2016

Annual Report

BERLIN INSTITUTE OF HEALTH

Charité & Max Delbrück Center

24
scientific events with more than 6,000 participants

> 4,000
researchers and clinicians at MDC and Charité

59.608
million euro of institutional funding

311
persons financed via BIH

4
scientific sites in Berlin

2
central BIH buildings in planning

225
publications

54
open access publications

315
participants included in clinical studies

5
registered patents

85
researchers at https://science-match.tagess-piegel.de/future-medicine-2017

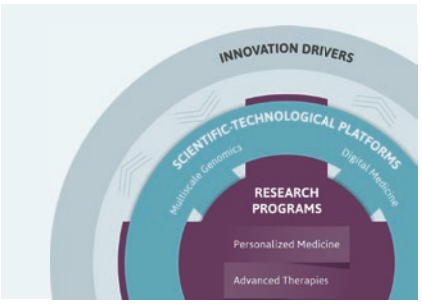
260
persons funded by the Private Excellence Initiative of Stiftung Charité

Berlin Institute of Health

2016 Annual Report

Contents

Strategy

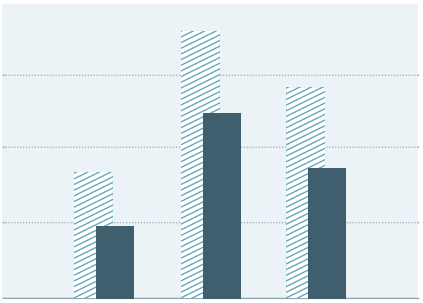


Research

People

Innovation

Facts and Figures



Key events in 2016

1

JANUARY

BIH has been operating as an institutionally funded corporation under public law since the beginning of the year.

Tenure track for women: BIH and Stiftung Charité publish a call for W2 professorships, the BIH Johanna Quandt Professorships.

First BIH symposium »Exploring Systems Medicine« with international keynote speakers and more than 200 guests

2

FEBRUARY

The Executive Board launches the strategy process for the »BIH Strategy 2026«.

Inauguration event: Erwin Böttinger is Chief Executive Officer

New members on the Scientific Advisory Board: Cell physiologist and Nobel laureate Thomas C. Südhof (Stanford University, USA) and endocrinologist Alan R. Shuldiner (Regeneron Genetics Center, University of Maryland, USA)

3

MARCH

Rolf Zettl takes office as full-time member of the Executive Board and Chief Financial Officer.

Three new Twinning Research Grant projects (TRGs) are launched.

Launch and »open doors« of the Clinical Research Unit at Charité Campus Benjamin Franklin

4

APRIL

Martin Lohse takes offices as Scientific Directorate of MDC and becomes the newest member of the BIH Executive Board.

Wir machen mit! Girls'Day Mädchen-Zukunftstag

Girls' Day: BIH offers girls a program in translational medicine in the Department of Pediatrics, Division of Oncology and Hematology at Charité Campus Virchow-Klinikum.

5

MAY

The senate of the state of Berlin appoints the new BIH Supervisory Board, replacing the existing Founding Supervisory Board.

Initial »BIH Annual Special Lecture« with John P.A. Ioannidis (Stanford University, USA) on reproducibility and quality in biomedical research

Captain T cell (MDC research team with SPARK program funding and support from Stiftung Charité) wins the *OneStart accelerator competition* (largest competition worldwide for start-ups in the field of life sciences and health).

6

JUNE

The Supervisory Board approves the »BIH Strategy 2026« at its inaugural meeting.

Completion of Biobank building at Campus Berlin Buch

JULY

7

Five-year anniversary of the »BIH Charité Clinician Scientist Program« with international symposium

Completion of Biobank building on Charité Campus Virchow-Klinikum

AUGUST

8

A joint open access representative for BIH and Charité commences with her duties.

SEPTEMBER

9

BIH confers the »BIH Award for Early-Career Women Scientists in Computational Biology«.

Einstein Foundation Berlin approves the proposal for foundation of the Einstein Center Digital Future. Erwin Böttinger takes on the role of spokesperson for the research area »Digital Health«.

OCTOBER

10

The Charité Faculty Council approves the fast-track procedure for an accelerated recruiting process at BIH.

NOVEMBER

11

The Supervisory Board approves the »BIH Strategy Implementation Plan 2017–2020«.

Andreas Diefenbach assumes the Professorship for Microbiology at Charité and is associated with BIH via the »BIH Professorship for Precision Medicine with a Focus on Microbiome Research at Charité«.

Berlin Science Week: BIH holds a Science Match on »Future Medicine«. More than 80 scientists present their cutting-edge research.

The German Bundestag grants BIH special funding (two million euro) for the expansion of digital medicine in the pilot project »Digital Health Accelerator«.

Launch and »open doors« of the Clinical Research Unit at Campus Charité Mitte

DECEMBER

12

New members on the Scientific Advisory Board: Nobel laureate Elizabeth Blackburn, (Salk Institute for Biological Studies, La Jolla, USA) and Stefanie Dimmeler (Institute of Cardiovascular Regeneration/ Goethe University, Frankfurt/Main)

It is not the wind that determines the course, but the sails!

Dear Reader,

Being forward-thinking – that is and has been a guiding principle of Berlin Institute of Health (BIH) from the very beginning. BIH aims to play a pioneering role in cutting-edge biomedical research and to help shape global trends in medicine and research. But questions such as »What exactly is BIH?«, »Who is part of BIH?« and »What does BIH aim to achieve?« are questions that we, the members of the Executive Board and colleagues in the teams, are often asked.

Prof. Erwin Böttinger
Chief Executive Officer

Dr. Rolf Zettl
Chief Financial Officer

BIH builds on the expertise of more than 4,000 researchers and clinicians at MDC and Charité.

Our answers: In Germany, BIH is a unique institute, both scientifically and with regard to the science and research system. Charité – Universitätsmedizin Berlin and Max Delbrück Center for Molecular Medicine in the Helmholtz Association (MDC) are the founding institutions which shape BIH. We capitalize on the expertise and collaboration between MDC and Charité and use cutting-edge findings from the field of biomedical research to improve human health by working together with international partners. The members of BIH are professors employed full time by the Charité as well as research group leaders of the MDC. Our mission is to maintain or restore health and quality of life for people with progressive diseases. We can do this by providing new solutions for better predictions and advanced therapies – thereby turning standardized medical therapy into personalized, value-based treatment.

Since the beginning of 2016, BIH has been an independent institutionally funded corporation under public law. Charité and MDC are independent member entities within BIH. We have pooled our collaborative research in a translational research commons. This means that at BIH, there are collaborative and interdisciplinary research projects as well as independent activities for increasing the value of research, for fostering and training early-career scientists, and for technology transfer. This also means that independent projects and research activities will continue to advance, interacting with BIH at meaningful interfaces.

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

Prof. Axel Radlach Pries
Charité – Universitätsmedizin Berlin, Dean

Prof. Martin Lohse
Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Scientific Directorate

Let us look back on the year 2016. It was a demanding year, but the efforts paid off. With the »BIH Strategy 2026«, we hoisted our sails and set off for the future. Since April 2016, there have been five members on the Executive Board – Martin Lohse and Rolf Zettl joined us in spring – and already in the middle of the year, we agreed upon which future topics would be the focuses in the years ahead. Together, we embarked upon a new path at the end of 2016 to fulfill our public mission: Maintaining health and quality of life and creating real value.

In this report, we present to you selected BIH activities and achievements in 2016. They include research highlights, people who are taking translational medicine to new heights at BIH, but also individual activities at Charité and MDC which characterize the excellence of the over 4,000 scientists at these two institutions and define BIH.

We would like to take this opportunity to thank all our partners from the scientific and business community, the Supervisory Board, the Scientific Advisory Board, the Scientific Committee, and the political representatives from the federal government and the state of Berlin for the strong and trustful collaboration. We hope you enjoy reading our annual report.

Executive Board of the Berlin Institute of Health

Setting the course for the next ten years

2016 was a trailblazing year for BIH. It was a year of significant milestones: The end of the founding phase and the commencement of institutional funding as a corporation under public law, visible research achievements, and the development of the »BIH Strategy 2026«.

»Fit for the future« – All of the BIH Executive Board's activities in the past year were characterized by this motto. Above all, the emphasis was on the development of the »BIH Strategy 2026«, and hence on the scientific focus. Our decisions were characterized by three key questions when deciding on the essential points: What does BIH stand for? Which research topics should we concentrate on? And: How can we create translational innovations? In order to answer these questions, we held discussions with internal and external stakeholders from the research, business, political, and administrative communities, and consulted around 40 persons in one-on-one interviews, workshops, and sounding boards in spring. Our ideas were also discussed in-depth with the Scientific Advisory Board and the Scientific Committee. Subsequently, the Supervisory Board approved the new scientific focus.

From the beginning, one thing was clear: We want to determine today what we will be doing, what will guide us in the coming ten years, and where we will be investing. Increasingly enlightened citizens, controlled access to and controlled use of patient data, the digitalization of healthcare provision, and integrated research teams with partners from the private sector were just some of the key factors that were taken into account when developing our strategy.

It was also important to us to define the »BIH Strategy 2026« in a manner that was as consistent as possible with the guidelines and scientific strategies of the member entities of BIH: Charité and MDC. The background: By law, BIH is an independent legal corporation under public law, and MDC and Charité are autonomous member entities within it. Together with MDC and Charité, this creates a translational research commons at BIH, which also interacts with other departments of both institutions.

Interdisciplinary research approaches and new scientific alliances are crucial for successful translation.

The profile of BIH is characterized by its precision medicine approach and innovative therapies for progressive diseases. This also includes entrepreneurial thinking and a new innovation culture which are crucial to BIH's mission.

→ ***Diagram showing the structure of the Charité and MDC's translational research commons of BIH*** *Page 13*

Progress in research

Things have progressed in the field of research as well: New projects for cardiac metabolism diseases, heart muscle failure, and glioblastoma research were launched, while others presented significant scientific findings. These include e.g. publications in high impact journals such as *Nature*, *Science*, and the *New England Journal of Medicine*.

Numerous patients were recruited and admitted for initial clinical studies in the Clinical Research Unit.

→ ***More research highlights***
Pages 18 and 19

New buildings

The challenges of where research groups would be housed, where patients could be examined, and where scientific and technical units were to be located continued to occupy us in 2016. At Campus Berlin Buch, the Biobank building with automated deep-freeze storage areas for the long-term storage of liquid biological samples was completed in collaboration with MDC, and the competitive procedure for the construction of the new Käthe-Beutler Building (KBH; formerly Robert-Rössle Institute) was completed along with other construction plans.

↗ ***History of BIH***
www.bihealth.org/en/institute/history/

The BIH-Charité Biobank at Charité Campus Virchow-Klinikum (CVK) is one of the first laboratory buildings in Germany to be constructed of wood.

Headway in all construction projects: CRU premises, Biobank building, and the new BIH buildings in Buch and Mitte

At the main offices of BIH in Berlin-Mitte, the construction of a new, modern building for translational medicine is in the works. The former operations and intensive care wing at Robert-Koch-Platz on Campus Charité Mitte will be used for this purpose. The advantage: The new BIH building will be located directly adjacent to the clinical care units at Charité, right next to the main building. We made great progress here in 2016. All the necessary resolutions were passed, all audits from public authorities received favorable assessments, and the preliminary planning was commissioned.

The objective here is to unite BIH's patient-centric translational research and Charité's clinical care system under one roof – for closer interaction between patients and researchers, housing the BIH research groups, bringing together units which are scattered across the geographical limits of the city, and for identity-building. Envisioned here is a common translation, innovation, and patient center, including training rooms and offices. In total, the renovation will result in around 13,000 square meters of floor space; an area of around 9,230 square meters has been reserved for BIH.

A Biobank constructed of biological materials

At Charité Campus Virchow-Klinikum (CVK), a special research building was completed in 2016. The BIH-Charité Biobank is one of the first laboratory buildings in Germany to be built of wood. Advantages of this construction method include weight, construction time, costs, and sustainability criteria.

↗ *MDC report*
www.mdc-berlin.de/RR2016

↗ *2016 at Charité*
https://biobank.charite.de/en/

The Biobank will house more than two million samples and offer a wide range of services. After all, in the era of personalized medicine, excellent biobank structures play a decisive role: In order to research the causes and mechanisms of diseases, researchers require high-quality biological materials, such as blood, urine, and tissue samples, as well as comprehensive clinical information. The biobank at the CVK is a »clinical biobank«, which will primarily gather, store, and process biological samples from patients in a manner that complies with data privacy laws, and also associate it with clinical information. It is an important link between clinical care and science.

Operating as a corporation under public law

With effect from January 1, 2016, BIH now operates as a corporation under public law (KdöR, Körperschaft des öffentlichen Rechts). Numerous administrative processes were defined and established for this purpose, including the financial management for institutional funding from the federal and state governments, the articles of incorporation and bylaws of the Executive Board, as well as the systems for operational activities such as double-entry accounting and *standard operating procedures (SOPs)*.

Outlook

Our objectives for 2017 are ambitious: Successful strategic implementation in all activity areas (programs, research platforms, innovation drivers), additional recruitments, progress in the field of medical informatics, and in particular the linking of various data, participation in networks and partnerships, as well as the consistent implementation of the Berlin open access strategy. We look forward to taking the next few steps towards the future of BIH together with all researchers, clinicians, and management teams who are already actively contributing to the institute.

↓ ***BIH law***
www.bihealth.org/uploads/pics/BIG_Gesetz.pdf

BIH Strategy 2026

The »BIH Strategy 2026«, which was established in 2016, paves the way for BIH to become a successful and and innovative scientific institution. It defines the scientific focus and provides a decision-making and orientation framework for outstanding research and innovation.

The new strategy specifies the BIH's programs, platforms and defines overarching innovation drivers. In this strategy, early-career scientists, the quality of biomedical research, and the transfer of research findings into clinical practice play a decisive role.

Our focus

Progressive diseases, such as cardiovascular conditions, dementia, arthritis, Parkinson's, kidney failure, or cancer have a huge negative impact on the lives of those affected, and additional complications often make their daily lives even more difficult. However, treatment options are limited – we still do not truly understand how a disease can develop differently in different people, and how individual patients react to standard therapies. Hence, numerous medical problems which patients experience remain unresolved.

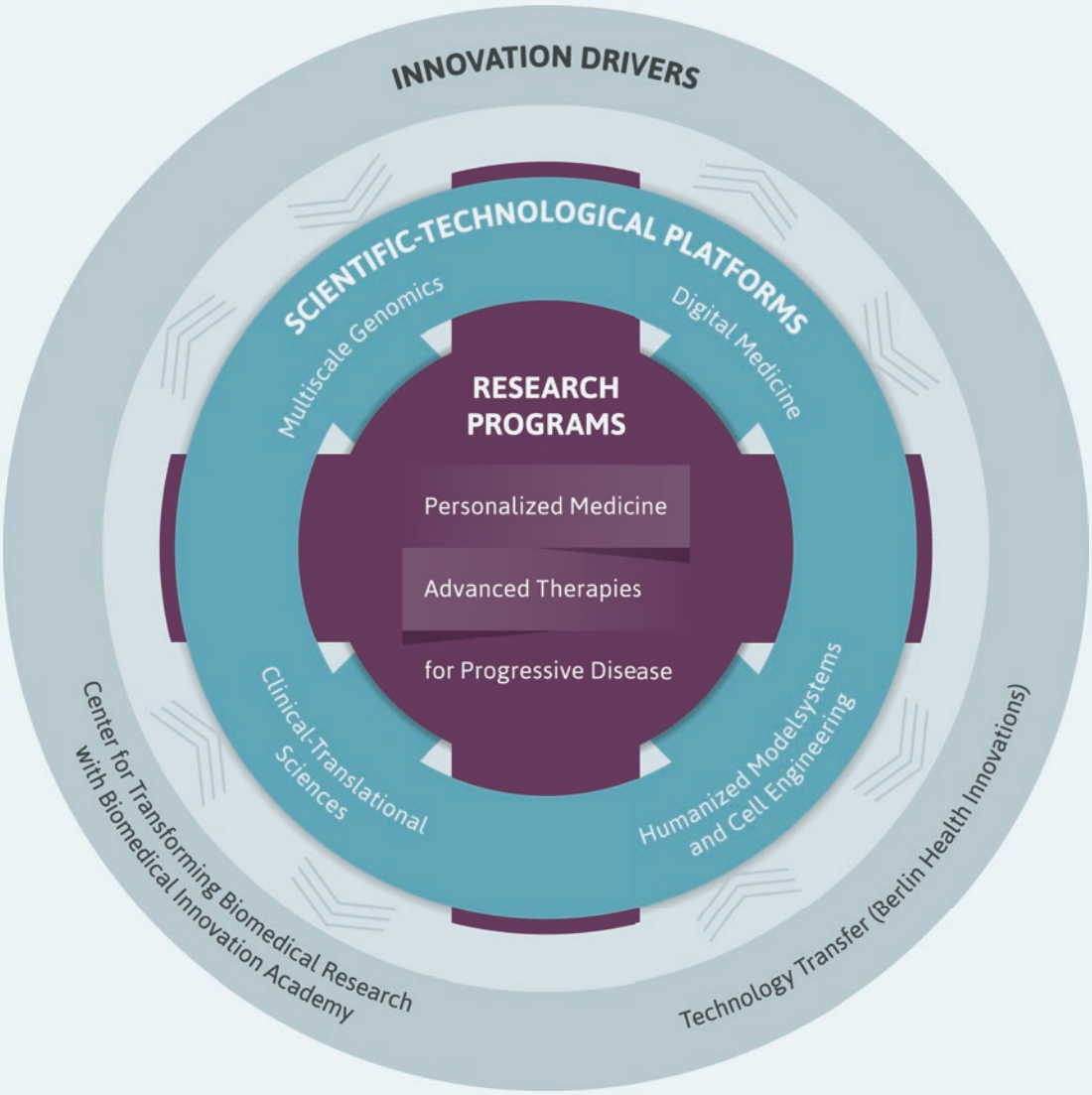
Our mission

Our objective is to maintain and improve quality of life for patients with progressive diseases. To this end, we aim to develop predictive instruments and innovative therapies, particularly where they are urgently needed or do not even exist yet (unmet medical needs). With cutting-edge translational research and innovations, we pave the way for for a personalized, value-based healthcare model.

