Berlin Institute of Health

Mission and Implementation

bihealth.org

BIH Berlin Institute of Health
Charité & MDC

Turning Research into Health.

Executive Summary

The mission of the Berlin Institute of Health is medical translation. To this aim, BIH establishes a comprehensive Translational Ecosystem with the clinical environment of Charité, in which experts jointly develop effective therapies, innovative diagnostics, and strategies for individual disease prevention for patients and citizens.

BIH's approach focuses on disease processes arising from the interaction of various organs and systems in the body. The research and development initiatives at BIH therefore specifically address cross-cutting issues (e.g. digital medicine, cell-based therapies) and are not organ-specific (e.g. cardiology, cancer research).

The Translational Ecosystem of BIH is a catalyst for cultural change in biomedical research, establishing innovative structures, incentives and new models for cooperation. This includes the following components:

The Innovation Enablers

create the underlying structures for a translational environment and the mindset for all involved in this process. In order to achieve this, they establish incentives and mechanisms and they support the faculty through all the phases of the translation process.

The Focus Areas

implement concrete translational research and development projects which have a high potential for success in translation, using systems medicine approaches to deal with medical questions.

The Translation Hubs

pool topics and technologies that will revolutionize medicine across disciplines in the years ahead. The hubs develop state-of-the-art technology, further improve it, and connect the community of the participating institutions that make these technologies available for translation.

The Excellence Fund

attracts important expertise to BIH for specific goals and networks BIH with national and international players in translational research.

At BIH, the success of translational research is not measured primarily using the typical scientific parameters such as the number and impact factor of publications or the acquisition of third-party funding. Nor is it assigned exclusively to individuals. A prerequisite for a new culture of translation is to develop and apply new criteria for the success of translational projects. Together with international partners, in particular the Wellcome Trust in the UK, BIH is also working on new incentives for translational research.

Following its integration into Charité from 2021, BIH will act as a prototype for direct federal funding for a medical university. The clinical and scientific environment at Charité – University Medicine is an essential prerequisite for effective translation, while MDC – Max Delbrück Center for Molecular Medicine – is BIH's central partner for the development of innovative technologies and new mechanistic approaches.

Mission

The mission of the Berlin Institute of Health is medical translation. Our goal is to deliver relevant medical benefits for patients and citizens. To this purpose, and in conjunction with the clinical environment of Charité, we have established a comprehensive Translational Ecosystem. We rely on an understanding of disease and health across different organs and indications, promoting a cultural change in translation within biomedical research.

Translation

We understand medical translation as the transfer of knowledge from biomedical research into novel approaches for personalized prediction, prevention, diagnostics and therapy. In parallel, we develop new research approaches based on clinical observations. We look at the entire spectrum from the level of a single cell to society as a whole.

Medical Need

Health systems in Germany and around the world are facing major challenges. With aging populations leading to more patients, and at a time that there are fewer health professionals and care workers, medical research will be pivotal in providing us with fresh insights into new models of care and treatment. In addition, while digitization promises to deliver a network of information from a wide variety of sources that support research, the medical world must become more successful in bringing solution-oriented observations and the questions raised by everyday clinical practice into translational research. The reverse process, the transfer of observations from the laboratory back to everyday clinical practice, also needs to be improved and accelerated.

With no long-term treatment options currently existing for many diseases, the hope of future successes in treatments for a range of conditions hinges on the rapid technological progress being made in basic research and information technology. Such a scenario makes it vital to combine innovative technologies and research activities with clinical expertise that is driven by medical need, thus establishing new medical, technical and digital solutions within a reasonable timeframe. This is one of the core tasks of BIH.

Being based in Berlin, BIH sits in the ideal location for fulfilling this mission by offering easy access to biomedical research from a large number of university and non-university working groups. Charité, as Europe's largest university clinic, is not only able to deliver clinical excellence in a wide range of areas, but also has a broad spectrum of patients - all the components needed for the successful development of new forms of therapy within this biomedical Ecosystem.

