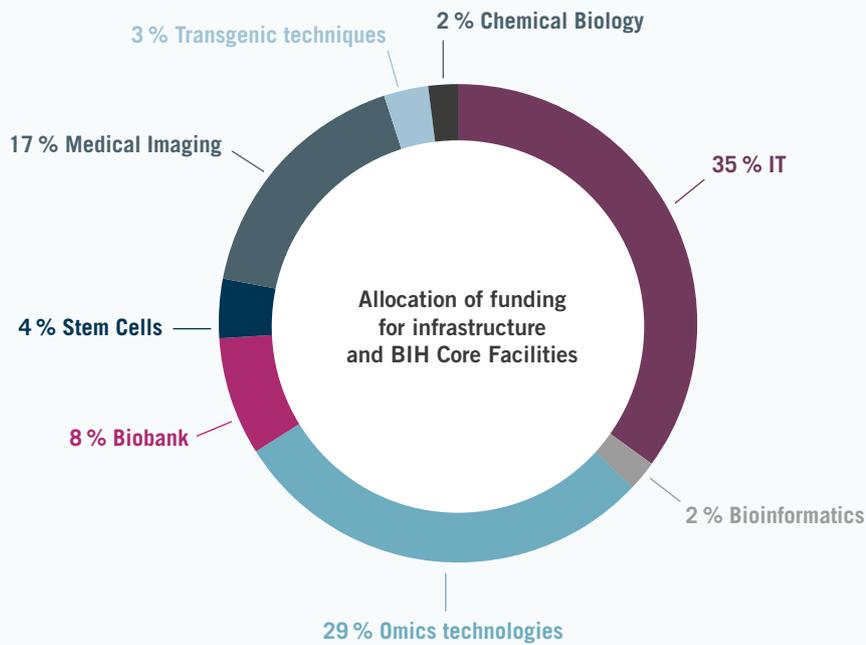


* Including 3.3 million euros which take effect in 2015.

Allocation of funding according to types of cost



Allocation of funding for infrastructure and BIH Core Facilities



Allocation of funding for construction measures

In 2014, various construction measures were planned, and their implementation was commenced step by step. This includes the construction measure Robert-Rössle-Institut at Campus Buch with both the expansion of the Clinical Research Unit and research laboratories, the accommodating of the BIH Omics Core Facility in the long term, and, in addition, the construction of a new building for the Clinical Research Unit at Charité Campus Virchow-Klinikum. Here, spending focused in particular on planning activities for a feasibility study of Mitte and Virchow.

In order to quickly ensure the ability of the research groups to commence activities, the laboratories required for the omics technologies on Campus Buch were initially extended in the context of the measure “Interim accommodation of omics technologies”. Reconstruction measures were completed in 2014. The core facilities’ equipment was successfully accepted in 2014, as planned. The construction measure “BIH Computer Center at Campus Buch” was concluded in 2014.

For the Biobank, expenditure in 2014, above all, comprised preparatory measures for construction such as planning, clearing and partial demolishing.

BIH offices and space for BIH laboratories are being provided at the Biomedical Research Center (BMFZ) at Campus Virchow-Klinikum. They were prepared step by step in 2014 and handed over to user groups (e.g. Biobank).

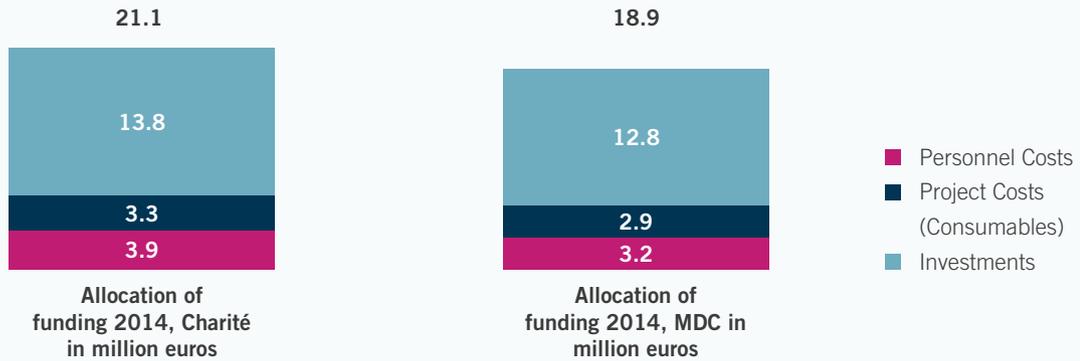
Allocation of funding for management activities

The BIH's management activities include all activities of and services for the various decision-making and advisory committees at BIH, e.g. the Supervisory Board, the Scientific Advisory Board, the Board of Directors as well as the Head Office. Funding is administrated by **Funding Resources Management** at the Head Office.