Key research areas

With our strategy, we have defined two key areas of research programs. They build on the expertise and collaboration between MDC and Charité:

1. We intend to improve the diagnostic options for outcome prediction in progressive diseases and
2. develop advanced therapies for the personalized treatment of progressive diseases.



Translational medicine

Translational medicine links research with patient care. This is precisely what BIH stands for with its two research programs. Every research program is supported by four scientific and technical research platforms. In order to overcome the translational obstacles and to promote an entrepreneurial research spirit, two additional units and innovation drivers have been assigned a special significance: Technology transfer and a center for the transformation of biomedical research and training.

The translational research commons of Charité and MDC shows how deeply our activity areas are connected.

↓ ***BIH Strategy 2026***
www.bihealth.org/uploads/pics/BIH-Strategie-2026_Booklet.pdf

»An entirely new approach«

Chief Executive Officer Erwin Böttinger speaks about BIH's strategy in the pioneering field of personalized medicine

The topic of personalized medicine is one of the two new research programs at BIH. Why will personalized medicine be important in the future?

Conventional medicine, as it has been practiced so far and generally continues to be practiced, is ultimately based on average findings. Imagine 20,000 patiens in a clinical study, 10,000 with one drug, 10,000 with a placebo, and at the end statistical methods are used to identify significant differences. But this is inadequate in light of what we now know about diseases. We now have entirely different information, which enable a completely new approach.

What is this information you mentioned and what approaches do they make possible?

Individual factors exist for the risk of contracting a certain disease, as well as for the probability of responding to a particular treatment. Such factors include e.g. the environment or a person's own genetic makeup. Correspondingly, drugs that are prescribed in this country only have the desired effect in a certain number of patients. With increasing frequency, the predispositions which influence whether a drug will help can be determined even before the active ingredient is consumed, in part thanks to the massive improvements in genomic diagnostic technology. This is what personalized medicine is, and it is revolutionizing health research and the provision of healthcare.

Personalized medicine

Individually and optimally treating each person based on their genetic and molecular profile – that is the exciting idea of personalized medicine. Numerous advances in medicine have made this possible: Samples from patients can now be characterized individually at the molecular, genetic, and cellular level. This enables in-depth understanding of the cause of diseases and lays the foundation for targeted therapy. Patients are categorized into subgroups according to these characteristics. At the same time, ineffective treatments and undesirable side effects can mostly be avoided. Large-scale research programs are pushing forward with the development of this concept worldwide.

» The prerequisite for cutting-edge research: The digital, real-time availability of harmonized health data in real time «

What role does BIH play in this?

With our technologies, scientific methods, and our expertise, we can contribute to enabling more precise classifications. In a nutshell: We relate complex diseases to genetic and biochemical information and other psychosocial factors of the persons we are examining. Such individualization ultimately allows for a better prediction of the course that diseases will take or a more effective treatment.

What exactly does BIH research? Could you give an example of what you are currently working on?

The scientists at MDC and Charité are involved in numerous research projects with personalized approaches that aim to enable better predictions for individual disease progressions. In one BIH project, for example, multiple teams led by Professor Erich Wanker (MDC) and Professor Frank Heppner (Charité) are researching the functional relationships in neurons which are impaired in Alzheimer's, and how they can intervene in the disease progression at the molecular level in order to develop new therapies. One other example is Professor Holger Gerhardt from MDC, who also holds a BIH Professorship. With his team, he is investigating the role and mechanisms of blood vessels in diseases and their significance for symptoms. Blood vessels play a crucial role in progressive diseases, in particular cardiovascular diseases and cancer.

So BIH will be focusing on progressive diseases in future? Why?

Yes, but current research projects will of course continue. With our research, we intend to contribute to increasing the quality of life for those who are suffering from a disease. In most cases, progressive diseases greatly reduce quality of life for those affected. We intend to redouble our efforts in this area in future. With the excellent expertise of Charité and MDC and the scientific and technical infrastructure, we are optimally equipped to do so.

Progressive diseases

worsen over the course of the disease, whether in a temporary or chronic sense. Examples include:

- Heart attacks, heart failure, strokes in the case of vascular diseases
- Dementia in the case of neurodegenerative illnesses such as Alzheimer's or in the case of systemic vascular diseases such as high blood pressure
- Arthrosis or arthritis in the case of degenerative joint diseases or autoimmune diseases
- Paralysis in the case of neurodegenerative, autoimmune, or muscular diseases such as Parkinson's, multiple sclerosis, and spinal cord injuries
- Respiratory failure in the case of lung diseases, asthma, or pulmonary fibrosis
- Kidney failure in the case of diabetes, high blood pressure, or autoimmune diseases
- Metastasis and tissue infiltration in the case of tumor-causing diseases

Research

Our research focuses on understanding the causes and complex mechanisms of severe disease progressions and to define the individual risk for patients. This allows predictions to be improved for progressive diseases and innovative therapies to be developed and utilized for personalized treatments.

Our research is collaborative and interdisciplinary. In more than 100 research projects, coordination teams and committees, scientists from MDC and Charité are already collaborating successfully. They shape the translational successes of the institutions. The following pages present selected examples from the year 2016.

Research in brief

↗ ***More research highlights from MDC and Charité***
https://insights.mdc-berlin.de/en/tag/research-highlight-en/
https://www.charite.de/en/research/

An end to hunger

The sensation of being full, as it emerges during an extended meal, comes from a complicated signaling cascade. One major component in this cascade is the protein proopiomelanocortin (POMC), which is secreted in the hypothalamus. In the case of a hereditary POMC deficiency, this signaling pathway is not even triggered in the first place. The result is constant hunger, resulting in massive obesity. A team of researchers led by the physician Peter Kühnen carried out a study at Charité and BIH with two female patients suffering from a POMC deficiency. They were treated with a new medication which activates the satiety center in the brain. Within twelve weeks, one patient who initially weighed 152.8 kilograms lost 20.5 kilograms. The other patient lost even more weight – 51 kilograms – for a final weight of 104 kilograms. Due to the success of the study, the researchers now intend to investigate whether the drug might also work with adipose persons who do not have the hereditary disease.

Proopiomelanocortin Deficiency Treated with a Melanocortin-4 Receptor Agonist
New England Journal of Medicine. 2016 July
Kühnen, P., Clément, K., Wiegand, S., Blankenstein, O., Gottesdiener, K., Martini, L.L., Mai, K., Blume-Peytavi, U., Grüters, A., Krude, H.

Arteries under pressure

The process of angiogenesis is a lifelong one, and also plays a role e.g. in the growth of tumors, as the growing sections of new tissue require blood vessels to provide them with nutrients. But numerous processes in a healthy body also require the formation of new blood vessels, such as when wounds heal. Hence, it is of enormous importance for medical science to understand these mechanisms, which we currently know very little about. In 2016, Holger Gerhardt, who leads a research group at MDC and holds a BIH Professorship for experimental cardiovascular research at Charité, discovered together with his team that blood pressure is the driving force behind angiogenesis. The researchers were able to use the zebrafish as a model organism to show how blood pressure forces invaginations in the cell membranes of vascular cells and how a continuous vascular tube grows out from them as a result.

Blood flow drives lumen formation by inverse membrane blebbing during angiogenesis in vivo. Nature Cell Biology
New England Journal of Medicine. 2016 April
Gebala, V., Collins, R., Geudens, I., Phng, L., Gerhardt, H.

↗ ***More scientific details:***
https://insights.mdc-berlin.de/en/2016/01/role-model-stem-cells-how-immune-cells-can-self-renew/

A new perspective of the immune system

Epitopes are fragments of bacterial or viral proteins. They are presented on the surface structures of cells and trigger the defensive reactions of the immune system to substances that are foreign to the body. Using a new method, researchers led by Michele Mishto in the research group of the BIH research project »T cell gene therapy for cancer« by Peter-Michael Kloetzel at the Institute for Biochemistry at Charité have now mapped the surfaces of cells and discovered that almost a third of all existing epitopes are composed of two different fragments. These »spliced epitopes« were considered a rarity for a long time. Among other things, their frequent occurrence can now also explain the great flexibility of the immune system, and the findings could contribute to the development of immunizations and cancer immunotherapy.

A large fraction of HLA class I ligands are proteasome-generated spliced peptides
Science. 2016 October
Liepe, J., Marino, F., Sidney, J., Jeko, A., Bunting, D., Sette, A. Kloetzel, P.-M., Stumpf, M., Heck, A. Mishto, M.

Inflammation of the placenta disrupts the flow of nutrients to the fetus

Pre-eclampsia is one of the most common pregnancy complications. However, its causes are unknown. The team led by Florian Herse, who works as a researcher at MDC, Charité, and BIH, demonstrated that those affected by the condition had less of the receptor protein CD74 on the surface of macrophages in placental tissue, and that certain inflammatory factors were elevated. In healthy tissue, the macrophages interact directly with other cells in the placenta, the trophoblasts, stimulating them. If CD74 presentation is reduced, the structure of the placenta is disrupted, and the fetus does not receive sufficient nutrients. The relationship between the CD74 receptor and pre-eclampsia presents a new starting point for therapy directed at the causes of the condition, and not just its symptoms.

CD74-Downregulation of Placental Macrophage-Trophoblastic Interactions in Preeclampsia
Circulation Research. 2016 May

Przybyl, L., Haase, N., Golic, M., Rugor, J., Solano, M.E., Arck, P.C., Gauster, M., Huppertz, B., Emontzpohl, C., Stoppe, C., Bernhagen, J., Leng, L., Bucala, R., Schulz, H., Heuser, A., WeedonFekjaer, S., Johnsen, G.M., Peetz, D., Luft, F.C., Staff, A.C., Mueller, D.N., Dechend, R., Herse, F.

How macrophages regenerate

For the regeneration of cells, the body is usually dependent on a few stem cells in the tissue, as the vast majority of the differentiated cells can no longer divide and are unable to produce new cells. It was only recently discovered that certain immune cells, the macrophages, are able to divide almost indefinitely, allowing them to regenerate themselves. A Franco-German team led by the Einstein BIH Visiting Fellow Michael Sieweke investigated the genetic mechanism behind this phenomenon and discovered that the immune cells activate a gene network similar to that of embryonic stem cells. However, the transcription factors and gene-regulating elements which control the network are entirely different and highly specific for the respective cell type. In future, the findings may reveal innovative approaches for regenerative medicine, thereby leading to therapeutic benefits.

Lineage-specific enhancers activate self-renewal genes in macrophages and embryonic stem cells
Science 351(6274). 2016 February
Soucie, E., Weng, Z., Geirsdóttir, L., Molawi, K., Maurizio, J., Fenouil, R., Mossadegh-Keller, N., Gimenez, G., VanHille, L., Beniazza, M., Favret, J., Berruyer, C., Perrin, P., Hacohen, N., Andrau, J.-C., Ferrier, P., Dubreuil, P., Sidow, A., Sieweke, M.

Equipping the body's own cells for the battle against cancer

Immunotherapy has developed into a promising treatment alternative for cancer patients. In the BIH research project »Mutation-specific T cell receptor gene therapy for cancer«, which was launched in 2014 and is led by Thomas Blankenstein from MDC/Charité and Peter-M. Kloetzel from Charité, the researchers are driving forward this approach in seven sub-projects, researching the basic mechanisms, and developing solutions in cooperation with other promising methods. The focus here is on therapy with mutation-specific T cell receptors.

The human immune system actually provides the perfect defense mechanisms against infectious diseases. However, in the case of cancer, the millions of immune cells patrolling the body often fail to do their job because although they recognize the tumor, they do not destroy it. After all, it is made of the body's own cells. And the immune system generally does not attack its own body. Hence, scientists around the world are attempting to develop strategies which allow the immune cells to recognize cancer cells as foreign invaders and combat them. With cancer immunotherapy, which aims to support the patient's own defense mechanisms, the first few promising approaches have been created. This was also the case in this BIH research project.

The researchers' objective is to genetically modify T cells – one of the immune system's main weapons – in the laboratory to enable them to specifically target tumor cells while sparing healthy tissue. When doing so, it is not the entire immune cell which is modified, but only the T cell specific surface receptor which is responsible for recognizing structures that are foreign to one's own body. But which specific structures are they? The consortium is also working on this question.

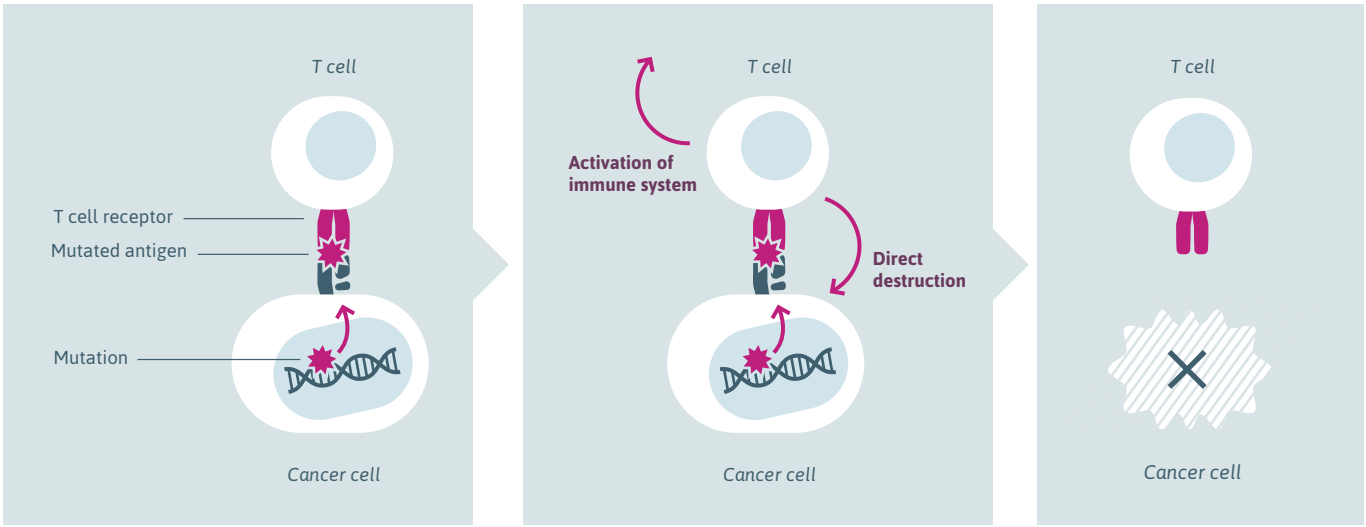
The research project is co-funded by the German Research Foundation (SFB TR36). Einstein Foundation Berlin awarded Hans Schreiber a Visiting Fellowship, enabling him to conduct his research in Berlin.

The idea is to use T cells to specifically target proteins on the surface of cancer cells which were created via mutations and are therefore highly specific for a tumor – called antigens. But not every mutation occurs at the same time during carcinogenesis, and hence does not occur in all cancer cells. However, an antigen which is suitable as a therapy target must occur in all tumor cells, even in metastases. Another challenge: Some tumor cells do not present enough of the mutated antigens and remain undetected by the T cells.

Milestones

The team of researchers celebrated milestones back in 2010 and 2015 when they developed transgenic mice which produced human T cell receptors that were effective at targeting certain tumor cells. In petri dishes, these receptors were then transferred to T cells from the blood.

In two projects in 2016, the Berlin-based team of researchers led by Matthias Leisegang, Thomas Kammertöns, Wolfgang Uckert and Thomas Blankenstein (MDC/Charité), collaborating with the Einstein Visiting Professor Hans Schreiber from the University of Chicago, succeeded in further realizing their idea in the mouse model and in identifying specific



T cells recognize the mutated antigen on the cancer cell and are able to destroy it and activate other immune cells.

mutations as a target for attack: They analyzed the genes of a tumor from the mouse and identified a mutation which occurred in all regions of the tumor and which also found its way to the surface as an antigen. T cells from the mouse were equipped with a mutation-specific T cell receptor and administered to the animal. By doing so, the tumor was almost completely repressed.

In the second project, the researchers realized that although certain mutations turned out to be a suitable target for therapy in cell culture experiments, this was not the case in vivo. Hence, the BIH consortium established a humanized mouse model in April 2016 in which suitable mutated human tumor antigens could be investigated for therapeutic purposes.

How tumor cells escape therapy

In October 2016, the research group led by Thomas Blankenstein and Peter Kloetzel made another breakthrough. Their intention was to use an animal model to find out why tumors often re-occurred, despite their initially good gene therapy results with tumor-specific T cell receptors. They determined that two antigens which appeared highly similar at first glance were very different in terms of suitability as targets for T cell receptor gene therapy. They decoded a mechanism by which tumor cells, depending on the target antigen selected, were able or unable to escape the T cell attack. These experiments will allow for a better prediction of suitable target antigens in future.

Ultimately, the intention is for mutation-specific T cell receptor gene therapy to be used in clinical applications. Preparations are currently underway for an initial study financed by the Federal Ministry of Education and Research (BMBF) with 15 patients, in which a non-mutated tumor antigen which is expressed in tumors, but not in normal cells, will serve as the target of the T cells with modified T cell receptors. This study will pave the way for future T cell receptor gene therapy studies against mutated antigens. Blankenstein is optimistic: »I have very little doubt that in ten to 15 years, most patients will be treated using personalized, mutation-specific T cell therapy.« But before this happens, a wide range of regulatory conditions will need to be fulfilled and improvements made to the systems for tumor analysis, antigen and receptor selection, some of which are highly cost-intensive. Once this is done, there will be little standing in the way of researchers to equipp the body's own cells for the battle against cancer.