Challenges

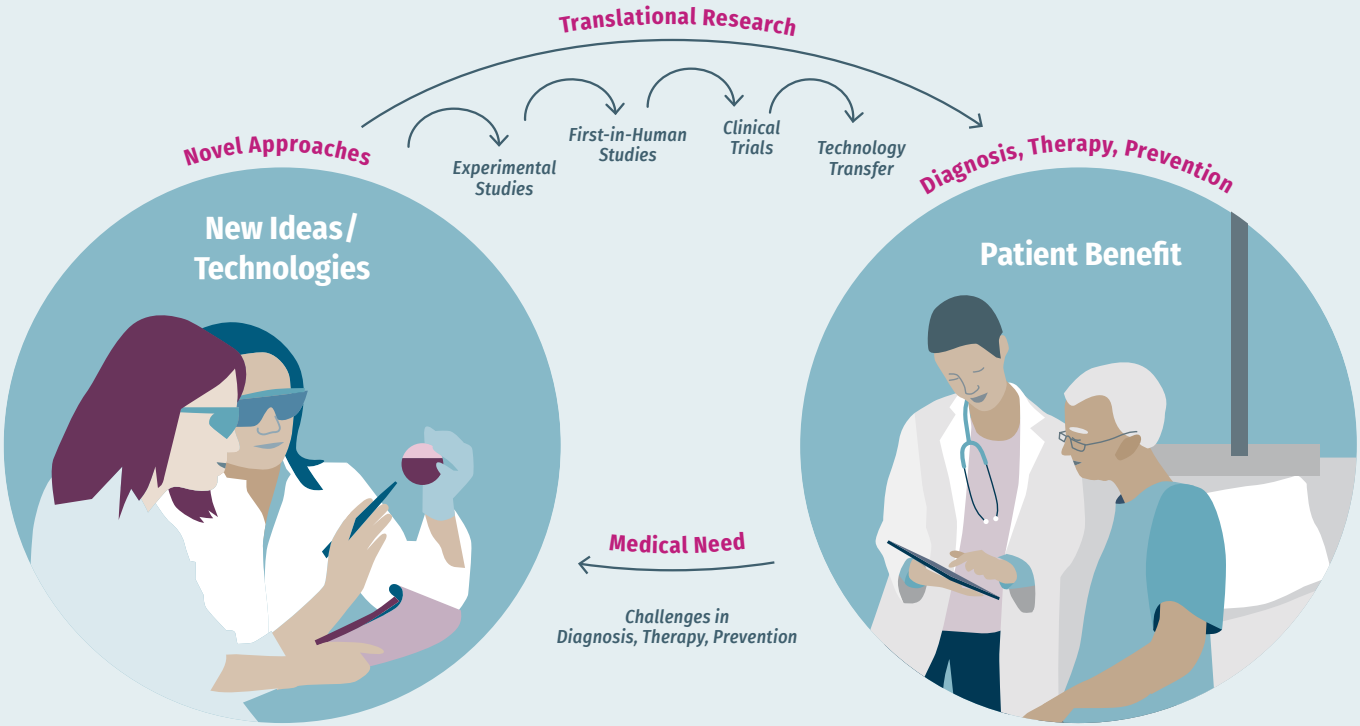
Currently, the translation of innovative approaches into clinical practice requires much in the way of time and resources, and unfortunately is often not as successful as it could be. Available data shows that the number of approved drugs per billion USD (adjusted for inflation) in research investments has on average halved every nine years between 1950 and 2010.[1]

A major reason for this is the complexity of the steps required along the translational value chain, from innovative idea to real-world clinical application. In addition, a multitude of infrastructures and technologies, as well as professional groups with different skill sets, are required to contribute to the process and work towards a common goal.

Another challenge lies in the combinations of people involved in these various stages, who often have different priorities, speak different languages and work in different communities. For scientists working in basic research, an understanding of new molecular mechanisms – and subsequently publishing results in well-known journals – is crucial. Sitting opposite this, for translational research to be successful in delivering achievement from preclinical and clinical studies, there is a need for all clinical partners and researchers involved in the process to share common goals and cooperate closely from the very beginning. Greater cohesion is of the utmost importance here – underlining the importance of those involved in both basic and translational research to possess the capabilities and skill sets needed to master the complex requirements for the preparation and approval of clinical trials. These steps, however, require considerable time and resources and may not always seem worthwhile in the basic research environment. Such hurdles and difficulties exist at many interfaces of translational value creation and can lead to the development of separated silos, endangering the effectiveness of the translational process.