By the reference date of 31 December 2014, in addition to the Chairman of the Board of Directors and the Managing Director, 14 fulltime employees were employed.

Allocation of funding according to types of cost (MDC, Charité)

Out of the total funding spent in 2014, approx. 21.1 million euros were allocated to Charité and 18.9 million euros to MDC.



Personnel

By the reference date of 31 December 2014, within the funding lines, 145 fulltime employees (fulltime equivalent, FTE) or 198 individuals were funded by BIH (systems medicine, translation, infrastructure and core facilities, education and career paths, recruitment).

Funding lines (as of 31 December 2014)	Charité		MDC		BIH, total	
	FTE*	Staff	FTE*	Staff	FTE*	Staff
1. Systems medicine	26,3	38	18,5	23	45,1	61
2. Translation	46,7	66	2,7	3	49,3	69
3. Core Facilities	13,7	18	19,9	22	33,6	40
4. Education and career paths	5,7	11	5,0	9	10,7	20
5. Recruitment	3,4	5	2,5	3	5,9	8
	95,8	138	48,8	60	144,6	198

Funding lines (as of 31 December 2014)	FTE* BIH, total		Scientists**		Doctoral candidates***		Science supporting staff		BIH, total	
	female	male	female	male	female	male	female	male	female	male
1. Systems medicine	14,5	10,3	4,8	6,5	7,1	2,0	26,4	18,8		
2. Translation	16,9	12,8	0,0	0,0	17,8	1,9	34,7	14,7		
3. Core Facilities	4,9	15,5	0,5	0,0	4,7	8,0	10,1	23,5		
4. Education and career paths	2,3	3,5	2,5	1,0	1,4	0,0	6,2	4,5		
5. Recruitment	0,0	5,4	0,5	0,0	0,0	0,0	0,5	5,4		
	38,6	47,5	8,3	7,5	30,8	11,9	77,7	66,9		