→ ***Overview of persons involved and sub-projects***
Page 63

How DNA folding regulates genes

Changes in the folding of DNA can trigger diseases. With this knowledge, tests for hereditary deformities can be developed.

Julian has six toes on his right foot, and Charlotte's middle and index fingers are fused together. Around one out of 10,000 newborns is affected by a skeletal deformity. »If we understand what triggers the deformities, we can also develop diagnostic tests and advance personalized medicine«, explains Stefan Mundlos. The director of Charité's Institute of Medical Genetics and Human Genetics and Ana Pombo from MDC are sub-project leaders in the BIH research project »Genomic analysis of inherited children's diseases«. In 2016, under the leadership of Stefan Mundlos and with Ana Pombo as co-author, a study was published in the scientific journal *Nature* reporting that mutations may lead to skeletal deformities by modifying certain DNA domains of the genome, called TADs.

Folding determines deformities

»Our genome is a molecule measuring almost two meters in length that is packed into a minuscule cell nucleus. Nothing about it is a coincidence«, says Stefan Mundlos. »The folding takes place according to a complicated, controlled mechanism, and the TADs are an important component in this process.« Mundlos was able to demonstrate that TADs determine whether genes are activated or deactivated, and whether or not deformities occur. In this case, the modifications do not take place in the sequence of the genome, but are of a structural nature. One thing is clear for the researcher: »The TADs are of enormous importance for the proper regulation and hence functioning of the genes.«

Shared strengths

The TADs were discovered via progress in the field of mapping chromatin contacts, in particular via the development of new molecular methods based on

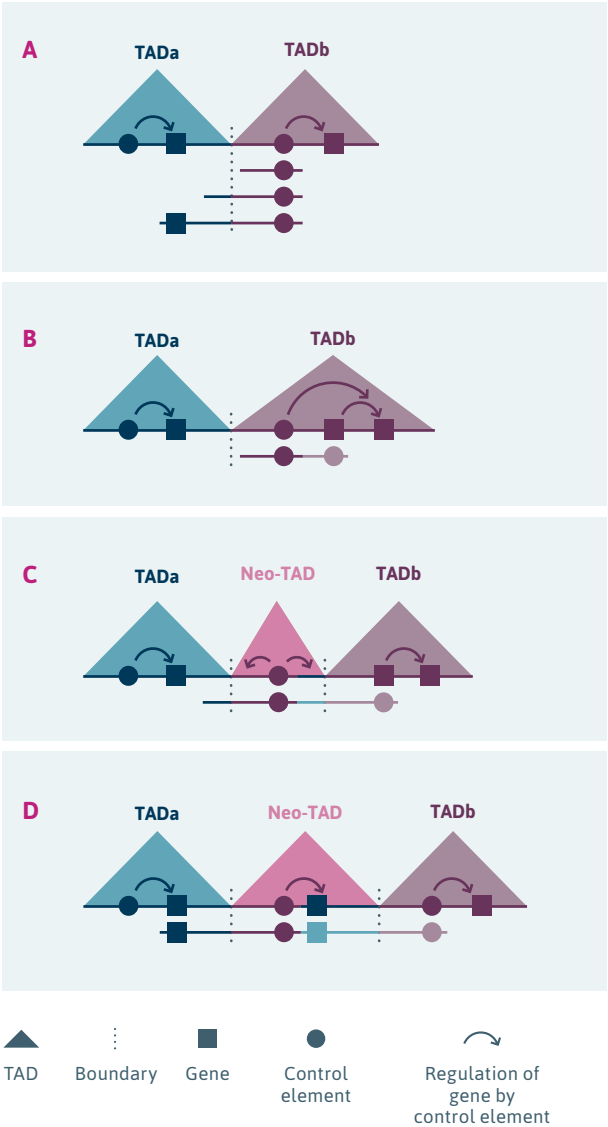
next-generation sequencing. »Ana Pombo is one of the leading experts in the field of 3D genome regulation, and contributes a great deal of knowledge regarding chromosome folding to this aspect of our BIH project«, says Stefan Mundlos. He himself has been researching the molecular cause of skeletal deformities for many years. The combination of basic research and clinical expertise enables particularly effective collaboration, permitting a better understanding of TADs and their role in diseases.

Markers and methods for rapid diagnosis

Since the publication in *Nature*, it has become increasingly clear that such folding not only results in double toes and fused fingers, but may also lead to cancer. »We are only beginning to understand what effects the TADs have«, says Stefan Mundlos. Numerous research groups are now interested in the findings obtained by these two scientists. Their common objective is to discover new markers and methods for predicting and diagnosing hereditary diseases. Four to six percent of children are born with genetic defects. Parents ask themselves how these deformations occur – and if the child's next sibling will also be affected. It is only with rapid diagnosis that conclusions can be made regarding the progression of the illness and the administration of possible therapies can begin, explains the scientist.

Translational research

Already back in 2016, he made a small diagnostic breakthrough. Working together with pediatricians from the Children's Hospital Charité, his team launched an interdisciplinary pilot study with 200 pediatric patients. All of them had a hereditary deformation with an unknown diagnosis. The research group led by Stefan Mundlos developed a test which allows all of the 3,000 currently known disease genes to be tested and the results to be evaluated using an analysis tailored to the patients. »Ultimately, we were able to provide a quarter of the patients with a diagnosis«, says a visibly delighted Stefan Mundlos. In future, says the 58-year-old, he hopes to have a test that allows all genetic diseases to be tested right away in one single procedure.



TADs determine whether genes are activated or deactivated.

A *TADs in a healthy genome*

B *Duplication takes place within a TAD; the overarching structure of the genome is not affected. Incorrect regulation of the affected gene takes place within the TAD.*

C *Duplication also affects the boundary between two TADs, resulting in a new TAD (neo-TAD). It only contains control elements, but no gene. Hence, there is no effect on the organism.*

D *Duplication affects the boundary between two TADs and a gene of the neighboring TAD. The neo-TAD contains the control mechanisms of the orange TAD and a gene from the blue TAD, which is therefore incorrectly regulated.*

#research and #treatment – entirely #digital

Cutting-edge digital applications and technologies are revolutionizing medicine and research. They open up new treatment, therapy, and healthcare options for patients, doctors, researchers, and the healthcare system. With numerous projects and studies, Charité, MDC, and BIH are also focusing on the digital future.

The objective of pioneering digital technology is clear: It aims to allow diseases to be detected sooner, be treated better with personalized therapies, overcome supply bottlenecks, and save on costs. According to industry predictions, the global digital healthcare market will more than double by the year 2020. Experts are confident that the future of medicine belongs to wireless research information systems, electronic medical records, and standardized data warehouses.

Charité, MDC, and BIH are at the heart of this digital revolution as well. In various projects and studies, clinical employees, researchers, and IT experts are driving forward the digital future of medicine.

Significant progress was made in 2016. In September 2016, Einstein Foundation Berlin approved the proposal for the foundation of the Einstein Center Digital Future in Berlin. This center focuses on various societally relevant topics, including digital health. Erwin Böttinger has taken on the role of the spokesperson for this topic. Three junior professorship positions had already been advertised for this area in 2016. These positions cover the topics of genomic data analysis, new methods for the use of clinical data, and the evaluation of systems medicine data.

In order to enable individually customized therapy for patients, it is imperative that research data and clinical data be combined. It is only by doing so that personalized medicine becomes possible at all. However, this makes data standardization, archiving, availability, and security major topics. This is what BIH and numerous partners from clinics, universities, IT companies, and health insurance providers are working to address as part of the consortium proposal »Medical Informatics« for the funding initiative of the Federal Ministry of Education and Research. After the submission of the proposal »*Health Data for Care and Research (HD4CR)*« approval was granted at the end of July 2016 for the conception phase, which was completed in late April 2017. The quintessential component of the plan is a data warehouse.

↗ ***Einstein Centers Digital Future***
www.digital-future.berlin

BIH's information warehouse

For this purpose, BIH began building a health data platform at the end of 2016. The objective is to create a system of various IT services which develop improved diagnostic, therapeutic, and preventative procedures. Establishment of the required systems and the existing systems was subdivided into three project phases which were slated to be completed over the course of three years.

The first phase started with the necessary requirements for data definitions and documentation and with the gathering of all clinical data in a »Plain Data Repository«. In this repository, existing clinical data in various source systems are consolidated and combined in order to provide information on patients that is as complete as possible. One important aspect is the availability of a central identification and pseudonymization procedure for the data. Upcoming phases will address standardized vocabulary and the option of allowing users to integrate research data as their own sources, thus allowing new research data and clinical data to »flow« from *bedside to bench* and back to *bedside* (i.e. from the patient's bed to the laboratory and from the laboratory back to the patient's bed).

Other digital projects by Charité in 2016

TBase

Development of a web-based electronic patient record which provides patient data at the right time at the right location, and, as an integrated outpatient research system, will run on mobile devices such as smartphones, tablets, and PCs in future, as well as be made available to outpatient clinics and research units at Charité and BIH – in compliance with data protection provisions.

MACSS (Medical Allround Care Service Solution)

Development (in collaboration with research and industry partners) of a service platform for chronically ill patients which collects their medical data and is able to transmit it to the attending physicians – from medical results to patient diaries. The objective: Improving quality of life for patients, avoiding hospital stays, and saving costs.

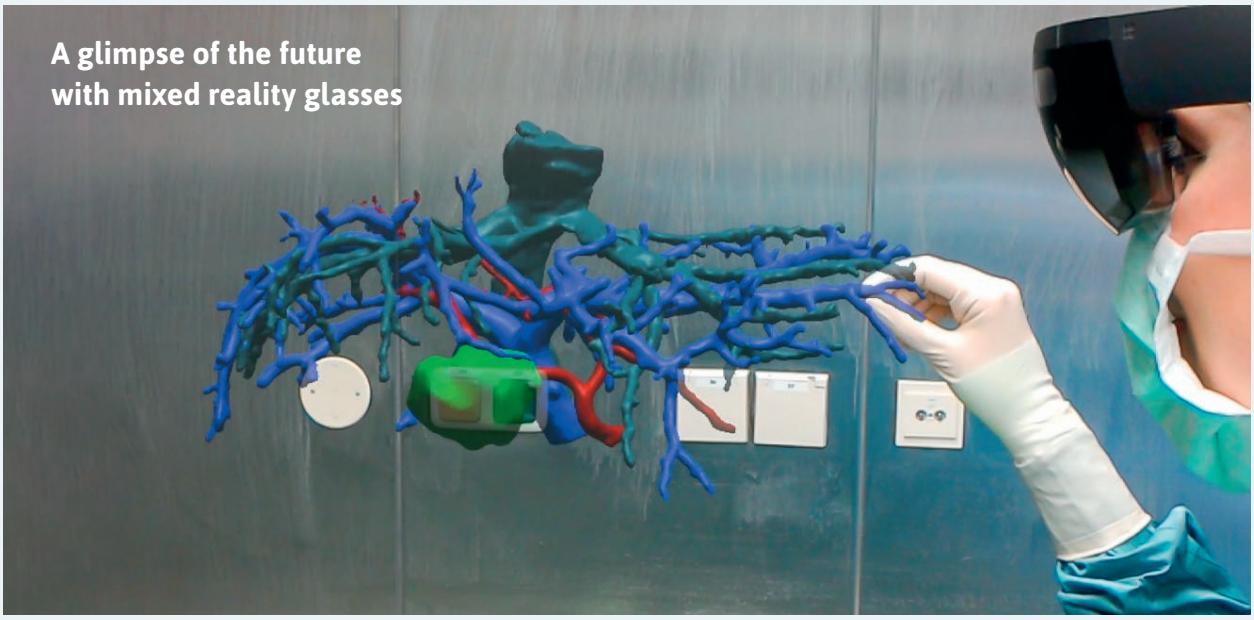
Computational microscope for the brain: The Virtual Brain

Petra Ritter has an ambitious goal: With the help of detailed brain simulations, the medical researcher aims to make visible how changes in brain processes affect learning or aging, but also how they impact the cause and development of diseases. In future, her models could help devise better treatments for diseases such as stroke, epilepsy, and schizophrenia.

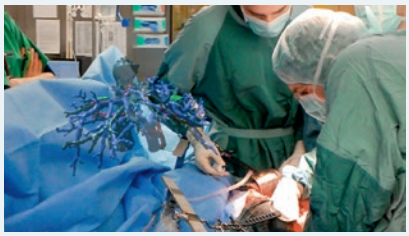
All of this will be made possible by the multimodal simulation platform »The Virtual Brain (TVB)«, which Ritter and her team from Charité's Department of Neurology with Experimental Neurology has developed in collaboration with international partner institutions. On this platform, the medical researchers accumulate enormous datasets from patients which are created during examinations such as electroencephalography, magnetic resonance tomography, and magnetic field measurements. »The data provides us with insight into the architecture of each individual brain and the routes of the neural pathways«, says Ritter. »The challenge here is to ultimately compile all the data collected in one model of the brain.«

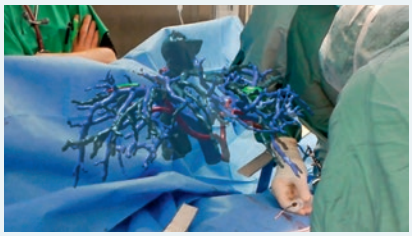
In order to provide better therapy in future, researchers require a more exact understanding of how the individual components of the brain interact. »Via TVB, we can collect comprehensive knowledge on how the brains of healthy and sick people function. This allows better measures to be developed for preventing, delaying, or treating diseases«, says Ritter.

»Our objective is also to create an awareness for the brain and how it functions among the general population«, says Ritter. BrainModes apps run on devices such as smartphones, allowing people to view in real time what happens during various activities. What does Ritter hope to achieve through all this? »To encourage people to live a better, healthy lifestyle – with balanced nutrition, exercise, and a cultural and social life.«



A glimpse of the future with mixed reality glasses





Lying on the operating table is a patient, his abdominal cavity open. Two surgeons in green scrubs and white masks are hunched over him. The medical experts are wearing giant glasses which allow them to see things that would otherwise not be visible: An exact three-dimensional model of organs and blood vessels. And of a tumor that is located within the complex vascular anatomy of the patient's liver.

Even though it sounds like something out of a science fiction movie, this is already possible today – at least technically. It is made possible by a concept which experts call mixed reality. In order to make use of this technology, surgeons wear special glasses into which three-dimensional structures, which were previously generated using the patient's MRT and CT data, are projected. But what makes this procedure so special is that the surgeons can not only see the simulated blood vessels, arteries, and tumors, but also continue to see their environment.

Such mixed reality systems are already being tested at Charité as well. Professor Igor Maximilian Sauer and his team from the Department of Experimental Surgery and Regenerative Medicine are working on concepts for the use of this technology in real-world medical procedures. For this purpose, the team is collaborating with software experts and game developers and has already tested glasses and software in initial pre-clinical studies. »Mixed reality makes it possible to have ›digital x-ray vision‹«, says Sauer. One major advantage of this technique: During an operation, surgeons need to rely on precise anatomical knowledge. »If I can see the structures at the same time while performing the operation, everything is made significantly easier – and hence also safer for the patient«, says Sauer.

»Our research fits together perfectly«

Stiftung Charité supports pioneering projects and persons at BIH. With the Einstein BIH Visiting Fellowships, leading researchers from overseas receive funding for a position at BIH. The researchers continue to be employed at their home institutes, but at the same time work in a new research group in Berlin. Since 2016, Professor Rolf Bodmer and Professor Silke Rickert-Sperling (Charité/MDC) have been conducting research together. The molecular and development biologist comes from the Sanford-Burnham-Prebys Medical Discovery Institute in California, USA. Together, they investigate genetic and molecular causes in persons with hereditary heart defects. An interview.

What does your research focus on?

RICKERT-SPERLING My research group investigates the genetic and molecular causes of hereditary heart defects. In particular, we look at genes associated with diseases and epigenetic factors, i.e. chemical compounds which activate and deactivate genes. Almost one percent of newborns suffer from a congenital heart defect, whereby Tetralogy of Fallot (TOF) is the most common cyanotic heart defect. This complicated disease consists of multiple simultaneous abnormalities: A hole in the cardiac septum, a narrowing of the pulmonary valve, and a thickening of the musculature of the right ventricle. Furthermore, the aorta, the main artery, is not located at the right position, which results in blood that is not enriched with oxygen entering the circulatory system. These infants suffer from »blue baby syndrome« – or cyanosis. Children with Tetralogy of Fallot generally undergo surgical treatment when they are infants. In order to discover the molecular basis of this and other congenital heart defects, it is important to combine various approaches – including molecular biology, bioinformatics, systems biology, and clinical approaches.

BODMER I, too, investigate the causes of congenital heart defects. However, I approach the topic from a different perspective. I work with a model organism – the fruit fly *Drosophila*. Even though *Drosophila* only possesses a heart tube (dorsal vessel) and not a four-chamber heart like humans or mice, it is an excellent tool for investigating the basics of certain heart diseases, as the embryonic and active genetic blueprints of the heart muscle cells of the fly are similar to those of humans in a significant number of respects; it has been evolutionary conserved.

Above all, what I am interested in is the molecular and genetic regulation of all those processes which are crucial to the development of the heart. For example, I discovered the first cardiogenetic transcription factor in the fruit fly – a control protein which plays an important role in gene regulation. It is only through this discovery that we are now able to understand the influence molecular mechanisms have in the development of the heart. We were able to establish *Drosophila* as a model organism for heart research.

You have been coolaborating since 2016. How does that work?

RICKERT-SPERLING We have known each other for years. I had invited Rolf Bodmer as a speaker to a congress and was impressed with his latest technological development, the »SOHA« method for the analysis of cardiac function *in vivo* in *Drosophila*. It was exactly what I had been looking for: A quick and convenient method for testing – in a living system – the effects of multiple genetic modifications which we had identified in patients with congenital heart defects. Until then, we had only been working with cell culture systems and mice in Berlin.