1 Scannell, Blanckley, Boldon et al. Diagnosing the decline in pharmaceutical R&D efficiency. Nature Reviews Drug Discovery 11, 191–200 (2012). Link: https://doi.org/10.1038/nrd3681 (Website last accessed on 06.05.2020)

FIGURE 1
The Translational Value Chain



Yet translation cannot, and should not, be divided into basic scientific knowledge on the one hand and implementation in clinical practice on the other. On the contrary, translation-oriented teams and facilities must both be anchored in the clinic, and in the laboratory. Professionals working in daily clinical practice observe medical need through contact with patients or through the help of innovative big data processes, whilst pathophysiological research approaches and therapy concepts can be developed through interaction with scientists in basic research and reviewing them based on medical need. The necessary mindset for translation can only arise within this context.[2]

Another challenge for medical translation is the pathophysiological limits of traditional, organ-oriented concepts in medicine and research. These promote a deep understanding of individual structures, but do not take sufficient account of the fact that the different functions and structures within an organism are closely linked; physiological and pathological mechanisms overlap, and genetics and the environment affect all organs and systems simultaneously. Most chronic diseases occur when processes that affect the whole body fail. These include the body's immune system and inflammatory processes, blood circulation or the regeneration of tissue lost through trauma or degeneration.

At the same time, fundamentally new opportunities are opening up for translational medicine through the digital revolution including new technologies such as: machine learning/artificial intelligence, biomimetic materials, 3D printing, human-on-a-chip, pluripotent stem cells, organoids, genome editing, the dramatically increasing level of detail and speed of molecular analysis (omics: genomics, proteomics, metabolomics), as well as new approaches in diagnostics and therapy development at the cellular level. As an example, Novel Therapies (Advanced Therapy Medicinal Products – ATMP) – a new class of personalized therapeutics at the cellular basis (Living Medicines) – offer new options for more effective translation in the area of academic research.

2 Volk, Stevens, Mooney, Grainger, Duda. Key elements for nourishing the translational research environment. Science Translational Medicine 7, 282 (2015). Link: https://stm.sciencemag.org/content/7/282/282cm2 (Website last accessed on 06.05.2020).

See also the DFG position paper on translation: https://www.dfg.de/download/pdf/dfg_im_profil/reden_stellungnahmen/2019/190919_stellungnahme_empfehlung_ag_translation.pdf (Website last accessed on 06.05.2020)

BIH Approach

Cross-Organ Systems Medicine

BIH is not a typical research institute. Its innovative approach is to utilize a novel concept of clinically anchored cross-organ systems medicine in a comprehensive Translational Ecosystem to significantly increase the speed and effectiveness of medical translation.

The primary partner for effective translation is the clinical and scientific environment at Charité and across Berlin, enabling a high degree of interaction due to the proximity of different partners. MDC (Max Delbrück Center for Molecular Medicine) is central to the development of technologies and new mechanistic approaches.

BIH focuses on cross-cutting issues: for example, digital medicine, and cell-based therapies as innovative drivers; and not organ-specific approaches such as cardiology and cancer research. BIH, thus, works across systems medicine, examining processes that arise from the interaction of various organs and systems in the body.

The systems medicine translation approach at BIH is therefore a necessary addition to the disciplinarily oriented approach of the German Centers for Health Research, which uses a decentralized network of expertise at several locations, with each focusing on widespread diseases.

BIH's Translational Ecosystem

BIH is able to implement its mission of medical translation by establishing comprehensive and coordinated structures in one location. Such an approach enables the various professional groups involved to use their expertise to develop new preventive strategies, new diagnostics and effective therapies, and to discover how these options can be effective for patients. Together with Charité and MDC, BIH establishes a comprehensive translational value creation system.