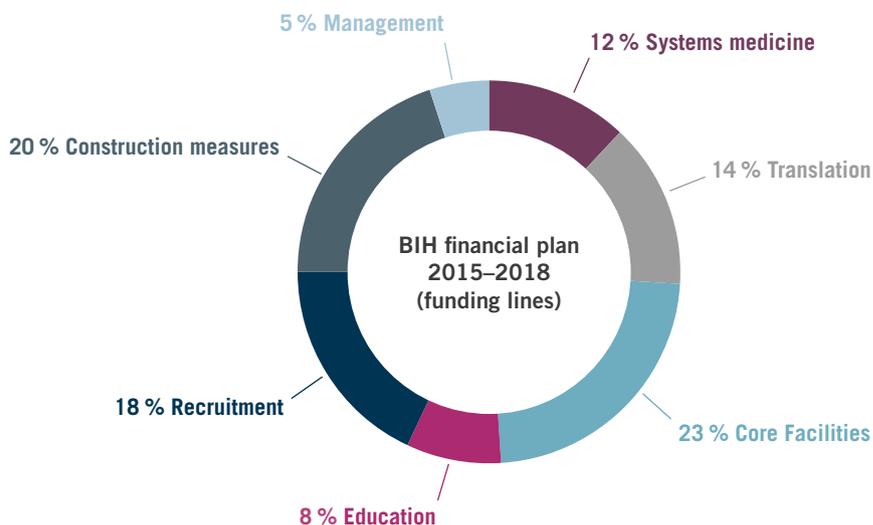
* Fulltime equivalent, FTE

** Scientists: Post docs, physicians

*** Doctoral candidates: all persons working towards their PhD.

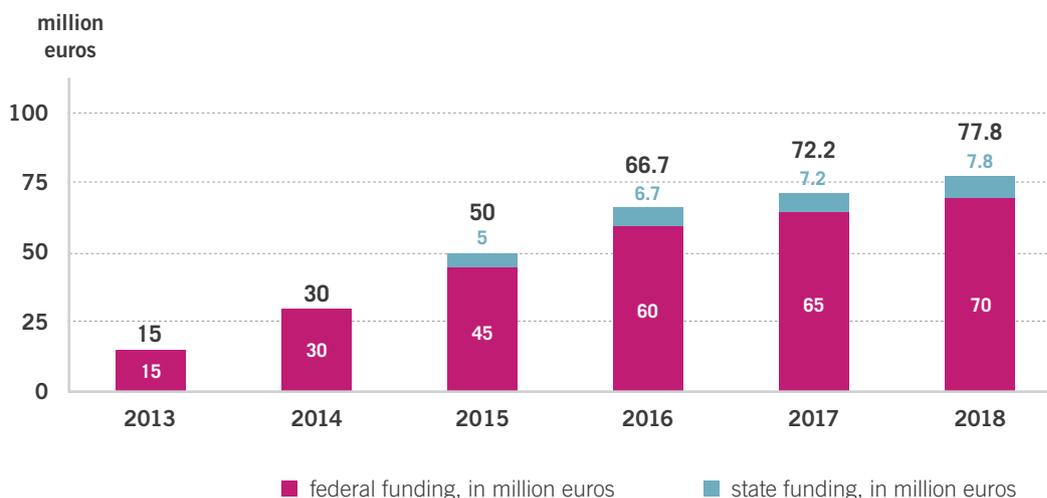
Medium-term BIH financial plan 2015–2018

For 2015, compared to the budget 2013/2014, more resources are available for the funding of scientific projects and the education of early-career researchers. Nevertheless, the establishment of research infrastructure is going to require a major share of the financial resources in order to create the framework conditions for excellent translational and systems medicine-oriented research.



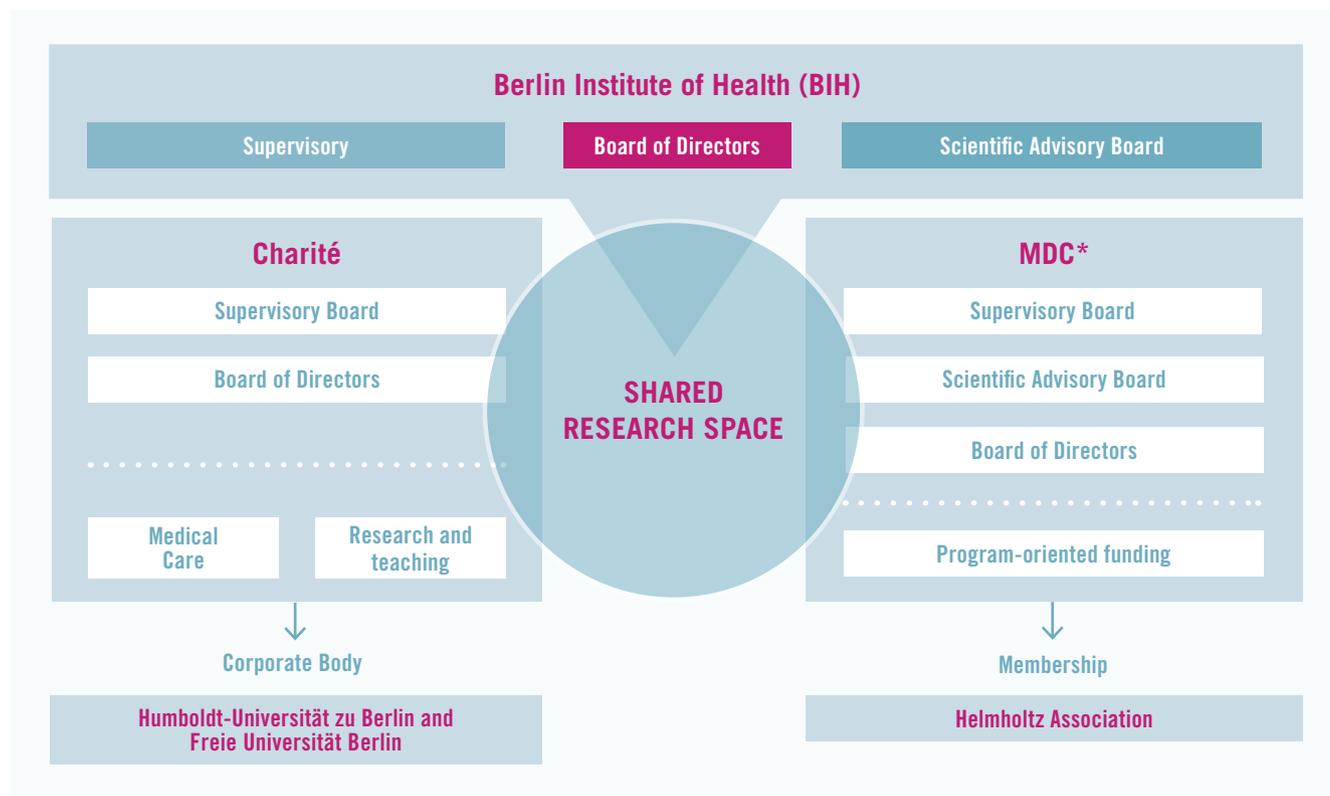
Overall funding 2013–2018 (in million euros*)