BODMER And I was searching for a way to make the model organism *Drosophila* usable for human heart genetics. That was when we quickly realized that we made the perfect combination.

Do you already have initial successes to tell us about?

BODMER Oh yes. Based on Silke Rickert-Sperling's genetic data from patients with Tetralogy of Fallot, we began investigating rare mutations which occurred individually in patients – or more frequently in combination – in *Drosophila*. Hence, for the first time, we now have candidates which could be the cause for this type of heart disease. What is particularly interesting in this case is that a percentage of the affected genes come from the group of structure proteins in muscles, which could have possible implications for the long-term progression after the operation.

Hence, we are currently developing a series of genetically modified *Drosophila* in which we have specifically deactivated individual genes with the help of CRISP/Cas9 technology. This will allow us to verify if the candidates we have discovered are in fact responsible for the abnormalities.

Stiftung Charité
Private Excellence Initiative
Johanna Quandt

With the Private Excellence Initiative Johanna Quandt, Stiftung Charité has promoted the establishment and further development of BIH since 2013. For this Private Excellence Initiative, Johanna Quandt provided special 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.

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.

In the Private Excellence Initiative, 260 individuals have received or continue to receive funding (not including follow-up funding).

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

↗ ***Stiftung Charité***
www.stiftung-charite.de/en/funding/private-excellence-initiative-johanna-quandt/bih-johanna-quandt-professorship.html

→ ***More information under »Facts and Figures«***
Pages 73–75

How do you benefit from each other?

RICKERT-SPERLING Personal contact is extremely important – we share information and ideas every week. Only by doing so can we achieve our research objective. With this fellowship program, we were able to bring Rolf Bodmer's methods to Berlin and set up a fly laboratory. Here, we directly test the genes which we have categorized as potentially relevant for patients. Furthermore, we also transfer the technology to other colleagues in Berlin who are performing cardiac research. Another crucial aspect is that, through our transatlantic »bridge«, we are now able to exchange information directly with scientists focusing on clinical and basic research via Rolf Bodmer's American network, and of course the contact with our European partners. This has helped all parties progress.

How can people benefit from your research?

RICKERT-SPERLING Fortunately, children with congenital heart defects can now receive excellent treatment via surgery and drug therapy. This has resulted in a new group of patients for us: Adults with a congenital heart defect. A number of them suffer from heart failure or arrhythmia during the course of their lives. Our object is to determine early on which of these persons are particularly at risk. We surmise that not all of them face the same risks.

In future, we also wish to find new approaches for preventing heart defects. Perhaps epigenetics will help us in this endeavor. We hope very much that research into epigenetic modulations in heart development will become a new research area and contribute to the development of preventative options.

Research platforms in brief

→ *Overview of research platforms expenditures*
Page 56

Research platforms and their initiatives sat BIH are structured as functional organizational units. Within these BIH Research Platforms, cutting-edge technologies, methods, and research structures are developed that generally exceed the capabilities of individual research groups. The research platforms serve to further develop scientific findings for the state-of-the-art technologies and to provide services for researchers in the BIH Research Programs.

The previously established Core Facilities were integrated into the research platforms as essential elements in 2016 and are accessible to scientists from the BIH Translational Research Commons. The services offered are geared to the needs of researchers in the research commons at BIH, as well as all members of BIH.

In the following, you will find basic information about the research platforms and their contact persons.

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.

Clinical Research Unit (CRU)

In 2016, activities previously initiated for the structural development of the CRU continued. The main focus was on preparations for conducting a cardiovascular pilot study (BeLOVE: Berlin Longterm Observation of Vascular Events). In this regard, the development of structures always takes place with an emphasis on the systems medicine approach, in this case with the involvement of the cardiology, neurology, endocrinology, and nephrology departments.

The objective of the pilot study is to establish the CRU across campuses such that the optimal prerequisites are provided for future BIH cohort studies with more than 10,000 patients. Apart from drafting the regulatory documents for the pilot study, the various steps for conducting the study were planned in detail, such as patient recruitment, specific laboratory management processes (sample collection, processing, and storage), the collection, storage, and evaluation of study data, and the setting up of reporting systems.

In 2016, two of the CRU site coordinators were able to successfully finish their habilitation qualification, and one CRU site coordinator was conferred a W2 professorship at Charité.

CRU site coordinators
Campus Charité Mitte (CCM): Prof. Knut Mai; Prof. Sein Schmidt
Charité Campus Virchow-Klinikum (CVK): Prof. Frank Edelmann, PD Dr. Anne Flörcken
CRU OCC-Operative Critical Care (CVK): PD Dr. Steffen Weber-Carstens, PD Dr. Undine Gerlach
Charité Campus Benjamin Franklin (CBF): Dr. Joachim Weber
Charité Campus Buch/Experimental and Clinical Research Center (ECRC): Dr. Michael Boschmann

Biobank

The Biobank allows for the long-term storage of fluid samples from subjects as well as patients from trials, but also the storage of fluid and tissue samples taken from patients for diagnostic purposes within the scope of their medical care. Millions of samples will be stored at temperatures of down to minus 160 degrees Celsius at the two Biobank locations.

- The »BIH Biobank Building« in Buch was completed in June 2016, and the commissioning of the automatic sample storage facility is planned for June 2017.
- The »BIH Biobank Building« at Campus Virchow-Klinikum was completed in July 2016 and the laboratories were put into operation in mid-August. The automatic cryogenic storage facility was installed in August 2016 (handover will only take place after a detailed site acceptance test (SAT) currently planned for June 2017). The inauguration of the Biobank at Campus Virchow-Klinikum took place on December 1, 2016. The BIH-Charité Biobank is one of the first laboratory buildings in Germany to be built of wood. Advantages of this construction method include weight, construction time, costs, and sustainability criteria. The Biobank will store more than two million samples and has storage capacity for up to six million samples.

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

Research Platform »Multiscale Genomics«

This platform investigates the genetic causes of diseases and the role of genes, gene variations and mutations, as well as the role of the microbiome in the development of progressive diseases. The characterization of gene variants in the DNA sequence of individuals and their association with phenotypic traits as well as the characterization of regulatory processes in biological models for a better understanding of pathogenic mechanisms are also highly relevant for translational research at BIH.

Recruitments

Dr. Birte Kehr, previously of deCODE genetics in Iceland, was recruited to BIH. In November 2016, she began establishing her junior research group in the area of »Genome Informatics« in Berlin.

Dr. Martin Kircher, previously of the University of Washington, Seattle, USA, began establishing his junior research group »Statistical Genetics« in Berlin in March 2017.

Contact person: Prof. Erwin Böttinger

Omics Core Facilities

BIH's Omics Core Facilities are specialized in high-throughput technologies and the processing and analysis of clinical samples. It combines genomics, proteomics, and metabolomics, three state-of-the-art omics technologies which are used for the analysis of genes, proteins, and metabolic products, as well as their interactions. The individual BIH Omics Core Facilities have been headed by MDC researchers on an interim basis since they were founded. The management positions for all three omics units were filled in 2016.

Contact persons: Core Facility Genomics:
Dr. Sascha Sauer (since August 1, 2016/Head of the BIMSB Core Facility Genomics at MDC),
since April 1, 2017 Dr. Tomasz Zemojtel (Charité)
Core Facility Proteomics: Dr. Stefan Kempa (MDC),
from August 2017: Dr. Philipp Mertins
Core Facility Metabolomics: Dr. Jennifer Kirwan (MDC)

Bioinformatics

The BIH Bioinformatics Core Unit moved to the Campus Charité Mitte, Invalidenstrasse 80/Virchowweg 20, in January 2017, and is responsible for the further processing and scientific evaluation of data.

Contact person: Dr. Dieter Beule (BIH)

High Performance Computing (HPC)

The High Performance Computing Cluster at the MDC campus in Buch has been in operation since summer 2015, and is actively used by BIH researchers: Utilization of the HPC's CPU currently accounts for approximately 45% of capacity. Approx. 40 percent of the HPC's storage capacity (DDN) is currently in use.

Contact person: Dr. Alf Wachsmann (MDC)

Research Platform »Humanized Model Systems and Cell Engineering«

Among other things, this research platform is aimed at the further development of advanced technologies in stem cell research and modeling, the development of high-throughput methods based on humanized models, and their application in the study of therapeutic target molecules and active substances.

Core Facility Stem Cells

The Core Facility Stem Cells provides high-quality standard operating procedures (SOPs) for the acquisition, processing and tissue-specific differentiation of stem cells. It also provides genome editing techniques for the targeted manipulation of stem cells such as CRISPR/CAS9 and TALEN. In addition, this research platform is specialized in the generation of disease-specific isogenic iPS cell lines for basic and clinical research.

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

Research Platform »Digital Medicine«

This research platform focuses on the use and development of digital technologies to improve the usability of data in research and clinical settings. This also includes the IT infrastructure and services, activities, and three junior professorship vacancies for the Einstein Center Digital Future (ECDF) in Berlin, as well as the consortium proposal »Medical Informatics« (HC4CR) for the funding initiative of the Federal Ministry of Education and Research.

Contact persons: Prof. Erwin Böttinger,
Martin Peuker (Charité)

People

Two resources are absolutely essential for our successes in health research: People and their ideas. That is because innovations are created through the stamina, patience, and the thirst for knowledge of individuals.

Our scientists at MDC and Charité are among the best. However, in order to achieve our objectives, we strive to grow and improve ourselves. Our progress is based on scientific excellence, the promotion of talent, equal opportunities, the diversity of ideas, and new alliances with leading minds – both in Germany and beyond national borders.

Mission: Recruitment

Investing in people via training and recruiting the brightest minds in translational research is a central principle at BIH for achieving success in international competition. In 2016, BIH further developed its recruitment strategy. Equal opportunity is a prerequisite!

BIH Chairs

At the end of the year, BIH prepared its call to recruit for the first BIH Chairs in the following fields. In 2017, candidates will be recruited for these initial key positions:

- Transforming biomedical research
- Digital health
- Clinical translational sciences
- Disease modeling
- Gene and cell therapies
- Medical genomics

We strive to grow. Charité, MDC, and BIH. In 2016, we enhanced the BIH recruitment strategy. Being part of the »BIH Strategy 2026«, it aims to recruit outstanding scientists for Berlin via the new, attractive positions, but also via support for appointments at Charité and MDC. These researchers will shape BIH's profile with their scientific expertise. Hence, we will be focusing on best practice approaches, internationalization, and equal opportunity. One aspect of the recruitment strategy involves significantly increasing the number of women at all levels of the scientific system. At least 50 percent of all new positions in the junior research groups at BIH are to be filled by women, and at least 40 percent for the BIH Chairs and BIH Professorships.

Together with Charité's Faculty Council, we approved an accelerated recruitment procedure in October 2016. This »fast-track procedure« corresponds to the requirements of international competition with regard to tighter deadlines and more structured workflows, but also the academic principles of university appointments. Apart from the Appointment Committee, a Search Committee will be defined for this procedure, thereby allowing the process to be accelerated.

Successful recruitments in 2016

Two principal investigators were recruited in 2016: Professor Andreas Diefenbach, former director of the Institute for Medical Microbiology and Hygiene at the University of Mainz, accepted a W3 professorship for microbiology at Charité in November 2016. Moving from Iceland to Berlin to take up her new appointment was Dr. Birte Kehr, previously of deCODE genetics. In November 2016, she began establishing her junior research group in the area of »Genome Informatics«. Two other junior research groups have now also been filled. Dr. Martin Kircher (University of Washington in Seattle), at BIH since March 2017; Dr. Dagmar Kainmüller (HHMI Janelia Research Campus, USA) will begin work in 2018.

The *Johanna Quandt Professorships* (temporary W2 professorships with a true *tenure track*) were created in collaboration with Stiftung Charité at the end of 2015. This program is aimed specifically at female scientists. Preselection and selection in the relevant committees took place in 2016. The appointment procedures were initiated in 2017.

Recruitments at BIH
The categories

BIH Junior Research Groups

Researchers and scientists at the beginning of their career

BIH Professorships

These scientists pursue successful research at the highest level and are characterized by internationally recognized success. They augment the profile of BIH, MDC, and Charité.

BIH Chairs

Researchers with an excellent academic track record who will become pioneers for research programs and research platforms

Selection criteria for candidates at all career phases include scientific excellence and whether their skills are a good match for the key research areas.

New career paths are drivers of innovation

The Biomedical Innovation Academy is the centerpiece of training and professional development at BIH. Five programs are managed by the Academy, and we intend to continue to expand it in 2017. Professor Duska Dragun about the Academy

I am a medical specialist and a passionate translational researcher. My generation is that of the »after-work researcher«, who worked for half the night in the laboratory after finishing the day job in the clinic. That is why my objective is to make it possible for young researchers to have more time to conduct their research with the BIH Charité Clinician Scientist Program. At the same time, we want to train a new generation of »translators« who not only perform biomedical research, but also continue to gather real-world clinical experience.

BIA's training and professional development activities

- **Core lecture series and clinic and industry visits**
- **Clinician Scientist Program Curriculum**
- **Good Clinical Practice refresher course**
- **Good Practice in Peer Review**
- **Biostatistics**
- **Soft skills/personal skills training**
- **MSc offerings (a selection)**
  - »Animal models in translational science« (blended learning)
  - »Blood brain barrier« (blended learning)
  - »Critical thinking in translational medicine«

Four other programs are housed under the roof of the Biomedical Innovation Academy (BIA): Translational PhD & Postdoc Grants, Biomedical Entrepreneurs, and the research scholarships for students of human medicine and dentistry. These programs are targeted at young medical experts and theoretical researchers at various career stages, ranging from students to postdocs. We currently oversee and support more than 130 *fellows* and their mentors.

2016 – A trailblazing year

In Germany, but also internationally, the focus of promoting early-career researchers is on project funding. BIA's programs focus explicitly on nurturing individuals. By doing so, we fill a gap in the strategic personnel development of young talent in biomedicine. 2016 once again demonstrated that we are on the right track. In July, we organized a symposium with 150 guests celebrating »Five Years of the Clinician Scientist Program«. The fellows invited their favorite clinician scientists from prestigious institutes such as the Harvard Medical School in Boston or the John Hopkins University in Baltimore. Together, they formed thematic tandems, gave lectures, and held talks. I am glad that the idea of the program was so well-received and continues to grow since it was launched. Currently, the »Berlin Model« is also being replicated across Germany.

Professor Duska Dragun
is the senior attending clinician of the Division of Nephrology and Internal Intensive Care Medicine at Charité, and director of the BIH Academy.

Another highlight was the Clinician Scientist Retreat with 80 fellows at Genshagen Castle in Brandenburg. Together with their mentors and department directors, the fellows discussed their research and the strategic direction of the program. Response was so good that we met again in January 2017 for a second retreat on the key future topic of »Entrepreneurship and Innovation«.

A glimpse of the future

In the fall of 2016, we opened up the Clinician Scientist Program to returnees from overseas for the first time. By doing so, we hope to recruit even more preeminent young clinicians for Charité. In an era characterized by Brexit and changes in US science policy, Germany will become increasingly interesting for researchers as a science hub – and this is a trend we cannot and do not wish to ignore. Furthermore, we are currently developing a pilot program for talents with cutting-edge ideas, the Biomedical Innovator. The idea: The fellows will transform translational research findings into new diagnostics, medical products, or cutting-edge therapies, and supervise the entire process of bringing them to market. We will support them via intensive specialist mentoring and network them with experts so that they can continue to develop their ideas and innovations.

On the search for genetic variation

Birte Kehr is a researcher at the start of a promising career. Her research is successful and pioneering – together with her team she develops computational methods for the analysis of genome sequencing data. Specifically, she focuses on identifying and analyzing structural variations in the genome sequence and their influence on diseases.

Her work at BIH is in its early stages, as she only took up her position in November 2016. Since then, her main priority has been getting set up, establishing the team, and obtaining an overview of MDC, Charité, and BIH. To date, the team comprises a postdoc and a doctoral student. All of them work next door to the BIH Bioinformatics Core Unit, which is headed by Dieter Beule and which provided support for the processing and evaluation of raw data for more than 20 projects from the MDC/Charité research commons in 2016. The spatial proximity is promising for all.

Algorithms for daily tasks in the clinic

How susceptible a person is to developing a disease and how a patient will respond to a particular form of medical therapy can be influenced by individual variation within the genome sequence. In order to better understand this relationship, Kehr and her team develop computer programs which filter out such variations from large amounts of sequencing data. »It would be wonderful if our algorithms were used routinely for daily tasks in the clinic one day«, says Kehr. This is the goal she and her team are working towards with full commitment and ambition.

Before Birte Kehr began her work in Berlin, she gained experience at deCODE genetics in Iceland working with sequencing datasets from all over the country. That was where her passion for structural variation in the context of disease developed, she says. She completed her doctoral thesis on algorithms and data structures for multiple genome alignment in 2014 at Freie Universität Berlin, within the framework of the International Max Planck Research School for Computational Biology and Scientific Computing.

In 2016, BIH was able to fill positions for yet another junior research group in the field of genome informatics. Martin Kircher will primarily be analyzing and evaluating the sequencing datasets starting in spring 2017. Back in 2016, Kircher and I had already begun discussing and coordinating our activities, says Birte Kehr. Together, the duo will work closely to continue advancing the state-of-the-art sequencing data evaluation at BIH, Charité, and MDC.

»We are striving to optimize the efficiency and reproducibility of research«

An interview with Professor Ulrich Dirnagl on the validity, robustness, and reproducibility of scientific findings.

Professor Ulrich Dirnagl
has been committed to achieving new quality standards in biomedical research for many years. He is also the director of the Center for Stroke Research Berlin and the founding director of QUEST – Center for Transforming Biomedical Research at BIH.

