

Annual Report

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About the Berlin Institute of Health (BIH)

The Berlin Institute of Health (BIH) as a research institution focuses on translational biomedical research and precision medicine. The only institute of its kind in Germany, its guiding mission aims to improve and sustain the health and quality of life of patients suffering from progressive diseases – a mission that involves the development of concrete solutions for better disease prediction whilst simultaneously supporting the advancement of groundbreaking personalized therapeutic options. The BIH was jointly founded by Charité – Universitätsmedizin Berlin and the Max Delbrück Center for Molecular Medicine in the Helmholtz Association (MDC). Charité is one of Germany's leading university hospitals with a staff of 3,950 physicians and scientists dedicated to world-class medical research, teaching, and patient care. The MDC, which is home to over eighty principal investigators, ranks amongst the world's top twenty research institutes for molecular biology and genetics. As a vanguard translational research platform, the BIH unites the collaborative research expertise of the two institutions, thus translating innovative biomedical research findings into tangible improvements for human health.

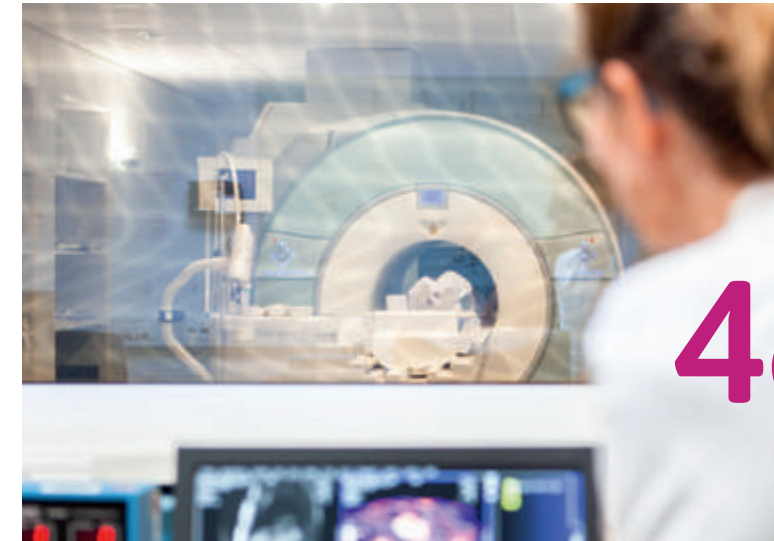
**Berlin Institute
of Health**
Annual Report 2017

Table of contents

- 04 Timeline
- 06 Foreword
- 08 Report by the Executive Board
- 11 With pace and persistence
- 13 Successful recruitment processes up to April 2018

Research

- 16 Research in brief
- 18 Detecting risk factors for recurring events
The beginning of the BIH study BeLOVE
- 22 Cooperation is the undisputed currency of translation
- 24 Three questions to...
Interview with Sylvia Thun
- 25 Dangerous LDL cholesterol reduced by half
- 26 Five millimeters of brain in a Petri dish
A model for stroke research
- 28 »How are you today?«
PROMIS® survey instrument



People

- 32 Time for research
Dr. Michael Sigal and Prof. Peter Krawitz: a close-up
- 34 »Knowledge about diseases is stored in massive data volumes«
Roland Eils on data, diagnoses and breakthroughs
- 36 Understanding thinking
BIH Johanna Quandt Professor Petra Ritter
- 38 Monitoring system for cancer
BIH Johanna Quandt Professor Il-Kang Na
- 40 The explorer
BIH Johanna Quandt Professor Ute Scholl
- 42 More than a visit to Berlin
Private Excellence Initiative Johanna Quandt
- 44 Expertise squared
Growth for the Scientific Advisory Board of the BIH
- 45 No small difference
The BIH Excellence Award for Sex and Gender Aspects in Health Research
- 46 Promoting the transfer of knowledge

Innovation

- 50 A faster implementation with Berlin Health Innovations
- 53 Start of a Digital Health Accelerator Program
- 56 Startup aid in the market launch for Digital Health spin-off companies
Startupbootcamp network
- 57 Mentoring for academic innovations
- 58 Climate change also in biomedical research
QUEST Center for Transforming Biomedical Research
- 61 Closing the gap:
The electronic lab notebook

Facts and Figures

- 65 Legal framework and institutional milestones
- 65 Members of the corporation under public law
- 65 Financing and financial situation 2017
- 67 Personnel 2017
- 68 Organization and committees
- 72 Sites
- 72 Scientific performance
- 90 Private Excellence Initiative Johanna Quandt
- 96 Imprint

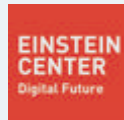
Significant events 2017

FEBRUARY



Official launch of Berlin Health Innovations, the joint technology transfer unit of the BIH and Charité, in cooperation with SPARK Berlin.

APRIL



Opening of the Einstein Center Digital Future. Charité takes over the speaker function for the research area Digital Health.

The QUEST Center launches the electronic laboratory notebook for BIH scientists.

Bioinformatician Tomasz Zemojtel takes over the management of the second BIH genomics site on the Campus Virchow-Klinikum.

JUNE

First BIH Charité Digital Health Roundtable for the development of a Digital Health community.



Long Night of the Sciences: For the first time, the BIH offers visitors an insight into translational medicine at Clinical Research Units (CRU) sites.

The BIH Charité (Junior) Clinician Scientist Program: The first trainees receive a certificate for completing the program successfully.

All under one roof: The employees of the QUEST Center, the BIH Biomedical Innovation Academy, Berlin Health Innovations and the head office move into joint spaces on Anna-Louisa-Karsch-Straße.

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JANUARY



Clinician Scientist Retreat: Early-career scientists, their mentors and clinic managers convened for the annual scientific exchange at Schlos Genshagen.

In cooperation with Stiftung Charité, the BIH awards the Paper of the Month for the first time: Angela M. Kaindl receives the award for her work on the origin of microcephaly.

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MARCH

Christian Drosten takes over the BIH Professorship Virology at Charité and starts developing a BIH research unit for virology in line with the research program Personalized Medicine.



Martin Kircher assumes his role as leader of a new junior group for bioinformatics. He previously worked in the Department of Genome Sciences at the University of Washington in Seattle, USA.

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MAY



Dr. Rolf Zettl opens the 10th Charité BIH Entrepreneurship Summit with 400 international guests.

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JULY



Geraldine Rauch takes over the BIH Professorship Biometry at Charité and starts the development of a Biometry Service Unit.

The pilot study of the project Berlin Longterm Observation of Vascular Events – (BeLOVE) starts successfully with the recruitment of the first patients.

SEPTEMBER



Cooperation between Berlin Health Innovations and Startupbootcamp in the context of the Digital Health Accelerator Program.

NOVEMBER

Ute Scholl starts the BIH Johanna Quandt Professorship »Hypertension and molecular biology of endocrine tumors«.

Berlin Health Innovations is presented at the international partnering conference BIO-Europe®.

Official opening of the QUEST – Center for Transforming Biomedical Research



The BIH participates in the Berlin Science Week: Martin Lohse opens the second science match »Future Medicine«, which takes place in cooperation with the Tagesspiegel.

The new pilot program of the BIH Biomedical Innovation Academy and Stiftung Charité is launched: Innovator for the promotion of entrepreneurial spirit and innovation.

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OCTOBER

The BIH, Charité and the MDC sign a cooperation agreement with Sanofi in Germany.

Petra Ritter takes over the BIH Johanna Quandt Professorship for brain simulations and thus becomes the first BIH Johanna Quandt Professor.



Digital Health Accelerator of Berlin Health Innovations starts with three teams.

DECEMBER

Il-Kang Na takes over the BIH Johanna Quandt Professorship »Therapy-induced re-modeling in immuno-oncology«.

The MDC celebrates its 25th birthday with around 550 invited guests.

Foundation of Charité's »Charité 3R – Replace, Reduce and Refine« with the aim to radically change research based on animal testing following the 3R principles.



First Hacking Health Hackathon by Berlin Health Innovations and Hacking Health.

Berlin Health Innovations advertises the validation fund for translational projects for the first time.

Exemplary characters: the BIH awards two international female scientists with the BIH Excellence Award for Sex and Gender Aspects in Health Research.

A year of change, development and progress!

Dear readers,

2017 was the first year in which we were able to consistently put our strategy – the BIH Strategy 2026 – into action. In late 2016, we set the course for this strategy, with the aim of fulfilling our mission for society: maintaining health and quality of life whilst simultaneously creating value. If you have been accompanying the Berlin Institute of Health's (BIH) journey from afar or following its activities with interest, you will have noticed that 2017 was also a year of change, development, and progress. The BIH took great strides forward despite having to overcome a significant hurdle.

In early summer, the departure of Erwin Böttinger necessitated a fundamental change within the BIH Executive Board. Indeed, Böttinger's official departure last July has meant that we have not only to reorganize the tasks of the Executive Board but have also reassigned responsibilities. As a result, Martin Lohse has taken over the role of BIH Executive Board Spokesperson and we have devoted ourselves intensively to priorities for the current year.

Our annual report presents selected BIH activities and achievements that took place in 2017. These achievements are perhaps best reflected in the fact that the BIH was able to successfully attract numerous excellent scientists to Berlin. Together with the existing

» Excellent scientists are working together with the scientific community at the MDC and Charité to breathe fresh life into BIH's strategy. «

scientific community at the MDC and Charité, these new arrivals are breathing fresh life into BIH's strategy. Additionally, »Berlin Health Innovations«, the joint technology transfer unit of BIH and Charité was founded, thus continuing to ensure that innovative healthcare research is swiftly translated into concrete benefits for our patients. Furthermore, in the autumn of 2017, the QUEST (Quality | Ethics | Open Science | Translation) Center was inaugurated focusing on the quality of biomedical research. BIH has also consolidated its interdisciplinary work. As such, ongoing research projects have strengthened and expanded collaboration, whilst new alliances and communities are constantly emerging. These dynamics form the very basis for creative innovation.



Prof. Karl Max Einhäupl
Charité – Universitätsmedizin
Berlin, Chief Executive Officer



Prof. Martin Lohse
Max Delbrück Center
for Molecular Medicine in the
Helmholtz Association, Scientific
Directorate, Spokesman of the
BIH (Executive Board)



Prof. Axel Radlach Pries
Charité – Universitätsmedizin
Berlin, Dean

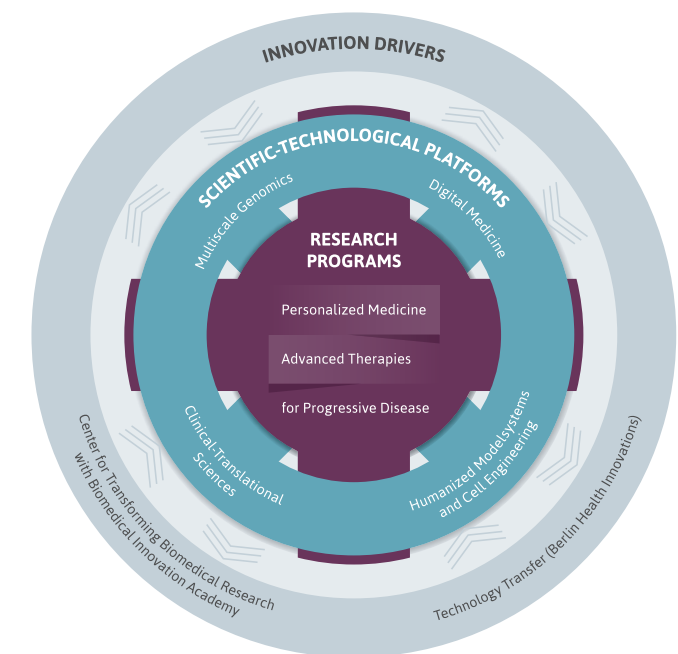


Dr. Rolf Zettl
Chief Financial Officer

We would like to thank all our partners in the fields of politics, science, and industry as well as the BIH Supervisory Board, the Scientific Advisory Board, the Scientific Committee, members of the BIH and all committed individuals for their intensive and fruitful cooperation over the past year.

We sincerely hope you will enjoy reading about the BIH highlights in 2017.

Executive Board of the Berlin Institute of Health



The elements of the "BIH Strategy 2026"

A focus on recruiting and community building

The year 2017 focused on the implementation of the BIH strategy. Charité's and MDC's strengths provide a solid basis for securing crucial institutional progress. These ranged from recruitment successes, milestones of »innovation drivers«, completing key construction planning phases as well as the development of a cohort study through strengthening the scientific community and governance structures.



»What's happening at BIH?« We've been asked this question repeatedly by numerous interested parties. Reflecting on the past year the answer is clear: we have been implementing BIH's Strategy 2026, a strategy that focuses on personalized medicine and advanced therapies. The objective is to establish a research center for translational medicine – together with our partner institutions Charité and the MDC and their expertise.

The cornerstones of BIH's Strategy 2026 comprise of two central research programs, the associated scientific-technological platforms as well as two overarching organizational units. These are »Berlin Health Innovations«, a reorganized technology transfer office

dedicated to fostering a new innovation culture and entrepreneurial mindset, and the »QUEST Center for Transforming Biomedical Research«, which aims to increase the value and quality of biomedical research.

For tomorrow's medicine

Excellent scientific practice and value-based health-care can only be driven forward by the very best and brightest minds. Of course, the MDC and Charité are already home to numerous researchers who fit this profile. However, in order to remain successful in the face of global competition, we have made the recruitment of translation-focused scientists an integral component of our strategy. Until March 2018, we have

been able to recruit a total of twenty BIH Chairs, BIH Professorships and BIH Junior Research Group Leaders – all senior scientific positions. Further recruitment procedures are currently underway. This means that key requirements for driving expansion in priority areas have already been secured and that BIH's faculty is undergoing significant growth. Two key chair positions are worth highlighting: Professor Ulrich Dirnagl (Founding Director of the QUEST Center for Transforming Biomedical Research) and Professor Roland Eils (Founding Director of the BIH Center Digital Health). Furthermore, in 2017, we launched calls for four additional chairs in Cell and Gene Therapy, Clinical-Translational Sciences, Disease Modeling and Genomic Medicine and have been swiftly enacting recruitment procedures. The BIH Chairs will be responsible for organizing the areas under their management, whilst simultaneously guiding the development of BIH programs and platforms.

Dialogue is vital

Building a scientific community has been one of BIH's key aims since its foundation. This mission is rooted in the fundamental understanding that interdisciplinary exchange is essential to successful translational research. As a result, our 2017 priorities focused on scientific exchange, novel collaborations and academic networking. Major contributing factors have been large scientific events in addition to event series such as the Clinician Scientists Retreat, the Scientists Retreat and the Core Technologies Retreat, each of which drew in over 120 participants from the scientific community. Event formats such as the BIH Lectures by visiting international scientists and their Berlin partners furthermore strengthened scientific exchange – both at the discipline-specific and interdisciplinary level. These events were regularly attended by up to sixty participants. Additionally, we have pushed on the development of scientific-technological platforms. As a result, two series of workshops were organized around the Digital Medicine and Clinical-Translational Sciences platforms, with participants including

scientists from the translational research commons and representatives from the relevant research infrastructures. These workshops allowed the scientific community to determine research activities that should be carried out within the platform context. The overall objective was to create synergies between Charité and the MDC whilst concurrently identifying needs that research platforms could meet.

Committed participants

BIH also made important progress in terms of fostering cooperation between all strategic areas. This included establishing a truly effective governance structure. This includes bottom-up decision-making via relevant steering committees and the BIH Scientific Committee, the latter serving as an internal scientific advisory body. In addition, two members of the Scientific Committee are to be co-opted to the BIH Executive Board, thus ensuring that the Executive Board's aims are closely coordinated with the BIH scientific community. The recruitment of further chair professors marks the beginning of operational development concerning the afore mentioned strategic areas. This in turn means that the new governance structure swiftly comes into effect. As such, all BIH members can actively participate in the translational research commons and help shape the research direction.

Other key milestones in the implementation of the BIH Strategy 2026 included the opening of the QUEST Center and the successful launch of Berlin Health Innovations, the joint technology transfer unit of the BIH and Charité. Both divisions have quickly established themselves as innovative drivers facilitating creative solutions thus further strengthening the role of the BIH within the scientific community.

→ **QUEST Center**
Pages 58–60

➤ **One year of Berlin Health Innovations**
www.youtube.com/watch?v=q915uGdvb6l

Monitoring the interplay between systems medicine factors

The Berlin Long-term Observation of Vascular Events (BeLOVE) study, which was launched in 2017 is just one example of the very unique character of BIH research. BeLOVE seeks not only to better understand the interplay between the various systems medicine factors responsible for the onset of cardiovascular and metabolic diseases, but also to identify markers that could enable early detection of diseases and predict disease progression. The study will enroll 10,000 patients suffering from acute diseases such as stroke, heart attack, and renal failure. Results and banked biosamples will subsequently serve as valuable resources that can be employed to develop new studies and therapies.

Creating physical proximity: construction projects on schedule

The pursuit of innovative research and a swiftly growing faculty mean that finding additional physical space for basic and clinical research is essential.

In 2017, the BIH continued to drive its two large construction projects forward. These include the BIH building at Charité Campus in Mitte, which will serve as an outpatient, translation, and innovation center, and the Käthe Beutler Building at Campus Buch, which will both play a key role in strengthening identity. The responsible federal and state authorities have reviewed the construction planning documents and issued building permits for both projects and renovations to the Käthe Beutler Building got underway in summer 2017. Construction of the BIH building in Berlin-Mitte is set to commence in spring 2018. It will be situated directly adjacent to Charité's clinical care units, just next to the Luisenstraße tower block. The project includes demolition and structural work as well as the creation of a new courtyard and expansion of the former facilities. All this will result in a highly modern and welcoming building.

→ **Founding director of the Center for Digital Health**
Pages 34–35

High visibility in Berlin-Mitte

The renovation will create a total of approximately 14,500 square meters of floor space distributed over six floors with some 9,230 square meters reserved for BIH. This includes raising the roof structure and building an additional floor. This in turn will create circa 1,500 additional square meters, which will house the BIH Digital Health Center research groups. The building's other five floors will each have a surface area of between 2,000 and 2,300 square meters. Four of the six floors will have direct access to Charité's tower block.

Outlook for 2018

In late 2017, we decided to make regenerative therapies a priority field within the Advanced Therapies Program. To this end, we first conducted a comprehensive evaluation of potential synergies with the translational research commons and subsequently undertook a multi-day international review of the Berlin-Brandenburg Center for Regenerative Therapies (BCRT). Evaluation results were positive and signal that in 2018, we need to be more tangible when defining partners, projects, goals, and milestones whilst continuing to identify synergies between established activities and ground-breaking research eg. in areas such as humanized cell models and cell and gene therapies.

We will also vigorously implement our strategy. Two top priorities include recruitment successes in key positions and providing new BIH research groups with the necessary physical space to facilitate scientific progress and networking. Additionally, we must focus on strengthening the entrepreneurial mindset of our employees whilst building new bridges in the field of industry. Last but not least, we will be promoting tangible results in the field of digital medicine, thus ensuring swift translation of research results which will inevitably lead to improved health and quality of life.

→ **More information on the BeLOVE study**
Pages 18-21, 80-81

With pace and persistence

Global competition for excellent researchers remains fierce. Worldwide, top-level scientists continue to be in high demand, and will relocate based on best research conditions. Together, the BIH, Charité, and the MDC achieved numerous recruitment successes in 2017.

Interview with Martin Lohse and Axel Radlach Pries on last year's goals and activities:

An integral component of the BIH Strategy 2026 is the recruitment of outstanding researchers to Berlin. As a result, BIH is currently in the process of creating new scientific positions and intensively supporting appointments to both Charité and the MDC. In this context, what have you achieved in 2017?

LOHSE We recruit staff at various levels – from junior research group leaders to mid-career researchers to senior scientists. We can proudly say that 2017 was a very successful year.

PRIES Last year alone, we successfully launched nine appointment procedures; some are already completed whilst others remain ongoing. Since BIH was founded, a total of twenty senior, junior, and key positions have been filled– some with international candidates and under tough competitive conditions. We have carried out further parallel measures to ensure our ambitious recruitment aims stay on target.*

Can you provide us with an example?

PRIES Last year we optimized our organizational structure creating a joint Recruitment and Onboarding Office which ensures closer cooperation between all people involved. This facilitates the standardization and acceleration of recruitment procedures.

LOHSE One example is the extremely swift progress concerning recruitment procedures for key scientific positions in the fields of Transforming Biomedical Research, Digital Health, Clinical-Translational Sciences and Disease Modeling. This was largely thanks to the huge commitment of scientists from Charité, the MDC and external institutions who serve on the relevant appointment and selection committees.

PRIES That's correct. This joint effort has facilitated the continuous and successful advancement of a large number of recruitment procedures in parallel. In addition to numerous committee meetings, this also involved dedicated support for and organization of on-site candidate visits in Berlin.

* This information is current as of April 2018

» The increase of the validity, quality and reproducibility of scientific results are important core elements of the BIH strategy. «

Which success stories are you particularly proud of?

LOHSE That's a difficult question to answer. Each appointment is unique and strengthens key BIH, Charité, and the MDC research areas – and thus in turn our faculty. Our selection criteria include scientific excellence and suitability in terms of our scientific priorities.

PRIES I would like to highlight one example: the appointment procedures for the BIH Johanna Quandt Professorships. We established these new tenure-track W3 temporary professorships at the end of 2015 with the help of the Stiftung Charité and were able to successfully fill positions by 2017. Petra Ritter, Il-Kang Na, and Ute Scholl - all outstanding scientists - began working for us in 2017. Petra Ritter's research focus is personalized brain simulation. This contributes to a better understanding of disease processes in the brain and allows new therapeutic approaches to be developed. Il-Kang Na focuses on improving treatment success in cancer patients via personalized therapy decisions. These are based on improved molecular and functional characterization of tumors, their microenvironments and the immune system. Ute Scholl is working on a particular form of hypertension caused by overproduction of the hormone aldosterone. To date, Ute Scholl's research has made a significant contribution towards understanding the causes of this form of endocrine hypertension.

