

Berlin Institute of Health (BIH)

BIH: From Research to Health

Mission

The mission of the BIH is translational medicine. The BIH aims to translate insights from biomedical research into novel approaches to personalized prediction, prevention, diagnosis, and therapy, and conversely to develop new research approaches based on clinical observations. The goal is to generate significant medical benefits for patients.

Challenges

Health care systems in Germany and worldwide face some major challenges. Aging populations mean more and more patients, as well as fewer and fewer doctors and nurses. Concurrently, medical research is delivering a steady stream of new research findings. Similarly, digitalization promises to make great strides by exploiting the insights gained by linking together information from diverse sources.

There are many diseases for which there are still no effective long-term treatments. Consequently, medicine needs to get a lot better at translating laboratory results into real clinical applications. Conversely, it also needs to get a lot faster at transferring clinical observations back into the laboratory. The BIH's core role and mission lies in this translational medicine process.

Berlin is the perfect place to pursue this mission. As Europe's largest university hospital, the Charité is home to outstanding biomedical research by a plethora of university and non-university research groups, boasts clinical excellence in almost all fields of medicine, and houses an extraordinarily broad spectrum of patients. In terms of the biomedical ecosystem needed for successfully developing novel diagnostics, preventive measures, and treatment, every element is in place.

Translational medicine

At present, successful outcomes from efforts to turn innovative approaches into clinical applications are few and far between – it takes too long and costs too much. One of the key reasons for this is that translational medicine requires significant infrastructure, a wide range of technologies, and the involvement of multiple professions with a wide range of different skills all working towards a common goal.

The BIH is convinced that translational medicine can't simply be split into basic science on one side and clinical implementation on the other. On the contrary, it calls for teams with a translational focus both in the clinic and in the laboratory. It needs clinical staff working with patients to identify medical needs, and to work with scientists in-

involved in basic research to develop and jointly test research approaches and therapy concepts rooted in sound pathophysiology. In order to foster a translational mindset, this kind of collaboration is essential.

A systems medicine approach

Most chronic diseases occur when processes fail which affect the body as a whole. These include, for example, problems involving the innate immune defenses, inflammatory processes, circulation, or tissue regeneration caused by injury or degenerative processes. Consequently, the BIH pursues an organ-independent systems medicine approach, focusing on interdisciplinary topics such as digital medicine and cell therapy, and non-organ-specific approaches such as cardiology and oncology.

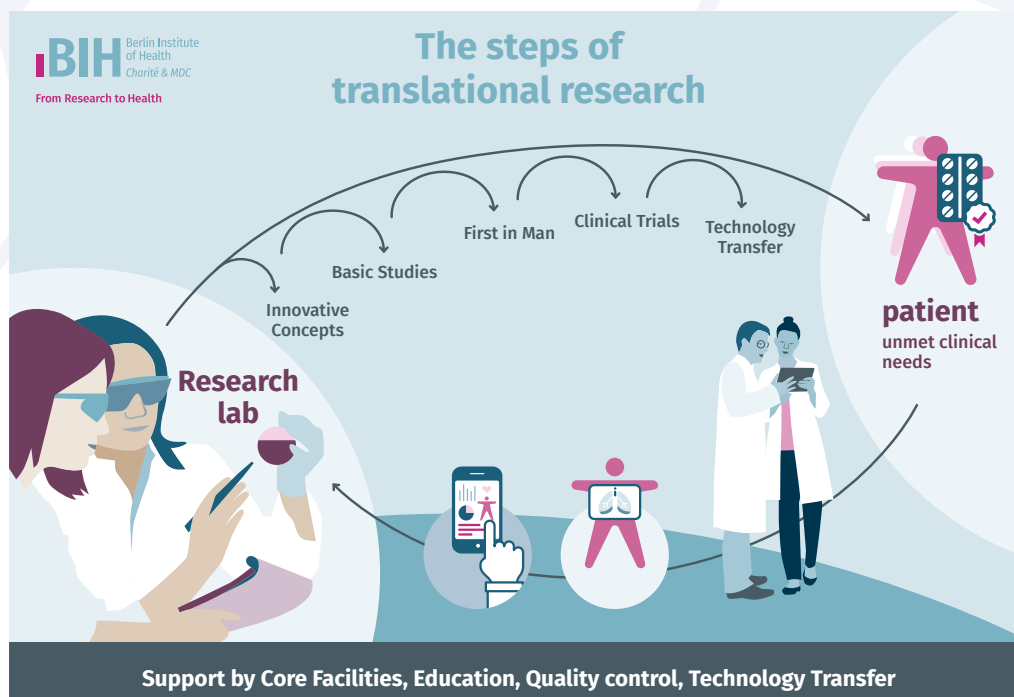
To enhance the efficacy of its translational activities, BIH partners with the Charité – which carries out an enormous range of clinical and scientific activities – and, for developing technologies and approaches involving entirely novel mechanisms, with the Max Delbrück Center. This enables staff from all three organizations to share information and ideas freely, and ensures that the key elements of innovation, hospital, and implementation are available on site, with no institutional barriers. This is a particular advantage in the case of clinical data, which can be used for research while maintaining the highest level of data protection. The translational science community at the BIH encompasses medical professionals, scientists involved in basic research, innovators, engineers, digital experts, data scientists, business developers, entrepreneurs, businesses, health system experts, users, and, in particular, patients.