In total, approx. 312 million euros are available to Berlin Institute of Health (BIH) via the Federal Government and the State of Berlin from 2013–2018. This includes the Federal Government’s special funding for the construction of the Berlin Institute for Medical Systems Biology (BIMSB)*.



* including approx. 29 million euros in Federal Government special funding for the construction of the Berlin Institute for Medical Systems Biology (BIMSB). (2013: 3 million euros, 2014: 4 million euros, 2015: 6 million euros, 2016: 7.1 million euros, 2017: 6.6 million euros, 2018: 2.3 million euros)

Committees and Organizational Structures



The **Board of Directors** heads BIH, and its responsibilities include strategic planning and the implementation of the BIH research plan. As a rule, the Board meets every three weeks (every two weeks until August 2014). The members of the Board are the Chairman of the Board of Directors, the Chairman of the Board of Directors of Charité, the Dean of the Medical Faculty of Charité and the Chairman of the Directorate of Max Delbrück Center for Molecular Medicine. Following the transformation of BIH into a corporation under public law, the Board is to be extended by a further administrative Board Member. BIH is supported by a **Scientific Advisory Board**. The Advisory Board is responsible for supporting the Board and the Supervisory Board in scientific and strategic matters with external expertise. The Advisory Board meets twice a year. In 2014, the Scientific Advisory Board consisted of 13 of potentially 14 members.

The **Supervisory Board** supervises all BIH's activities and is responsible for essential decisions (e.g. research and integration plan and annual implementation plan, budget plan and appointment plans). In the period up to the founding of BIH as a corporation under public law, a Founding Supervisory Board was appointed comprising one representative each of the State of Berlin, the Federal Government and Helmholtz Association and a joint representative of the Berlin universities. Following the transformation of BIH into a corporation under public law, a new Supervisory Board is to be appointed with a larger membership. Until it has been appointed, the present Founding Supervisory Board is to perform the supervisory law tasks. The **Head Office** supports the work of the BIH committees and is responsible for the essential administrative and coordinating procedures relating to BIH. **Funding Resources Management** is responsible for the management of funding. The Head Office is seated in Berlin-Mitte (since November 2014: Kapelle-Ufer 2). In addition, the Coordinator Equal Opportunity is assigned to the Head Office.

In 2015, an internal Scientific Committee comprising BIH members is to be appointed. Its task will be to advise the Board on central scientific and strategic issues.

* With the law for the establishment of BIH coming into effect, the legal form and the committees of the Max Delbrück Center for Molecular Medicine also change (until April 2015: Board of Trustees as Supervisory Board and Scientific Advisory Board in scientific and programmatic matters).

SCIENTIFIC ADVISORY BOARD

Prof. Jörg Hacker**Chairmen**

German National Academy of Sciences
Leopoldina, (Halle, Germany)

Prof. Veronica van Heyningen**Vice-Chairman**

University of Edinburgh/Institute of
Genetics and Molecular Medicine
(Edinburgh, Scotland)

Prof. Robert C. Bast, Jr.