Which chair positions – considered to be key BIH positions – were you able to fill?

PRIES BIH has set itself the important strategic goal of improving the validity, robustness and reproducibility of scientific results. Professor Ulrich Dirnagl holds the relevant Chair and serves as Founding Director of the QUEST Center for Transforming Biomedical Research. Under his leadership, the QUEST Center achieved pivotal milestones: It established a core team, appointed a scientific advisory board, started its first projects, raised third-party funds and initiated a recruitment procedure. These initial undertakings are already being reaped throughout the faculty.

LOHSE The procedure for the BIH Chair for Digital Health was also completed in 2017. Professor Roland Eils is now founding director of the new BIH Digital Health Center and a tenured professor of Digital Health. With Professor Eils, BIH has gained a recognized expert in biomedical informatics, genomics, and personalized medicine to lead this center. As such, he is assuming responsibility for one of BIH's main scientific priorities. We are very happy about this huge success. External reviews have been obtained for all other procedures and candidates, and negotiations are ongoing.

How will recruitment activities move forward in 2018?

PRIES We are sticking to our goals and hope to attract further excellent translational scientists to Berlin for employment at BIH, Charité and the MDC. For us, this also means further strengthening the immense interdisciplinary diversity of the biomedical faculty, thus enabling scientific exchange and community networking, which are essential for medical innovation.

Successful recruitment processes up to April 2018

BIH Chairs

Transforming Biomedical Research

Prof. Ulrich Dirnagl

Digital Health

Prof. Roland Eils

BIH Professorships

BIH Johanna Quandt Professorship

»Therapy-Induced Remodeling in Immuno-Oncology«

Prof. Il-Kang Na

BIH Johanna Quandt Professorship for Brain Simulations

Prof. Petra Ritter

BIH Johanna Quandt Professorship

»Hypertension and the Molecular Biology of Endocrine Tumors«

Prof. Ute Scholl

W3 Professorship

for Pediatric Pneumology and Immunology

Prof. Marcus Mall

W3 Professorship for Biometry

Prof. Geraldine Rauch

W3 Professorship for Virology

Prof. Christian Drost

W3 Professorship for Microbiology

Prof. Andreas Diefenbach

W3 Professorship

for Experimental Cardiovascular Research

Prof. Holger Gerhardt

W3 Professor of Interventional Cardiology

Prof. Ulf Landmesser

W3 Professor of Cardiology

Prof. Burkert Pieske

W3 Professorship

for Mathematical Modeling of Neuronal Learning

Prof. Robert Güting

Director of eHealth and Interoperability

Prof. Sylvia Thun

W3 Professorship

for Environmental Epigenetics and Lung Research

Prof. Irina Lehmann

BIH Junior Groups

Genome Informatics

Dr. Birte Kehr

Computational Genome Biology

Dr. Martin Kircher

Biomedical Image Analysis

Dr. Dagmar Kainmüller

The following management positions were filled for the eight BIH Core Facilities

Biobank

Prof. Michael Hummel and Prof. Tobias Pischon

Bioinformatics

Dr. Dieter Beule

IT / Core

Michael Mallach and Martin Peuker

IT / High Performance Computing

Dr. Dieter Beule

Genomics

Dr. Sascha Sauer and Dr. Tomasz Zemojtel

Metabolomics

Dr. Jennifer Kirwan

Proteomics

Dr. Philipp Mertins

Stem Cells

Dr. Sebastian Diecke and Dr. Harald Stachelscheid



Research

Our mission maintaining patients' health and quality of life and creating values.

In more than 100 research projects, coordination teams and committees, scientists from the MDC and Charité work successfully together in a collaborative and interdisciplinary manner. They shape the translational successes which create new approaches for better predictions and innovative therapies in severe disease progressions and unresolved health problems, in order to restore or preserve people's quality of life. Here we present selected success stories from the year 2017.

Research in brief

➤ **Other research highlights by the MDC and Charité**
www.mdc-berlin.de/news
www.charite.de/en/research

Pancreas from the lab

The so-called islets of Langerhans are tissue areas in the pancreas which make up only a tiny part of the organ but produce an extremely important hormone: insulin. With diabetes type 1, the body's own defense system attacks this cell structure in an autoimmune response. As a consequence, too little insulin is produced. Diabetes has been considered incurable so far. The BIH Charité Clinician Scientist Benjamin Strücker has now been able to publish a promising approach with his colleagues *Science Reports*. The team succeeded in removing all the cellular components in the pancreas of rats, i.e. the factors which the recipient's immune system would reject in case of a transplant. In a subsequent step, the researchers managed to re-colonize the islets of Langerhans regions with insulin-producing cells. The presented technology is an important step for the production of suitable and functioning pancreases for patients with diabetes type 1.

➤ **Engineering an endocrine Neo-Pancreas by repopulation of a decellularized rat pancreas with islets of Langerhans**
Science Reports. February 2017

Napierala H., Hillebrandt KH., Haep N., Tang P., Tintemann M., Gassner J., Noesser M., Everwien H., Seiffert N., Kluge M., Teegen E., Polenz D., Lippert S., Geisel D., Reutzel Selke A., Raschzok N., Andreou A., Pratschke J., Sauer IM., Struecker B.
 doi: 10.1038/srep41777

Salt, gut bacteria, immune system – everything is linked

That an increased salt intake can have a negative effect on blood pressure is well-known, but that different types of gut bacteria are also sensitive to too much salt is still a very recent discovery. Dominik Müller of the MDC and his team investigated this in more detail in a study which has appeared in *Nature*. The researchers found a regular chain of consequences here: Increased salt intake evidently affects especially a type of gut bacteria called *Lactobacillus murinus*; furthermore, the number of specific defense cells – so-called TH17 helper cells – which could also turn against themselves within autoimmune reactions rises. The team speculates that there is a link between all of these aspects which can be traced back to the concept of an intestine-immune-axis. The scientists could therefore demonstrate in mice that an administration of *Lactobacillus murinus* in case of higher salt intake not only evidently lowers blood pressure, but also reduces the changes in the TH17 helper cells.

➤ **Salt-responsive gut commensal modulates TH17 axis and disease.**
Nature. 2017 November

Wilck N., Matus M. G., Kearney S. M., Olesen S. W., Forslund K., Bartolomaeus H., Haase S., Mähler A., Balogh A., Markó L., Vvedenskaya O., Kleiner F.H., Tsvetkov D., Klug L., Costea P.I., Sunagawa S., Maier L., Rakova N., Schatz V., Neubert P., Frätzer C., Krannich A., Gollasch M., Grohme, D.A., Côte-Real B.F., Gerlach R.G., Basic M., Typas A., Wu C., Titze J.M., Jantsch J., Boschmann M., Dechend R., Kleinewietfeld M., Kempa S., Bork P., Linker R.A., Alm, E.J., Müller D.N.
 doi:10.1038/nature24628

Potential weakness found in brain tumor

Glioblastoma is the most frequent malignant brain tumor, and so far can only be treated badly despite intense research efforts. The average survival time is currently just under 15 months. The study published in *Oncotarget* by the BIH Charité Clinician Scientist Josefine Radke brings hope for better treatment options. With her team, she could prove that a variant of a specific enzyme, pAXL, is produced by the tumor in the majority of glioblastoma patients. There is considerable evidence that pAXL is significant for the tumor to survive. To that effect, an inactivation

of pAXL, for instance, could cause a reduction of the tumor substance. Radke and her colleagues are currently following this approach.

➤ **Phospho-AXL is widely expressed in glioblastoma and associated with significant shorter overall survival**
Oncotarget. 2017 June

Onken J., Vajkoczy P., Torka R., Hempt C., Patsouris V., Frank LH., Radke J. doi: 10.18632/oncotarget.18468

How side effects of chemotherapy can be limited

Chemotherapeutic agents can be a powerful weapon against specific forms of cancer, but they also have massive side effects on the whole body. The undesirable effects of chemotherapeutic agents on the nervous system are known, but have been researched little so far. For example, there are so-called chemotherapy-induced memory disorders. Neurologist Matthias Endres of Charité and his team have examined where the chemotherapeutic agent paclitaxel collects in the brain of mice and to what extent. They discovered that the hippocampus is especially affected; an area of the brain which is important for memory and learning. In the next stages of the study, which appeared in *Translational Psychiatry*, the scientists examined

the damage mechanism in more detail. They were also able to develop a first approach for a prevention strategy: The administration of lithium seemed to protect the neurons well at least in animal and cell model.

➤ **A novel preventive therapy for paclitaxel-induced cognitive deficits: preclinical evidence from C57BL/6 mice**

Translational Psychiatry. 2017 August

Huehnchen P., Boehmerle W., Springer A., Freyer D., Endres M. doi: 10.1038/tp.2017.149.

A 3D map of the genes

For the around 1.8-meter DNA strand with the human genome to fit into the nucleus, the genes must be arranged in a folded and winding pattern and be organized. This creates a special structure between the genes and the switches that influence gene activity. In the *Nature*, Ana Pombo of the MDC and her colleagues presented a method with which the three-dimensional topography of the genome can be mapped. Thanks to the team's »genome architecture mapping«, the spatial proximity of specific gene regions can also be measured against one another. They thus discovered that specific particularly active gene regions are spatially in contact with one another through a respective organization of the folding across great distances within the DNA.

With this new method, many new findings can still be made on what influence the folding of the DNA has on the transcription of genes (and the occurrence of diseases).

➤ **Complex multi-enhancer contacts captured by genome architecture mapping**
Nature. 2017 March

Beagrie RA., Scialdone A., Schueler M., Kraemer DC., Chotalia M., Xie SQ., Barbieri M., de Santiago I., Lavitas LM., Branco MR., Fraser J., Dostie J., Game L., Dillon N., Edwards PA., Nicodemi M., Pombo A.
 doi: 10.1038/nature21411

Detecting risk factors for recurring events - the BeLOVE study

In mid 2017, the pilot phase of the BIH study BeLOVE (Berlin Longterm Observation of Vascular Events) was started with the recruitment of the first patients. Professor Kai-Uwe Eckardt, Director of the Department of Nephrology and Medical Intensive Care as well as acting spokesman of the BeLOVE Study Committee, and Professor Matthias Endres, Director of the Department of Neurology, explain the cross-campus Berlin project.

What is the aim of the prospective observational study BeLOVE?

ECKARDT With BeLOVE, we want to identify new and yet unidentified pathophysiological mechanisms of progression of cardiovascular diseases and examine them more accurately. We monitor the course of disease in patients with a high cardiovascular risk, and want to specifically detect risk factors for recurring events.

ENDRES The long-term study should help detect and prevent unfavourable courses early on in patients with cardiovascular disease. The long-term objective is to develop effective preventive measures as well as personalized therapies.

ECKARDT In the next few years, methodological developments in medicine will open up entirely new opportunities to identify molecular processes in individual people with a level of detail which has been unimaginable so far. However, medical care can only benefit from these developments if there are patient cohorts which can be applied to these techniques, and if detailed information on organ functions and the course of a disease also exists with which molecular data can be compared. BeLOVE will therefore combine these two aspects.



Prof. Kai-Uwe Eckardt



Prof. Matthias Endres

The capital city study with up to 10,000 patients has been designed for a period of at least ten years. What does the project also stand out for?

ENDRES An essential aspect of BeLOVE is that we are not limited to one disease or one organ. In fact, in the study we include patients who have severe heart problems, a stroke, acute renal failure or are diabetic with various organ disorders at the same time. We therefore want to have a better understanding of why different problems are at the forefront in patients and how the functional restriction of an organ influences the function of other organs and causes complications. We also want to find out why a patient lives for ten years without further restrictions, while the next has a relapse or has a disorder in another organ despite an allegedly similar starting point.





ECKARDT A characteristic of the study is also the collaborative approach of various specialities. Scientists from many clinics, specialist departments and institutions of Charité and the MDC collaborate intensively in the planning as well as the analysis. In this way, new processes and structures are set up between the BIH, Charité and the MDC – and this benefits the entire research community. BeLOVE will supply a wealth of data and samples which scientists of the BIH community can draw on for many years to answer different scientific questions. Setting up transparent partnerships with the industry is also a particular goal of the project. The practical application and the clinical benefit of new research results should be promoted from an early stage.

BeLOVE started with a pilot study in July 2017. What was the first phase of the project like?

ECKARDT We are very happy with the pilot phase, in which the recruitment as well as the long-planned processes are tested and implemented. Overall, both have worked well so far. It is the first big interdisciplinary BIH study implemented jointly by Charité and the MDC. This involves a tremendous amount of commitment by many colleagues and especially by the teams in the Clinical Research Unit (CRU) of the BIH.

ENDRES The patients' willingness to take part in the study is also very encouraging. In the course of the year, we will intensively analyze the experiences from the pilot phase and certainly make important adjustments. Then the establishment stage follows, in which we complete our infrastructure and thus determine our processes so that we can transfer them to the main phase, which begins in 2019.

How does the study then proceed specifically?

ECKARDT The majority of patients are enrolled during their inpatient treatment at Charité after an acute event. Three months later, a detailed examination is carried out at a CRU site of the BIH, which takes one to two days. Regardless of which primary event led to the inclusion in the study, a whole range of organ functions is examined. After two years, the patients are then invited again for a detailed examination. We further conduct annual phone interviews to record the course of the disease.



The study helps to promote biomedical research. Alongside its value for society, is there a personal benefit for participating patients?

ENDRES At Charité, all patients are treated to the highest standards and according to international guidelines regardless of their participation in the study. If we come across conspicuous results in the scientific examinations conducted within the context of the BeLOVE study, we naturally tell the patients about them – if this was agreed beforehand. The patient also has the opportunity to receive an easily comprehensible report of the results.

ECKARDT The examinations, which go far beyond the usual preventive examinations, are assessed very positively by the study participants. Because we examine patients who are already restricted by the effects of their disorder, they are very willing to contribute to an improvement of future therapies. The feedback is, for example: »I think it's great that you care about how I'm getting on beyond the acute treatment.«



About BeLOVE

The **Berlin Longterm Observation of Vascular Events** (BeLOVE) study is a long-term observation of up to 10,000 patients with vascular events. By monitoring study participants over at least ten years, BeLOVE enables the investigation and the understanding of the interplay of organ-specific and disease-spanning factors which are responsible for the origin and course of cardiovascular diseases. The interdisciplinary research project is promoted by the BIH and carried out by a high-ranking consortium with members of Charité and the MDC. The recruitment of patients with indications such as acute heart failure, acute stroke, acute coronary syndrome, acute renal failure and diabetes mellitus type 2 takes place at the three inpatient sites of Charité. Further multi-day examinations and annual surveys are part of the study concept.

Cooperation is the undisputed currency of translation

A close collaboration between various disciplines and different institutions is generally regarded a crucial premise for successful translation – partnership projects and exchange create a greater medical benefit through new scientific findings.

Interdisciplinary cooperation is the founding mission of the BIH, together with the integration of clinical research and basic research. With various established structures and Core Facilities as well as services, the interplay of all relevant disciplines could be consolidated and developed in 2017. More than 40 new cooperations with national, international or industrial partners have been established alone through the ongoing collaborative research projects on T-cells therapy, hereditary diseases, Alzheimer's, heart and metabolic diseases as well as neuroblastoma. For instance, these include new academic cooperations with the

Children's Hospital in Chicago, the Harvard Medical School in Cambridge (both USA) and the Netherlands Cancer Institute in Amsterdam. Alongside new academic bridges, cooperations were also set up nationally with industrial partners, including for the development of xenogeneic animal models or the isolation of circulating tumor stem cells.

The CRU – the Clinical Research Unit with its four sites in Berlin – also ran a significant network expansion last year. Through joint (steering) committees across campuses, clinics, specialist areas and institutes, new links have been created between the participating researchers which were and still are used for an exchange of knowledge and ideas beyond the CRU and the BIH and from which different cooperations or project ideas have emerged. Among these is, for instance, the quality management circle, which was established by the CRU together with the Center for Stroke Research (CSB). In three meetings in 2017, ideas were exchanged on QM-related topics between various Charité clinics and study research institutions, the Biobank, the Central Quality Management (QM) of Charité and the business area Strategic Business Development.

The Clinical Research Unit of the BIH

The CRU is a translational organizational unit for the interdisciplinary and cross-campus implementation of clinical studies. Research and treatment are conducted under one roof at four sites: collaborating clinicians and researchers have treatment units, examination rooms, research laboratories and their own administration and documentation at their disposal. In this way, complementary expertise is incorporated into a joint translational research space.

➤ **CRU range of services**
www.bihealth.org/cru-leistungsangebot

» All the activities of research groups, organizational units and involved individuals have one goal: creating something that improves health and serves the patients «

Furthermore, the great interdisciplinary vascular study BeLOVE with five participating clinics of Charité and the MDC enhances the networks and community building at the BIH.

A growing translation community

In research platforms, the translation community could be expanded with a series of scientific workshops. Dedicated scientists from the Digital Medicine and Clinical-Translational Sciences research platforms organized workshops to determine the research activities of the platforms that should be promoted from the point of view of the community. On the one hand, it is about using the current synergy potential of Charité and the MDC, and, on the other, about defining necessary requirements which can be addressed through research platforms.

2017 was also a remarkable »Digital Health Community Year«. With the Digital Health Roundtable Berlin Health Innovations established a new series of events with and for experts and interested parties – researches, doctors, creative minds, investors, programmers, engineers and entrepreneurs. The growing expert network for teams of the Digital Health Accelerator Program and the first hackathon »Hacking Health Hackathon powered by Berlin Health Innovations« contributed to a further growth of the community. Because all the activities of research groups, organizational units and involved individuals have one goal: creating something that improves health and quickly serves patients.

→ **Details on the BeLOVE study**
 Pages 18-21, 80-81

→ **BIH research platforms**
 Pages 77-84

Three questions to...

BIH Professor Sylvia Thun on the Digital Health Community at the BIH.

Why does Digital Health attract so many scientists?

Today, Digital Health concerns everybody: Patients, doctors, nurses, therapists – and scientists. It is therefore no surprise that a kind of Digital Health Community has been formed at and through the BIH. I deal with IT standards for the barrier-free exchange of medical data and I am consulted several times a day.



» I am consulted every day by researchers and clinicians.«

What role does the Digital Health Community play at the BIH?

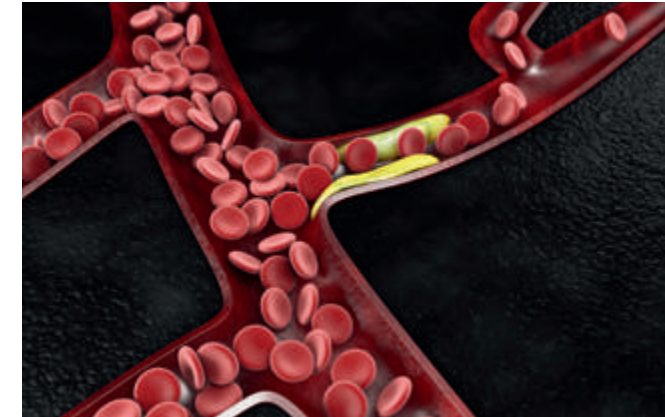
Digital Health plays not only one role but several roles. On the one hand, more and more capacities are created, and the unit »eHealth and Interoperability«, which I'm setting up at the BIH, is only one example of this. At the same time, however, more and more people exchange views at the BIH through Digital Health – even if it isn't their special field or they haven't received project funding. There is a great need for exchange between various special fields and it is growing. We will establish a strong Digital Health network.

What challenges does this network face at the BIH?

The challenges are diverse – and many individual solutions are developed. It is about intelligent analyses and specifications for new digital applications and research based on Health Data, which open up brand new research areas and are all aimed at better patient care. For this reason, exchange is extremely important.

Dangerous LDL cholesterol reduced by half

By means of the so-called RNA interference method, a BIH researcher team managed to reduce the activity of a gene responsible for a high LDL cholesterol level in the blood. Their study was published in the *New England Journal of Medicine*.



In a study published in the *New England Journal of Medicine*, a total of 501 high-risk patients with increased LDL cholesterol levels were treated with the active principle of the so-called RNA interference («small interfering RNA»). This can specifically silence certain genes and block them to some extent. With this method, both lead authors of the study, Professor Ulf Landmesser, Director of the Clinic of Cardiology at Charité, and Professor Kausik Ray, Imperial College London, and their team succeeded in shutting down the activity of the gene responsible for the production of PCSK9. The result: The LDL cholesterol levels in the blood dropped by up to 52.6 percent. The long-lasting effect was particularly interesting, as the LDL cholesterol level was still reduced after a single administration even after nine months. The treatment is currently being further developed as a new therapy for high-risk patients in a large clinical study program.

Ideally, a problem should be tackled directly at the source before it develops, becoming bigger and more and more difficult to resolve. Charité and BIH scientists, together with colleagues from London Imperial College, chose this early intervention approach 2017 for one of the crucial risk factors of cardiovascular diseases: LDL cholesterol. If there is too much so-called LDL cholesterol in the blood, the risk of atherosclerosis and diseases such as heart attack and stroke rises significantly. High-risk patients that suffer from very high LDL cholesterol values due to a hereditary disease are especially vulnerable. In them, the root of the problem lies in the fact that a protein called PCSK9 prevents the liver from removing LDL cholesterol from the blood. The scientists start from the genes responsible for the production of this protein.