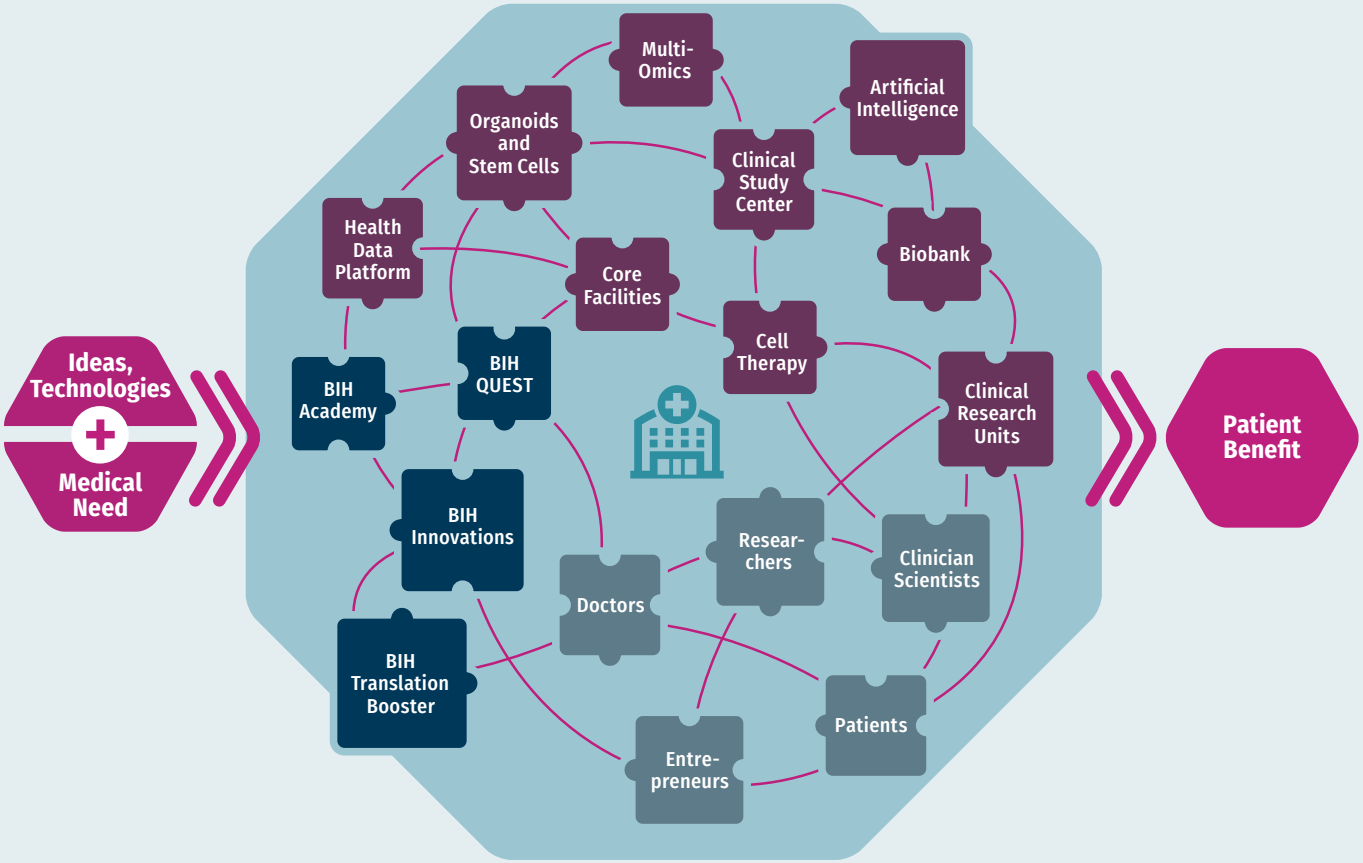
In order to transfer new concepts into clinical practice faster and more effectively, it is important that the parties involved are networked in a translation-oriented environment – the Translational Ecosystem.

BIH's Ecosystem bundles a variety of competencies and infrastructures in the vicinity of Charité's clinical facilities, confirming the findings that:

- translational processes are usually not linear and targeted, as suggested by the concept of the translational value chain; and
- a variety of skills, infrastructures and support mechanisms are essential for effective translation.

This Ecosystem is unique to BIH. It encompasses the necessary critical mass of all professions and skills required, and provides the necessary structures and services for translation. As such, this environment allows continuous optimization of ideas and solutions in one iterative »bench to bedside« and »bedside to bench« process. Crucial for the achievement of BIH's mission is the continuous development of the Ecosystem as a learning system. The experience gathered from all projects and processes, and new ideas and concepts from the faculty and benchmarks from other institutions, contribute to this.

FIGURE 2
The Translational Ecosystem of BIH



The elements presented here are exemplary for the components of the Ecosystem, the graphic shows their complex interaction.

Innovation Enablers

Technologies and infrastructures in the Translation Hubs

Active players

Clinical environment of Charité

Principles

The way BIH works can be described by the following principles:

Full Circle

Together with Charité and other stakeholders, BIH is building a comprehensive translational value creation system. Ideas from the laboratory are transferred to the bedside and checked there (»bench to clinical reality«). The observations in the clinic are carried back to the laboratory (»clinical challenges to bench«) and stimulate the development of new ideas and technologies.