The University of Texas MD Anderson
Cancer Center (Houston, USA)

Prof. Ewan Birney

EMBL-European Bioinformatics Institute
(Hinxton/Cambridge, UK)

Prof. Leena Bruckner-Tudermann

Universitäts-Klinik für Dermatologie und
Venerologie (Freiburg, Germany)

Prof. Alastair Buchan

Medical School und Medical Sciences
Division, University of Oxford (UK)

Prof. Amanda Fisher

Imperial College/Institute of Clinical
Science (London, UK)

Prof. Matthias Hentze

European Molecular Biology Laboratory
(EMBL) (Heidelberg, Germany)

Prof. J. Larry Jameson

University of Pennsylvania/Perelman
School of Medicine (Pennsylvania, USA)

Prof. Maria Leptin

European Molecular Biology Organisation
(EMBO), European Molecular Biology
Laboratory (EMBL) (Heidelberg, Germany)

Prof. Sibrand Poppema

University of Groningen (Groningen, NL)

Prof. Dame Nancy Rothwell

University of Manchester (UK)

Prof. Günter Stock

Berlin-Brandenburg Academy of Sciences
and Humanities (Berlin, Germany)

**Meetings of the Scientific Advisory
Board in 2014**

27 + 28 February | 8 + 9 December

BOARD OF DIRECTORS

Prof. Ernst Th. Rietschel

Chairman of the Board of Directors

Prof. Karl Max Einhäupl

Charité – Universitätsmedizin Berlin
Deputy: Prof. Matthias Endres

Prof. Annette Grüters-Kieslich

(up to 31 December 2014)

Prof. Axel Radlach Pries

(from January 2015)

Charité – Universitätsmedizin Berlin
Deputy: Prof. Christian Hagemeier

Prof. Walter Rosenthal

(up to 14 October 2014)

Max Delbrück Center for Molecular
Medicine

Deputy: Prof. Thomas Sommer

Prof. Thomas Sommer

(from 15 October 2014)

Max Delbrück Center for Molecular
Medicine

Deputy: Prof. Nikolaus Rajewsky

HEAD OFFICE

Dr. Falk Fabich

Managing Director

Marcel Gätjen

Executive Assistant to the Chairman

Maike Kohlmorgen

Personal Assistant to the Chairman

Alexandra Hensel

Head of Communications

Caren Kunze

Coordinator Equal Opportunity

Administration**Cathleen Biesen**

Head of Administration

Katrin Meike, Wen-Yu Bünger, Yusuf Taner

Funding Resources Management

Antje Albrecht

Controlling

FOUNDING SUPERVISORY BOARD

State Secretary Dr. Georg Schütte

Federal Ministry of Education and
Research

State Secretary Sigrid Klebba

Senate Department for Education,
Youth, and Science, Berlin

*Deputy: State Secretary Knut Nevermann
(up to 12 December 2014)*

*State Secretary Steffen Krach (from 13
December 2014)*

Prof. Jürgen Mlynek

Helmholtz Association of German
Research Centres

Dr. Martina Frost

Humboldt Universität zu Berlin

Deputy: Prof. Jan-Hendrik Olbertz

**Meetings of the Founding Supervisory
Board in 2014**

3 February | 11 June | 20 November

Science Operations**Dr. Nicola Isendahl**

Head of Science Operations

Dr. Iwan C. Meij

Coordinator BIH Biomedical Academy

Jennifer Stewart

Administrator BIH Biomedical Academy

Dr. Christian Hirsch, Dr. Silke Mühlstedt

Research Coordinator

Dr. Ljudmila Borisenko

Coordinator Core Facilities

Kati Jegzentis

(from January 2015)

Coordinator Clinical Research Unit

Awarded Scientists and Projects

Funding line Systems medicine

COLLABORATIVE RESEARCH GRANTS

Prof. Thomas Blankenstein and Prof. Peter-M. Kloetzel:
 “Targeting somatic mutations in human cancer by T cell receptor gene therapy”

PRINCIPAL INVESTIGATORS AND SUBPROJECTS

1	Peter Kloetzel (Charité)	Identifying immunogenic mutant epitopes
2	Thomas Blankenstein (MDC)	Mutation-specific T cell receptors
3	Hans Schreiber (Charité)	Targeting unique tumor-specific antigens
4	Wolfgang Uckert (MDC)	Tumor rejection capacity of mutant-specific TCRs
5	Zsuzsanna Izsvák (MDC)	A transposon-based TCR gene transfer for clinical use
6	Michael Hummel (Charité)	Identification of cancer-specific immunogenic mutations and their expression
7	Antonio Pezzutto (Charité)	Moving mutation-specific TCR gene therapy into the clinic and preclinical efficacy comparison to lymphoma lineage-specific TCRs