➤ Ray KK*, Landmesser U*, Leiter LA, Kallend D, Dufour R, Karakas M, Hall T, Troquay RP, Turner T, Visseren FL, Wijngaard P, Wright RS, Kastelein JJ. *Inclisiran in Patients at High Cardiovascular Risk with Elevated LDL Cholesterol*. *N Engl J Med*. 2017 Mar 17. www.nejm.org/doi/full/10.1056/NEJMoa1615758 [Epub ahead of print] PubMed PMID: 28306389.

*Both authors contributed equally.

Five millimeters of brain tissue in a Petri dish

Scientists at Charité and the BIH use human induced pluripotent stem cells for developing a human stroke model that has the potential for making animal experiments obsolete.



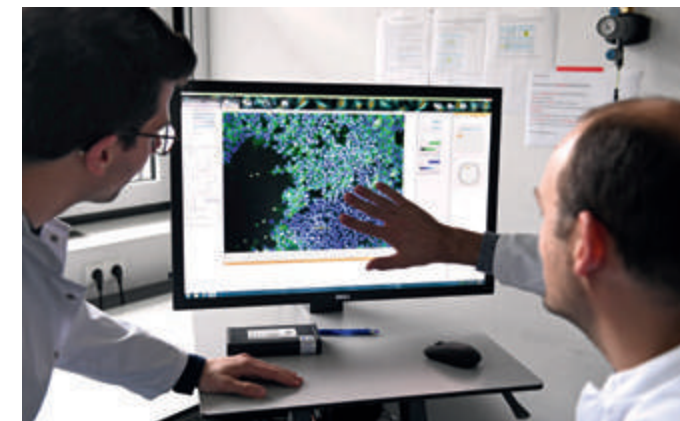
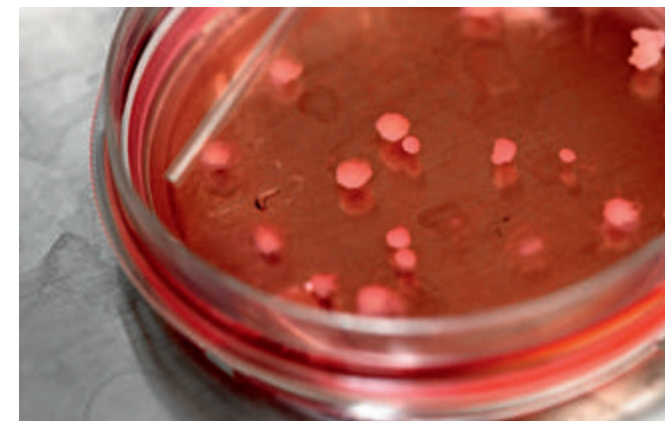
Dr. Mergenthaler

is a neuroscientist and physician in the Departments of Experimental Neurology and Neurology and a Fellow of the BIH Charité Clinician Scientist Program.

Dr. Stachelscheid

is a scientist at the Berlin-Brandenburg Center for Regenerative Therapies and Head of the BIH Core Facility Stem Cells.

» Human stem cell derived neurons and brain organoids represent an intermediate step in research between conventional cell culture and traditional animal testing. These models lead to a reduction of animal testing, but also significantly contributes to a higher validity and reproducibility of results particularly in the area of stroke research.«



The network of nerves, which is similar to a clump of brain tissue, fits in a small Petri dish. It takes 30 to 40 days for human pluripotent stem cells to become a brain organoid four to five millimeters in diameter like this one »brain organoid« is the term the scientists use to describe their brain model. By that time, the brain organoid has formed networks and even generates electrical activity. On reaching this stage of development it can be used as a tool for stroke research.

Using these brain organoids, Philipp Mergenthaler and Harald Stachelscheid from Charité and the BIH are developing a model that in several ways may constitute a scientific breakthrough. On the one hand, it can help to reduce the need for animal experiments. That is why in 2017 the State of Berlin awarded the scientists a prize worth 12,500 Euros for research into alternatives to animal experiments. On the other hand, it might also provide valuable new insights into the pathophysiology of stroke, a disease for which so far almost 90 percent of patients can obtain no effective treatment.

Mergenthaler and Stachelscheid are already working on their first experiments. For example, they plan to expose the brain organoids to an environment deprived of oxygen and other nutrients, which is very similar to the situation that prevails in the human brain during a stroke. One of the research team's goals is to learn more about what happens in the brain at the cellular and molecular level during a stroke. Another goal using the brain organoids is to run large-scale tests in order to screen new drug candidates for treating stroke. The protocols for applying the developed models will be published in specialized journals, thus making such technical advances accessible to other researchers.

»How are you today?«

The BIH has established a new survey instrument to record the well-being of patients. PROMIS® has now also been in use in Germany since 2017.



Dr. Sein Schmidt



Patients can answer the PROMIS® questions electronically and autonomously

One of the BIH's main objectives is to preserve and improve patients' quality of life. But how can subjectively experienced well-being be measured objectively? In cooperation with Charité, the BIH introduced a survey instrument for this in 2017 which enables doctors to record the patients' quality of life and to derive new individual needs-oriented therapy concepts.

The Patient Reported Outcomes Measurement Information System – short form PROMIS® – was developed by the US-American National Institutes of Health (NIH) more than ten years ago. The system is used for an individual prediction of treatment procedures and enables doctors to assess the success of medical measures from the point of view of a sick person.

The BIH has taken the tested system to Berlin and is building a reference center in close cooperation and on a contractual basis with the NIH, which act as an exclusive national PROMIS® contact point and will advertise the system in the German-speaking area and make it available free of charge.

A common ground

The basis of PROMIS® consists of extensive questionnaires touching upon physical, psychological and social aspects in the life of those affected. In the clinic, various other measuring instruments are used for the illustration of health-related quality of life reported by the patients. The great disadvantage: These instruments can hardly be compared, since they are specific



to the disease and differ significantly in the level of detail and survey classification. With PROMIS®, the NIH has established a common ground so that the results of various established measuring instruments can be compared. Furthermore, doctors can use PROMIS® regardless of disease and age and refer to a wider choice of questions.

PROMIS® in Germany

To make PROMIS® available across Germany, the extensive questionnaire must first be translated into German in an NIH-defined process. In autumn 2015, under the leadership of the CRU coordinator Dr. Sein Schmidt and in cooperation with Professor Matthias Rose, Director of the Medical Clinic with a focus on

Psychosomatic Medicine at Charité, the Clinical Research Unit (CRU) started the translation of PROMIS®. 405 questions have already been translated and are being validated in the first studies at Charité. The new reference center will significantly promote the translation of around 1,000 questions in order to illustrate other clinical pictures and factors influencing the quality of life in relation to health. Along with the translation, the reference center will also deal with the validation of the German-speaking version and the development of a database for the German-speaking area. Schmidt and his team benefit from patient cohorts treated at the CRU which are using PROMIS®.



People

Our research success depends on the people who create and evolve it. Innovations rely on researchers' motivation, endurance, patience and thirst for knowledge.

We must grow to reach our goals, so we promoted our recruitment strategy extensively in 2017 and were able to gain excellent national and international scientists for our research projects. Cooperations were further consolidated and expanded and new alliances and communities have been formed.

Our progress is based on scientific excellence, talent promotion, equal opportunities and diversity.

Time for research

The BIH Charité Clinician Scientist Program is a model for success: It gives medical professionals a chance to carry out research - with impressive results. A close-up on two passionate doctors and scientists.

Michael Sigal was deeply immersed in his research in the labs of the American Stanford University when he heard this talk. »It was in Boston at a meeting of the German Academic Network (GAIN)«, he recalls from the scientists' conference today: Someone presented the Clinician Scientist Program (CSP) there – »and I knew straight away that it was the right thing for me«. Sigal is now back in Germany and is researching *Helicobacter pylori* at Charité and at the Max Planck Institute of Infection Biology; a bacterium that can colonize the stomach.

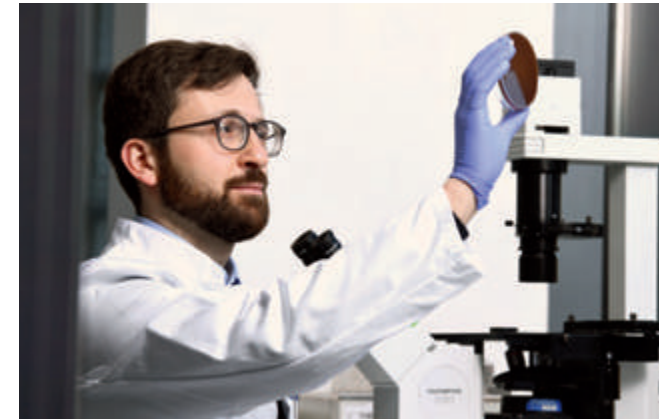
» I knew straight away that the program was the right thing for me. «

»I did clinical work in Germany before my residence in Stanford, and I noticed that it would be extremely difficult to carry out work in the lab at the same time«, Michael Sigal says. For him, the CSP is an »enormous advantage« – because he can finally pursue the research that fascinated him already during his medical studies: He was enrolled at the University of Rostock, and already in the preclinical stage he realized that he found physiology fascinating. »When later, during my clinical training, I saw how many gaps there were in fundamental questions, it was clear to me that I wanted to dig deeper into the subject«, he says. He studied hepatic cirrhosis for his doctorate, and in Stanford he researched the microbiological

foundations of the stomach bacteria *Helicobacter pylori* – a topic which he is consistently expanding on today as a research group leader at Charité, and which he also deals with as a doctor at the clinic. Thanks to the CSP, Michael Sigal is well on track with regard to his research – and the program is also a stroke of luck for him in his private life: His wife is also a doctor, and they both share a passion for research – so they both benefit from the BIH Charité Clinician Scientist Program. In the context of the CSP, it is possible to take a break for up to 18 months for parental leave, and the funding time is then extended this time period..

Meanwhile, Peter Krawitz moved from Berlin to Bonn: The medical professional has been head of the Institute of Genome Statistics and Bioinformatics at the local university since last year. Krawitz is therefore the first alumnus of the Clinician Scientist Program to be appointed for a W3 professorship. He ranked among the pioneers: He took part in the second year of the program. »A particularly commendable part of the program is the fact that the research period is taken into account for the specialist training«, he says in retrospect – »and of course the network also helped me a lot; the regular exchange with colleagues who are all active in research«.

Program Coordinator **Dr. Nathalie Huber**
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Dr. Michael Sigal



Prof. Peter Krawitz

A ground-breaking moment for Peter Krawitz was when he sat in front of a family of five at Charité. The three children suffered from a mental disability which is also known as Mabry syndrome – a genetic defect which Peter Krawitz was researching. »The relevant genes had already been analyzed in detail by a research group in Japan, but it was still not known whether there was a relevant medical phenotype«, Krawitz says. He took blood samples from all the family members, isolated the DNA – and made the breakthrough after one and a half years. His evidence was published in Nature Genetics and was an impressive demonstration that the combination of clinic and laboratory work funded by the program pays off even in the early stages of one's career.

In Bonn, Peter Krawitz is now further researching so-called monogenic diseases, which occur through the mutation of a single gene. He has long been mentoring young researchers in his work – seven years after he entered the Clinician Scientist Program himself as a young researcher.

About the BIH Charité Clinician Scientist Program

The Clinician Scientist Program was started in Berlin in 2011 at the initiative of Stiftung Charité. The pilot year first included eight participants. Seven years later, the Berlin program has been consolidated not only by the BIH, Charité and Stiftung Charité and has grown to over 100 people in total. The Science Council and the German research community also

recommend it as a model to improve the career paths of clinical researchers across the country. In the current coalition agreement of the federal government, a national funding program for Clinician Scientists – based on the Berlin model – was also announced.

The Clinician Scientist Program enables early-career scientists to combine medical research with clinical work. The program is jointly advertised by the BIH, Charité and Stiftung Charité. The participants obtain a post which is half funded by the CSP and thus enables to focus on research; the other half is borne by Charité, where doctors do clinical work with a part-time position.

Two tracks are offered within the CSP: The Junior Clinician Scientist Track is aimed at doctors in their first and second year of their specialist training; the Clinician Scientist Track is planned for clinicians starting from their fourth year. At the end of the program, the participant will have completed the specialist training and ideally the post-doctoral lecture qualification.

Program Coordinator **Professor Duska Dragun**
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»Knowledge about diseases is stored in massive data volumes«

To be successful, translational and personalized medicine must apply digitalized methods and technologies. The BIH has therefore established a new Center for Digital Health. With Professor Roland Eils, the center gained a renowned expert of biomedical informatics, genomics and personalized medicine as a founding director at the end of 2017. Roland Eils in an interview on data, diagnoses and breakthroughs.



As chair, you are also the founding director of the new BIH Center for Digital Health. What is the center like? Who works there?

We are a real multicultural research group characterized by various specialist disciplines and communities. Theorists as well as data analysts who develop mathematical models and transfer enormous streams of data work side by side here with experimental researchers recreating disease related processes in the laboratory. Our employees work closely with patients as well as completely digitally on a computer. What unites us and drives us all is the firm conviction of revolutionizing the understanding of diseases with our digital concepts.

Mr Eils, how do you explain to friends who do not work in science what you do as chair for Digital Health in Berlin?

We develop methods to bring together complex data from the research world with those from medical care. In combination with mathematical models that illustrate complex disease processes from molecular to organ level, we try to gain a deeper insight into disease-causing mechanisms. We therefore transfer enormous amounts of data from fundamental research and medical care – these are data volumes similar to those that are for example generated daily in the short message service Twitter. With our methods, we contribute significantly to an improved personalized diagnosis and therapy.

The new center is a part of various activities in the area of the BIH platform Digital Medicine. What role does interconnectivity play?

Without the interconnectivity of highly complex data, from a molecular to an organismic level, from the laboratory to the hospital bed, from the computer to the laboratory and back, Digital Medicine would be inconceivable. Knowledge about diseases is stored in these massive data volumes, just like world knowledge is somehow mapped in the worldwide network. One must extract the findings »only« from these streams of data.

So you collect data, and how are diseases then cured?

Cure is a big word. Our ambition is to understand the mechanisms of disease origin and development. This then provides the fundamental basis for the detection and treatment of diseases. Combined with large amounts of data which we collect on specific clinical pictures from various directions, we can express a significantly better informed diagnosis and therapy recommendation. If a patient is then cured at the end, this is of course a great success.

How do you work, what does your typical work day look like?

My work consists of a lot of fun in discovering new things. This is a kind of childlike curiosity, combined with the joy in scientific insight, and finally the gratification in making a contribution to a better treatment or cure of diseases with my work. More specifically, my working day consists of a variety of interactions – with people and data, in that order!

» We are firmly convinced that we will revolutionize the understanding of diseases with our digital concepts. «

Which clinical pictures do you focus on? Give us a concrete example.

In the past, I focused on cancer diseases. This is related to my previous location at the German Cancer Research Center in Heidelberg. There, together with colleagues from oncology and genomics, I radically changed the way we diagnose and treat cancer for hundreds of cancer patients. The results show that our approach in the deep molecular characterization of cancer diseases, combined with highly specialized bioinformatics and data analyses approaches, led to a breakthrough in the treatment of specific types of cancer. At the BIH, we will systematically expand the processes and methods developed for oncology in Heidelberg to other disease areas. Here, we specifically started with lung diseases and heart failure, where we see exciting connecting factors at Charité. I will place a structural emphasis on bringing together the most important partners from science and industry at the BIH in order to develop Berlin into a globally visible location for digital health.

Understanding thinking

Petra Ritter has been recently received one of three new Johanna Quandt Professorships at the BIH. She intends to do nothing less than create a personalized simulation of the brain on the computer.



She goes jogging once a day; this is now the constant in Petra Ritter's very diversified life. »I go out into the fresh air and run for at least five kilometres – whether I'm in New Delhi or it's already midnight«, Ritter says. For someone who has already run marathons and triathlons, this is pure relaxation. Time to think. Or maybe once in a while not to think, but simply to experience life and return from the world of computer models and simulations to the real world. To then be able to devote herself with new energy to her great challenge: learning to better understand the human brain – and to simulate it.

Together with her team at the Clinic of Neurology, with Experimental Neurology of Charité and with international partners, Ritter built the informatics platform »The Virtual Brain«, with which processes in the human brain are simulated on a computer. The

virtual brain has been constantly learning based on new data: Ritter and her colleagues continuously integrate new input into the complex program, such as the data of patients who have suffered a stroke or have a brain tumor. The vision behind this: »People should be able to plan the treatment of brain disease in the future with a digital double on the computer«, Ritter says. Which means: All the risks and chances of different therapy options can be tested in advance in the simulation, so that the ideal therapy can be selected for sick patients. Petra Ritter is pursuing this goal with her BIH Johanna Quandt Professorship, which she received last year.

What does it take to get there? Interchange, Ritter says and laughs. But it's not just about data.

»The challenges that highly specialized research faces today are so complex that one can hardly tackle them alone«, Ritter says. This is why professional exchange is extremely important. Not only to be able to gain new thought patterns and ideas. The problems are often so multifaceted that one person's knowledge is hardly enough to even comprehend it, let alone solve it. Ritter also regards the much acclaimed interdisciplinarity as the solution. She herself is the best example of this.

A medical professional by education, Petra Ritter taught herself how to program on the computer. She also completed various online university courses, including on the basics of engineering. »Through this vast acquired knowledge, I find it easier to better understand experts from any field I may work with«, Ritter says. But Ritter's broad positioning is also

» People should be able to plan the treatment of brain disease in the future with a digital double on the computer. «

important in the management of her team. »I must and want to also inspire my team. And I can only do this by thinking outside the box.«

In the end, after all the thinking outside the box and an in-depth interdisciplinary exchange, it comes down to compressing everything again. »Anyone who must absorb and process a lot of information often runs the risk of getting lost in the variety. You must remind yourself constantly of what the goal is and which levers bring you there«, Ritter says. So Ritter tries to extract the most important part, the essence, from the

stream of data, information, approaches and specialist areas. Sometimes this is a great challenge. In Ritter's opinion, this also comes down to a good team: »There is no requirement for a person to be right. On the contrary, if someone changes their mind during a discussion, this is the sign of a good exchange«, Ritter says. And at the end of these discussions there are new results, ideally new findings. For instance, this could mean that specific spreading patterns are identified for epilepsy. And this – after some delay – not only benefits the patients. It also brings Petra Ritter one step closer to her main goal: understanding the brain.



Monitoring system for cancer

Il-Kang Na is one of the three new Johanna Quandt professors at the BIH. She wants to understand what changes in the body during cancer therapy.

When Il-Kang Na is in the lab holding a small tube with a blood sample in her hand, she can often picture the face of the patient. Based on the label of the blood sample, however, you only know that it is the blood of a patient with B-cell lymphoma. This applies to almost all blood samples in Na's lab. They are people who receive an optimal and modern therapy a few miles further at Charité. But what effects does the therapy actually have on the body and on the tumor? And what consequences do these have for the immune system? And how do these changes affect the tumor? These are questions that Na has dealt with for a couple of years.

»The systems in the body are interlocked like gear

wheels. If something goes wrong, then it also affects the other systems. I want to understand how this all ties together«, says Na, who started a BIH Johanna Quandt Professorship in December. Based on these findings, Na's goal is to establish a monitoring system that provides precise information on important disease and immune parameters during the treatment. And this would eventually improve the patients' treatment.



Na can picture a face for almost every blood sample, also because she treats the people from whom the blood samples come from. Na works as a senior physician at the Campus Virchow-Klinikum of Charité in the Medical Department, Division of Hematology, Oncology and Tumor Immunology and at the Berlin-Brandenburg Center for Regenerative Therapies (BCRT). Here she looks after patients, especially those with B-cell lymphoma. Na researches this disease – also at the Experimental and Clinical Research Center (ECRC) of the MDC and Charité in north-east Berlin. But the 40-year-old medical professional's variety of duties does not stop here.

Along with her work in the lab and in the clinic, she also teaches, giving lectures to students. And everything is interconnected. At least thematically. Spatially, Na sometimes has to cover a considerable distance several times a day.

Because the clinic and the Campus Buch are more than ten kilometres apart. Na tries to plan her days so that she only has to be in one place, but that doesn't always work. And then she sometimes has to drive or travel by metro or suburban railway for an hour or more through Berlin. This is already a journey in itself – also due to the sheer size of Berlin. But this also has its advantages, for example a lively scientific community. »Through the years, I have built up myself an extensive network of collaborations and scientific exchange here in Berlin. I cannot appreciate this enough«, Na says. It was only possible because Berlin facilitates a variety of new projects and initiatives thanks to its size and wealth of research institutions. So it sometimes applies to research too: size matters.