One Campus

Interdisciplinary translation is made possible at BIH as all participants are able to continuously exchange ideas. The essential prerequisites of innovation, the clinic and implementation, are available on site and can be utilized without institutional barriers. This particularly applies to clinically obtained data, which is made available to research, whilst ensuring the highest levels of data protection.

Decide-Early

BIH continuously analyzes projects at all levels of the translational value chain in order to either specifically promote them, or where necessary, to terminate them early. This increases overall effectiveness and reduces the risk of failure in the later, cost-intensive, stages.

Value

Research at BIH must be trustworthy, robust, resilient and transparent.
It must be effective for science and of benefit to the wider society, and it must be proportionate to the risks and burdens taken.

Interdisciplinarity

BIH's translational scientific community includes medical professionals, basic research scientists, innovators (i.e. scientists who give the impetus for clinical application without commercial interest themselves), engineers, digital experts and data scientists, business developers, entrepreneurs, market players, health system experts, as well as the users, and particularly, patients.

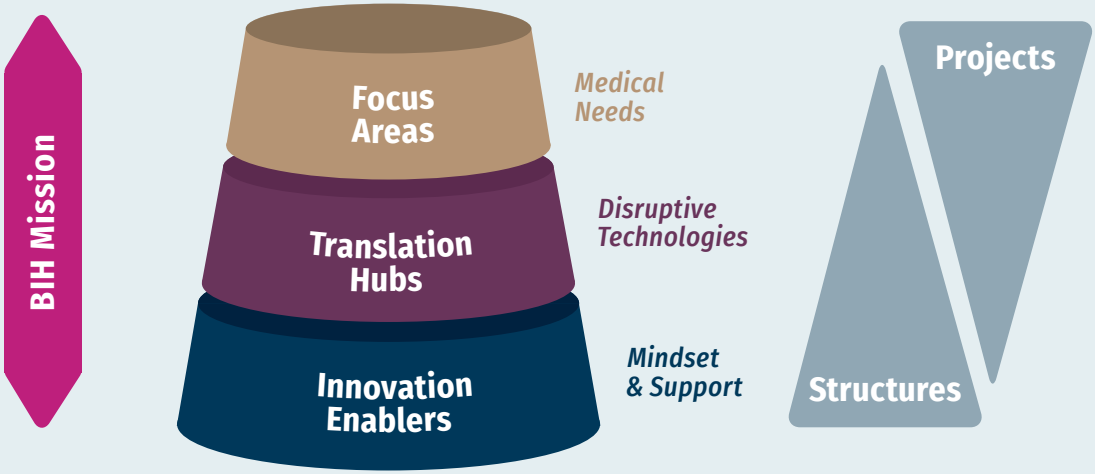
Partnering

To ensure excellence at all stages of the translation process and to be able to fund application-related phases, BIH adds to its expertise and resources through cooperation with prominent partners from science and industry.

Responsibility

BIH takes its responsibility towards patients and citizens extremely seriously. This is reflected in their appropriate representation in BIH processes, in a gender- and diversity-sensitive organizational culture and in a continuous focus on relevant medical needs.

FIGURE 3
The Components of BIH



The Innovation Enablers
create the underlying, permanent structures for the translational mindset and environment for all those involved in the process.

The Translation Hubs
bring together topics and technologies that have the potential to revolutionize medicine over the coming years - designed for the long term but constantly adapting to new developments.

The Focus Areas
implement concrete translational research and development projects designed for a defined period of time.

BIH as a dynamic system

To fulfill its mission, BIH has established three components that build on one another and provide different support mechanisms for the translational process and the implementation of specific projects with a high level of innovation and translational potential. The development of the translational environment is a continuous task that affects the entire faculty, while in the Focus Areas, experts address highly relevant questions.

Implementation of the mission

The Innovation Enablers

The basis of the Ecosystem is the translation-oriented mindset of all stakeholders involved in the process and the constant support of the faculty in all phases of translation. Developing this is the task of the Innovation Enablers. BIH Academy promotes translational competencies, designs specific training programs to this end and defines innovative career paths for clinician scientists and medical scientists. BIH QUEST Center has developed and implemented new approaches to ensure the quality and sustainability of research through all phases of the value chain. BIH Translation Booster develops mechanisms and incentives to overcome the hurdles along the chain. BIH Innovations promotes the early, and targeted, transfer of innovative ideas into products and clinical solutions at all levels of translation.