BIH has defined the augmentation of the validity, robustness, and reproducibility of scientific findings as an important strategic objective. The quality and in particular long-term translational value of research achievements in pre-clinical and clinical research at BIH is to be continuously verified, evaluated, and further developed, as is the efficiency of the research processes and projects. In order to achieve these objectives, in 2016 the »BIH Strategy 2026« detailed the establishment of *QUEST – Center for Transforming Biomedical Research*. QUEST stands for the key aspects of *Quality*, *Ethics*, *Open Science* and *Translation*. Since March 2017, the center has been headed by Professor Ulrich Dirnagl, who is also in charge of the Department of Experimental Neurology at Charité – Universitätsmedizin Berlin and director of the Center for Stroke Research Berlin.

Mr. Dirnagl, improving the quality and reproducibility of research findings is a matter that is very close to your heart. Where do the challenges lie?

At the moment, there is a lot of talk about the replication crisis – it turns out that many laboratory findings, in particular frequently the spectacular ones, cannot be reproduced. Initially, this was noticed by the pharmaceutical industry, where it was often not possible to reproduce findings that were published in academic biomedicine. In addition, many diseases can be treated with great success in animal models, but it is only seldom that these therapies are successful in patients – we call this the translational roadblock.

In order to change this, you are actively engaged in the field of meta-research in addition to your scientific research on the pathophysiology of strokes. What exactly does this entail?

We work on optimizing the efficiency and reproducibility of research. It is particularly in the basic research and pre-clinical domains of biomedicine where there is a significant need for improvement in order to e.g. avoid bias, to increase statistical significance, or also where publication practices are concerned. At the same time, I have also noticed in my seminars on experimental design, statistics, and »Good Scientific Practice« that there is also a great need for improvement where methodological competency is concerned.

How do you intend to achieve improvements? What are your objectives for the coming year as the founding director of QUEST?

One of our initial measures will be to introduce an electronic lab notbook in which researchers will receive assistance with the planning and analysis of experimental studies and the establishment of quality assurance measures, or which will assure that *reporting guidelines* are adhered to. Other measures

will include e.g. promoting the publication of »negative« findings as well, or setting up a fund for the replication of particularly important findings. Furthermore, measures in which the appointment, funding and career advancement of researchers are not determined solely via the impact factor of their publications will also play an important role. The key aspect will be to create incentives for more »quality-conscious« publications, where it is important that the findings are significant for clinical applications, for example. It will be important to provide academic supervision for the implementation of such offerings and measures in order to investigate their effectiveness and to develop additional, improved approaches. They can then also serve as »blueprints« for other research institutions.

With the right measures, BIH can achieve a leading global position in light of the international discussion on *reducing waste and increasing value*, while at the same time optimizing the long-term value of the research performed at BIH.

Innovation

It is important that new research findings straight out of the laboratory rapidly find their way into real-world medical applications, where they can improve quality of life for patients as soon as possible. But realizing new ideas and promising therapies in practice is one of the most difficult tasks in biomedical research.

It can only succeed with a holistic innovation culture: Researchers need to receive targeted funding, motivation, and training. They require business know-how and a tight network of advisors at their side.

Berlin Health Innovations

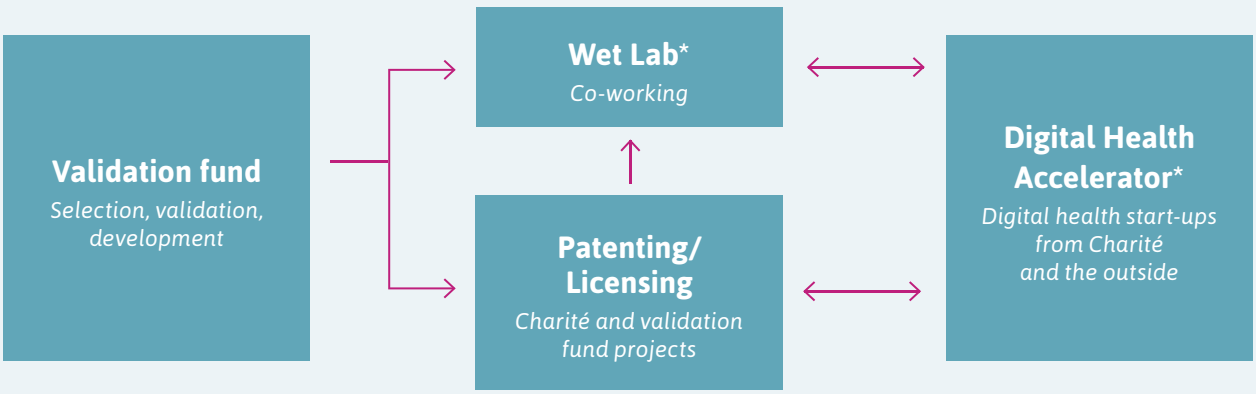
BIH and Charité's newly established joint technology transfer unit

The year 2016 was characterized by the decision of the Executive Boards of BIH and Charité to merge their respective technology transfer units and activities into a single entity, »Berlin Health Innovations« (BHI), and in doing so to lay the foundation for ambitious, professional technology transfer that comprehensively coveres the pharmaceutical, medical technology, and digital health fields. Creating this kind of joint entity was recommended by multiple external assessor groups which, among other things, were commissioned by Stiftung Charité; it was also proposed in the external expert assessment of the initial BIH concept in 2013.

This decision was preceded by an intensive conceptual dialogue regarding a complete restructuring of the technology transfer of BIH, Charité, and MDC: Back in spring 2016, the BIH Executive Board members agreed as part of the »BIH Strategy 2026« on the expansion of technology transfer as a central innovation driver for translational medicine, and on the development of an ambitious concept.

The core instruments of the technology transfer unit »Berlin Health Innovations«

** In the evaluation phase*



Advisory (powered by SPARK Berlin and Ascenion) and Cooperations

» Digitalization is transforming healthcare systems worldwide. The ambitious technology transfer strategy by BIH and Charité focuses on digital health in business and industry, and in doing so caters to the cross-industry demand for data-driven products and business models. Stiftung Charité welcomes the fact that ›Berlin Health Innovations‹ is stimulating this development for researchers and entrepreneurs. «

Jürgen E. Zöllner, Stiftung Charité Executive Board

A joint entity

In summer 2016, a dialogue began between BIH and Charité on the merger of the respective technology transfer units, which was completed successfully with the signing of a corresponding contract on February 9, 2017. Since then, the joint technology transfer unit has been in operation as »Berlin Health Innovations« with a joint team and joint management. Berlin Health Innovations has since then become Charité and BIH's central point of contact for internal innovators, industry and investors (one face to the customer).

MDC intends to incorporate its wide range of funding programs for technology transfer into the BIH/Charité concept, thereby contributing to an overall concept that provides a range of programs that is as diverse as possible. This will allow BIH and Charité researchers to benefit from the successful programs that have been established at MDC.

Three fields of action

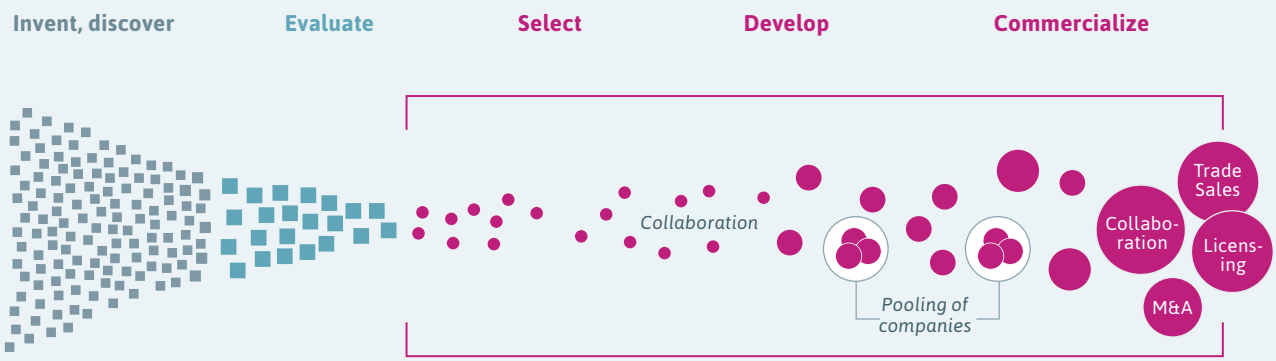
The Berlin Health Innovations concept aims to significantly reinforce existing technology transfer competencies and capacities; it focuses on the following three fields of action:

- Improving the framework conditions for technology transfer
- Strengthening the appropriate incentive systems
- Continued professional development of the technology transfer team

These fields of action are intended on the one hand to take the transfer culture to a significantly higher level and, on the other hand, to enable important components in the innovation and value chain to be implemented while still within academic context, before commercialization takes place in the second step.

For the operationalization of these fields of action, five instruments were developed which, in addition to Charité's contributions to BHI up to the year 2020, will receive around 24 million euro of funding from BIH based on resolutions by the Executive Board and Supervisory Board regarding the BIH Strategy.

»Asset Pipeline«



BIH, Charité, MDC and university partners

Berlin Health Innovations –
The joint technology transfer of BIH and Charité
Incl. partners (Ascenion, SPARK Berlin, Stiftung Charité, BIH Innovation Academy)

Ideas, data · Innovations · Projects, companies

Chart with reference to Karolinska Development

Focus on digital health

The core instrument is a validation fund, that combines the existing smaller-scale funding instruments and adds the component »Digital Health«; its aim is to enable the implementation of larger value-added projects, also as part of strategic partnerships with the industry.

In addition, opportunities for researchers to advance their projects, e.g. to spin-off companies, in the areas of »Medical Technology«, »Pharmaceuticals«, and »Digital Health« will also be significantly improved. In November 2016, the German Bundestag decided to increase BIH funding for 2017 by an additional two million euro in order to advance the field of digital health, in particular the pilot proposal »Digital Health Accelerator«. Implementation of this pilot proposal began the very same year, in 2016:

- An experienced manager was recruited for the area »Digital Business Models«
- Exploratory discussions were initiated with international partners for the operation of a Digital Health Accelerator, and
- Initial projects were identified for inclusion in the Digital Health Accelerator.

The objective of all these activities is to develop an »asset pipeline«, a continuous establishment of innovations with long-term value which can be licensed to the industry or turned into spin-off companies. It is only when the number of such innovations of long-term value remains permanently high that pharmaceutical and medical technology companies, as well as investors, can be interested in engaging in a constant dialogue with the technology transfer unit at BIH, Charité, and MDC.

Progress in the implementation of existing technology transfer funding lines

The funding instrument BIH Technology Transfer Fund – Pharmaceuticals and Medical Technology

The BIH Technology Transfer Fund supports projects with identifiable economic potential, that need to generate evidence of economic viability and for which an investment by industrial partners or the establishment of a startup are still considered too risky. A total of seven projects were funded in 2016, of which three were from the category »Pharma« and four from »Medical Technology«. Total funding amounted to around 350,000 euro. Additional calls for the submission of projects were published at the end of 2016. Funding has been increased significantly as part of the new transfer strategy.

Two selection procedures were held in 2016:

1. BIH Technology Transfer Fund – Pharmaceuticals
   19 project proposals; three funding grants
2. BIH Technology Transfer Fund – Medical Technology
   20 project proposals; four funding grants

Funding instrument: SPARK Berlin

In 2015, SPARK Berlin joined with Stiftung Charité to launch a new funding activity in the field of technology transfer based on the model at Stanford University, California. In addition to financial funding, SPARK Berlin is also establishing a mentoring network for the areas of Pharmaceuticals and Medical Technology to provide the projects funded with personalized support during the entire funding term. Moreover, SPARK Berlin is organizing a series of seminars for professional development in the field of technology transfer. It is open to all interested scientists and clinicians. In 2016, seven projects were funded by SPARK Berlin, with 27 individuals and teams receiving mentoring. Supported by SPARK Berlin, the funded programs have already submitted two patent applications with four further applications currently in the works.

»More innovations are possible«

Dr. Rolf Zettl and Professor Axel Radlach Pries speak about the role of technology transfer and a new innovation culture

In the »BIH Strategy 2026«, technology transfer was assigned a significantly larger role than in the initial years of BIH. What are you now doing differently?

ZETTL Technology transfer was completely redefined in 2016. The starting point is a programmatic and holistic approach which is closely interwoven with our research activities. For us, it is important that the entire transfer culture changes and that innovation and transfer are »taken into consideration and also rewarded« from the very beginning in all research activities.

What are you doing to ensure this?

ZETTL We are improving the overall framework conditions which need to be right in order for innovation to emerge. We are increasing incentives which motivate, and are reinforcing the technology transfer team with colleagues who have business experience.

» Technology transfer is a major innovation driver. «

PRIES With these measures, we intend to bring together what BIH and Charité have to offer, in doing so take the transfer culture to a whole new level and stimulate important steps in the innovation and value creation chain in the academic sector in order to make commercialization possible.

What is the status of this endeavor as of early 2017?

PRIES We are in the early stages of implementing a highly ambitious concept. But we have already reached a significant milestone: We have merged the technology transfer units of BIH and Charité to create the joint unit »Berlin Health Innovations« (BHI). In summer 2016, the basic aspects for a collaboration contract between BIH and Charité were defined which regulates this merger.

What specifically do you hope to achieve by merging the Charité and BIH units?

PRIES In the new unit, we bring together competencies and capacity, create processional service structures and new instruments – thus making it far easier for the biomedical hub of Berlin to play to its strengths!

ZETTL It is envisioned that this joint unit – »Berlin Health Innovations« – will become a one-stop-shop for commercialization, focusing on the needs of

Dr. Rolf Zettl
is the Chief Financial Officer and the representative for technology transfer on the BIH Executive Board.

healthcare provision and the industry. The relevant representatives from »Berlin Health Innovations« will supervise researchers from the idea to the application: This is where they will receive advice, funding, entrepreneurial know-how and access to a wide network of advisors. However, the key aspect is that we are truly creating a new innovation culture which stimulates the creativity of the researchers, makes innovations visible, and enables real cultural exchanges with industrial partners, either in joint laboratories or in the companies. This will open the door to even more innovation.

What is it based on?
Are you imitating successful models?

ZETTL Naturally, we had a look at successful transfer units, such as at the Karolinksa Institute in Sweden or at Imperial Innovations and MRC Technology in England. However, it would not be possible to transpose the concepts, as the innovation culture in Germany is simply different. Success-critical elements must be adapted to the framework conditions here. Naturally, we also attempt to learn from the experiences of the best in this field.

Do you focus on certain areas or applications?

ZETTL Our »native« industries are the medical technology and pharmaceutical industries. However, we hope that in the future, we will also have the opportunity to supervise an increasing number of high-quality »digital« research projects and insights all the way up to their application in medicine.

PRIES We evaluate the applications – regardless of where the ideas arose – according to quality and potential and support the ones that are the most promising.

Professor Axel Radlach Pries
is the dean of Charité's medical faculty.

How attractive is »Berlin Health Innovations« for partners and investors?

PRIES We are highly attractive, because we meet them at their level. We understand industrial processes, framework conditions, and how industries think. Furthermore, we give industrial partners access to the comprehensive expertise of our facility and deliver a »critical mass« for clinical research.

ZETTL Our research activities perfectly match the fields which investors from the pharmaceutical, biotech, medical technology, and digital health fields view as attractive and having long-term value; for example patient-oriented research, cell-based therapies, and big data as the basis for the development of e.g. diagnostic markers and IT solutions in digital and mobile health.

What are your priorities for 2017?

ZETTL Processes and structures are important, but without a good and experienced team, our concept is difficult to put into practice. With the merger and the creation of a joint unit, we will first need to ensure that the team has been judiciously established. Every single person must have a task and a role. It will certainly not be easy. On the business side of things, we intend to launch promotion of validation, establish a Digital Health Accelerator, and negotiate initial strategic partnerships.

PRIES Furthermore, it is also important that we standardize the rules for spin-offs as well as draft and finalize unified and transparent use policy regulations for BIH, Charité and MDC. Of course, it would also be great to see visible initial approaches and successes from our new initiatives!

Facts and Figures

Facts and Figures

1. Legal framework and institutional milestones

Berlin Institute of Health (BIH) was founded as an non-university biomedical research facility in cooperation with Charité – Universitätsmedizin Berlin (Charité) and 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 MDC, the partners included the Federal Republic of Germany, the state of Berlin and 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, MDC, the Federal Ministry of Education and Research and the Senate Administration for Education, Youth and Science in Berlin, as well as 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, BIH was converted into a corporation under public law. Under the law, BIH is a new, non-universitary independent institution (corporation under public law *[KdöR]*) in the field of biomedicine with the member entities Charité and MDC. 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 MDC and Charité.

Institutional milestones

July 2011	Memorandum of understanding
2012–2013	Scientific concept
January 2013	Administrative agreement *(Verwaltungsvereinbarung)*
March 2013	Founding agreement *(Gründungsvertrag)*
	BIH is a civil law association *(Innengesellschaft bürgerlichen Rechts)*.
May 2013	Evaluation of scientific concept
March 2015	The Berlin House of Representatives passes the BIH Act *(BIG-G)*.
January 2016	BIH now operates as a corporation under public law.
June 2016	The Supervisory Board approves the »BIH Strategy 2026«.
November 2016	The Supervisory Board approves the »BIH Strategy Implementation Plan 2017–2020«.