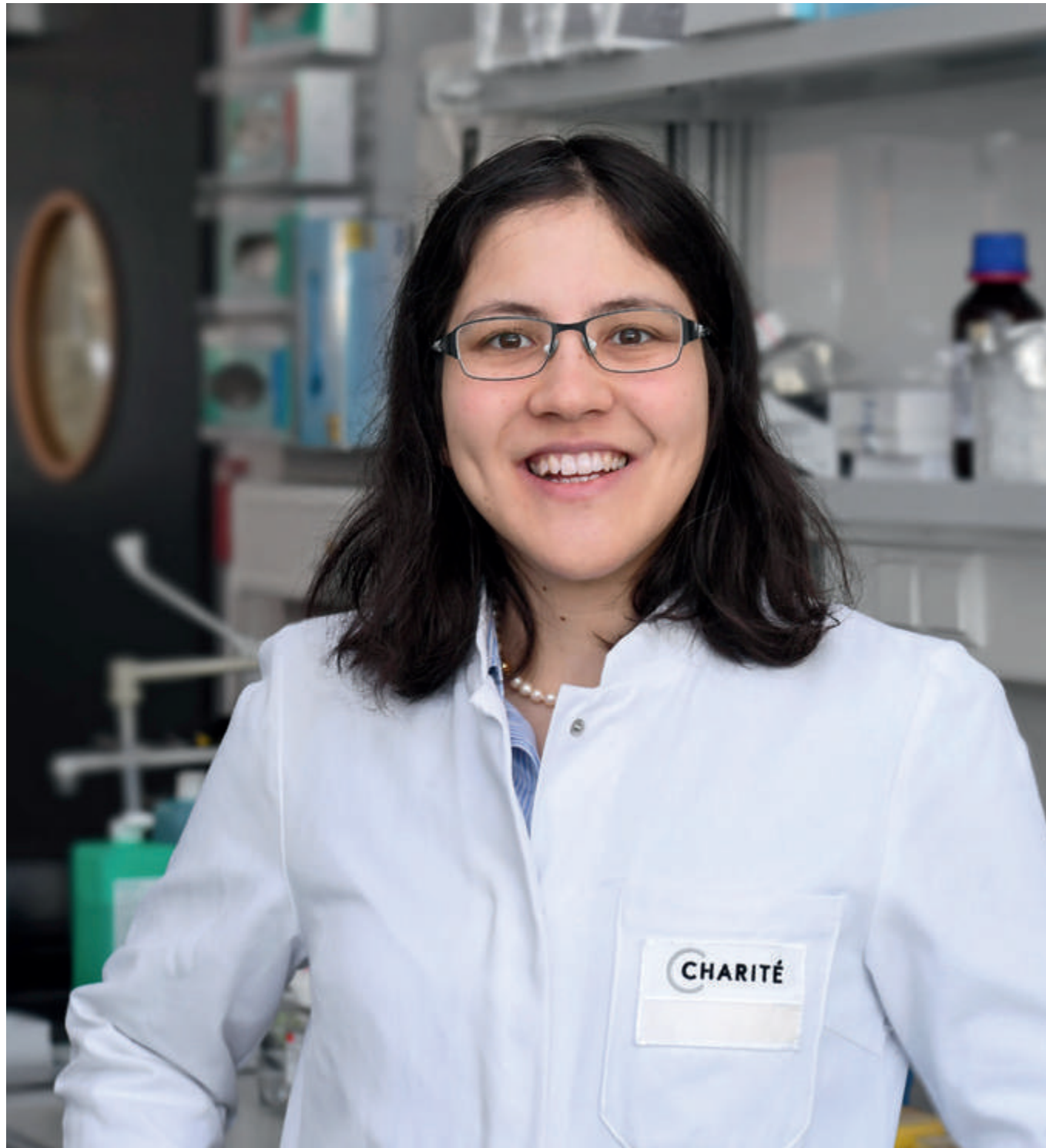
» My extensive Berlin network of scientific collaborations and scientific exchange is the basis for good research, new projects and initiatives. «



It's also thanks to this wide network that Na has the ideal preconditions to achieve further ground-breaking success in her research projects. During her Johanna Quandt Professorship, she wants to characterize the changes occurring in the body during therapy on a large scale. »My focus are the longitudinal changes, the risks that come with the treatment, further chances that possibly occur for the patients and the point in time when this relationship tips«, Na says. The monitoring system that is being established should sound the alarm in time. Na's research is currently focused on B-cell lymphoma. But she also wants to tackle other types of cancer in the long term. Her motivation always comes from the exchange with her patients: Na wants her research and medicine in general to be able to provide them with more.

The explorer

Ute Scholl has been recently received one of three new BIH Johanna Quandt Professorships at the BIH. Her research area is widely known: high blood pressure.



When Ute Scholl found her first disease gene, she was 25 years old and a postdoc in the USA. She excitedly went to her former boss and said: »I think I've found a disease gene.« But at first he did not have time to discuss her findings, because he had a deadline to meet. Only later did he stop by the lab – and was enthusiastic.

» Research is fun. «

At the BIH, the whole thing will probably be reversed. If somebody makes a great discovery, they will knock on the door of Ute Scholl, who received the BIH Johanna Quandt Professorship »Hypertension and Molecular Biology of Endocrine Tumors« on 1st November 2017. »And then perhaps I won't be on a deadline«, Ute Scholl says, laughing. Then she would come to the lab directly and share their joy.

Ute Scholl, 34, owes her steep scientific career to her research success. Her research topic is well-known and widespread like few others: high blood pressure (hypertension). Scholl focuses on a special form of hypertension that is caused by an overproduction of the hormone aldosterone. Aldosterone is produced in the adrenal gland and triggers increased salt resorption in the kidney, which in turn can lead to high blood pressure. Scholl's previous work has contributed significantly to the understanding of the causes of this form of hypertension. For example, she could demonstrate that special mutations of ion channels in benign hormone-producing adrenal gland tumors contribute to this form of high blood pressure. Scholl was awarded several prizes for her laboratory findings.

Ute Scholl spends little time in the lab these days, which she thinks is a pity because direct research in the laboratory is basic joy for her: »Children act as researchers in the garden, either consciously or unconsciously. I basically do the same, only I get paid for it«, Scholl says. What more could you want?

But this doesn't mean that research is child's play. In the lab, one small detail is enough to obtain incorrect results after several weeks of tests. In this case, major questions are: Was my working hypothesis wrong? Or was there a mistake somewhere? But where? Sometimes it can take weeks and months to find out what the problem was. Scholl sees this sometimes painstaking process more as a chance than a burden: »As a researcher, I don't try and conjure up a specific result, I rather approach the tests as impartially as possible. And when it doesn't go as planned, this doesn't mean that it hasn't worked. It's just a different result from what you might have expected«, Scholl says. »And much can be learned from this result, too, if you look at it closely and have a little patience.« Scholl certainly owes her success also to this perseverance in research.

It has also long benefited the research group Scholl supervises. Scholl wants to continue her previous research consistently within her BIH Johanna Quandt Professorship. She will be using modern sequencing techniques to find genetic mechanisms of hypertension and understand disease-causing links. Scholl's focus is on basic research, but her work area will likely be expanded soon: She would like to undertake a first clinical trial with patients soon.

More than just a visit to Berlin

With its Private Excellence Initiative Johanna Quandt, the independent and non-profit Stiftung Charité promotes the building and further development of the BIH. The focus lies in the promotion of excellent people in all stages of scientific development, from studies to a professorship. The Private Excellence Initiative is made up of 13 different funding programs altogether, which a total of 275 people from the life sciences and medicine have benefited from in Berlin. An important program of the Private Excellence Initiative is the »Einstein BIH Visiting Fellows« program. The funding program takes place in cooperation with the Einstein Foundation Berlin.

» With the Einstein BIH Visiting Fellows, we succeed in attracting internationally highly renowned scientists for the BIH who are highly acclaimed worldwide – among them are three Nobel prize winners. Berlin is therefore becoming more and more of a global hub for life sciences. «

E. Jürgen Zöllner, Executive Board of Stiftung Charité

Einstein BIH Visiting Fellows are leading international scientists who come to the BIH to form a research group, but remain employed and active at their home institutions abroad. With funding for an initial period of three years, the fellows can hire scientific staff in Berlin, purchase devices and research material and come to work meetings in Berlin several times a year. This ensures that they can supervise the research group in Berlin continuously, that they are available for junior scientists and that they also consolidate and develop a collaboration with the hosts at Charité and the MDC in the medium and long term.

Programs of the Private Excellence Initiative Johanna Quandt

- Einstein BIH Visiting Fellows (in cooperation with the Einstein Foundation Berlin)
- BIH Visiting Professors
- BIH Johanna Quandt Professors
- Recruiting Grants
- Humboldt Research Fellowships at the BIH (in cooperation with the Alexander von Humboldt Foundation)
- BIH Clinical Fellows
- BIH Charité Clinician Scientists
- Entrepreneurship and innovation program (pilot)
- BIH Delbrück Fellows
- Deutschlandstipendien
- BIH Investment Fund
- BIH Paper of the Month
- BIH Public Health Initiative

➤ **The funding program Einstein BIH Visiting Fellows**
www.stiftung-charite.de/en/funding/the-private-excellence-initiative-johanna-quandt/einstein-bih-visiting-fellows

➔ **More information under Facts and Figures**
 Page 63

Fellows with research start in 2017

Prof. Brian Kobilka

Stanford University, USA

Host: Prof. Christian Spahn (Charité)

Research project: »In silico GPCR: 'A computational microscope to determine receptor – G protein coupling specificity and functional selectivity«

The Nobel Prize winner Brian Kobilka, in close cooperation with Professor Peter Hildebrand and Professor Christian Spahn from the Institute of Medical Physics and Biophysics of Charité, runs a research lab in Berlin dedicated to the study of G protein-coupled receptors with the aid of the latest computer-assisted simulations. The team is investigating how G proteins are activated and which factors influence the binding preferences of G proteins. With a better understanding of these processes, precise medication can be developed with fewer side effects.

Prof. David Gutmann

Washington University School of Medicine, USA

Host: Prof. Helmut Kettenmann (MDC)

Research project: »Biology and treatment strategies of low-grade gliomas«

The neurologist and cell biologist David Gutmann researches in the new Berlin laboratory on brain tumors that can cause visual impairment. This cancerous disease is one of the most common types of cancer in children and adolescents. Together with Helmut Kettenmann of the MDC, Gutmann is investigating the development of the tumor in its own ecosystem to understand the interactions between various cell types and signals in the diseased tissue and to derive better therapies from this. Because so far the therapies available for children and adolescents are too aggressive for a brain which is still not fully developed.

Prof. Mario Nicodemi

Università di Napoli Federico II, Italy

Host: Prof. Ana Pombo (MDC)

Research project: »Understanding chromatin folding and gene regulation in disease associated genomic rearrangements«

The expert of theoretical physics in molecular biology, Mario Nicodemi, is researching chromatin folding in Berlin and its influence on gene expression, which play a significant role in hereditary diseases. He thus developed a method for a more precise analysis of great volumes of patient data. In particular, it is about a better analysis of genome mappings created by Ana Pombo from the MDC for hereditary diseases of the nervous system and the skeleton. This collaboration in the new lab should be able to provide personalized diagnosis and therapy options.

Prof. Stefan Guenther Tullius

Harvard Medical School, USA

Host: Prof. Johann Pratschke (Charité)

Research project: »Vascular Composite Tissue Allotransplantation (VCA): an integrated, multidisciplinary Basic and Clinical Research Program for abdominal wall, hand, and uterus transplantation«

The transplant specialist Stefan Tullius is establishing a research focus on the transplant of complex tissue structures which is still unique in Germany. Unlike most organ transplants, whole parts of the body such as the hand, the abdominal wall or the uterus are transplanted in the procedure applied by the new research group. Tullius will set up the clinical research environment and a corresponding transplantation program in cooperation with Johann Pratschke.

Expertise squared

Renowned growth for the Scientific Advisory Board of the BIH: Miriam Merad, Professor of Cancer Immunology, and Jan Geißler, cancer patient representative and advisor in medical research, patient participation and EU health policy, bring a high level of expertise and new perspectives into the Scientific Advisory Board.



» A great amount of research activity ignores real patient requirements because it pursues more academic, commercial or political goals instead of dealing with unmet needs. «

Jan Geißler

Jan Geißler represents the important perspective of the patients as a new member of the Scientific Advisory Board at the BIH. The diagnosis of »Chronic Myelocytic Leukemia (CML)« in 2001 pushed the business graduate to get involved in the health sector on a voluntary basis and from 2008 in full-time employment. »The goal of all health research must be to improve the life and the living situation of patients who are affected by a serious disease. This sounds obvious, but, in reality, decisions are often made for the patients without including them in the decision-making process«, Jan Geißler says, who has also worked as a patient representative in various patient organizations and EU committees for many years. After he started the European Cancer Patient Coalition (ECPC) together with other cancer patients in 2003, Geißler also founded the CML Advocates Network in 2007, which today links 118 patient organizations in 88 countries. As the managing director of Patvocates GmbH, he works as an independent advisor especially in capacity building and patient involvement in the areas of medical research and health policy. Jan Geißler wants to bring his know-how as a patient expert and that of

other patient organizations to the council of the BIH, »so that what the BIH does and promotes takes patients' preferences into account, actually translates into a benefit for the patients and fills therapeutic gaps«.

The second new member of the Scientific Advisory Board certainly keeps the patients' benefit in mind too: Professor Miriam Merad, who has researched and taught in the field of Cancer Immunology at Mount Sinai School of Medicine in New York since 2004, is an internationally acclaimed representative of translational medicine. The pioneer in the mapping of the regulatory network of dendritic cells relies on interdisciplinary cooperation to transfer preclinical research quickly and successfully to clinical development. In her laboratory, scientists as well as clinicians from various specialist departments work together to develop new therapies which interact synergetically with conventional antitumor therapies.

No small difference

Louise Pilote and Rhonda Voskuhl, two pioneers of Gender Medicine, have been awarded the BIH Excellence Award for Sex and Gender Aspects in Health Research. With the new prize created in 2017, the BIH honors scientists who increasingly integrate gender aspects into biomedical research.



Louise Pilote



Rhonda Voskuhl

Studies prove: Men and women differ in terms of the frequency of new diseases, the age of onset and also their response to different therapies. To draw attention to the importance of gender-specific aspects in medicine and to promote the development of research in this area, the BIH has conferred the BIH Excellence Award for Sex and Gender Aspects in Health Research for the first time. The choice was made by a renowned international jury consisting of five female professors and one male professor.

The first prize winners are two excellent representatives of gender medicine: Professor Louise Pilote from the McGill University in Canadian Montreal has specialized in social gender differences, i.e. the gender roles of women and men, in the area of cardiovascular diseases. Thanks to the »Gender Score« developed by her, she investigates the possible aspects of social gender differences on medical issues and compiles respective therapeutic approaches.

The second prize winner, Professor Rhonda Voskuhl from the University of California, USA, is researching biological gender differences in degenerative diseases such as multiple sclerosis, and is developing gender-specific biomarkers for new therapies. The scientists, who both stand out for their strong translational approach, share the prize money in the amount of 20,000 euro. They will also bring their expertise in gender medicine during a guest residence in joint projects at the BIH, the MDC and Charité.

Promoting the transfer of knowledge

In 2017, we provided the basis for a close scientific exchange with various event formats.



Scientific exchange, new collaborations and connections had a high priority at the BIH in 2017. Big scientific events as well as series of events including the Clinician Scientists Retreat, the Scientists Retreat and the Core Technologies Retreat have especially contributed to this with more than 120 scientists respectively.

Also formats such as the BIH Lectures with international guest scientists and their hosts and up to 60 guests each promoted subject-specific and interdisciplinary scientific exchange. Community events such as the BIH Digital Health Roundtables, workshops and lectures from the field of equal opportunities and the

FMP-MDC-BIH-Charité Postdoc Day with about 200 postdocs encouraged scientific exchange. Big multi-day events such as the Charité BIH Entrepreneurship Summit, the World Health Summit, Science Match FUTURE MEDICINE and the Hacking Health Hackathon also facilitated the consolidation and establishment of the BIH community.





Innovation

So that innovations can lead to an increase of quality and efficiency in health care, results from medical research must be transferred into useful technologies for patients.

Only this can create real medical progress.



A faster implementation with Berlin Health Innovations

February 2017 marks a significant milestone at the BIH: The BIH and Charité signed a cooperation agreement, and therefore started the official integration of two technology transfer teams to »Berlin Health Innovations« (BHI).



Berlin Health Innovations has been the central point of contact for scientists of Charité and the BIH as well as industry partners and venture-capital organizations since 2017. Dr. Rolf Zettl, Chief Financial Officer of the BIH, is responsible for the new innovation unit. Dr. Klaus Nitschke took over the management for an interim period in 2017.

→ [More on the Digital Health Accelerator Program](#)
Pages 53-55

In 2016, in line with the BIH Strategy 2026, it was established to expand technology transfer as a central »innovation driver« for translational medicine. The new technology transfer concept of Berlin Health Innovations comprises three areas of activity:

- Improvement of framework conditions for technology transfer
- Consolidation of suitable incentive systems
- Professionalization of the technology transfer team

The core instruments of the Berlin Health Innovations



For the operationalization of these areas of activity, Berlin Health Innovations has expanded and further developed six core instruments.

In focus 2017: Validation fund and BHI Digital Labs

In 2017, activities were particularly focused on the areas of »validation fund« and »BHI Digital Labs«.

In partnership with SPARK Berlin, Berlin Health Innovations formed an internal »validation fund« team. This was expanded with external experts (Senior Advisors for the segments of pharmaceuticals, medtech, digital health). These Senior Advisors support the entire team of Berlin Health Innovations within the scope of professionalization. The first call for the new joint validation fund began in December 2017, accompanied by informational events at all BIH sites in Berlin. People showed great interest: 75

applications by researchers and clinicians of the BIH, Charité and the MDC for translational projects were submitted from all the innovation areas of pharmaceuticals/drug development, medtech, diagnostics and digital health. The call includes two tracks. Track 1 is aimed at project teams applying for support for projects in the early stage (funding amount under 50,000 euro). Track 2 targets project teams with more sophisticated products and funding amounts over 50,000 euro. The selection of project teams for track 1 began in spring of 2018 within a pitch session. An external jury with experts from the industry, venture-capital companies and scientists was obtained for this. The selection of the track 2 project team is planned for the second quarter of 2018.

→ [More on the cooperation with Startupbootcamp](#)
Page 56

» In 2017, we focused on the development and structure of our Digital Health activities. We therefore activated the community, brought momentum to the topic and promoted the development of new digital business models. We were thus able to make the first start-up teams fit for the market. «

Dr. Rolf Zettl, Chief Financial Officer of the BIH and and the Board Member responsible for Berlin Health Innovations

A growing Digital Health community

Along with the endeavor to increase the value chain (pipeline of assets) with the incentive of the validation fund, in 2017 the focus was on the development and expansion of Digital Health activities, brought together under the roof of »BHI Digital Labs«.

To support the translation of innovations to an application for patients or to the market, three service areas have been set up. These range from community building (Meet + Ideate) such as monthly Digital Health Roundtables and an internationally visited Health Hackathon in December 2017, a first successful run of the Digital Health Accelerator program with four innovation teams from Charité to turn concepts into prototypes (Prototype + Build) to the partnership with the network Startupbootcamp Digital Health Berlin for the positioning of spin-off companies of Charité for market traction and growth, to be able to implement innovative solutions (Launch + Grow). Furthermore, BHI Digital Labs combines innovative Digital Health start-ups specifically with contact partners to explore opportunities for joint development or validation of new Digital Health solutions (Match + Connect).

Industrial cooperations

Measurable progress was also obtained in other core instruments. This includes:

- Strengthening of the team by an experienced cooperation manager from the industry
- Elaboration of a uniform IP guideline of the BIH, Charité and the MDC
- Conclusion of a framework contract with Sanofi for the implementation of joint research projects

Research and development partnership with Sanofi



In October 2017, a joint framework agreement was signed between Sanofi and the BIH, Charité and the MDC through a research and development partnership. The aim is for research results to reach patients more quickly. The first joint project activities are also focusing on autoimmune diseases. The partners will define scientific challenges together in the next few years, and are already working together in early research stages (laboratory).

Start of a Digital Health Accelerator Program

Turning innovations into future-oriented digital applications and shaping the medicine of the future.



With the »Digital Health Accelerator«, Berlin Health Innovations started a pilot program in 2017 which contributes to the promotion of digitalization in medical care.

Health apps and other digital aids in the lab and in hospital routine are increasingly finding their way into all life and work areas. Berlin Health Innovations helps researchers and clinicians convert their new Digital Health solutions from the idea to the market and application. The program targets innovation teams from the BIH, Charité and the MDC and provides specialist exchange with experts as well as the necessary professionalization for this transfer to medical application.

The program started in spring of 2017 with a call. Four interdisciplinary teams from Charité were selected for this first round and joined the program. The pro-

gram includes: Work and development in a co-working area of the BIH, intensive coaching and mentoring including in the areas of data science, patient-oriented product development, regulation, development of business models and design. The teams were also supported in matters of knowledge transfer, start-up consultancy and with networking with investors.

After four months, the innovation teams presented their new Digital Health products and solutions in January 2018 to a wide and interested audience. Not only colleagues from research and the clinic were there, but also representatives from the industry, politics and potential investors.

Innovation projects from the BHI Digital Health Accelerator Program 2017

Prof. Marc Dewey

Radiology (two projects)

Cardiac Risk App and Automated Cardiac CTA; fractal-analysis-assisted diagnostic method (together with Dr. Florian Michallek)

With the aid of artificial intelligence, the team around Marc Dewey analyzes radiological image files with the aim of identifying coronary artery disease in patients, detecting individual treatment options as well as optimizing treatment processes.

Prof. Georg Duda

Julius Wolff Institute of Biomechanics and Musculoskeletal Regeneration and Berlin-Brandenburg Center for Regenerative Therapies (BCRT)

3D-movement analysis for pre- and post-operative biomechanical analyses

With his three-dimensional patient-specific analysis, Georg Duda and his team developed an internationally unique solution for a quick assessment, analysis and treatment of orthopedic and biomechanical problems as well as a sound clinical and rehabilitative assessment in the pre and postoperative course.

Dr. Alexander Meyer

Clinic of Cardiovascular Surgery and DHZB

Prediction of severe postoperative complications in the cardiological intensive care ward

Alexander Meyer and his team want to improve the early detection of postoperative incidents in patients at the intensive care ward. Their development should contribute to the proactive avoidance of emergency situations.