Prof. Erich Wanker and Prof. Frank Heppner:
 “Elucidating the proteostasis network to control Alzheimer’s disease”

PRINCIPAL INVESTIGATORS AND SUBPROJECT

1	Frank Heppner (Charité)	Repurposing, validating and mechanistically understanding IL-12/23 and NALP3 inhibitors as novel preclinical and clinical Alzheimer’s disease modifiers
2	Erich Wanker (MDC)	Effects of small molecule modulators of proteostasis and protein aggregation on dysfunction and neurotoxicity in Alzheimer’s disease
3	Thomas Willnow (MDC)	APOE receptors as targets for prevention of A β oligomerization and neurotoxicity in Alzheimer’s disease
4	Elke Krüger (Charité)	Perturbations of proteostasis networks in Alzheimer’s Disease: focus on the ubiquitin proteasome system
5	Oliver Peters (Charité)	Proteostasis and long-term disease progression in Alzheimer’s dementia
6	Josef Priller (Charité)	Repurposing of approved drugs impacting on proteostasis for the treatment of Alzheimer’s disease
7	Nikolaus Rajewsky (MDC)	Expression and function of circular RNAs and micropeptides in Alzheimer’s disease

Prof. Christian Rosenmund and Prof. Carmen Birchmeier:
 “Towards a better understanding and diagnosis of congenital disease”

PRINCIPAL INVESTIGATORS AND SUBPROJECT

1	Christian Rosenmund (Charité) Angela Kaindl (Charité)	Common pathways and transcription network control in intellectual disability and microcephaly
2	Carmen Birchmeier (MDC) Heiko Krude (Charité)	Towards a better understanding of congenital endocrine diseases
3	Stefan Mundlos (Charité) Ana Pombo (MDC)	Mis-regulated chromatin folding as a cause of congenital disease
4	Wei Chen (MDC) Dominik Müller (Charité)	Integrative omics-based dissection of molecular mechanisms underlying congenital abnormalities of the kidney and the urinary tract
5	Uwe Ohler (MDC) Silke Rickert-Sperling (Charité)	Transcription network controlling heart development and congenital heart disease

TWINNING RESEARCH GRANTS	
NAME/ORGANIZATION	PROJECT TITLE
Jonas Busch (Charité) Walter Birchmeier (MDC) Wei Chen (MDC)	Systems medicine in kidney cancer: towards cancer stem cell-directed therapy
Nils Blüthgen (Charité) Markus Landthaler (MDC)	Systems medicine of BRAF-driven malignancies
Simon Jacob (Charité) James Poulet (MDC & Charité)	The role of corollary discharge and the dopamine system in controlling sensory processing: elucidating a core mechanism in the pathophysiology of psychotic disorders
Carmen Birchmeier (MDC) Jens Fielitz (Charité & ECRC) Steffen Weber-Carstens (Charité)	Inflammation-induced skeletal muscle atrophy in critically ill patients: Identification of molecular mechanisms and preventive therapies

Funding line Translation

TECHNOLOGY TRANSFER FUND	
NAME/ORGANIZATION	PROJECT TITLE
Ralph Buchert (Charité)	easyDAT: web-based service platform for real-time evaluation of FP-CIT SPECT
Hendrik Fuchs (Charité)	ApOptiLink als Plattformtechnologie zur Herstellung zielgerichteter Therapeutika in der Tumorbehandlung
Ulrich Gohlke (MDC)	Novel compounds for the therapy of prostate cancer
Julian Kamhieh-Milz (Charité)	Entwicklung eines PCR-basierten Schnelltests zur nicht-invasiven, pränatalen Diagnostik einer Trisomie 21 (Down Syndrome) auf der Basis von extrazellulären MikroRNAs (miRNAs)