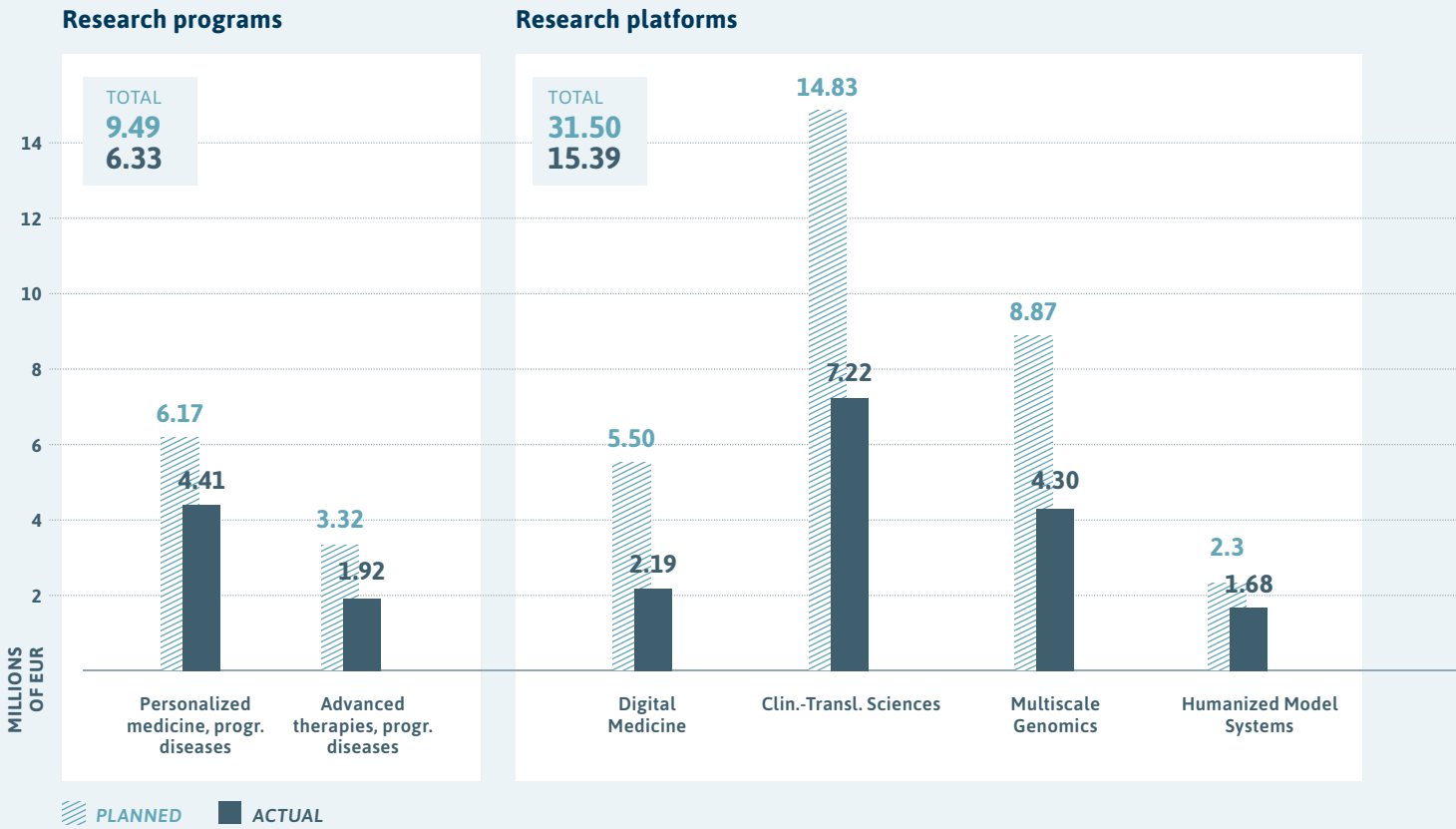
2. Members of the corporation under public law

The members of BIH are professors employed full time by the Charité (professors, junior professors), as well as research group leaders of the MDC. As of December 31, 2016, more than 250 researchers were involved in BIH research activities. In order to achieve the objectives of the BIH Strategy 2026, BIH will be extensively recruiting numerous chair positions, professorships, and junior research group leaders in the coming years.

3. Financing and financial situation 2016

BIH is financed based on the joint administrative arrangement with the federal government (90 percent) and the state of Berlin (10 percent). With effect from January 1, 2016, 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 BIH to forward funds to Charité and MDC in accordance with the specified utilization regulations. Furthermore, the federal government has also authorized 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 Helmholtz Association of German Research Centres.

In accordance with the approval by the federal government dated October 14, 2016 and by the state of Berlin dated October 4, 2016, BIH was awarded institutional funding totaling 59.608 million euro. Of this, the federal government provided 52.908 million euro, and the state of Berlin 6.7 million euro. In addition, there were also grant funds for discretionary use from 2015 totaling 9.08 million euro.

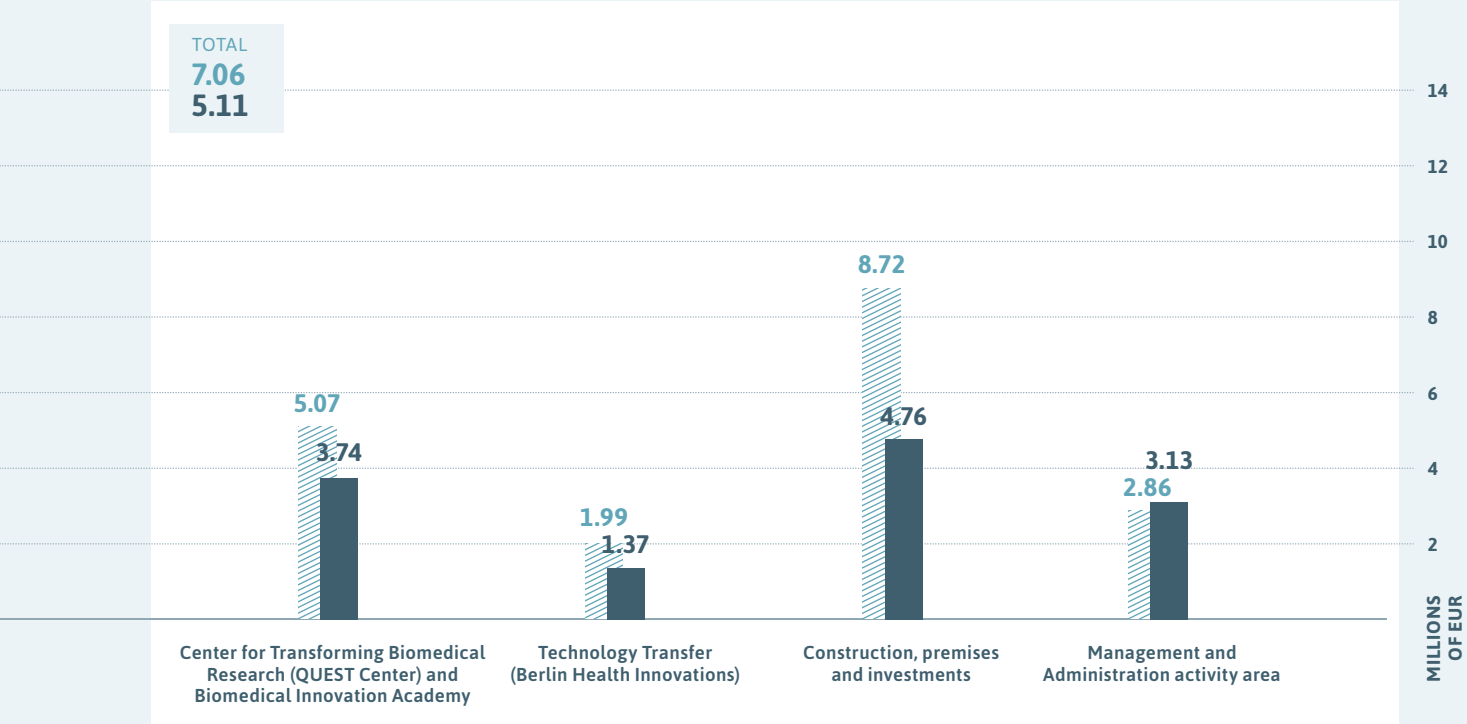


From the funding available, BIH drew down 34.556 million euro in the year 2016, of which 31.25 million euro came from the federal government and 3.307 million euro from the state of Berlin. Of this, Charité received 21.265 million euro, and MDC 9.057 million euro. Furthermore, 2.232 million euro were drawn down by Stiftung Charité and forwarded to the member entities.

Hence, the outflow of funds was significantly lower than specified in the original plan from the year 2012. One of the main reasons for this was the strategy process initiated by the Executive Board, which led to radical changes, namely the abandonment of a »funding agency« approach with a wide range of funding interests to a focus on a small range of fields and the reinforcement of topics identified through new recruitments. After adopting the strategy, implementation and the initiation of the recruitment and appointment processes began immediately in the year 2016.

According to section 3(4) of the BIH Act *(BIG-G)*, 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.

Innovation drivers



4. Personnel 2016

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

As of December 31, 2016, 18 female employees and 8 male employees (a total of 24.87 full time equivalents; figures include the two full-time Executive Board members) were employed at the BIH corporation under public law.

Scientific and clinical personnel; management and administration

As of December 31, 2016, 226.5 FTEs (*full time equivalents*) or 311 persons were being financed by BIH within the research commons (programs, structures, recruiting, management).

Of which	FTEs	Persons
Female	128.61	174
Male	97.9	137

Personnel in research commons (in detail/FTEs)

	FTEs	Definition
Scientists (female)	57.38	Employees who • receive remuneration equivalent at least to *BAT II A* or *TVöD* remuneration group 13, • have a university degree, • have acquired a doctorate or do not wish to pursue a doctorate, • belong to a primarily scientific or scientific/technical organizational unit, • are directly active in advancing science,
Scientists (male)	76.16	
Doctoral students (female)	16.30	Persons who are working on their PhD and using the resources provided for this purpose.
Doctoral students (male)	13.25	
Research assistants (female)	55.93	Employees (e.g. holders of degrees from universities of applied sciences, technical assistants) who are assigned to appointment category I or II or directly to a specific program.
Research assistants (male)	8.49	

5. Organization and committees

Organs and committees of the corporation under public law

By law, the organs of 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. The Supervisory Board convened twice in 2016 (June 29/Nov 2).

5 out of 15 positions on the Supervisory Board are occupied by women (33 percent). The 8 seats for which state equal opportunity laws apply have equal representation from both genders.

↗ *bihealth.org/en/institute/organization/the-supervisory-board/*

Executive Board

There were two personnel changes on the Executive Board in 2016: Rolf Zettl assumed his position as Chief Financial Officer on March 1, 2016. On April 1, 2016, Martin Lohse took up his position as Scientific Director at MDC and hence also a seat on the BIH Executive Board. Thomas Sommer was named as deputy to Martin Lohse for MDC; his previous position was as acting director of MDC.

The percentage of women is 0 percent.

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

Scientific Advisory Board

The Scientific Advisory Board consists of 14 experts. In 2016, the Supervisory Board appointed four new members in total: Alan Shuldiner (Regeneron Genetics Center, Vice President and Co-Head), and at the suggestion of Stiftung Charité Nobel Prize laureate Thomas C. Südhof (Stanford University), both on February 1, 2016, as well as Stefanie Dimmeler (Goethe University, Frankfurt am Main) and Nobel laureate Elizabeth Blackburn (Salk Institute for Biological Studies, La Jolla), who were appointed on December 1, 2016. The Scientific Advisory Board convened twice in 2016 (April 14/15; October 13/14, 2016). The meetings of the Scientific Advisory Board in 2016 focused on the »BIH Strategy 2026« in particular. The new scientific strategy was unanimously welcomed.

6 out of 14 positions are occupied by women (43 percent).

↗ *bihealth.org/en/institute/organization/the-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 MDC as well as between basic and clinical research. The Scientific Committee advises the Executive Board in all research-relevant aspects. The points of focus in 2016 were the »BIH Strategy 2026« and the associated topics of appointment strategy and project funding.

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

↗ *bihealth.org/en/institute/organization/scientific-committee/*

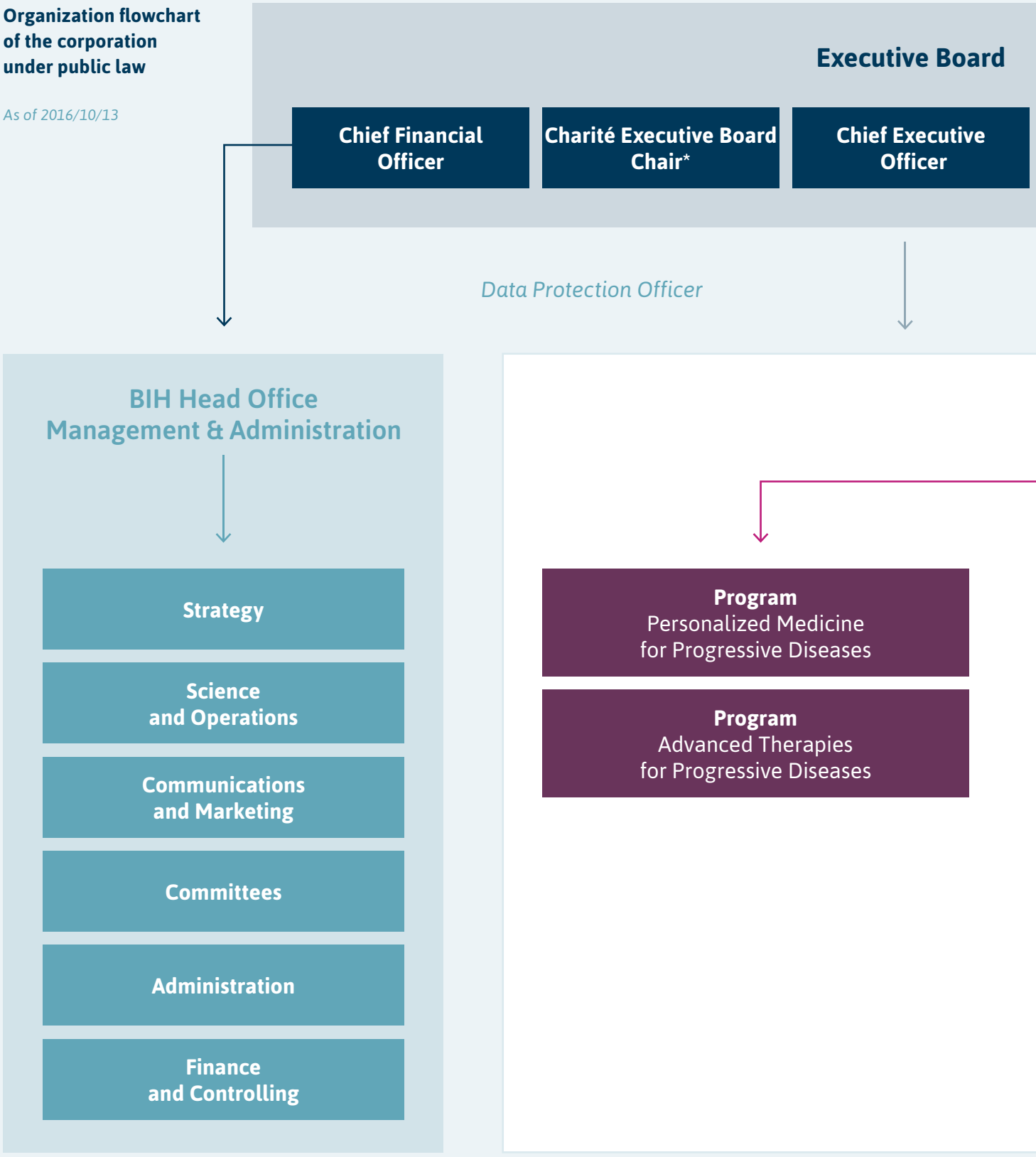
Head Office

As specified in the BIH Act, BIH established a Head Office which is managed by the Chief Financial Officer. The Head Office is based in Berlin-Mitte. It supports the work of the Executive Board in planning and implementing the strategy and is responsible for all administrative procedures associated with research.

↗ *bihealth.org/en/institute/organization/head-office/*

Organization flowchart of the corporation under public law

As of 2016/10/13



Dean of Charité *

Scientific Directorate MDC*

Supervisory Board

Scientific Advisory Board

Anti-Corruption Officer

Research Commons

Research Platform
Digital Medicine

Research Platform
Clinical-Translational Sciences

Research Platform
Multiscale Genomics

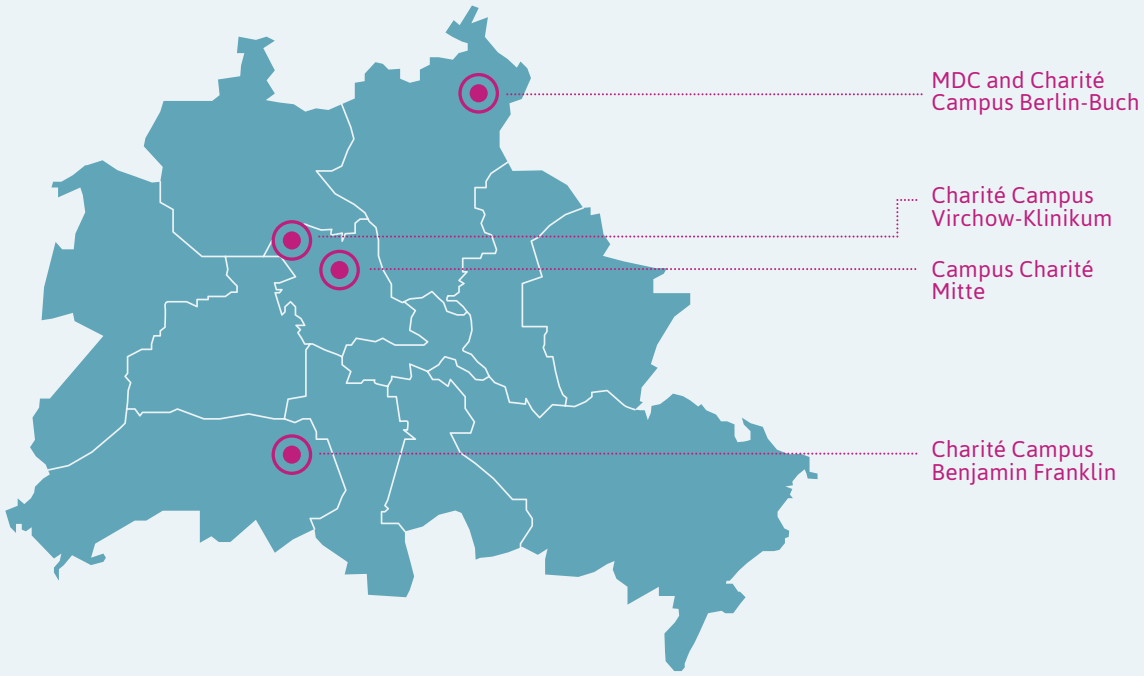
Research Platform
Humanized Model Systems and Cell Engineering

Innovation Driver
Center for Transforming Biomedical Research (QUEST) with BIH Academy

Innovation Driver
Technology Transfer (Berlin Health Innovations)

** Part-time Executive Board members*

6. Sites



7. Scientific performance

7.1 Overview of research projects

During its founding phase, the BIH developed two funding instruments for strengthening translational research between 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 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«.