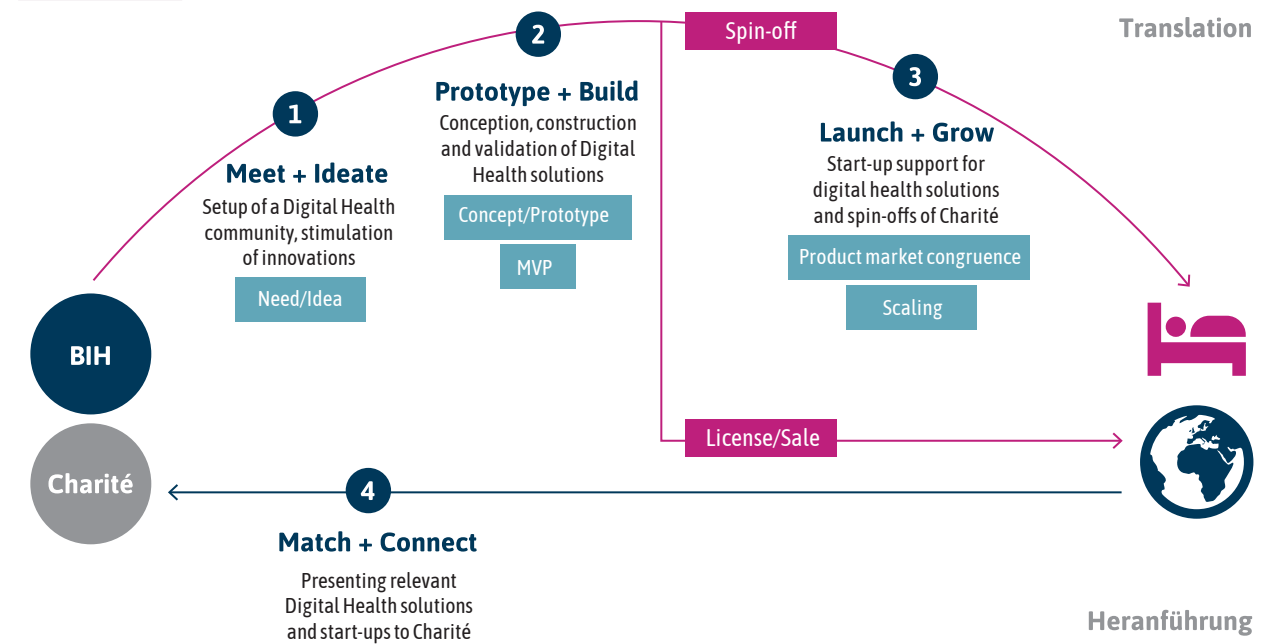
Dr. Dietmar Frey

Neurosurgery

PREDICTioN2020 – Stroke prediction through artificial intelligence

Dietmar Frey and his team developed a simulation program for stroke prognosis to develop optimal treatment strategies for stroke prevention.

Digital Labs



All Digital Health Accelerator-related activities are part of the innovation instrument BHI Digital Labs. With BHI Digital Labs, a Digital Health ecosystem leading on a national level should be set up in which Digital Health solutions become a driving force for a greater benefit in medical care – for patients and therefore for society. The idea is: To promote digital health solutions or their ideas at Charité and bring in Digital Health expertise at the same time.

In line with the cooperation with the technology transfer unit of the MDC, Berlin Health Innovations services are also accessible to the MDC on request.

The range of services of BHI Digital Labs has been in great demand already in its first year. The activities are therefore being continuously developed. A new call for the Digital Health Accelerator program started in the spring of 2018.

The following four service areas are provided

1. Meet + Ideate

Setup of a Digital Health community and stimulation of innovations

2. Prototype + Build

Conception, construction and validation of digital health products and services

3. Launch + Grow

Start-up support for Digital Health spin-off companies

4. Match + Connect

Bringing relevant Digital Health solutions and start-ups to Charité

➤ **BHI Digital Labs**

www.berlinhealthinnovations.com/services/bhi-digital-labs/

Start-up assistance for market entry of Digital Health spin-offs

Alongside the established network Startupbootcamp, entrepreneurs and potential founders receive support in their first steps into the commercial market.



BocaHealth

Not only with its own program – the Digital Health Accelerator – does Berlin Health Innovations fund entrepreneurs from Charité and the MDC in the spin-offs of their Digital Health solutions and products. In 2017, Berlin Health Innovations entered a multi-year partnership with Startupbootcamp, Europe's leading digital accelerator.

Startupbootcamp is a global network of industry-oriented start-up accelerators running 20 programs on five continents and with a wide mentor and alumni network in over 30 countries. Startupbootcamp relies on a broad experience from the company's eight-year history, and has its roots in Copenhagen. Startupbootcamp Digital Health Berlin is a funding program in Europe and supports innovative companies combining medical knowledge with new technologies.

Per selection round, the Startupbootcamp network provides ten internationally selected digital health start-ups with practical mentoring by over 150 industry experts, logistics support, office spaces in Berlin and access to a global network of business partners



Motognosis

and investors from the healthcare industry. In 2017, two start-ups from the Charité environment were chosen to participate at the Startupbootcamp Digital Health Berlin. They work together as entrepreneurs in residence – i.e. on site – on the program to benefit from knowledge transfer with startups and mentors:

With Motognosis, Sebastian Mansow-Model has developed a video-analysis-based solution for the clinical assessment of motor symptoms in patients with neurological diseases such as multiple sclerosis and Parkinson's disease.

➔ www.motognosis.com

Dr. Alessandro Faragli of BocaHealth has developed a mobile sensor to monitor the fluid balance for patients with cardiovascular and renal diseases.

➔ www.boca-health.com

Mentoring for academic innovations

Together with Stiftung Charité, SPARK Berlin was founded in 2015 based on the model of the original SPARK program of Stanford University in the USA, and has been a partner of the validation fund of Berlin Health Innovations since autumn 2017.



SPARK Berlin is a mentoring program which promotes academic inventions through coaching and funding and speeds up their translation to clinically relevant medication, diagnostics and therapies. Teams can apply every year with their translational projects. After an evaluation phase, which includes a selection round (pitch session), projects are accepted on the program. Along with financial support, SPARK project teams also benefit from a growing network of experts, including from the areas of pharmaceuticals, diagnostics, medical technology, patenting and medicinal chemistry. They support the teams over the whole period, which can vary depending on the project and depends on the actual requirements. Financial support is usually provided for the period of one year.

But SPARK Berlin offers even more: a regular series of lectures and seminars open to all interested researchers and clinicians on various topics of technology transfer and expertise for business start-ups.

Partners of BIO-Europe®

In 2017, a cooperation was started with BIO-Europe®, Europe's biggest partnering conference at the service of the global biotech industry. BIO-Europe® allows international SPARK programs to hold this kind of pitch session. The first session was held in Berlin, where six of the teams from Charité and the MDC supported by SPARK Berlin presented their projects. The aim of this new event is to make industrial partners and investors aware of innovative biomedical projects. Partnering translational research teams and the industry gets collaboration, licensing and funding off the ground. The pitch session should now be carried out every year by the respective SPARK team of the BIO-Europe® host country.

Global networking for translational medicine

The SPARK program is growing. After the program start of SPARK Jena in Germany, talks were held with other universities, for instance in Heidelberg and Neuss, to establish other SPARK programs in Germany. The SPARK Global network is also growing worldwide. There are currently programs at 26 international universities, another 14 are now being planned. New programs were started in Finland and Norway in 2017. Universities in Israel and South Africa are also in discussions with Craig Garner, the founder of SPARK Berlin. Individual SPARK teams are constantly exchanging views and form a consistently growing global network of experts.

Climate change also in biomedical research

Validity, and reproducibility of scientific results are important strategic goals of the BIH which are implemented in the QUEST Center for Transforming Biomedical Research. In November 2017, the center was officially opened with various scientific talks on the theme of »reducing waste – increasing value«.



Are the common indicators by which research performance is measured still relevant today? How must research results be published so that they are available to everyone? Which incentives must be created so that »negative« results may also be published? What measures are required to increase the quality of research and therefore the reproducibility of scientific results?

» *The special feature of our center is that we conduct general research as well as work internally on our subjects, and initiate projects at the BIH for better quality.* «

Ulrich Dirnagl, Founding Director of QUEST Center

These and other questions that the QUEST Center deals with were the focus of the scientific opening event. The event was moderated by the Founding Director of the QUEST Center Ulrich Dirnagl, who presented more than ten ongoing projects.

These include the introduction of the electronic laboratory notebook; an anonymous survey on the institutional research climate; an addition of criteria within the recruitment procedures for Charité professorships; a study on the publication rate of clinical studies in German university clinics as well as measures to increase the number of open-access publications; and

the foundation of a cooperative society in which citizens become members and can therefore manage and control their own personal data themselves.

After a keynote lecture with the title *The quest for better behavior in science* by David Moher (Ottawa Hospital Research Institute, Canada), a brief scientific symposium was held on the second day, where internationally acclaimed scientists presented their work, ideas and possible solutions on the key topic of »reducing waste – increasing value«.

» *This is about research on research. There is an urgent need for this. We must rethink the system and understand where we stand. I therefore congratulate the QUEST Center.* «

Frank Miedema, University Medical Center Utrecht, Netherlands

Some of the speakers were Ernst Hafen (ETH Zurich; Switzerland), Trish Groves (The BMI, UK), Frank Miedema (University Medical Center Utrecht, NL), Ivan Oransky (New York University School of Medicine, USA) and Londa Schiebinger (Stanford University, USA).

➤ **QUEST Center**
www.bihealth.org/en/quest

Mission & approaches of the QUEST Center

The aim of the QUEST Center is to improve the quality and especially the intrinsic value of research performance in the preclinical and clinical research of the BIH and beyond and increase the efficiency of research processes and projects.



Quality assurance

The QUEST Center promotes compliance of preclinical as well as clinical research with standards and guidelines on design, conduct, analysis and reporting..



Open Science

The QUEST Center improves the accessibility and transparency of the BIH research and its results through open access and open data.



Meta Research

The QUEST Center identifies opportunities for improving research practice and obtain evidence for the impact of its activities through 'research on research'



Incentive and rewards

The QUEST Center develops new incentive systems in research, e.g. by selecting appropriate novel indicators and metrics for the assessment of research performance of researchers and institutions. QUEST assist in the implementation and evaluation of these novel systems.



Research for and with the public

The QUEST Center fosters research for and with the public to enhance public outreach and public involvement in the BIH research.



Bioethics of translation

The QUEST Center develops and implements innovative, science-based guidelines and training modules for the quality of research and protection of humans and animals.



Thinktank

The QUEST Center acts as advisors to stakeholders in biomedicine from funders to politics.



Education & Training

The QUEST Center develops and implements training and teaching resources on experimental and study design, methods to reduce bias, new modes of publishing, the digital footprint of academics, as well as open science.

Closing the gap: The electronic lab notebook

Handwritten to digital: The BIH introduced the electronic laboratory notebook (eLN) at Charité in April 2017. Dr. Philipp Böhm-Sturm, group leader at the MRI lab in the department of Experimental Neurology at Charité, outlines how the electronic documentation system simplifies his work routine.



What other benefits does the electronic laboratory notebook have?

It also prevents writing and reading errors as well as redundancies. And you can structure the data much better. For instance, specific experiments, measurement data or test parameters can be found easily via a search function and the keywording option, even years later. With paper lab notebooks this is very time-consuming. labfolder is also quite flexible: I can sketch a test setup, insert images and link to other sources. And collaboration in joint projects and across individual research groups is easier.

Do you miss the paper laboratory notebook?

Not one bit. My field, experimental MRI, is very data-intensive. We also come across a lot of digital imaging data – and documenting it in a handwritten laboratory notebook was not ideal and took a long time. labfolder, which is what the electronic, browser-based lab software is called, simplifies and improves data collection in experimental neurology immensely. For example, we can now document all the research stages without any media disruption.

How so?

As a core facility, we provide our services across the campus and also for the industry. Because our devices are relatively unique, we are requested for many collaboration projects. With labfolder, we can now set up a joint project and document all the experiments centrally. For external collaboration partners, we can convert and send the collected data via a PDF – all those involved are thus always up to date and can exchange information widely.



Facts and Figures

Is an electronic lab notebook useful for each field?

This is something that each person must check for themselves. In my opinion, the electronic laboratory notebook closes a big gap in the necessary digitalization of scientific work processes. As a group leader, I work a lot on the computer, bring the experimentally generated data together and, for instance, utilize it for scientific publications. For this reason, the eLN is very important for my work. But someone who works in the lab on cell culture and still writes data down can also bring this into the new system: Instead of typing it all out again, he or she can for instance take a photo of the data with a smartphone and insert it into the electronic laboratory notebook.

And what about data security?

The BIH version of labfolder is modified in such a way that it runs on the Charité servers. All the data and documents remain in the intranet and therefore in a closed system. For security, in each project you can also determine who exactly has access to which data and who can make entries. Furthermore, you can seamlessly trace who changed what and when.

Facts and Figures

- 65 1. Legal framework and institutional milestones
- 65 2. Members of the corporation under public law
- 65 3. Financing and financial situation 2017
- 67 4. Personnel 2017
- 68 5. Organization and committees
- 72 6. Sites
- 72 7. Scientific performance
- 90 8. Private Excellence Initiative Johanna Quandt: Funding decisions 2017

1. Legal framework and institutional milestones

The Berlin Institute of Health (BIH) was founded as an non-university biomedical research institution in cooperation with Charité – Universitätsmedizin Berlin and the Max Delbrück Center for Molecular Medicine in the Helmholtz Association (MDC), initially in the form of a partnership under civil law (Innen-GbR) according to the German Civil Code (BGB). Apart from Charité and the MDC, the partners included the Federal Republic of Germany, the state of Berlin and the Helmholtz Association of German Research Centres. In January 2013, the German federal government and the state of Berlin signed the administrative arrangement on the »Establishment, Organization and Financing of Berlin Institute of Health«. Charité, the MDC, the Federal Ministry of Education and Research and the Senate Administration for Educa-

tion, Youth and Science in Berlin, as well as the Helmholtz Association of German Research Centres, signed the founding agreement on March 25, 2013.

With the BIH Act (BIG-G), which entered into force on April 23, 2015, the BIH was converted into a corporation under public law. Under the law, the BIH is a new, non-university independent institution (corporation under public law [KdöR]) in the field of biomedicine with the member entities Charité and the MDC. The BIH unites the clinical research and basic research of its member entities and processes the development of this research. It promotes translational research and interdisciplinary collaboration between the MDC and Charité.

2. Members of the corporation under public law

The members of the BIH are professors employed full time by the Charité (professors, junior professors), as well as research group leaders of the MDC.

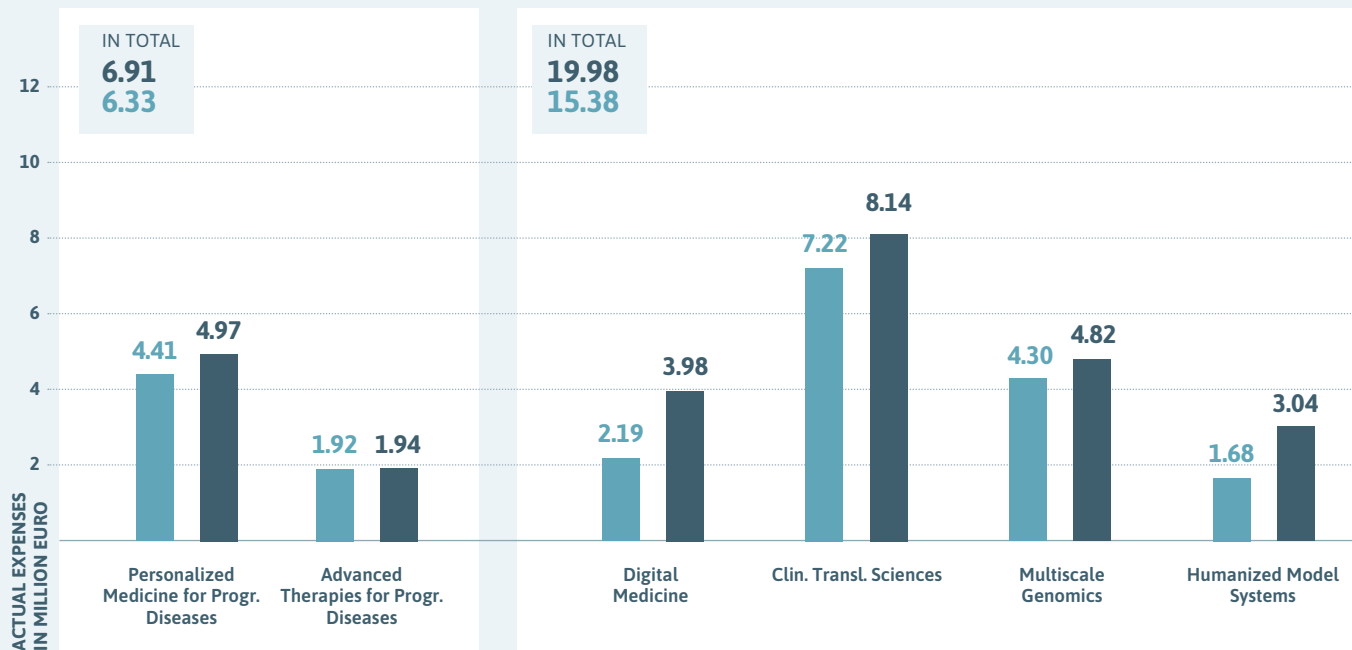
3. Financing and financial situation 2017

The BIH is financed based on the joint administrative arrangement with the federal government (90 per cent) and the state of Berlin (10 per cent). With effect from January 1, 2016, the BIH now operates independently as a corporation under public law (Körperschaft des öffentlichen Rechts). The utilization of funding takes place in accordance with the funding approval by the federal government and the state of Berlin, which authorizes the BIH to forward funds to Charité and the MDC in accordance with the specified utilization regulations. Furthermore, the federal government has also authorized the BIH to utilize the regulations for the federal remuneration scheme for professors (W-scheme) and the respective applicable regulations for supplementary payments for the various centers of the Helmholtz Association of German Research Centres.

In accordance with the approval by the federal government dated March 22, 2017 and by the state of Berlin dated April 4, 2017, the BIH was awarded institutional funding totaling 70.2 million euro. Of this, the federal government provided 63 million euro, and the state of Berlin 7.2 million euro. In addition, there were also grant funds for discretionary use from 2016 totaling 34.132 million euro.

Research programs

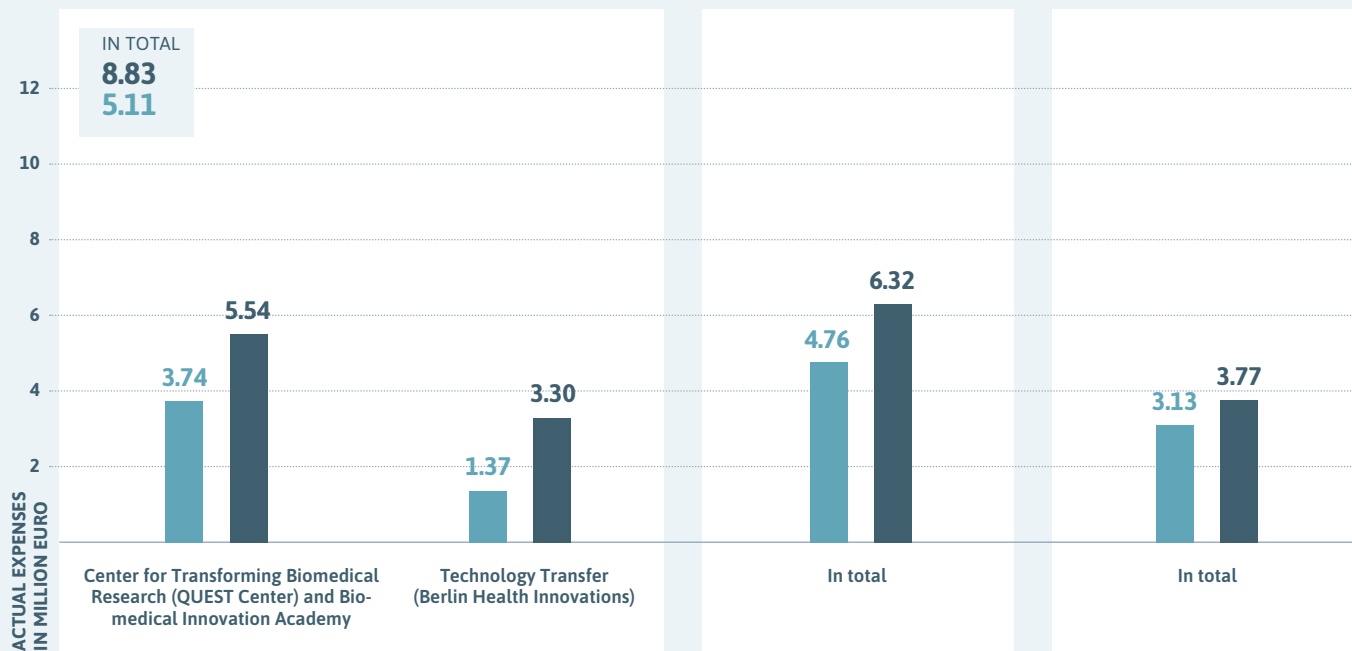
Research platforms



Innovation drivers

Construction, areas and innovations

Performance range management and administration



2016 2017

From the funding available, the BIH drew down 45.682 million euro, of which 36.711 million euro to be transferred to the member entities (Charité: 26.028 million euro, MDC: 10.683 million euro). Within self-management, 58.650 million euro were carried over to 2018, of which 52.591 million euro of federal government funds and 6.059 million euro of state funds (end-of-year cash remainders in the state of Berlin).

Significant business plan positions, in which independently generated revenues were made by the BIH, are construction projects costing less than 2.5 million euro as well as recruitments and related infrastructural measures. The funds are committed to measures which could no longer be implemented by the end of 2017, contrary to the original plan.

Stiftung Charité transferred 1.734 million euro to the BIH 2017 in line with the programs. Of this, 1.620 million euro was to be forwarded and 114 thousand euro was to be used at the BIH.