Funding line Education

TRANSLATIONAL PHD GRANTS	
NAME/ORGANIZATION	PROJECT TITLE
Divisha Bhatia (MDC)	Regulatory mechanisms of lymphocyte trafficking in homeostasis and immunopathogenesis
Amanda Luisa de Andrade Costa (MDC)	The role of human microglia for glioma progression
Mirjam Karber (Charité)	Regulation of pro- and anti-inflammatory mechanisms mediated by fatty acid metabolites in metabolic liver damage – a role for omega-3 fatty acids in prevention?
Larissa Kraus (Charité)	RNA-edited glycine receptor as marker and therapeutic target in intractable epilepsy
Julia Löffler (MDC)	Impact of energy metabolism on bone regeneration
Carmen Lorenz (MDC)	Investigation of the energy expenditure of human iPSC-derived basal ganglia neurons from patients with Leigh Syndrome
Laura Moreno Velásquez (Charité)	Modulation of neonatal olfactory cortex spontaneous synchronized activity in the GLUK2 KO model of mental retardation
Bernadette Nickl (MDC)	Functional characterization of osteoactivin/Gpnmb in myocardial infarction
João Miguel Parente Fernandes (MDC)	Targeting alternative translational initiation of oncogenes in cancer cells
Markus Petermann (MDC)	Identifying the mechanisms of antidepressant drug action in mice lacking brain serotonin

BIH CLINICAL SCIENTIST		
NAME	CLINICS/INSTITUTES	PROJECT TITLE
Claudia Brockmann	Department of Ophthalmology	Interaktion zwischen pathologischer Angiogenese und retinaler Neurodegeneration
Philipp Enghard	Medical Department, Division of Nephrology and Internal Intensive Care Medicine	Zelluläre Urinomics – Durchflusszytometrische Analyse von Urinzellen als noninvasives Instrument zur Erforschung und Diagnose von Nierenerkrankungen
Michaela Golic	Department of Obstetrics	Fötale Wachstumsretardierung in einem neuen Rattendiabetesmodell – Untersuchung der vermuteten fötalen und adulten Insulinresistenz
Konrad Klinghammer	Medical Department, Division of Hematology, Oncology	Präklinische Tumormodelle zur Identifikation neuer Zielstrukturen und neuer Substanzen zur Behandlung des Kopf-Hals-Karzinoms
Agustin Liotta	Department of Anesthesiology and Operative Intensive Care Medicine	Postoperative Delirium and Hippocampal Network Oscillations
Hendrik Nogai	Medical Department, Division of Hematology, Oncology and Tumor Immunology	Analyse der Immunmodulation bei malignen Lymphomen und deren gezielte Beeinflussung durch pharmakologische Inhibitoren von Signalkaskaden
Rosa Bianca Schmuck	Department of General, Visceral, Transplantation Surgery	Modulation von Tumorstammzellen in epithelialen Tumoren der Gallengänge und des Pankreas durch Notch-Inhibitoren
Christoph Treese	Department of Gastroenterology, Infectiology and Rheumatology	Entwicklung prognostischer und prädiktiver Marker für das Magenkarzinom durch Analyse therapieinduzierter Genregulierung

BIH JUNIOR CLINICAL SCIENTIST		
NAME	CLINICS/INSTITUTES	PROJECT TITLE
Viktor Arnhold	Department of Pediatrics, Division of Oncology and Hematology	Pharmakologische Reaktivierung des p53-Signalweges durch mdm2-Inhibition im Neuroblastom
Magdalena Balcerek	Department of Pediatrics, Division of Oncology and Hematology	Fertilität nach Chemo- und Strahlentherapie im Kindes- und Jugendalter, FeCt-Nachkommenstudie
Anja-Maria Davids	Department of Ophthalmology	Der Fractalkine Rezeptor CX3CR1 und seine Rolle bei der Pathogenese der choroidalen Neovaskularisation und Strahlenretinopathie
Julius Emmrich	Department of Neurology with Chair in Experimental Neurology	Mechanisms of neuronal dysfunction and death in critical illness-associated cognitive impairment
Aitomi Essig	Medical Department, Division of Hematology, Oncology and Tumor Immunology	Etablierung eines Patienten-individualisierten humanisierten Lymphom-Stroma/Immun-Mausmodells zur funktionellen Pathogenese-Dissektion, Therapie-Prädiktion und Biomarker-Entwicklung
Laura Hatzler	Department of Pediatrics, Division of Pneumonology and Immunology	Pathogen-specific T cells as diagnostic markers of immune-related disease exacerbations in cystic fibrosis patients
Christian Hoffmann	Department of Neurology with Chair in Experimental Neurology	Endothel-spezifische Stat3-Aktivierung durch Transferrinrezeptor-targeted Colivelin zur Regenerationsförderung nach Schlaganfall
Judith Holstein	Medical Department, Division of Nephrology	Involvement of functional antibodies targeting GPCRs in glomerular disease of native kidneys and transplants
Andreas Horn	Department of Neurology	Das strukturell-funktionelle Konnektom bei Patienten mit Dystonie
Vanessa Lembke	Center for Musculoskeletal Surgery	Sekundäre Immunsuppression durch nicht-traumatische Rückenmarksverletzung (NTSCI)