Implementation within the BIH

To achieve its mission, the BIH's translational ecosystem is based on three components: **innovation enablers**, **translational hubs** and **focus areas**. These three components all support the translational process in different ways. They are highly complementary and help implement specific projects with high innovation and translational potential. While developing the translational environment is an ongoing task involving the faculty as a whole, the focus areas are driven by experts in the relevant translational fields and continuously adapt to new scientific and clinical developments.

Innovation enablers

The ecosystem is based on everyone involved having a translational mindset, and support from the faculty at all stages of the translational process. Developing this is the job of the BIH's innovation enablers. The **BIH Academy**



provides ongoing support for doctors and scientists with skills relevant to and an interest in translational medicine, designs tailored training programs for them, and defines translational career paths for clinician scientists. The **BIH-QUEST Center** develops and implements new approaches aimed at ensuring the quality and sustainability of research and development at all points in the translational value chain. **BIH-Translations-Booster** develops mechanisms and incentives for overcoming obstacles along the translational value chain. **BIH-Innovations** supports targeted early-stage transformation of innovative ideas into products and clinical services at all levels of the translational process.

In an academic environment, translational activities are usually focused on identifying whether new concepts and ideas are amenable to scientific and clinical implementation. But such a narrow view often results in project failure in later project phases and high resource use. BIH-Innovations and BIH-Translations-Booster scrutinize concepts with high translational potential at an early stage to deter-

mine whether there are any technological, legal, financial or organizational barriers to implementation. This 'decide early' principle enables us to launch a large number of innovative, high-risk projects within our translational ecosystem.

The services and offerings provided by innovation enablers are available to all members of the scientific community.

Translational hubs

Translational hubs represent topics and technologies that, over the next few years, are set to revolutionize broad swaths of medicine, and which are capable of making a significant contribution to BIH's translational mission and to improving clinical options for patients.

The **Digital Medicine** translational hub facilitates the exploitation of data-focused concepts, **Multi-omics** concentrates on high quality phenotyping, and **Organoids & Cell Engineering** facilitates the use of selective modulation of cells and 3D organoids for innovative precision medicine

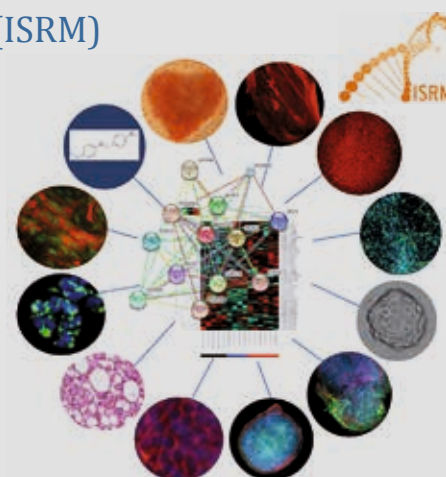
Institute for Stem Cell Research and Regenerative Medicine (ISRM)

Regenerative Medicine at a glance

At the institute for stem cell research and regenerative medicine we adopt a systems biology approach to better understand normal development (hepatogenesis, neurogenesis and nephrogenesis), ageing and disease mechanisms (Steatosis/Non Alcoholic Fatty Liver Disease, Alzheimer's Disease, Nijmegen Breakage Syndrome, Crigler-Najjar Syndrome and Acute Kidney Injury). We are actively involved in the EU/FP7 funded project AgedBrainSYSBIO (<http://agedbrainsysbio.eu/>) where we study mechanisms underlying late onset Alzheimer's Disease (LOAD). Mechanisms underlying the induction and maintenance of pluripotency and

the derivation of patient specific induced pluripotent stem cells (iPSCs) **differentiated into relevant cells types (2D and 3D) are core to these efforts.** Omics-based datasets (transcriptome, proteome, methylome and secretome) Bioinformatics, mathematically modeling, pathway reconstruction and data management are central to our research.

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applications. Research and development in these fields is supported by effective translational research at the **Clinical Translation** translational hub. The goal of the hubs is to facilitate networking between experts and build a research community, develop innovative technologies and methods, and provide outstanding scientific services (core facilities).