According to section 3(4) of the the BIH Act (BIG-G), the BIH is seen as directly and exclusively serving non-profit purposes according to the subsection »Tax-privileged purposes« of the fiscal code, in particular scientific purposes.

4. Personnel 2017

The BIH stands for equal opportunity in the appointment of management positions, committees, and reviewer groups. The BIH offers family-friendly, flexible working hours and professional development measures for (future) management staff.

As of December 31, 2017, 33 female employees and 23 male employees (a total of 53.16 full-time equivalents; figures include the full-time Executive Board members) were employed at the BIH corporation under public law. Three people were sent from Charité to the BIH (Berlin model). Based on a contractual agreement, the BIH also reimbursed Charité for the staff costs for another person.

Scientific and clinical personnel; management and administration

As of December 31, 2017, 276.76 FTEs (full-time equivalents) or 363 persons were being financed by the BIH within the research commons (programs, structures, recruiting, management). Three of them were sent from Charité to the BIH (Berlin model).

Of which	FTEs	Persons
Female	151.78	193
Male	124.98	170

Development of personnel in the research commons (in detail/FTEs)

	2016	2017	Definition	
Scientists (female)	49.61	51.43	Employees are considered BIH scientists if: 1. their staff positions are financed with the BIH funds, 2. they are reimbursed at least according to the collective agreement for the public service of states or to the public service pay grade 13 and are postdocs, 3. they have a university degree, 4. they either have a PhD or do not aspire to have a doctorate, 5. they are assigned to an organizational unit focused on scientific or scientific-technical matters, 6. they carry out valuable scientific tasks directly, 7. they work as doctors.	
Scientists (male)	68.54	80.55		
Doctoral students (female)	16.30	17.95		
Doctoral students (male)	14.25	20.20		
Research assistants (female)	62.69	82.40		Research assistants are employees whose staff positions are financed through the BIH (e.g. university of applied sciences graduates, technical assistants). However, this also includes people from the collective agreement for the public service of states or for the public service pay grade 13 who have coordinating or administrative functions, i.e. do not carry out scientific work directly.
Research assistants (male)	15.11	24.23		

5. Organization and committees

Organs and committees of the corporation under public law

By law, the organs of the BIH consist of the Supervisory Board, the Executive Board, and the Scientific Advisory Board. The members of these organs and the duties of the organs are defined in the BIH Act. The internal workings and division of tasks on the Supervisory Board and Executive Board are regulated in the bylaws of the Supervisory Board dated June 2016, the bylaws of the Executive Board dated October 2015 and the articles of incorporation dated July 2016, and in an additional business distribution plan for the Executive Board.

Supervisory Board

The Founding Supervisory Board was replaced by the Supervisory Board pursuant to a letter from the Senate Administration for Education, Youth and Science dated May 11, 2016 detailing the

appointment of the Supervisory Board members. In 2017, State Secretary Steffen Krach (State Secretary for Science and Research, Berlin Senate Chancellery) and Sonja Jost (DexLeChem GmbH, Berlin) were appointed new members of the Supervisory Board. Senator Sandra Scheeres (Senate Administration for Education, Youth and Family Berlin) and Jan Eder (IHK Berlin) left the Supervisory Board.

In the 2017 reporting period, the Supervisory Board met twice, on July 6, 2017 and on November 17, 2017. State Secretary Steffen Krach was elected deputy chairman of the Supervisory Board in the July session.

6 out of 15 positions on the Supervisory Board are occupied by women (40 percent). The 8 seats for which state equal opportunity laws apply have equal representation from both genders.

www.bihealth.org/en/supervisory-board

Executive Board

In the reporting period, there was a personal change on the Executive Board: On July 6, 2017, Professor Erwin Böttinger was dismissed by the Supervisory Board as full-time Chief Executive Officer with effect from July 31, 2017. From then on, the Executive Board consisted of four members. Professor Martin Lohse took over the function as acting Spokesman of the Executive Board on August 1, 2017.

In this reporting period, the Executive Board met for 13 regular sessions and an extraordinary session as well as for other closed meetings. The focus of these sessions and closed meetings was on the implementation of the »BIH Strategy 2026«, the 2017 - 2020 implementation plan, the 2018 business plan and the areas of recruitment and construction/areas.

The percentage of women is 0 percent.

Prof. Karl Max Einhäupl, Charité –
Universitätsmedizin Berlin, Chief Executive Officer
Prof. Martin Lohse, Max Delbrück Center
for Molecular Medicine in the Helmholtz
Association, Scientific Director – Acting Spokesman
of the Executive Board
Prof. Axel Radlach Pries, Charité –
Universitätsmedizin Berlin, Dean
Dr. Rolf Zettl, Chief Financial Officer

Scientific Advisory Board

The Scientific Advisory Board consists of 14 experts and elected Stefanie Dimmeler as the new chairwoman from the members of the Scientific Advisory Board in 2017.

In 2017, four new members were appointed into the Scientific Advisory Board from the Supervisory Board: Jan Geissler (Patvocates GmbH, Riemerling) and Miriam Merad (Icahn School of Medicine, Mount Sinai Health System Hospitals, New York) as of October 1, 2017, as well as Sarah Teichmann (Wellcome Sanger Institute Hinxton) and Georg Stingl (Medical University of Vienna) as of December 1, 2017.

The Supervisory Board also appointed the members Robert Bast, Alan Buchan, Amanda Fisher, Jörg Hacker, Veronika van Heyningen and Sibbrand Poppema for a second term of four years as of 1st October 2017.

In the reporting period, the Scientific Advisory Board met twice, on June 15/16, 2017 and on October 12/13, 2017. During its meetings in the reporting period, the Scientific Advisory Board especially dealt with the »BIH Strategy 2026«, the approval of the 2018 implementation plan and consultation for BIH appointments as well as the setup of a focus on regenerative therapies in the New Therapies research program.

5 out of 14 positions are occupied by women (36 percent).

www.bihealth.org/en/scientific-advisory-board

Scientific Committee

According to the BIH Act, the Executive Board may appoint a Scientific Committee consisting of BIH members. The Scientific Committee consists of up to 21 members, whereby there must be a balance between the members of Charité and the MDC as well as between basic and clinical research. The Scientific Committee advises the Executive Board in all research-relevant aspects. In 2017, the key topics were the »BIH Strategy 2026« with the related topics of appointment strategy and project funding.

7 out of 21 positions are occupied by women (30 percent).

www.bihealth.org/en/scientific-committee

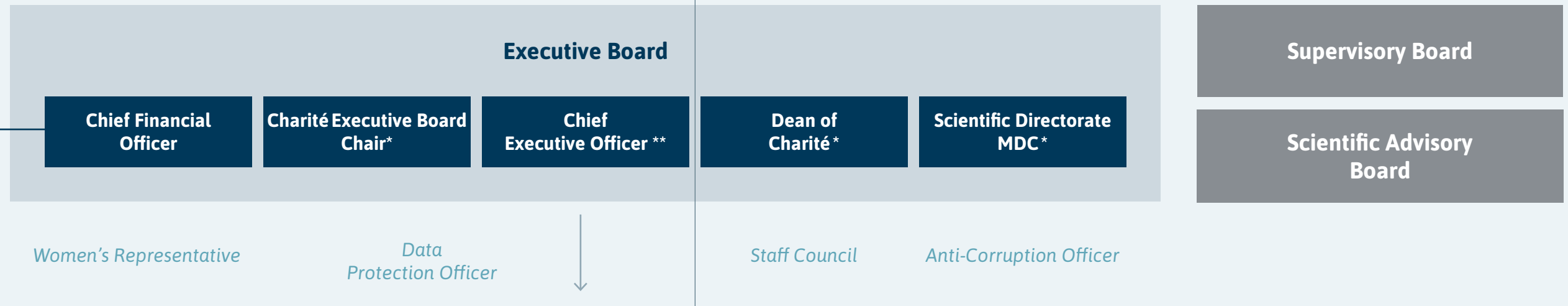
Head Office

According to the BIH Act, the BIH established a Head Office which is managed by the Executive Board. The Head Office is based in Berlin Mitte, and in mid-2017, it moved into new premises in the Spreepalais on Anna-Louisa-Karsch-Straße near the Hackescher Markt, to be able to have all departments of the Head Office in one place. This supports the work of the Executive Board in the planning and implementation of the strategy and of the research program, and manages all research-related administrative procedures.

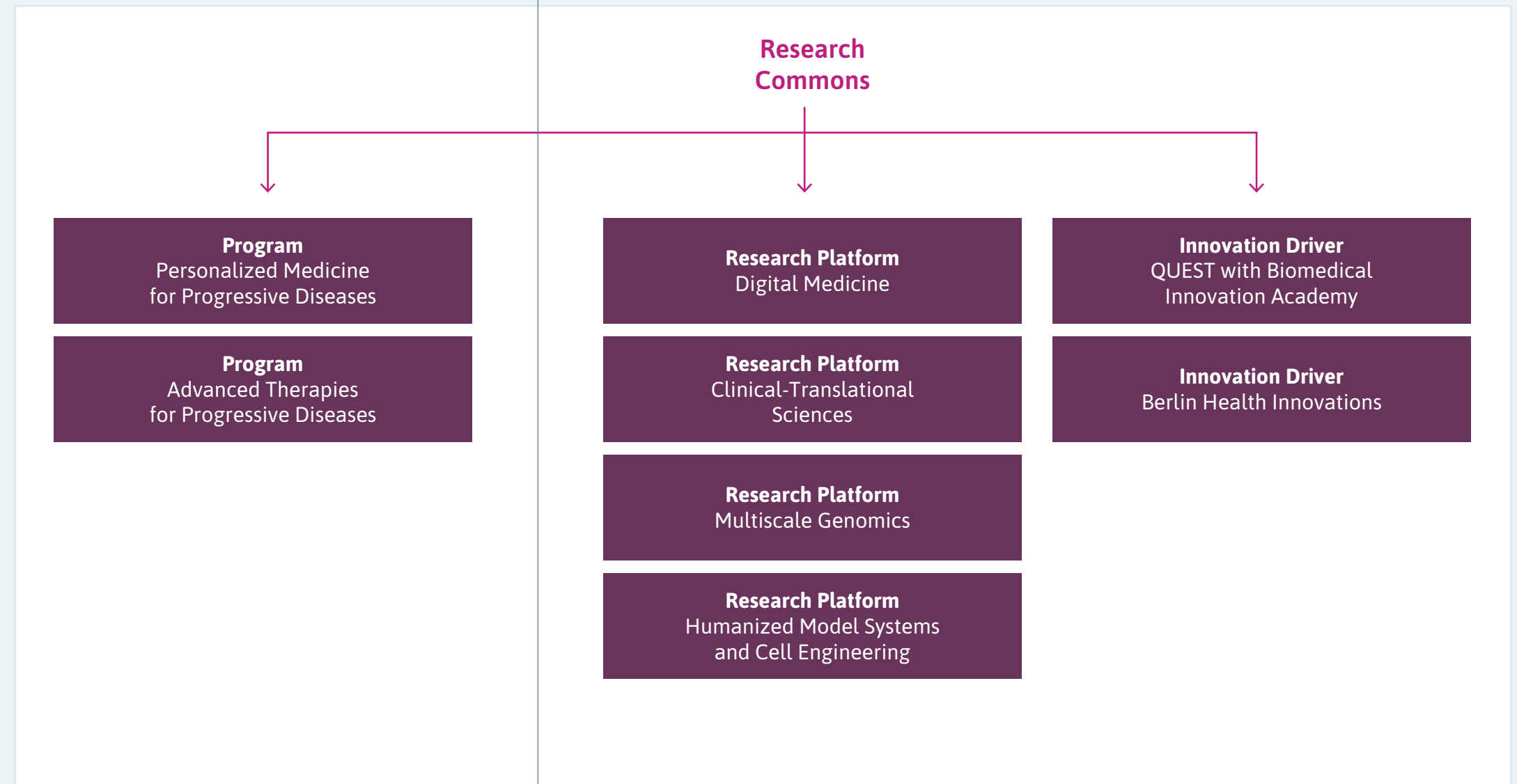
www.bihealth.org/en/head-office

Organization flowchart of the corporation under public law

As of 2018/03/09



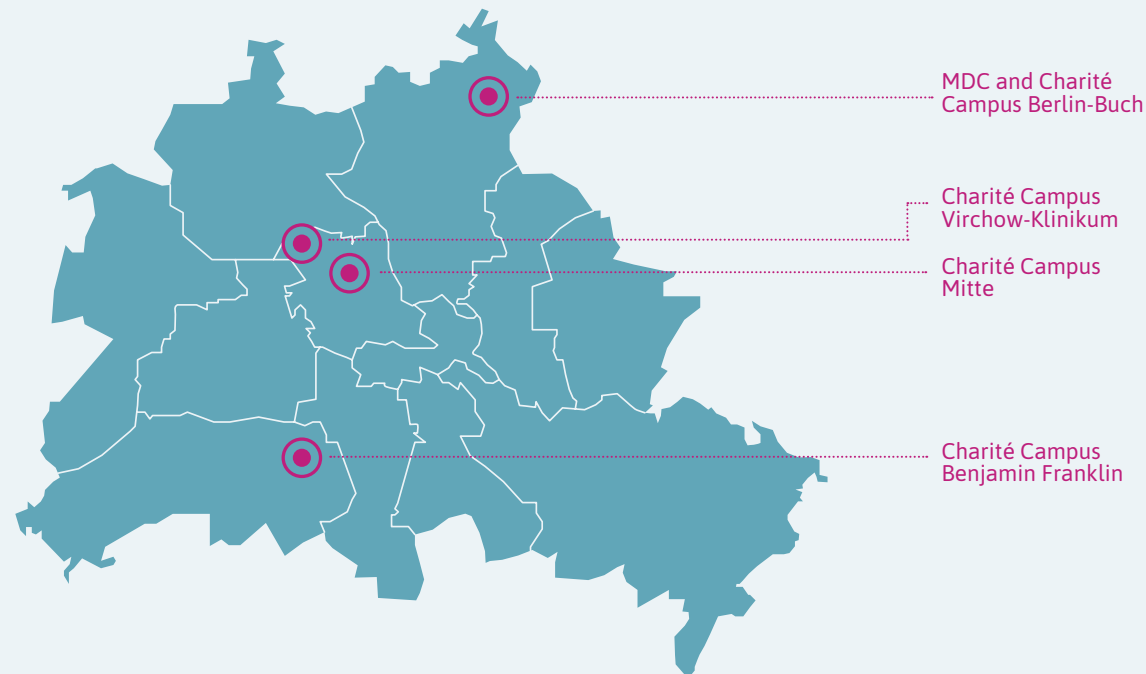
BIH Head Office Management & Administration



* Part-time Executive Board members

** vacant since 07/2017; spokesman role assumed by the Chief Executive Officer of the MDC

6. Sites



7. Scientific performance

7.1 Translational research projects and the BIH Research Groups

During its founding phase, the BIH developed two funding instruments for strengthening translational research between the MDC and Charité. The Collaborative Research Grants (CRGs) support large-scale collaboration teams over a period of four years. The Twinning Research Grants (TRGs) are smaller teams of two to three group leaders who jointly represent the areas of basic and clinical research at the MDC and Charité. The funding period of TRGs is two years.

CRG 1 is part of the program »Advanced therapies of progressive diseases«; all other projects belong to the program »Personalized medicine of progressive diseases«.

➔ www.bihealth.org/en/research/projects

7.1.1 Program »Personalized Medicine for Progressive Diseases«

The aim of the program is to develop and apply better predictive markers and models for the prediction of the progressions and therapy successes of progressive diseases. The program is made up of several research

initiatives in which researchers of the MDC and Charité and cooperating institutions deal work on their own topics in their specific strategic focus.

CONSORTIUM: CRG 2A PROJECT TERM: 06/14–05/18

Elucidating the proteostasis network to control Alzheimer's disease

Prof. Erich Wanker and Prof. Frank Heppner

Principal investigators and subprojects

Frank Heppner (Charité)

Repurposing, validating and mechanistically understanding IL-12/23 and NALP3 inhibitors as novel preclinical and clinical Alzheimer's disease modifiers

Erich Wanker (MDC)

Effects of small molecule modulators of proteostasis and protein aggregation on dysfunction and neurotoxicity in Alzheimer's disease

Thomas Willnow (MDC)

APOE receptors as targets for prevention of A β oligomerization and neurotoxicity in Alzheimer's disease

Elke Krüger (Charité)

Perturbations of proteostasis networks in Alzheimer's Disease: focus on the ubiquitin proteasome system

Oliver Peters (Charité)

Proteostasis and long-term disease progression in Alzheimer's dementia

Josef Priller (Charité)

Repurposing of approved drugs impacting on proteostasis for the treatment of Alzheimer's disease

Nikolaus Rajewsky (MDC)

Expression and function of circular RNAs and micropeptides in Alzheimer's disease

CONSORTIUM: CRG 2B PROJECT TERM: 05/14–04/18

Towards a better understanding and diagnosis of congenital disease

Prof. Christian Rosenmund and Prof. Carmen Birchmeier

Principal investigators and subprojects

Christian Rosenmund (Charité)

Angela Kaindl (Charité)

Common pathways and transcription network control in intellectual disability and microcephaly

Carmen Birchmeier-Kohler (MDC)

Heiko Krude (Charité)

Towards a better understanding of congenital endocrine diseases

Stefan Mundlos (Charité)

Ana Pombo (MDC)

Mis-regulated chromatin folding as a cause of congenital disease

Wei Chen (MDC; since summer 2016: South University of Science and Technology in Shenzhen, China)

Christian Hinze (MDC)

Dominik Müller (Charité)

Integrative omics-based dissection of molecular mechanisms underlying congenital abnormalities of the kidney and the urinary tract

Uwe Ohler (MDC)

Silke Rickert-Sperling (Charité/MDC)

Transcription network controlling heart development and congenital heart disease

CONSORTIUM: CRG 4 PROJECT TERM: 08/15–07/19

From Cancer Diagnostics to Precision Medicine: Model Neuroblastoma

Prof. Angelika Eggert and Prof. Matthias Selbach

Principal investigators and subprojects

Angelika Eggert (Charité)

Clinical Coordination, Biobanking and Phenomics

Matthias Selbach (MDC)

Proteomics, Integrative Genomics, Transcriptomics and Epigenomics

Carsten Denkert (Charité)

Dr. Hedwig Deubzer (Charité)

Metabolomics

Ulrich Keilholz (Charité)

Liquid Biopsies

Johannes Schulte (Charité)

Animal Models

Nils Blüthgen (Charité)

Altuna Akalin (MDC)

Computational NB Biology and Data Management

Thomas Blankenstein (Charité)

Annette Künkele (Charité)

Genetically engineered T Cells

CONSORTIUM: TRG 1 TERM: 02/15–01/18

Systems Medicine of BRAF-driven malignancies

Principal investigators

Nils Blüthgen (Charité)

Markus Landthaler (MDC)

CONSORTIUM: TRG 2 TERM: 02/15–01/18

Systems Medicine in Kidney Cancer:

Towards stem cell-directed therapy

Principal investigators

Jonas Busch (Charité)

Walter Birchmeier (MDC)

Wei Chen (MDC; since summer 2016: South University of Science and Technology in Shenzhen, China)

CONSORTIUM: TRG 3 TERM: 01/15–12/17

Inflammation-induced skeletal muscle atrophy in critically ill patients:

Identification of molecular mechanisms and preventive therapies

Principal investigators

Carmen Birchmeier-Kohler (MDC)

Jens Fielitz (Charité and ECRC)

Steffen Weber-Carstens (Charité)

CONSORTIUM: TRG 4 TERM: 05/15–05/18

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

Elucidating a core mechanism in the pathophysiology of psychotic disorders

Principal investigators

Simon Jacob (Charité; since spring 2015: Technical University of Munich, from where he continues to supervise the project)

James Poulet (MDC and Charité)

CONSORTIUM: TRG 5 TERM: 02/16–01/18

Fetal programming of cardiometabolic disease

Principal investigators

Michael Bader (MDC)

Ralf Dechend (Charité)

Michael Schupp (Charité)

CONSORTIUM: TRG 6 TERM: 04/16–03/18

PRDM16 – a therapeutic target for heart failure

Principal investigators

Norbert Hübner (MDC)

Sabine Klaassen (Charité)

CONSORTIUM: TRG 7 TERM: 04/16–03/18

Heterogeneity of immune infiltration in glioblastoma and its implications for molecular diagnostics and personalized treatment decisions

Principal investigators

Helmut Kettenmann (MDC)

Christoph Harms (Charité)

BIH RESEARCH GROUP

Prof. Andreas Diefenbach

BIH Professorship Microbiology

Diefenbach's research activities are focused on the question: which mechanisms does the innate immune system use to detect infectious agents such as viruses, bacteria and cancerous cells? In the next few years, Diefenbach will increasingly research the role of the innate immune system in the physiological adaptation to the environment and in the regeneration of tissues and organs.

BIH RESEARCH GROUP

Prof. Christian Drosten

BIH Professorship Virology

Professor Drosten is particularly consolidating the focus areas of infection epidemiology, respiratory and tropical viral diseases as well as the field of so-called preparedness research. Findings from evolution and infection research should contribute to the detection of dangerous pathogens and the preparation for occurring epidemics.

7.1.2 Program »Advanced Therapies for Progressive Diseases«

The aim of the program is to develop and apply better markers and models to be able to better understand and predict advancing diseases and their individual progressions. Interdisciplinary research groups will use the most modern systems medicine techniques to research the role and interplay of defective biological

systems in progressive diseases. This approach is unique because it is based on a comprehensive, deep characterization of patients, extensive studies on the structure and interplay of biological systems as well as large-scale data analyses.