Funding line Recruitment

NAME	APPOINTMENTS
Holger Gerhardt (MDC)	BIH Professorship “Experimental Cardiovascular Research” at Charité Research group leader at MDC and W3 Professor of Experimental Cardiovascular Research at Charité since 2014/09/01
Ulf Landmesser (Charité)	BIH Professorship “Interventional Cardiology” at Charité Director of the Department of Cardiology at Charité Campus Benjamin Franklin since 2014/10/01
Burkert Pieske (Charité)	BIH Professorship “Cardiology” at Charité Director of the Medical Department, Division of Cardiology at Charité Campus Virchow-Klinikum and Director of Cardiology at the German Heart Institute Berlin since 2014/11/01

Private Excellence Initiative Johanna Quandt: Funding Decisions in 2014

FUNDING PROGRAM	NAME
BIH Clinical Fellows	Kaven Baeßler, Christian Bamberg, Daniel Baumgart, Christiane Montag, Stefan Röpke, Michael Synowitz
BIH Delbrück Fellows	Prateep Beed
Deutschlandstipendien	Stefan Appelhaus, Aline Azabdaftari, Sophie Bienia, Sanne Burkert, Karl Busch-Petersen, Wei-Long Dennis Chen, Ricardo Donners, Jan-Frederik Fischer, Anja Garbe, Ines Goppelt, Franziska Greiß, Franziska Hentschel, Doreen Herinek, Arnim Hohberger, Nils Hunselar, Kasra Karimi, Felix Kleefeld, Dörte Löffler, Tom Malysch, Ingo Mrosewski, Jonas Muallah, Sandra Peuker, Henning Plage, Tarik Alp Sargut, Leonhard Schleußner, Antonia Schulz, Leopold Vorwerk, David Paul Weber, Marie-Christin Weber, Till Weidner, Marcel Wittenberg
Einstein BIH Visiting Fellow	Thomas Südhof, Florian Sennlaub, Michael Sieweke
Humboldt Research Fellowships at BIH	Keisuke Sebara

BIH CLINICAL SCIENTIST		
NAME	CLINICS/INSTITUTES	PROJECT TITLE
Sabine Bélard	Department of Pediatrics, Division of Pneumonology and Immunology	Tuberculous granuloma formation in children, its biomarkers and related clinical containment of tuberculosis disease in children
Federico Colletini	Institute of Radiology	Beyond the margin of local ablation: perifocal immune response and tumor progression after image-guided ablative tumor therapies in a VX2 liver tumor model
Leif-Christopher Engel	Department of Cardiology	Nichtinvasive Diagnostik Vulnerabler Plaques der Koronargefäße mittels 3-Tesla-Magnet-Resonanz-Tomographie und Gabe eines Albumin-bindenden Kontrastmittels
Bernd Hewing	Medical Department, Division of Cardiology and Angiology	Impact of iRhom2 on the progression of atherosclerosis
Philipp Jakob	Department of Cardiology	Identification of microRNAs promoting proliferation and inhibiting apoptosis of adult cardiomyocytes derived from patients with ischemic cardiomyopathy using a functional high-throughput screening
Reiner Jumpertz-von Schwartzberg	Medical Department, Division of Endocrinology	Plasticity of the human gut microbiota in metabolic disease
Laura-Nanna Lohkamp	Department of Neurosurgery with Pediatric Neurosurgery	Impaired inflammatory resolution after spinal cord injury – the role and relevance of IL-6, IL-17 and IL-23
Josefine Radke	Institute of Neuropathology	Molecular genetic analysis of primary CNS lymphomas (PCNSL)
Katharina Schmack	Department of Psychiatry and Psychotherapy	The neurobiology of delusions – linking perceptual inference and dopamine
Benjamin Strücker	Department of General, Visceral, Transplantation Surgery	Humanized porcine liver

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