Focus areas

The role of the focus areas within the translational ecosystem is to implement specific translational research and development projects. The BIH has established three focus areas, each of which uses different elements of the BIH's translational value chain. These are

- **Regenerative Therapies**
- **Vascular Biomedicine**
- **Single Cell Technologies for Personalized Medicine**

The significance of the selected fields and the excellence of the staff involved, both directly and in a coordinating role, is made clear by the fact that two of these fields (regenerative therapies and single cell technologies for personalized medicine) made the final shortlist of six concepts – from right across the scientific spectrum – for consideration for European FET Flagship status. Focus areas are fundamentally dynamic and are continually adapted in response to scientific, technological, and translational developments.

In addition, to leverage its dynamics, the BIH has also set up an **Excellence Fund**. This provides time-limited funding for high risk, high potential projects. If they can demonstrate medical value during this time, they are much more likely to be able to secure external funding.

MultiPL*i* the FIRST virally inactivated human platelet lysate on the market



SAFETY

EFFICIENCY

STANDARDIZATION

QUALITY

Results consistency for stem cell expansion in defined, standardized and xeno-free conditions represents a major challenge for cell therapy. For that reason, we developed a complete range of human platelet lysate including a new sub-range VIRALLY INACTIVATED : **MultiPL*i***, that meets the requirements of adventitious agent transmission reduction (General Chapter 5.2.12.4 of the European Pharmacopeia).

For more information, visit our dedicated MultiPL*i* website: <https://platelet-lysate.macopharma.com>

Please contact your local sales team or Maco Pharma International GmbH to enquire about products' availability in your country. This product is not available for sale in all countries.

Digital approaches within a translational ecosystem can be used to develop medical options for patients relatively quickly. The **Digital Health Accelerator** at BIH-Innovations, for example, supports digital start-ups right from identification of innovation potential, through the development process, and on to exploitation (via licensing, a spin-off, a commercial partnership, etc.).

How does the BIH measure success?

It is not possible to measure the success of translational research in terms of the number of publications. In addition, this success can't generally be attributed to a specific individual. Specific criteria for measuring the success of translational projects need to be defined, as do new principles for evaluating scientists working in the translational medicine field.

The mission of the BIH focuses on medical benefit to patients. Any performance indicators used need to reflect this fact. Direct indicators meeting this objective include:

- the launch of new preventive, diagnostic, or therapeutic procedures
- products and product launches
- changes to treatment guidelines
- income from commercial exploitation (licenses, sales, etc.)

These can only be measured at the end of a successful translational project – a long time after the key preparatory stages. These early stages are, however, an essential element of the translational process, and can also be measured more immediately. It follows that they too need to

be evaluated and incentivized. Mechanisms include proof of principle studies, manufacturing permits, first in human and IIT trials, actually commercialized patents, licenses, spin-offs, and relevant partnerships.

Also relevant to the BIH's strategy are indicators designed to assess quality and sustainability at all levels of translational activity, such as open access publications, data disclosure, and publication of negative results or confirmatory studies. Over the last few years, the BIH-QUEST Center has, on behalf of the BIH and Charité, launched significant initiatives which have, for example, resulted in a significant increase in open data publications and have achieved national and international recognition.

To further develop translational structures and mechanisms, in 2019 BIH became the first organization from continental Europe to partner with the Wellcome Trust. That partnership is focused on developing performance indicators and incentives for the various stages of the translational process, and for the different fields and people within the translational ecosystem.

Outlook

The above structure means that the BIH represents a completely new type of scientific institution. From 2021 the BIH will be integrated into the Charité, making it a model for direct federal funding for higher education institutions. Integration with the Charité will enable the BIH to redesign translational medicine from scratch and pursue it with a new sense of purpose. We are confident that we will succeed in this venture – for the benefit of patients everywhere.

Berlin-Brandenburger Centrum für Regenerative Therapien (BCRT)

BIH Regeneration
BIH Center for Regenerative Therapies (BCRT)

The BIH Center for Regenerative Therapies (BCRT) is an interdisciplinary translational center with the goal of enhancing endogenous regeneration by cells, biomaterials, and factors which can be used to develop and implement innovative therapies and products. At the BCRT clinicians and researchers are working closely together on a personalized medicine that depends on the early recognition of patients' individual healing potential. The primary focus of the BCRT is on diseases of the immune system, the musculoskeletal system, and the cardiovascular

system supported by the interdisciplinary fields of tissue homeostasis & cachexia and molecular analysis/rare diseases for which currently only unsatisfactory treatment options are available. According to our results, the analysis and control of inflammation/immunity plays a key role in the successful restoration of tissue homeostasis. Early cooperation with industry, health insurers and regulatory authorities as well as other external partners boosts the chances of innovation and exploitation opportunities of new methods and provides access to flexible financing options.



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Photo: Peer Schröder