CONSORTIUM: CRG 1 PROJECT TERM: 04/14–03/18

Targeting somatic mutations in human cancer by T cell receptor gene therapy

Prof. Thomas Blankenstein and Prof. Peter-M. Kloetzel

Principal investigators and subprojects

Peter Kloetzel (Charité)

Identifying immunogenic mutant epitopes

Thomas Blankenstein (MDC)

Mutation-specific T cell receptors

Hans Schreiber (Charité)

Targeting unique tumor-specific antigens

Wolfgang Uckert (MDC)

Tumor rejection capacity of mutant-specific TCRs

Zsuzsanna Izsvák (MDC)

A transposon-based TCR gene transfer for clinical use

Michael Hummel (Charité)

Identification of cancer-specific immunogenic mutations and their expression

Antonio Pezzutto (Charité)

Moving mutation-specific TCR gene therapy into the clinic and preclinical efficacy comparison to lymphoma lineage-specific TCRs

BIH RESEARCH GROUP

Prof. Il-Kang Na

BIH Johanna Quandt Professor for Translational Medicine with a Focus on Therapy-Induced Remodeling in Immuno-Oncology

Malignant tumors develop differently in each individual. Scientists are understanding the reasons behind this more and more, and can tailor therapies to patients in a much more accurate and individual manner. But which effects does the selected treatment have on the tumor, immune system and their interactions? And how can the therapy be adapted and improved? Il-Kang Na is searching for answers to these questions, and, with her previous work, she was able to detect immunodeficiencies which are

caused by therapies and which are providing innovative ideas for new therapeutic approaches. With the aid of modern bioanalytical high-throughput technology, the Professor wants to develop a comprehensive instrument which records and controls molecular and genetic changes at different times during the therapy. In this way, the treatment of cancer patients can be adapted individually and significantly improved.

7.1.3 Research Platform »Digital Medicine«

The research platform Digital Medicine focuses on the use and development of digital technologies for the improvement of data usability in research and in the clinic. This also includes IT infrastructure and services, the setup of a Health Data Platform (HDP) for the standardized and interoperable integration of health and research data as well as the High Performance Computing (HPC), activities in the Einstein Center Digital Future and medical informatics activities.

IT infrastructure and services

The IT Core Facility provides the BIH with basic IT services and therefore forms an IT-basic setup for employees and researchers at the BIH. IT services comprise administrative services such as user support, network support, central files and storage services, email and groupware services as well as central server and computing power. Along with the provision of administrative services such as network and server infrastructure, the IT Core Facility deals with the setup of the Health Data Platform (HDP) for the standardized and interoperable integration of health and research data of Charité. The IT Core Facility also provides the necessary network resources and data interfaces for the High Performance Computing (HPC) facility. Significant projects carried out by the IT Core Facility in 2017 were support in the setup of the IT infrastructure for the cohort project BeLOVE and the development of a concept for a general laboratory information system (uLIMS).

BIH RESEARCH GROUP

Prof. Petra Ritter

BIH Johanna Quandt Professor of Translational Medicine with a focus on Brain Simulation

Petra Ritter's research focus is personalized brain simulation. Together with her team at the Clinic of Neurology, with Experimental Neurology of Charité and with international partners, she built the informatics platform »The Virtual Brain«, with which processes in the human brain are simulated on a computer. Ritter and her team integrate the data of patients who, for instance, have suffered a stroke or have a brain tumor into the simulations. This then creates models tailored to each patient which help

gain a better understanding of disease processes and allow for new therapeutic approaches. Within the BIH Johanna Quandt Professorship, she would like to expand the Virtual Brain platform with scientists from the research commons of Charité and the MDC.

7.1.4 Research Platform »Clinical-Translational Sciences«

An access to well-characterized patient groups and their samples within a good infrastructure is necessary for closely connected and translational research. This research platform represents a scientific development of existing methods; it provides services and supports clinical-translational research projects.

Research infrastructure

Core Facility Biobank

The biobank operates in two sites which have a consistent sample database and a consistent laboratory, information and management system. The Buch site is managed by Professor Tobias Pischon, while the Charité Virchow Klinikum site is managed by Professor Michael Hummel and operated both by Charité and the BIH. The biobank is useful for the long-term preservation of liquid samples by test subjects and patients from studies and for the storage of liquid and tissue samples taken from patients for the diagnosis in line with the medical care. In 2017, the automated deep-freeze warehouse was installed and tested and many new projects and studies were supervised.

Clinical Research Unit (CRU) and studies

The CRU is a »translational organizational unit« which collaborates with different disciplines. The CRU was set up and developed in all four sites of Charité and combines laboratory workstations and outpatient research clinics in one place. Different research modules are available for various projects, whereby the CRU places great importance on the standardization and reproducibility of processes. This guarantees that patients recruited for studies are examined under comparable conditions, regardless of which CRU or Charité site the research takes place in.

Since 2017, three clinical studies with a translational focus have been conducted with funding for two years (250,000 and 500,000 euro).

ADVIM-TREG PROJECT PERIOD: APPROVED UNTIL AUGUST 2018

First-in-man adoptive regulatory T cell (Treg) therapy in kidney transplant patients – scientific sub-project for the Research Grant: advanced immune monitoring of adoptive Treg therapy (AdvIm-Treg)
Prof. Petra Reinke and Prof. Wolfgang Uckert

Planned number of patients to be recruited
max. 18. Patients are recruited and the study is carried out on the Campus Virchow-Klinikum.

OPTICO-ACS PROJECT PERIOD: APPROVED UNTIL SEPTEMBER 2018

Clinical and molecular characterization of two different pathophysiologies leading to an acute coronary syndrome using novel high-resolution intra-coronary plaque imaging (optical-frequency domain imaging) and molecular high-throughput technologies

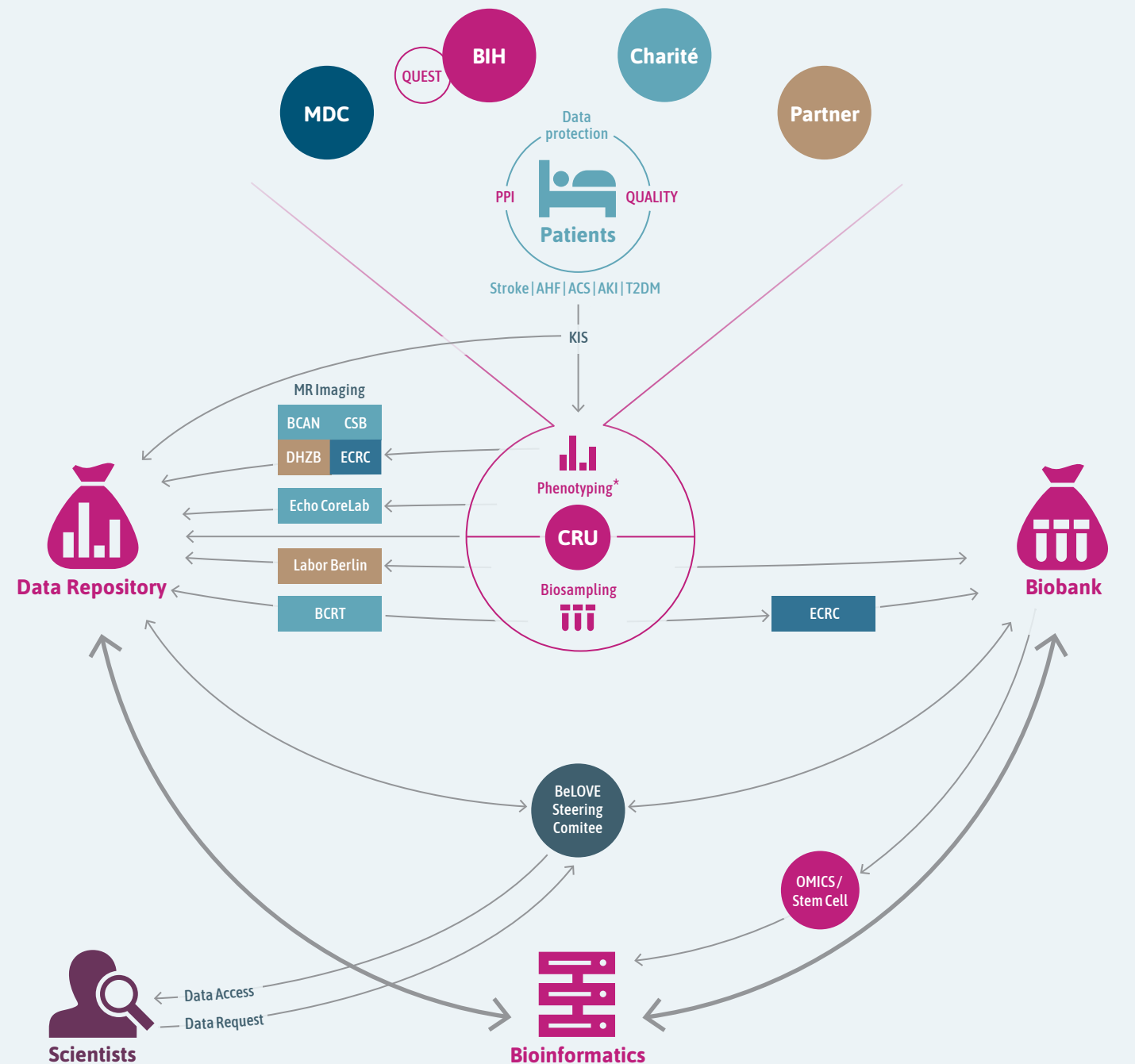
PD David Leistner and Prof. Ulf Landmesser

Planned number of patients to be recruited
414 ACS patients. Patients are recruited and the study is carried out on all three inpatient campuses of Charité (Charité Benjamin Franklin, Charité Virchow-Klinikum, Charité Campus Mitte).

GESPIC-CROHN PROJECT PERIOD: APPROVED UNTIL AUGUST 2018

The role of gut microbiota in the development of arthritis phenotype in patients with inflammatory bowel disease: a prospective cohort study
Prof. Denis Poddubnyy and Prof. Britta Siegmund

Planned number of patients to be recruited
100 patients with Crohn's disease, 50 patients with primary axial spondyloarthritis. Patients are recruited and the study is carried out on all three inpatient campuses of Charité.



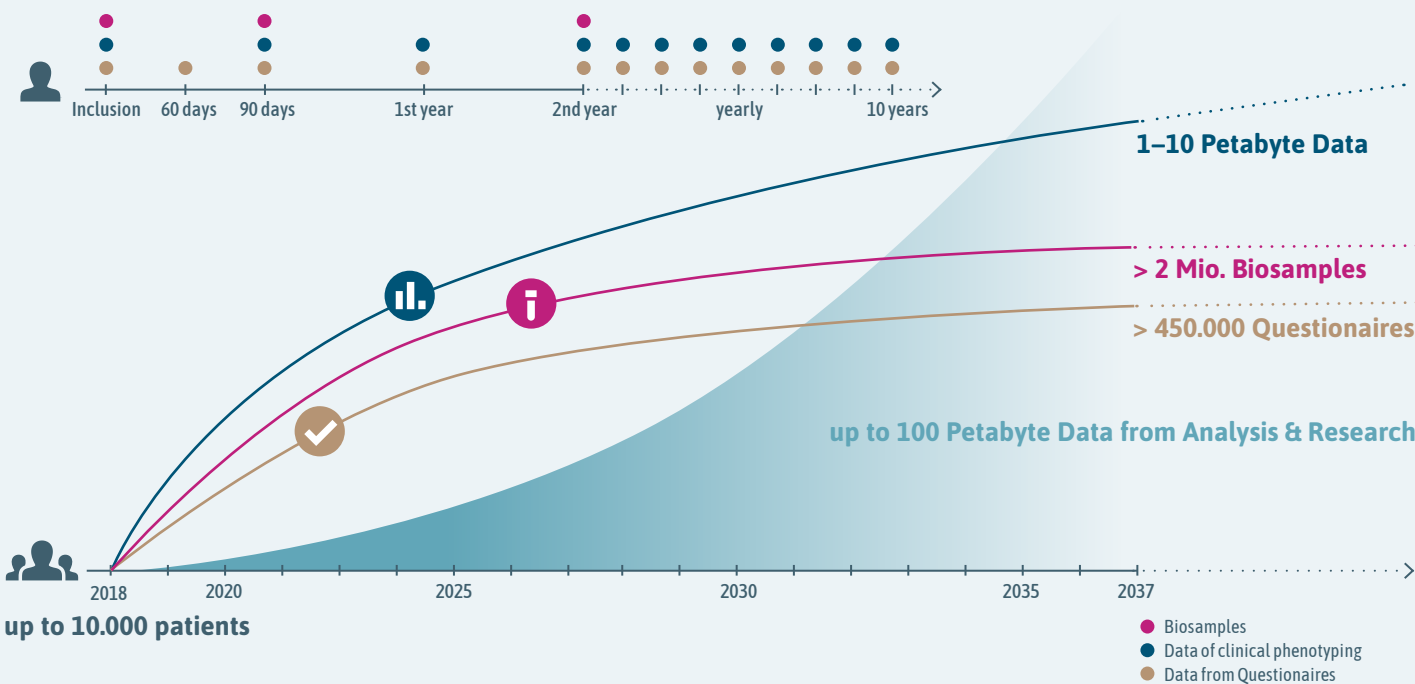
- *Organ specific phenotyping/Echocardiography/ Microbiome/Physical Assessment and Movement Analysis/Somatosensory and Pain Lab & EEG Lab/ Metabolic phenotyping/Patient Reported Quality of Life/Cognition/Sex & Gender
- AHF Acute Heart Failure
- ACS Acute Coronary Syndrome
- T2DM Type 2 Diabetes Mellitus
- AKI Acute Kidney Injury
- BCAN Berlin Center for Advanced Neuroimaging
- BCRT Berlin-Brandenburg Center for Regenerative Therapie
- CRU Clinical Research Unit
- CSB Center for Stroke Research Berlin
- DHZB Deutsches Herzzentrum Berlin
- ECRC Experimental and Clinical Research Center (MDC and Charité)
- OMICS Genomic, Proteomics and Metabolomic Core Facilities
- PPI Patient and Public Involvement
- QUEST Quality | Ethics | Open Science | Translation
- BIH (Berlin Institute of Health)
- Charité
- MDC (Max-Delbrück-Centrum)
- MDC & Charité
- External Institutions/Partner
- BeLOVE (members of MDC, Charité & BIH)

BeLOVE study

Observation study Berlin Longterm Observation of Vascular Events

BeLOVE was implemented in the summer of 2017 into a cross-campus pilot phase in the participating Charité clinics and CRU sites. Since the start of recruitment in July 2017, 100 patients could be recruited by December 31, 2017, of which 21 with an acute coronary syndrome (ACS), 17 with acute heart failure (AHF), 48 with an acute cerebrovascular disease (stroke / TIA) and 14 with diabetes mellitus type 2. The recruitment stage for acute kidney insufficiency (AKI) was implemented with a delay, which is why a recruitment start is not planned until the beginning of 2018.

Detailed phenotyping (taking two to three days per patient) has already been conducted on 31 patients, distributed around the CRU sites. This showed that 65 percent of the patients participated in the extensive studies at the CRU three months after their inclusion in the study.

**Participating scientists and physicians****BeLOVE steering committee****Prof. Kai-Uwe Eckardt**

Principle Investigator (Acute Kidney Injury)
Director, Medical Clinic with a focus on Nephrology and Internal Intensive Medicine, Charité

Prof. Frank Edelmann

Medical Clinic with a focus on Cardiology, Charité

Prof. Matthias Endres

Principle Investigator (Stroke)
Director, Clinic of Neurology, Charité

Prof. Holger Gerhardt

Principle Investigator (Induced Pluripotent Stem Cell)
Research group leader, Integrative Vascular Biology Cardiovascular Diseases, MDC

Prof. Norbert Hübner

Principle Investigator (Genetics and Genomics)
Research group leader, Genetics and Genomics of Cardiovascular Diseases, MDC

Prof. Tobias Kurth

Principle Investigator (Epidemiology)
Director, Institute of Public Health, Charité

Prof. Ulf Landmesser

Principle Investigator (Acute Coronary Syndrome)
Director, Medical Clinic of Cardiology, Charité

PD Dr. David M. Leistner

Medical Clinic of Cardiology, Charité

Prof. Knut Mai

Medical Clinic of Endocrinology, Charité

Prof. Dominik N. Müller

Principle Investigator (Metabolomics and Microbiome); Experimental and Clinical Research Center (ECRC) & Guest-Group Leader, MDC

Prof. Burkert Pieske

Principle Investigator (Acute Heart Failure)
Director, Medical Clinic with a focus on Cardiology at the Campus Virchow-Klinikum
Director, Clinic of Internal Medicine – Cardiology of the German Heart Center Berlin (DHZB)

Prof. Tobias Pischon

Principle Investigator (Epidemiology)
Group leader, Molecular Epidemiology Research Group, MDC

Prof. Geraldine Rauch

Principle Investigator (Biostatistics)
Head, Institute of Biometrics and Clinical Epidemiology, Charité

Prof. Kai Schmidt-Ott

Group leader, Molecular and Translational Kidney Research, MDC

Prof. Jeanette Schulz-Menger

Principal Investigator (Magnetic Resonance Imaging)
Group leader, Cardiac MRT, Experimental and Clinical Research Center (ECRC)

Dr. Bob Siegerink

Center for Stroke Research Berlin, Charité

Prof. Joachim Spranger

Principle Investigator (Diabetes mellitus Type 2)
Director, Medical Clinic of Endocrinology, Charité

Coordinators of CRU sites**Charité Campus Mitte (CCM)**

Prof. Knut Mai; Prof. Sein Schmidt

Charité Campus Virchow-Klinikum (CVK)

Prof. Frank Edelmann, Dr. Anne Flörcken

CRU OCC-Operative Critical Care (CVK)

Dr. Steffen Weber-Carstens, Dr. Undine Gerlach

Charité Campus Benjamin Franklin (CBF)

Dr. Joachim Weber

Charité Campus Buch/Experimental and Clinical Research Center (ECRC)

Dr. Michael Boschmann

7.1.5 Research Platform

»Multiscale Genomics«

The genetic causes of diseases, analyzes the role of genes, genetic variations and mutations and of the microbiome in the development of progressive diseases are analyzed. The characterization of genetic variations in the DNA sequence of individuals and their association with phenotypic characteristics are also highly relevant for translational research at the BIH. This is also the case for the characterization of regulatory processes in biological models for a better understanding of pathogenetic mechanisms.

Scientific infrastructures

Omics Facilities

The Omics Facilities of the BIH are specialized in high-throughput technologies and in the handling and analysis of clinical samples. With genomics, metabolomics and proteomics, they represent the three most modern omics technologies used for the analysis of genes, proteins and metabolic products as well as their interactions.

OMICS FACILITY

Genomics Core Facility

Dr. Tomasz Zemojtel; Dr. Sascha Sauer

The Charité Campus Virchow-Klinikum site is managed by Dr. Tomasz Zemojtel (since April 2017). The Buch site is integrated into the Genomics Facility of the Berlin Institute for Medical Systems Biology and is managed by Dr. Sascha Sauer. In particular, with around ten joint studies, BIH-funded Collaborative Research Grants are among the important users of the Genomics Core Facility.

OMICS FACILITY

Metabolomics Core Facility

Dr. Jennifer Kirwan

The Metabolomics Core Facility is managed by Dr. Jennifer Kirwan. The facility supports many projects, especially the BIH Collaborative Research Grant »Proteins at the focus of Alzheimer's research«. Close networking was also established with the Bioinformatics Core Unit. The two facilities are jointly developing a new software for data analysis in metabolomics.

OMICS FACILITY

Proteomics Core Facility

Dr. Philipp Mertins

The Proteomics Core Facility is managed by Dr. Philipp Mertins (since August 2017). Along with many services such as global proteome analyses and the detection of post-translational protein modifications such as phosphorylations, ubiquitinations and lysine acetylations, the team is establishing a method to analyze blood plasma samples.

OMICS FACILITY

Core Unit Bioinformatics

Dr. Dieter Beule

Core Unit Bioinformatics is located on the Campus Mitte of Charité and is managed by Dr. Dieter Beule. A subfield here is the standardized processing of data along the defined workflow, for example for the quality control and alignment of sequence data, variant calling and transcriptome quantification from RNA sequence data but also the management of omics data and metadata. The other subfield consists of bioinformatic support of specific projects, for example in the areas of rare diseases, cancer genomics, functional transcriptome analysis etc. The facility was used by around 30 research groups at the BIH, Charité and the MCD and supported a total of 66 projects in 2017.

BIH RESEARCH GROUP

Dr. Martin Kircher

BIH Junior Group Leader of Computational Genome Biology

The focus of the junior research group »Computational Genome Biology« is research into computer-based methods for the identification of functionally relevant genomic sequences and sequence variants. The group is developing and maintaining, together with cooperation partners, a frequently used variant effect scoring tool (Combined Annotation Dependent Depletion, CADD). Furthermore, the team analyzes experimental measurements of the effects of non-coding sequence alterations, for example of Massively Parallel Reporter Assays (MPRA), and uses these data to develop models of regulatory sequence effects, with the aim of understanding the functions of these sequences better.

BIH RESEARCH GROUP

Prof. Ute Scholl

BIH Johanna Quandt Professor of Translational Medicine with a Focus on Hypertension and Endocrine Tumors

Hypertension can occur in different ways. In particular, Ute Scholl deals with a special form of high blood pressure which is caused by an overproduction of the hormone aldosterone. Aldosterone is produced in the adrenal gland and triggers an increased salt resorption in the kidney which in turn can lead to high blood pressure. Scholl's previous work has contributed significantly to the understanding of the causes of this endocrine hypertension.