BIH projects and their terms

In total, BIH finances 50 group leaders and a total of 63 staff positions with the TRG and CRG consortiums. Significantly more researchers and clinicians support the TRG and CRG consortiums via their work, without being funded directly by BIH.

↗ *bihealth.org/en/research/projects/*

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 sub-projects

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

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 sub-projects

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 As 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 sub-projects

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 DiagnOMICS to Precision Medicine: Model Neuroblastoma

Prof. Angelika Eggert and Prof. Matthias Selbach

Principal investigators and sub-projects

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 & 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: TU Munich, where he continues to supervise the project***)***
James Poulet (MDC & 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)

CRU Clinical Research Grants

In early 2016, the Executive Board made a decision regarding the funding of three clinical studies of a translational nature; funding ranging from approx. 250,000 to 500,000 euro was granted for two years.

AdvIm-Treg

First-in-man adoptive regulatory T cell (Treg) therapy in kidney transplant patients – scientific subproject for the Research Grant: advanced immune monitoring of adoptive Treg therapy (AdvIm-Treg).

OPTICO-ACS

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

GESPIC-Crohn

The role of gut microbiota in the development of arthritis phenotype in patients with inflammatory bowel disease: a prospective cohort study.

7.2 Performance indicators

In 2016, BIH developed a comprehensive reporting system. It allows monitoring of project progress and measurement of performance indicators. After a pilot phase for a digital reporting system, the TRG and CRG consortiums submitted their progress reports in spring 2017. The reporting period ranges from the beginning of the respective projects up to January 2017.

Indicator	TRGs	CRGs	Σ
New collaborations with			
MDC or Charité	5	36	41
national institutions	4	10	14
international institutions	4	18	22
Industry	1	6	7
Publications			
Total	14	95	109
Cumulative impact factor	56	864	920
Publications with impact factor > 10	0	19	19
First or last author with BIH affiliation	14	56	70
Open access publications	5	49	54
New technologies in development			
Total	3	14	17
Intellectual property rights			
Reported inventions	0	3	3
Patent applications	0	5	5
Patents granted	0	1	1
Pre-clinical studies			
Total	0	7	7
Clinical studies			
Total	1	6	7
Participants currently included in studies	80	235	315
Planned number of participants	80	2,915	2,995
Academic qualifications			
Bachelor	0	1	1
Master	3	3	6
Dr. med.	2	0	2
Dr. rer. Nat.	2	7	9
PD (Privatdozent)	0	1	1
Professorship	0	2	2
Prizes and awards for project members			
Total	5	6	11
Scientific presentations and posters			
Total	16	87	103

7.3 Recruitments

In order to ensure success when competing internationally, a central principle of the »BIH Strategy 2026« is the recruitment of the brightest minds at every level – from junior (research) group leaders and mid-level career positions to leading researchers. To realize this ambitious goal, a series of new recruitments for BIH Chairs, BIH Professorships, and BIH Junior Research Groups across all of BIH's activity areas was launched during the reporting period and ongoing processes were accelerated, or in some cases were already concluded successfully. Furthermore, a fast-track procedure for the recruitment of BIH Chairs and leading BIH Professorships was established and approved in October 2016 by the BIH Executive Board, as well as by Charité's Faculty Council.

Joint appointments by Charité and BIH

Prof. Andreas Diefenbach
W3 Professorship for Microbiology (BIH Professorship)

Prof. Christian Drosten
W3 Professorship for Virology (BIH Professorship)

W2 professorships for microbiology/microbiome research and virology related to these recruitments have already been initiated. Additional joint appointments accelerated by Charité and BIH in 2016/2017 include the W3 Professorship for Biometry, the W3 Professorship for Academic Innovation, Entrepreneurship and Translational Career Paths, as well as the W3 Professorship for Bioethics in Translation.

The BIH Johanna Quandt Professorships (temporary W2 professorships with a true tenure track) were created in 2015 together with Stiftung Charité and its Private Excellence Initiative Johanna Quandt. This program is aimed specifically at female scientists, and is characterized by particular thematic freedom in the fields of translation and systems medicine. Hence, these professorships provide new impetus for promoting equal opportunity in the life sciences during the establishment phase, which has received little support in the scientific system to date. Originally, the funding of two professorships was planned. However, due to the number of outstanding applicants, Stiftung Charité's Scientific Advisory Board decided to fund four professorships in October 2016. The BIH Executive Board is currently in final talks with three of the four candidates selected to receive funding.

BIH Junior Research Groups

Dr. Birte Kehr
Head of the first genome informatics junior research group since November 2016. Her work focuses on the development of computer-assisted approaches for the analysis of genome sequence data with a focus on the detection of structural variation.

Dr. Martin Kircher
Head of the second junior research group (recruited in 2016; began work in March 2017). His research investigates computer-assisted approaches for the identification of functionally relevant genetic modifications in diseases and adaptations as well as the development of more sensitive diagnosis methods (exome, genome and cell-free DNA sequencing).

7.4 Overview of program participants at BIH Innovation Academy and alumni

Funding instrument	Participants	Percentage of women (%)	Alumni	Percentage of women (%)
Junior Clinician Scientist	43	18 *(42)*	3	2 *(67)*
Clinician Scientist 2015	59	25 *(34)*	21	4 *(19)*
Translational PhD Student	19	13 (68)	0	0 *(0)*
Translational Postdoc	2	1 *(50)*	0	0 *(0)*
Research Grants	11	4 *(36)*	20	8 *(40)*

As of: May 2017

7.5 Overview of BIH Technology Transfer Fund grants in 2016

Call BIH Technology Transfer Fund – Pharma	
Carmen Scheibenbogen *Charité*	Development of diagnostic tests for the detection of disease-specific autoantibodies against acetylcholine receptors
Heiko Funke-Kaiser *Charité*	First-in-class renin/prorenin receptor blockers (RERBs) – target deconvolution of an optimized small molecule compound
Prof. Hendrik Fuchs *Charité*	Development of a platform technology for the manufacture of targeted therapeutic agents in tumor treatment
Christiane Wetzel *MDC*	A STOML1 scaffold as a target to treat metabolic syndrome

Call BIH Technology Transfer Fund – Medical Devices	
Harald Prüß *Charité*	Specific therapeutic apheresis for the treatment of autoimmune encephalitis
Beate Rau *Charité*	Non-invasive optical methods for intraoperative tumor margin detection in visceral surgery
Fikates Panagiotis *Charité*	Stapling of solid organs with edge sealant using the »fish mouth procedure«
Susanne Koch *Charité*	Bedside screening tool for intensive care unit acquired weakness

7.6 Equal opportunity

Building on equal opportunity measures which had previously been successfully implemented, BIH, Charité, and 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 BIH will strive to eliminate structural and inter-actional 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, BIH will be focusing on four key aspects starting in 2017:

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

Contact person: Karin Höhne (BIH)

7.7 Overview of BIH publications in 2016

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. The calculations for the impact factor (IF) are based on the current Journal Citation Report that was published by Thomson Reuters in 2016.

Area	BIH-funded	Academy	Σ
Publications	141	84	225
Cumulative impact factor	1141	434	1575
High-impact publications (IF > 10)	32	9	41
Average impact factor	IF 8.1	IF 5.2	7.0

7.8 List of publications (selection: impact factor > 10)

BIH-funded

Kühnen, P., Clément, K., Wiegand, S., Blankenstein, O., Gottesdiener, K., Martini, L.L., Mai, K., Blume-Peytavi, U., Grüters, A. & Krude, H.
Proopiomelanocortin Deficiency Treated with a Melanocortin-4 Receptor Agonist. New England Journal of Medicine, 2016, doi:10.1056/NEJMoa1512693.

Blankenstein, T.
Receptor combinations hone T-cell therapy. Nat Biotechnol, 2016, doi:10.1038/nbt.3539.

Franke, M., Ibrahim, D.M., Andrey, G., Schwarzer, W., Heinrich, V., Schopflin, R., Kraft, K., Kempfer, R., Jerkovic, I., Chan, W.L., Spielmann, M., Timmermann, B., Wittler, L., Kurth, I., Cambiaso, P., Zuffardi, O., Houge, G., Lambie, L., Brancati, F., Pombo, A., Vingron, M., Spitz, F. & Mundlos, S.
Formation of new chromatin domains determines pathogenicity of genomic duplications. Nature, 2016, doi:10.1038/nature19800.

Wilhelm, K., Happel, K., Eelen, G., Schoors, S., Oellerich, M.F., Lim, R., Zimmermann, B., Aspalter, I.M., Franco, C.A., Boettger, T., Braun, T., Fruttiger, M., Rajewsky, K., Keller, C., Bruning, J.C., Gerhardt, H., Carmeliet, P. & Potente, M.
FOXO1 couples metabolic activity and growth state in the vascular endothelium. Nature, 2016, doi:10.1038/nature16498.

Liepe, J., Marino, F., Sidney, J., Jeko, A., Bunting, D.E., Sette, A., Kloetzel, P.M., Stumpf, M.P., Heck, A.J. & Mishto, M.
A large fraction of HLA class I ligands are proteasome-generated spliced peptides. Science, 2016, doi:10.1126/science.aaf4384.

Matcovitch-Natan, O., Winter, D.R., Giladi, A., Vargas Aguilar, S., Spinrad, A., Sarrazin, S., Ben-Yehuda, H., David, E., Zelada Gonzalez, F., Perrin, P., Keren-Shaul, H., Gury, M., Lara-Astaiso, D., Thaiss, C.A., Cohen, M., Bahar Halpern, K., Baruch, K., Deczkowska, A., Lorenzo-Vivas, E., Itzkovitz, S., Elinav, E., Sieweke, M.H., Schwartz, M. & Amit, I.
Microglia development follows a stepwise program to regulate brain homeostasis. Science, 2016, doi:10.1126/science.aad8670.

Soucie, E.L., Weng, Z., Geirsdottir, L., Molawi, K., Maurizio, J., Fenouil, R., Mossadegh-Keller, N., Gimenez, G., VanHille, L., Beniazza, M., Favret, J., Berruyer, C., Perrin, P., Hacohen, N., Andrau, J.C., Ferrier, P., Dubreuil, P., Sidow, A. & Sieweke, M.H.
Lineage-specific enhancers activate self-renewal genes in macrophages and embryonic stem cells. Science, 2016, doi:10.1126/science.aad5510.

Kieback, E., Hilgenberg, E., Stervbo, U., Lampropoulou, V., Shen, P., Bunse, M., Jaimes, Y., Boudinot, P., Radbruch, A., Klemm, U., Kuhl, A.A., Liblau, R., Hoevelmeyer, N., Anderton, S.M., Uckert, W. & Fillatreau, S.
Thymus-Derived Regulatory T cells Are Positively Selected on Natural Self-Antigen through Cognate Interactions of High Functional Avidity. Immunity, 2016, doi:10.1016/j.immuni.2016.04.018.

Goldmann, T., Wieghofer, P., Jordao, M.J., Prutek, F., Hagemeyer, N., Frenzel, K., Amann, L., Staszewski, O., Kierdorf, K., Krueger, M., Locatelli, G., Hochgerner, H., Zeiser, R., Epelman, S., Geissmann, F., Priller, J., Rossi, F.M., Bechmann, I., Kerschensteiner, M., Linnarsson, S., Jung, S. & Prinz, M.
Origin, fate and dynamics of macrophages at central nervous system interfaces. Nat Immunol, 2016, doi:10.1038/ni.3423.

Sarrazin, S. & Sieweke, M.H.
Eosinophils and masT cells: a lineage apart. Nat Immunol, 2016, doi:10.1038/ni.3446.

Gebala, V., Collins, R., Geudens, I., Phng, L.K. & Gerhardt, H.
Blood flow drives lumen formation by inverse membrane blebbing during angiogenesis in vivo. NaT cell Biol, 2016, doi: 10.1038/ncb3320.

Halle, M., Adams, V., Edelmann, F., Pieske, B. & Wisloff, U.
Benefit of Exercise in Atrial Fibrillation: Diastolic Function Matters! J Am Coll Cardiol, 2016, doi:10.1016/j.jacc.2015.09.115.

Kuhnen, P., Handke, D., Waterland, R.A., Hennig, B.J., Silver, M., Fulford, A.J., Dominguez-Salas, P., Moore, S.E., Prentice, A.M., Spranger, J., Hinney, A., Hebebrand, J., Heppner, F.L., Walzer, L., Grotzinger, C., Gromoll, J., Wiegand, S., Gruters, A. & Krude, H.
Interindividual Variation in DNA Methylation at a Putative POMC Metastable Epiallele Is Associated with Obesity. Cell Metab, 2016, doi:10.1016/j.cmet.2016.08.001.

Mochmann, H.C., Scheitz, J.F., Petzold, G.C., Haeusler, K.G., Audebert, H.J., Laufs, U., Schneider, C., Landmesser, U., Werner, N., Endres, M., Witzenbichler, B., Nolte, C.H. & Grp, T.S.
Coronary Angiographic Findings in Acute Ischemic Stroke Patients With Elevated Cardiac Troponin The Troponin Elevation in Acute Ischemic Stroke (TRELAS) Study. Circulation, 2016, doi:10.1161/Circulationaha.115.018547.

Wetzel, C., Pifferi, S., Picci, C., Gok, C., Hoffmann, D., Bali, K.K., Lampe, A., Lapatsina, L., Fleischer, R., Smith, E.S., Begay, V., Moroni, M., Estebanez, L., Kuhnemund, J., Walcher, J., Specker, E., Neuenschwander, M., von Kries, J.P., Haucke, V., Kuner, R., Poulet, J.F., Schmoranzer, J., Poole, K. & Lewin, G.R.
Small-molecule inhibition of STOML3 oligomerization reverses pathological mechanical hypersensitivity. Nat Neurosci, 2016, doi:10.1038/nn.4454.

Jakob, P., Kacprowski, T., Briand-Schumacher, S., Heg, D., Klingenberg, R., Stahli, B.E., Jaguszewski, M., Rodondi, N., Nanchen, D., Raber, L., Vogt, P., Mach, F., Windecker, S., Volker, U., Matter, C.M., Luscher, T.F. & Landmesser, U.
Profiling and validation of circulating microRNAs for cardiovascular events in patients presenting with ST-segment elevation myocardial infarction. Eur Heart J, 2016, doi:10.1093/eurheartj/ehw563.

Landmesser, U., John Chapman, M., Farnier, M., Gencer, B., Gielen, S., Hovingh, G.K., Luscher, T.F., Sinning, D., Tokgozoglu, L., Wiklund, O., Zamorano, J.L., Pinto, F.J., Catapano, A.L.
European Society of, C. & the European Atherosclerosis, S., European Society of Cardiology/European Atherosclerosis Society Task Force consensus statement on proprotein convertase subtilisin/kexin type 9 inhibitors: practical guidance for use in patients at very high cardiovascular risk. Eur Heart J, 2016, doi:10.1093/eurheartj/ehw480.

Simandi, Z., Horvath, A., Wright, L.C., Cuaranta-Monroy, I., De Luca, I., Karolyi, K., Sauer, S., Deleuze, J.F., Gudas, L.J., Cowley, S.M. & Nagy, L.
OCT4 Acts as an Integrator of Pluripotency and Signal-Induced Differentiation. Mol Cell, 2016, doi:10.1016/j.molcel.2016.06.039.

Leisegang, M., Kammertoens, T., Uckert, W. & Blankenstein, T.
Targeting human melanoma neoantigens by T cell receptor gene therapy. J Clin Invest, 2016, doi:10.1172/JCI83465.

Richter, M., Saydaminova, K., Yumul, R., Krishnan, R., Liu, J., Nagy, E.E., Singh, M., Izsvak, Z., Cattaneo, R., Uckert, W., Palmer, D., Ng, P., Haworth, K.G., Kiem, H.P., Ehrhardt, A., Papayannopoulou, T. & Lieber, A.
In vivo transduction of primitive hematopoietic stem cells after mobilization and intravenous injection of integrating adenovirus vectors. Blood, 2016, doi:10.1182/blood-2016-04-711580.

Richter, M., Saydaminova, K., Yumul, R., Krishnan, R., Liu, J., Nagy, E.E., Singh, M., Izsvak, Z., Cattaneo, R., Uckert, W., Palmer, D., Ng, P., Haworth, K.G., Kiem, H.P., Ehrhardt, A., Papayannopoulou, T. & Lieber, A.
In vivo transduction of primitive mobilized hematopoietic stem cells after intravenous injection of integrating adenovirus vectors. Blood, 2016, doi:10.1182/blood-2016-04-711580.