BIH RESEARCH GROUP

Dr. Birte Kehr

BIH Junior Group Leader
Genome Informatics

The junior research group »Genome Informatics« is developing analytical methods for genome sequence data to record genetic variation. Their focus is the identification of structural variation from the growing amounts of sequence data of complete genomes. Under the leadership of Dr. Birte Kehr, the team is also working on a new method of finding and genotyping deletions which can be applied to much bigger cohorts than previous methods. An analysis tool is also being developed for data and technologies which generate much longer, but more defective sequence reads than previous technologies. Another new technology generates sequence reads which are linked through barcodes.

7.1.6 Research Platform »Humanized Model Systems with Cell Engineering«

The goals of the research platform include the development of the highly modern technologies of stem cell research and modeling of clinical pictures, the development of high-throughput technology based on humanized models and their application for the research of therapeutic target molecules and active ingredients.

Research infrastructure

Stem Cell Core Facility

The Stem Cell Core Facility provides services for the extraction, treatment and tissue-specific differentiation of stem cells at two sites – Charité Campus Virchow-Klinikum under the leadership of Dr. Harald Stachelscheid and the MDC Campus in Buch under the leadership of Dr. Sebastian Diecke. Both sites are cooperating closely to support fundamental and translational research by providing all available technologies for the use of human induced pluripotent stem cells (hiPSC). This includes genome editing for the targeted manipulation of stem cells. The facility further specializes in the generation of disease-specific isogenic iPS cell lines for fundamental and clinical research. This comprises the extraction, differentiation and provision of human iPS cell lines.

BIH RESEARCH GROUP

Dr. Holger Gerhardt

BIH Professorship Experimental Cardiovascular Research

Professor Holger Gerhardt is investigating the principles of blood vessel formation in the development of organisms as well as in diseases.

The goal of his research is finding ways of stopping and correcting pathological vessel growth. Professor Gerhardt is involved in the planning and implementation of the BIH symposium, in the BIH Scientific Committee and in Appointment Committees for the recruitment strategy of the BIH.

BIH RESEARCH GROUP

Dr. Ralf Kühn

iPS Cell-based Disease Modeling

The research group uses genetic recombination systems which allow a targeted insertion of mutations and whole combinations of gene variants into mammalian cells. Combined with the use of human, induced, pluripotent stem cells (hiPS cells) which can be established through reprogramming, it is possible to have direct, experimentally based insights into people's genetic pathomechanisms for the first time. The group is currently studying the optimization of CRISPR/Cas9-induced mutations in hiPSCs and their subsequent differentiation in dopaminergic nerve cells. The group would like to use these to investigate the genetic factors leading to the loss of these cells in the neurodegenerative disease Parkinson's.

7.2 Performance indicators

Performance indicators of TRG and CRG consortia:

Indicator	TRG+CRG consortia 2016	TRG+CRG consortia 2017
New collaborations with		
MDC or Charité	41	55
national institutions	14	22
international institutions	22	31
Industry	7	11
Publications		
Total	109	82
Open access publications	54	31
First or last author with BIH affiliation	70	45
New technologies in the development		
Total	17	9
Intellectual property rights		
Reported inventions	3	3
Patent applications	5	4
Patents granted	1	2
Pre-clinical studies		
Total	7	11
Clinical studies		
Total	7	3
Participants currently included in studies	315	146
Planned number of participants	2,995	215
Academic qualifications		
Bachelor	1	1
Master	6	6
Dr. med.	2	2
Dr. rer. nat.	9	3
PD (Privatdozent)	1	0
Professorship	15	0
Prizes and awards for project members		
Total	11	15
Scientific presentations and posters		
Total	103	121

7.3 Recruitments

A main principle of the »BIH Strategy 2026« to be successful in the international competition is the recruitment of the brightest minds at each level – from junior group leaders and the middle career stage to principal investigators. To achieve this ambitious goal, a series of new recruitments of BIH Chairs, BIH Professorships and BIH Junior Groups have been initiated in the reporting period across all service areas of the BIH and ongoing procedures have already been promoted or in some cases have already been completed successfully.

Recruitments at the BIH mainly take place in three categories

BIH Chairs

Researchers with an excellent academic career who will become pioneers for research programs and research platforms.

BIH Professorships

Conduct successful research of the highest level and stand out for internationally acknowledged achievements. Strengthen the impact of the BIH, Charité and the MDC.

BIH Junior Research Groups

Scientists at the beginning of their career

Together with Stiftung Charité and its Private Excellence Initiative Johanna Quandt, the BIH Johanna Quandt Professorships (W2 professorships for a time with tenure track) started in 2015, specifically targeting scientists and standing out for thematic openness in the areas of translation and systems medicine. The professorships therefore represent a new impulse for the promotion of equal opportunities in the life sciences during the establishment stage in the scientific system, which still has little funding. The funding was originally planned for two professorships, but, in October 2016, the Scientific Advisory Board of Stiftung Charité decided to fund four professorships due to the excellence of the applicants. Three candidates were appointed after a phase of negotiations of the Executive Board.

An overview of this can be found in 7.1.

7.4 Overview of program participants at the BIH Innovation Academy and alumni

Funding instrument	Participants		Percentage of women (%)		Alumni		Proportion of women (%)	
	2016	2017	2016	2017	2016	2017	2016	2017
Junior Clinician Scientist	43	54	18 (42)	22 (41)	3	5*	2 (67)	3 (60)
Clinician Scientist	59	67	25 (34)	24 (68)	21	25*	4 (19)	4 (16)
Translational PhD	19	19	13 (68)	13 (68)	0	0	0 (0)	0 (0)
Translational Postdoc	2	2	1 (50)	1 (50)	0	0	0 (0)	0 (0)
Research Grants	11	16	4 (36)	7 (44)	20	4**	8 (40)	4 (100)

Version: March 2018

* After a new definition, alumni include the participants who received their degree certificate in the reporting year (previously: those who finished the program in the reporting year).

** The start of funding was postponed to April 1 (previous year: January 1), so that those funded from 2017 can finish the twelve-month program only in 2018 and can then be counted as alumni.

7.5 Overview of the the BIH Technology Transfer Fund 2017

In the reporting period, funding activities were also implemented which can be traced back to the period before the implementation of the "BIH Strategy 2026". This includes the BIH Technology Transfer Fund Pharma/Medical Devices.

Two selection procedures were held in 2017.

Call for bids and funding of the BIH Technology Transfer Fund – Pharma

Matthias Taupitz Charité	Development of diagnostic tests to determine disease-specific autoantibodies against acetylcholine receptors
Karl Skriner Charité	Early diagnosis in rheumatoid arthritis with the anti-MCA3 ELISA test
Prof. Hendrik Fuchs MDC	Use of circulating cell-free DNA methylation as a diagnostic tool
Ulrike Stein MDC	Cancer metastasis restriction using novel molecularly targeted therapies

Call for bids and funding of the BIH Technology Transfer Fund – Medical Devices

Wolf-Dieter Müller Charité	Validation of the osseointegration of an innovative dental implant made of the high-performance material polyether ether ketone
Markus van der Giet Charité	Serum amyloid A adsorber for dialysis patients

7.6 Validation fund and SPARK Berlin

A new call for tenders was published in mid-December 2017: the validation fund for translational projects from the areas of pharmaceuticals/drug development, medical technology, diagnostics and digital health. The fund is aimed at researchers and clinicians of Charité and the MDC. 75 applications for both tracks were submitted until the submission deadline in mid-January 2018:

- Track 1 (previous projects with funding amounts up to 50,000 euro)
- Track 2 (bigger, more mature projects with a funding requirement of more than 50,000 euro)

External expert juries selected the projects in the context of short presentations in the spring of 2018.

The fund of Berlin Health Innovations, the joint technology transfer unit of the BIH and Charité, was advertised in partnership with SPARK Berlin.

Together with Stiftung Charité, SPARK Berlin was founded in 2015 based on the model of the original SPARK program of Stanford University in the USA, and has been a partner of the validation fund of Berlin Health Innovations since autumn 2017.

2017

- Newly promoted teams in the SPARK program: 5
- Total number of teams in the SPARK program (newly accepted and from previous years): 20

Program components of SPARK Berlin

- **Promotion:** Financial support in the context of the newly established validation fund of Berlin Health Innovations; funding decisions: milestone-based
- **Education:** SPARK stipend holders (aka »SPARKees«) take part in regular seminars and lectures on the process of development and marketing of medication, medicinal products, diagnostics and digital health products.
- **Mentoring:** Each project team presents the progress of the project at regular meetings with all the SPARKees and mentors. Competent advisors provide project-related support in each phase of product development.
- **Consultation:** SPARK provides consultation, access to the global SPARK network and access to the Core Facilities as well as support with setting up partnerships with the industry and other academic institutions.

7.7 Equal opportunity

Building on equal opportunity measures which had previously been successfully implemented, the BIH, Charité, and the MDC agreed upon a gender- and diversity-sensitive organizational culture with family-friendly working conditions in the »BIH Strategy 2026«, in which a diverse range of role and gender models as well as modern working and living models are accepted. Anchored in the strategy is the fact that the BIH will strive to eliminate structural and interactional mechanisms which discriminate against persons due to gender, nationality, religion, age, or social/cultural/ethnic origin. For the implementation of the equal opportunity objectives specified in the strategy, the BIH is focusing on four key aspects since 2017:

Funding and duration

- The funding is usually an average of 50,000 euro per project/year for one year. Projects with higher financial requirements can receive funding over two years.
- The support is usually planned for one to two years, but can vary depending on the project and depends on the actual need. Participating in the SPARK program is only possible as long as the groups benefit from it.

1. Increasing the percentage of women in areas where they are underrepresented
2. Female Career@BIH (measures for furthering the careers of early-career female scientists)
3. Promoting the reconcilability of science and family duties
4. Taking into consideration gender and diversity aspects in research

7.8 Overview of the BIH publications in 2017

The following table gives an overview of publications which were the result of BIH financing or the use of BIH infrastructure. Joint publications from multiple BIH authors are only included once.

*no survey in 2016

	2016	2017
Publications	225	390
Open access publications	- *	157

7.9 Award-winning publications (Paper of the Month)

In 2017, the BIH introduced the BIH Paper of the Month to award excellent publications by the research commons of the BIH. The award, amounting to 500 euro,

is funded by Stiftung Charité and handed over to the management of the BIH Research Group.

January

Zaqout S et al. *CDK5RAP2 Is Required to Maintain the Germ Cell Pool during Embryonic Development* *Stem Cell Reports*. 2017 Feb 14.
doi: 10.1016/j.stemcr.2017.01.002

February

Napierala H et al. *Engineering an endocrine Neo-Pancreas by repopulation of a decellularized rat pancreas with islets of Langerhans* *Scientific Reports*. 2017 May 23.
doi: 10.1038/srep41777

March

Beagrie RA et al. *Complex multi-enhancer contacts captured by Genome Architecture Mapping (GAM)*. *Nature*. 2017 March 8.
doi: 10.1038/nature21411

April

Thomas Kammertöns et al. *Tumour ischaemia by interferon- γ resembles physiological blood vessel regression* *Nature*. 2017 Apr 26.
doi: 10.1038/nature22311

May

Florian Uhlitz et al. *An immediate-late gene expression module decodes ERK signal duration*. *Mol Syst Biol*. 2017 May 3.
doi: 10.15252/msb.20177554.

June

Julia Onken et al. *Phospho-AXL is widely expressed in glioblastoma and associated with significant shorter overall survival* *Oncotarget*. 2017 Jun 13.
doi: 10.18632/oncotarget.18468

July

(no publication selected)

August

Petra Huehnchen et al. *A novel preventive therapy for paclitaxel-induced cognitive deficits: preclinical evidence from C57BL/6 mice* *Transl Psychiatry*. 2017 Aug 1.
doi: 10.1038/tp.2017.149

September

Felix Lorenz et. al. *Unbiased identification of T cell receptors targeting immunodominant peptide-MHC complexes for T cell receptor immunotherapy*
Hum Gene Ther. 2017 Sep 26.
 doi: 10.1089/hum.2017.122

October

(no publication selected)

November

Two awards

Nicola Wilck et. al. *Salt-responsive gut commensal modulates TH17 axis and disease*
Nature. 2017 Nov 30.
 doi: 10.1038/nature24628

Anton G. Henssen et. al. *Therapeutic targeting of PGBD5-induced DNA repair dependency in pediatric solid tumors*
Sci Transl Med. 2017 Nov 1.
 doi: 10.1126/scitranslmed.aam9078

December

Martin Szyska et. al. *A Transgenic Dual-Luciferase Reporter Mouse for Longitudinal and Functional Monitoring of T Cells In Vivo*
Cancer Immunol Res. 2018 Jan 6.
 doi: 10.1158/2326-6066.CIR-17-0256

8. Private Excellence Initiative Johanna Quandt: Funding decisions 2017

With the Private Excellence Initiative Johanna Quandt, Stiftung Charité has promoted the establishment and further development of the BIH to support Berlin developing an international beacon in life sciences and medicine. It therefore contributes significantly to the consolidation of translational health research in Berlin. For this Private Excellence Initiative, Johanna Quandt provided separate funding – in addition to the foundation's assets – in the amount of 40 million euro for a period lasting from 2013 to 2022. It is one of the largest single private funds for the promotion of the German scientific community. The Private Excellence Initiative focuses on the funding of outstanding persons in all phases of scientific development, from their studies to a professorship.

Funding programs

The Private Excellence Initiative Johanna Quandt currently comprises 13 individual program lines. Ten of these programs focus on funding individual persons. Three other programs provide structural and investment funding. The programs are generally advertised in a public call, and the respective funding is awarded in standardized, transparent, and competitive selection procedures.

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Overview of program lines

Funding of individuals

Einstein BIH Visiting Fellows <i>In collaboration with the Einstein Foundation Berlin</i>	Recruitment of leading researchers from overseas for continuous, concurrent activities at the BIH, in particular to set up a research group in Berlin (max. 3 + 2 years plus possibility of follow-up funding for the fellow)
BIH Visiting Professors	Recruitment of renowned guest researchers from Germany or overseas for a temporary assignment at the BIH (max. 9 months)
BIH Johanna Quandt Professors	Setting up of W2 professorships with a true tenure track for the long-term recruitment of experienced researchers (affirmative action for women) from overseas or in the country in a freely chosen field of translational medicine
Recruiting Grants	Supporting of measures by the BIH and its partners for the targeted recruitment of experienced or leading researchers for the life sciences and Charité – Universitätsmedizin Berlin
Humboldt Research Fellowships at the BIH <i>(for postdoctoral researchers and experienced scientists (in collaboration with the Alexander von Humboldt Foundation))</i>	Recruitment of early-career scientists and established researchers from overseas for an assignment at the BIH (max. 2 years)
BIH Clinical Fellows	Funding of experienced senior physicians with exceptional performance in patient care at Charité for the execution of a scientific proposal (max. 3 years)
BIH Charité Clinician Scientists	Funding of clinical researchers as part of the professional development of medical specialists at Charité (max. 3 years)
Entrepreneurship and Innovation Program (Pilot)	Funding of individual clinicians with entrepreneurial ideas including the setting up of a pre-incubator in Berlin.
BIH Delbrück Fellows	Funding of early-career scientists at the BIH for the long-term establishment of an independent research unit (max. 5 years)
Deutschlandstipendien	Funding of students at the BIH and Charité with particularly high performance and commitment

Structural and investment funding

BIH Investment Fund	Funding of construction proposals and the acquisition of large pieces of equipment at the BIH
BIH Paper of the Month	Award for BIH publications
BIH Public Health Initiative	Funding for the establishment and expansion of a »Public Health« teaching and research unit at the BIH

Overview of funding decisions in 2017

Host	Fellow	Research project
Einstein BIH Visiting Fellows <i>in collaboration with the Einstein Foundation Berlin</i>		
Prof. Christian Rosenmund Charité	Prof. Thomas Südhof Stanford University, USA	1. The functional relevance of RIM and RBP in presynaptic calcium channel localization and trans-synaptic synapse function. 2. Electrophysiological and ultrastructural characterization of human induced neurons lacking RIM-BP. (continued funding, until 2019)
Prof. Dietmar Schmitz Charité	Prof. Edvard Ingjald Moser Norwegian University of Science and Technology, Norway	Role of the parasubiculum in interregional theta-synchrony in spatial navigation
Prof. Klaus Rajewsky MDC	Dr. Michael Sieweke Centre d'Immunologie de Marseille-Luminy (CIML), France	Engineered macrophages for cellular therapy (continued funding, until 2019)
Prof. Georg N. Duda Charité	Prof. Viola Vogel ETH Zurich, Switzerland	Mechanobiology of Tissue Growth and Regeneration
Prof. Olaf Strauß Charité	Prof. Florian Sennlaub Institut de la Vision Paris, France	Signaling at the blood/retina barrier in the recruitment of macrophages and accumulation in retinal disease (continued funding, until 2019)
Prof. Georg N. Duda Charité	Prof. David J. Mooney Harvard University (Cambridge), USA	Biomaterial based strategies to stimulate in situ tissue formation for bone and muscle regeneration (follow-up funding)

Host	Fellow	Research project
BIH Visiting Professors		
Prof. Axel Radlach Pries Charité	Prof. Sylvia Thun Hochschule Niederrhein, Krefeld	Establishment of an eHealth and Interoperability Core Unit
Prof. Peter Kloetzel Charité	Prof. Peter van Endert Université Paris Descartes, France	Optimising MHC Class I (Cross-) Presentation to promote tumor rejection by CD8+ T Cells
	Prof. Hans Lehrach Max Planck Institute of Molecular Genetics, Berlin	The Future of Healthcare
Dr. Rolf Zettl BIH	Prof. Robert Frigg Swiss Federal Institute of Technology Zurich, Switzerland	Funding of medical technology solutions and their translation into medicinal products
Prof. Christian Rosenmund Charité	Prof. Lu Chen Stanford University, School of Medicine, USA	How do plastic changes at synapses in a circuit enable learning, encode memory, and drive behavior?
Humboldt Research Fellowships at the BIH <i>in collaboration with the Alexander von Humboldt Foundation</i>		
Prof. Achim Kramer Charité	Dr. Nikhil KL Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore, India	Posttranscriptional control of circadian rhythms: the role of polyadenylation site selection
Prof. Benjamin Judkewitz Charité	Dr. Thomas Chaigne Université Pierre et Marie Curie, Laboratoire Kastler-Brossel, France	Control of scattered coherent light and photoacoustic imaging: toward light focusing in deep tissue and enhanced, sub-acoustic resolution photoacoustic imaging

Professor	Title
BIH Johanna Quandt Professors	
PD. Dr. Petra Ritter Clinic and University Outpatient Clinic for Neurology, Charité – Universitätsmedizin Berlin	BIH Johanna Quandt Professor for Translational Medicine with a focus on Brain Simulation
Prof. Ute Scholl Heinrich Heine University Düsseldorf	BIH Johanna Quandt Professor for Translational Medicine with a focus on Hypertension and Endocrine Tumors
PD Dr. Il-Kang Na Medical Clinic with a focus on Hematology, Oncology and Tumor Immunology, Charité – Universitätsmedizin Berlin & Experimental and Clinical Research Center (ECRC)	BIH Johanna Quandt Professor for Translational Medicine with a focus on Therapy-induced Remodeling in Immuno-Oncology

Fellow	Research project
BIH Clinical Fellows	
Dr. med. Mario Menk Clinic of Anesthesiology with a focus on Surgical Intensive Medicine, Charité	Creation of a database for the recording of clinical, demographic and intensive medical parameters in patients with acute respiratory failure at the ARDS/ ECMO Center of the Charité
Dr. Oliver Miera Clinic of Congenital Heart Defects/Pediatric Cardiology, German Heart Center Berlin, Charité	Antithrombotic therapy for children in the cardiac support system – a multi-center prospective study
Prof. Frank Buttgereit Medical Clinic with a focus on Rheumatology and Clinical Immunology, Charité	Optimization of the diagnosis and therapy in patients with glucocorticoid-induced osteoporosis
PD Dr. med. Kay-Geert Hermann Institute for Radiology, Charité	Charité Case Viewer
PD Dr. med. Patrick Hundsörfer Clinic for Pediatrics with a focus on Hematology/ Oncology/BMT, Charité	New therapeutic approaches in therapy-refractory or relapsed neuroblastoma
PD Dr. med. Dietrich Hasper Clinic for Nephrology/Internal Intensive Medicine, Charité	Renal elastography in patients with acute renal failure
PD Dr. Florian Connolly Clinic for Neurology, Charité	Neurosonology – specialization and expansion of ultrasound diagnostics in neurological diseases
Dr. Ursula Wilkeshoff Clinic for Cardiology, Charité	Gender-specific aspects in echocardiography: Preparation of an individual and gender-specific echocardiographic recording of the findings and implementation into the routine diagnosis

Deutschlandstipendien

Luisa Albert, Marco Nicolas Andreas, Stefan Appelhaus, Wei-Long Dennis Chen, Lisa Ehlers, Lilian Jo Engelhardt, Jan-Frederik Fischer, Jacob Gohlisch, Paola Gozzi, Franziska Greiß, Franziska Hentschel, Meltem Ivren, Lennart Kay, Felix Kleefeld, Philine Köln, Christin Kupper, Jonas Alexander Leppig, Joel Melcop, Till Fabian Mertens, Desiree Mohrbach, Ronja Mothes, Jonas Muallah, Miriam Müller, Sina Erhardt, Katrin Repkow, Kristina Marie Rieger, Stanislav Rosnev, Tarik Alp Sargut, Lara Katharina Assiya Staats, Kim Natalie Stolte, Stefka Stoyanova, Christopher Tacke, Marie-Christin Weber, Gabriele Weiß, Daniela Zurkan, Nora Frühauf, Jessica Graef, Henriette von der Waydbrink, Marina Schnauß, Regina Walter, Jelena Weiß, Elisa Rath, Shailey Twamley, Erdi Hoxhallari, Svenja Hoffmann

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