Louwersheimer, E., Wolfsgruber, S., Espinosa, A., Lacour, A., Heilmann-Heimbach, S., Alegret, M., Hernandez, I., Rosende-Roca, M., Tarraga, L., Boada, M., Kornhuber, J., Peters, O., Frolich, L., Hull, M., Ruther, E., Wiltfang, J., Scherer, M., Riedel-Heller, S., Jessen, F., Nothen, M.M., Maier, W., Koene, T., Scheltens, P., Holstege, H., Wagner, M., Ruiz, A., van der Flier, W.M., Becker, T. & Ramirez, A.
Alzheimer's disease risk variants modulate endophenotypes in mild cognitive impairment. Alzheimers Dement, 2016, doi:10.1016/j.jalz.2016.01.006.

Przybyl, L., Haase, N., Golic, M., Rugor, J., Solano, M.E., Arck, P.C., Gauster, M., Huppertz, B., Emontzpohl, C., Stoppe, C., Bernhagen, J., Leng, L., Bucala, R., Schulz, H., Heuser, A., Weedon-Fekjaer, M.S., Johnsen, G.M., Peetz, D., Luft, F.C., Staff, A.C., Muller, D.N., Dechend, R. & Herse, F.
CD74-Downregulation of Placental Macrophage-Trophoblastic Interactions in Preeclampsia. Circ Res, 2016, doi:10.1161/CIRCRESAHA.116.308304.

Viola, J.R., Lemnitzer, P., Jansen, Y., Csaba, G., Winter, C., Neideck, C., Silvestre-Roig, C., Dittmar, G., Doring, Y., Drechsler, M., Weber, C., Zimmer, R., Cenac, N. & Soehnlein, O.
Resolving Lipid Mediators Maresin 1 and Resolvin D2 Prevent Atheroprogression in Mice. Circ Res, 2016, doi:10.1161/CIRCRESAHA.116.309492.

Baufeld, C., Osterloh, A., Prokop, S., Miller, K.R. & Heppner, F.L.
High-fat diet-induced brain region-specific phenotypic spectrum of CNS resident microglia. Acta Neuropathol, 2016, doi:10.1007/s00401-016-1595-4.

Arumughan, A., Roske, Y., Barth, C., Forero, L.L., Bravo-Rodriguez, K., Redel, A., Kostova, S., McShane, E., Opitz, R., Faelber, K., Rau, K., Mielke, T., Daumke, O., Selbach, M., Sanchez-Garcia, E., Rocks, O., Panakova, D., Heinemann, U. & Wanker, E.E.
Quantitative interaction mapping reveals an extended UBX domain in ASPL that disrupts functional p97 hexamers. Nat Commun, 2016, doi:10.1038/ncomms13047.

Grabundzija, I., Messing, S.A., Thomas, J., Cosby, R.L., Bilic, I., Miskey, C., Gogol-Doring, A., Kapitonov, V., Diem, T., Dalda, A., Jurka, J., Pritham, E.J., Dyda, F., Izsvak, Z. & Ivics, Z.
A Helitron transposon reconstructed from bats reveals a novel mechanism of genome shuffling in eukaryotes. Nat Commun, 2016, doi:10.1038/ncomms10716.

Van Haute, L., Dietmann, S., Kremer, L., Hussain, S., Pearce, S.F., Powell, C.A., Rorbach, J., Lantaff, R., Blanco, S., Sauer, S., Kotzaeridou, U., Hoffmann, G.F., Memari, Y., Kolb-Kokocinski, A., Durbin, R., Mayr, J.A., Frye, M., Prokisch, H. & Minczuk, M.
Deficient methylation and formylation of mt-tRNA(Met) wobble cytosine in a patient carrying mutations in NSUN3. Nat Commun, 2016, doi:10.1038/ncomms12039.

Voigt, F., Wiedemann, L., Zuliani, C., Querques, I., Sebe, A., Mates, L., Izsvak, Z., Ivics, Z. & Barabas, O.
Sleeping Beauty transposase structure allows rational design of hyperactive variants for genetic engineering. Nat Commun, 2016, doi:10.1038/ncomms11126.

Kandalla, P.K., Sarrazin, S., Molawi, K., Berruyer, C., Redelberger, D., Favel, A., Bordi, C., de Bentzmann, S. & Sieweke, M.H.
M-CSF improves protection against bacterial and fungal infections after hematopoietic stem/progenitor cell transplantation. J Exp Med, 2016, doi:10.1084/jem.20151975.

Textor, A., Schmidt, K., Kloetzel, P.M., Weissbrich, B., Perez, C., Charo, J., Anders, K., Sidney, J., Sette, A., Schumacher, T.N., Keller, C., Busch, D.H., Seifert, U. & Blankenstein, T.
Preventing tumor escape by targeting a post-proteasomal trimming independent epitope. J Exp Med, 2016, doi:10.1084/jem.20160636.

Wallmeier, J., Shiratori, H., Dougherty, G.W., Edelbusch, C., Hjeij, R., Loges, N.T., Menchen, T., Olbrich, H., Pennekamp, P., Raidt, J., Werner, C., Minegishi, K., Shinohara, K., Asai, Y., Takaoka, K., Lee, C., Griese, M., Memari, Y., Durbin, R., Kolb-Kokocinski, A., Sauer, S., Wallingford, J.B., Hamada, H. & Omran, H.
TTC25 Deficiency Results in Defects of the Outer Dynein Arm Docking Machinery and Primary Ciliary Dyskinesia with Left-Right Body Asymmetry Randomization. Am J Hum Genet, 2016, doi:10.1016/j.ajhg.2016.06.014.

Academy

Wenger, N., Moraud, E.M., Gandar, J., Musienko, P., Capogrosso, M., Baud, L., Le Goff, C.G., Barraud, Q., Pavlova, N., Dominici, N., Minev, I.R., Asboth, L., Hirsch, A., Duis, S., Kreider, J., Mortera, A., Haverbeck, O., Kraus, S., Schmitz, F., DiGiovanna, J., van den Brand, R., Bloch, J., Detemple, P., Lacour, S.P., Bezard, E., Micera, S. & Courtine, G.
Spatiotemporal neuromodulation therapies engaging muscle synergies improve motor control after spinal cord injury. Nat Med, 2016, doi:10.1038/nm.4025.

Belard, S. & Kurth, F.
Pyronaridine-artesunate retreatment for malaria. Lancet Infect Dis, 2016, doi:10.1016/S1473-3099(15)00353-9.

Mochmann, H.C., Scheitz, J.F., Petzold, G.C., Haeusler, K.G., Audebert, H.J., Laufs, U., Schneider, C., Landmesser, U., Werner, N., Endres, M., Witzenbichler, B., Nolte, C.H. & Group, T.S.
Coronary Angiographic Findings in Acute Ischemic Stroke Patients With Elevated Cardiac Troponin: The Troponin Elevation in Acute Ischemic Stroke (TRELAS) Study. Circulation, 2016, doi:10.1161/CIRCULATIONAHA.115.018547.

Uluckan, O., Jimenez, M., Karbach, S., Jeschke, A., Grana, O., Keller, J., Busse, B., Croxford, A.L., Finzel, S., Koenders, M., van den Berg, W., Schinke, T., Amling, M., Waisman, A., Schett, G. & Wagner, E.F.
Chronic skin inflammation leads to bone loss by IL-17-mediated inhibition of Wnt signaling in osteoblasts. Sci Transl Med, 2016, doi:10.1126/scitranslmed.aad8996.

Moraud, E.M., Capogrosso, M., Formento, E., Wenger, N., DiGiovanna, J., Courtine, G. & Micera, S.
Mechanisms Underlying the Neuromodulation of Spinal Circuits for Correcting Gait and Balance Deficits after Spinal Cord Injury. Neuron, 2016, doi:10.1016/j.neuron.2016.01.009.

Young, E., Noerenberg, D., Mansouri, L., Ljungstrom, V., Frick, M., Sutton, L.A., Blakemore, S.J., Galan-Sousa, J., Plevova, K., Baliakas, P., Rossi, D., Clifford, R., Roos-Weil, D., Navrkalova, V., Dorken, B., Schmitt, C.A., Smedby, K.E., Juliusson, G., Giacopelli, B., Blachly, J.S., Belessi, C., Panagiotidis, P., Chiorazzi, N., Davi, F., Langerak, A.W., Oscier, D., Schuh, A., Gaidano, G., Ghia, P., Xu, W., Fan, L., Bernard, O.A., Nguyen-Khac, F., Rassenti, L., Li, J., Kipps, T.J., Stamatopoulos, K., Pospisilova, S., Zenz, T., Oakes, C.C., Strefford, J.C., Rosenquist, R. & Damm, F.
EGR2 mutations define a new clinically aggressive subgroup of chronic lymphocytic leukemia. Leukemia, 2016, doi:10.1038/leu.2016.359.

Mansouri, L., Noerenberg, D., Young, E., Mylonas, E., Abdulla, M., Frick, M., Asmar, F., Ljungstrom, V., Schneider, M., Yoshida, K., Skaftason, A., Pandzic, T., Gonzalez, B., Tasidou, A., Waldhueter, N., Rivas-Delgado, A., Angelopoulou, M., Ziepert, M., Arends, C.M., Couronne, L., Lenze, D., Baldus, C.D., Bastard, C., Okosun, J., Fitzgibbon, J., Dorken, B., Drexler, H.G., Roos-Weil, D., Schmitt, C.A., Munch-Petersen, H.D., Zenz, T., Hansmann, M.L., Strefford, J.C., Enblad, G., Bernard, O.A., Ralfkiaer, E., Erlanson, M., Korkolopoulou, P., Hultdin, M., Papadaki, T., Gronbaek, K., Lopez-Guillermo, A., Ogawa, S., Kuppers, R., Stamatopoulos, K., Stavroyianni, N., Kanellis, G., Rosenwald, A., Campo, E., Amini, R.M., Ott, G., Vassilakopoulos, T.P., Hummel, M., Rosenquist, R. & Damm, F.
Frequent NFKBIE deletions are associated with poor outcome in primary mediastinal B-cell lymphoma. Blood, 2016, doi:10.1182/blood-2016-03-704528.

Eccles, R.L., Czajkowski, M.T., Barth, C., Muller, P.M., McShane, E., Grunwald, S., Beaudette, P., Mecklenburg, N., Volkmer, R., Zuhlke, K., Dittmar, G., Selbach, M., Hammes, A., Daumke, O., Klussmann, E., Urbe, S. & Rocks, O.
Bimodal antagonism of PKA signalling by ARHGAP36. Nat Commun, 2016, doi:10.1038/ncomms12963.

Ejaz, S., Emmrich, J.V., Sitnikov, S.L., Hong, Y.T., Sawiak, S.J., Fryer, T.D., Aigbirhio, F.I., Williamson, D.J. & Baron, J.C.
Normobaric hyperoxia markedly reduces brain damage and sensorimotor deficits following brief focal ischaemia. Brain, 2016, doi:10.1093/brain/awv391.

8. Private Excellence Initiative Johanna Quandt: Funding decisions in 2016

With the Private Excellence Initiative Johanna Quandt, Stiftung Charité funds the establishment and further development of BIH in order to support Berlin in its endeavor to become an international beacon in life sciences and medicine. By doing so, it contributes significantly to translational health research in Berlin. For the Private Excellence Initiative, Johanna Quandt made available special 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 funding programs. Ten of these programs focus on funding individual persons. Three other programs are used to 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.

Overview of program lines

Funding of individuals	
Einstein BIH Visiting Fellows *in collaboration with Einstein Foundation Berlin*	Recruitment of leading researchers from overseas for continuous, concurrent activities at 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 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 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 BIH *for postdoctoral researchers and experienced scientists (in collaboration with the Alexander von Humboldt Foundation)*	Recruitment of early-career scientists and established researchers from overseas for an assignment at 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 cientific 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 BIH for the long-term establishment of an independent research unit (max. 5 years)
Deutschlandstipendium	Funding of students at 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 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 BIH

Overview of funding decisions in 2016

Host	Fellow	Research project
Einstein BIH Visiting Fellows *in collaboration with Einstein Foundation Berlin*		
Prof. Christian Spahn & PD Dr. Peter Hildebrand *Charité*	***Prof. Brian Kobilka*** *Stanford University, USA*	In silico GPCR: A computational microscope to determine receptor – G protein coupling specificity and functional selectivity
Prof. Helmut Kettenmann *MDC*	***Prof. David Gutmann*** *Washington University – School of Medicine, St. Louis, USA*	Biology and treatment strategies of low-grade gliomas
Prof. Ana Pombo *MDC*	***Prof. Mario Nicodemi*** *University of Naples, Italy*	Understanding chromatin folding and gene regulation in disease associated genomic rearrangements
Prof. Johann Pratschke *Charité*	***Prof. Stefan Guenther Tullius*** *Harvard Medical School, USA*	Vascular Composite Tissue Allotransplantation (VCA): An integrated, multidisciplinary Basic and Clinical Research Program for abdominal wall, hand, and uterus transplantation
Prof. Georg N. Duda *Julius Wolff Institut & BSRT*	***Prof. David J. Mooney*** *Harvard University, USA*	Biomaterial based strategies to stimulate in situ tissue formation for bone and muscle regeneration

BIH Visiting Professors

Prof. Dietmar Schmitz *Charité*	***Prof. Hannah Monyer*** *Heidelberg University and German Cancer Research Center (DKFZ)*	Inhibition in the context of cortical columnar organization
Prof. Gerd-R. Burmester *Charité*	***Prof. Steffen Gay*** *University of Zurich, Switzerland*	Development of Novel Biomarkers for the Detection of Response to anti-rheumatic drugs
Prof. Holger Gerhardt *MDC*	***PD Michael Potente*** *Max Planck Institute for Heart and Lung Research, Bad Nauheim*	Mechanisms of vessel size regulation – role of YAP/TAZ signaling

BIH Short-Term Fellows

Prof. Kay Raum *Berlin-Brandenburg Center for Regenerative Therapies (BCRT)*	***Juan Du*** *University Minnesota, USA*	Ultrasound contrast agents for cortical vascular porosity assessment

Humboldt Research Fellowships at BIH
(in collaboration with the Alexander von Humboldt Foundation)

Prof. Volker Hess *Charité*	***Dr. Darren Wagner, McGill University****, Montreal, Canada*	Animal Spirits to Electric Shocks: A Revolution in Enlightenment Neurology in Cultural Context

BIH Clinical Fellows

Dr. Necip Torun *Charité*		Investigation of alternative therapy strategies for the treatment of corneal endothelial diseases

Deutschlandstipendium

Luisa Albert, Marco Nikolas Andreas, Stefan Appelhaus, Khairi Ben Ltaief, Sophie Bienia, Georg Bölke, Karl Busch-Petersen, Wei-long Dennis Chen, Ramazan Dag, Ricardo Donners, Norman Drzeniek, Lisa Ehlers, Lilian Jo Engelhardt, Jan-Frederik Fischer, Jacob Gohlisch, Paola Gozz, Franziska Greiß, Franziska Hentschel, Doreen Herinek, Samaa Hijazi, Meltem Ivren, Lisa Johann, Kasra Karimi, Lennart Kay, Felix Kleefeld, Philine Köln, Christin Kupper, Jonas Alexander Leppig, Anne-Kathrin Mareike Loer, Dörte Löffler, Tom Malysch, Joel Melcop, Till Fabian Mertens, Desiree Mohrbach, Jonas Muallah, Miriam Müller, Henning Plage, Katrin Repkow, Kristina Marie Rieger, Stanislav Rosnev, Tarik Alp Sargut, Helen Schmidt, Dr. Jana Marie Schwarz, Kim Natalie Sollte, Stefka Stoyanova, Christopher Tacke, Arne Thiele, Ipek Tiryaki, Naomi Maria Mei-Lien Tjiang, Leopold Vorwerk, Gabriele Weiß, Marcel Wittenberg, Daniela Zurkan

Imprint

Published by
Berlin Institute of Health/
Berliner Institut für Gesundheitsforschung (BIH)
Anna-Louisa-Karsch-Str. 2 | 10178 Berlin
www.bihealth.org
@berlinnovation

Representative
Alexandra Hensel
(Head of Communications and Marketing)

Last update
June 2017

Design
NORDSONNE IDENTITY
www.nordsonne.de

Image editing
Peter Hansen

Printing
trigger.medien.gmbh

Image credits
Title page: BIH/Christian Kruppa

Page 4: Martin Lohse: Nikolaus Brade
Rolf Zettl: Helmholtz Association/
David Ausserhofer
John P.A. Ioannidis: BIH/Marvin Güngör

Page 5: July: BIH/Stefan Zeitz; BIH/Thomas Rafalzyk
August: BIH/Thomas Rafalzyk
September: BIH/Thomas Rafalzyk
November: Andreas Diefenbach

Page 6+7: Erwin Böttinger: BIH/Thomas Rafalzyk
Rolf Zettl: Helmholtz Association/
David Ausserhofer
Karl Max Einhäupl: BIH/Tom Maelsa
Axel Radlach Pries:
Charité – Universitätsmedizin Berlin
Martin Lohse: Nikolaus Brade

Page 9+11: BIH/Christian Kruppa

Page 10: Werner Huthmacher

Page 14, 22, 28, 30, 34-35, 36, 39, 41, 49, 50, 51:
BIH/Thomas Rafalzyk

Page 23: Neo-TADs, Max Planck Institute of Molecular Genetics, Berlin

Page 25, 43: labfolder

Page 26: Petra Ritter

Page 27: I. M. Sauer/Department of Surgery CCM, CVK, Charité

Page 40: BIH/Stefan Zeitz

Page 42: Ulrich Dirnagl

Page 43: labfolder

Page 44/45: Thorsten Kasper

Page 49: fotolia

With funding from

Federal Ministry of Education and Research

be Berlin

STIFTUNG CHARITÉ


CHARITÉ
UNIVERSITÄTSMEDIZIN BERLIN
MDC
MAX DELBRÜCK CENTER
FOR MOLECULAR MEDICINE
IN THE HELMHOLTZ ASSOCIATION