FIGURE 4
The Innovation Enablers of BIH

	BIH Academy	BIH QUEST	BIH Translation Booster	BIH Innovations
	Competencies	***Quality***	***Efficacy***	***Transfer***
Goal	Develop commitment and competence in translation	Ensure optimal use of resources	Increase the speed and effectiveness of translation	Use the potential of innovations and products
Approach	Promotion of individuals through innovative career paths	Establish quality and sustainability	Overcome hurdles	Establish structures and mechanisms for translation
Incentivization	Translational Talent Empowerment	Value-Incentives	Translation-Incentives	Innovation-Incentives

These four functions are essential for all steps and in all areas of medical translation. However, their comprehensive approach has thus far not been the focus of translational initiatives. To address this, and add a further dimension to the effectiveness of translation, BIH has set up the Innovation Enablers to optimize conditions for the development and maintenance of the translational mindset and support over the long term. The incentive mechanisms of talent empowerment, value, translation and innovation services complement established formats such as the classic performance-oriented allocation of funds, which rewards publications and third-party fundraising.

It is important to avoid an oversimplified interpretation of the translational value chain. The focus of translational efforts in the academic environment is usually a question of whether new concepts and ideas can be implemented scientifically and clinically. However, such a narrow view can often lead to project failure in later phases and to the inefficient use of resources. Reasons for this can include the inadequate validity and robustness of data from the earlier stages, or a lack of foresight when examining legal and economic aspects.

Such deficits are avoided in BIH's Translational Ecosystem through BIH Innovations and BIH Translation Booster examining ideas with high translational potential at the early stage with scientific and transfer aspects in mind and continuously supporting the parties involved in the process as early as possible. In this way, feasibility in terms of technology, legal, financial and organizational aspects can be clarified early on in order to launch larger numbers of highly innovative and riskier projects into the Translational Ecosystem based on this Decide-Early principle. The services offered by the Innovation Enablers are generally available to the entire scientific community, thus helping to continuously create the best conditions for concrete translational approaches.

FIGURE 5
The Role of the Innovation Enablers in the Translational Ecosystem of BIH

Translational Research

Training	*Incentives*	*Support*	*Expertise*
BIH Academy	**BIH QUEST**	**BIH Translation Booster**	**BIH Innovations**
Translational commitment and competences Translational career paths	Quality and robustness of biomedical research Cultural changes	Early assessment and support Team-based approach and mind-set	Technology and products Entrepreneurial instruments

The Translation Hubs

Each translational institution must select which research and development priorities it wants to focus its activities and resources on. This takes place at BIH within the Translation Hubs and Focus Areas. In accordance with the strategic decision for a cross-organ approach, BIH has selected topics that can make fundamental systems medicine contributions to translation.

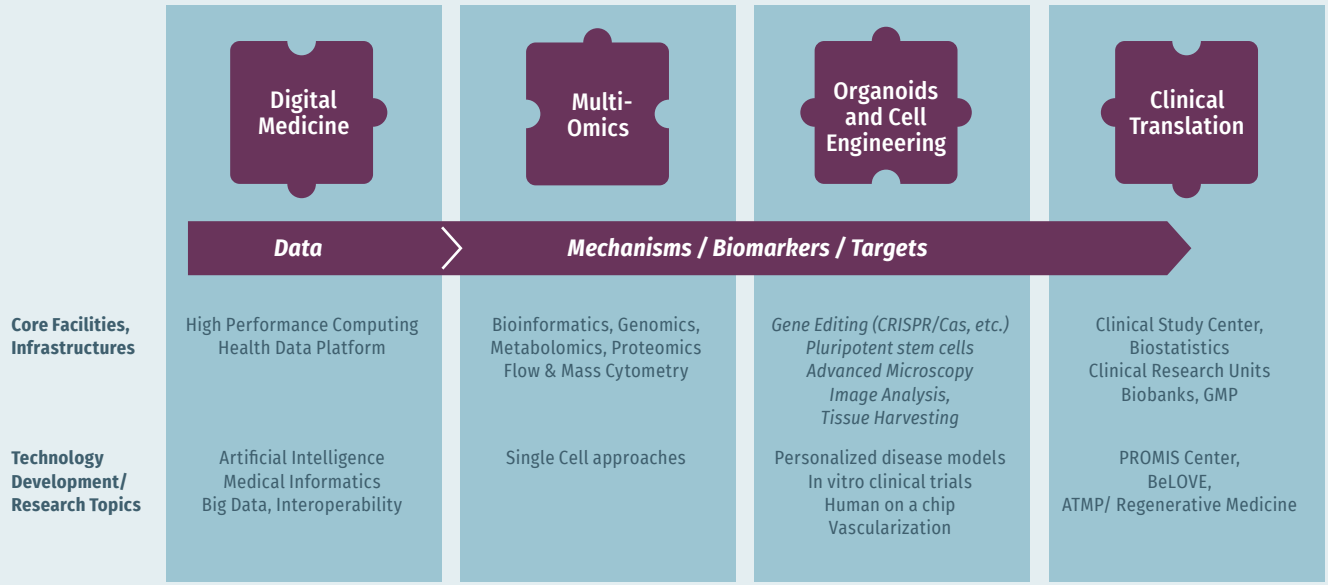
The Translation Hubs represent topics and technologies that will revolutionize medicine across various disciplines in the coming years:

- Digital Medicine
- Multi-Omics
- Organoids and Cell Engineering
- Clinical Translation

It is in these areas in particular that highly relevant contributions can be made to BIH's translational mission, so improving clinical options for patients. The Digital Medicine hub enables the extensive use of data-based approaches; Multi-Omics ensures phenotyping at the highest level; and Organoids and Cell Engineering make the targeted modulation of cells and 3D organ cultures usable for innovative, precision-based medical approaches. In these areas, the Translation Hubs support effective translational research through the Clinical Translation hub by:

- Networking experts and establishing a research community
- Developing innovative technologies and methods
- Providing excellence in scientific services (core facilities)

FIGURE 6
The Translation Hubs of BIH



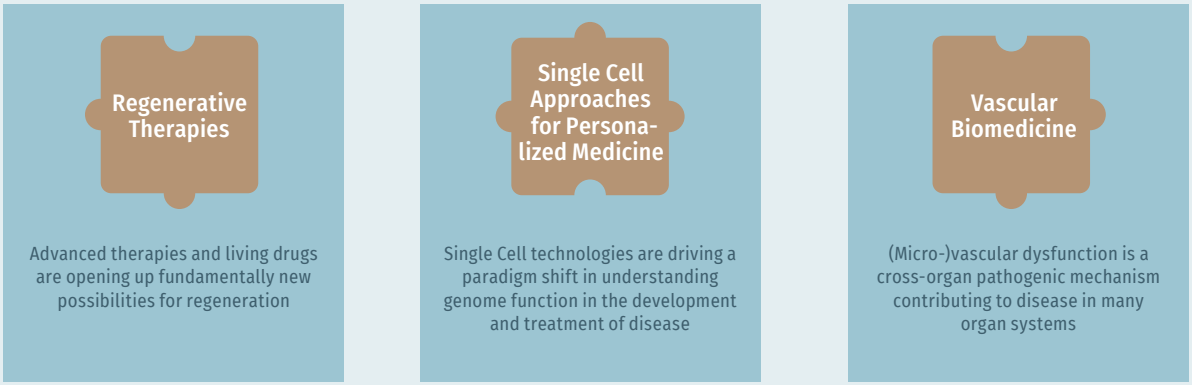
The Focus Areas

The Focus Areas bring concrete translational research and development projects into the Translational Ecosystem. These Focus Areas are characterized by:

- Taking a systems medicine approach
- Having a high potential for groundbreaking success in translation
- Successful and decisive implementation in the Translational Ecosystem

Three Focus Areas have been established at BIH, each using different elements of BIH's translational value chain: Regenerative Therapies, Single Cell Approaches for Personalized Medicine, Vascular Biomedicine . The relevance of these, as well as the excellence achieved by the parties involved, is clear from the extraordinary fact that from across all scientific fields, two of these Focus Areas – Regenerative Therapies and Single Cell Approaches for Personalized Medicine – have made it to the final selection round of the last six European FET Flagships. BIH's Focus Areas are fundamentally dynamic and are continuously adapting to scientific, technological and translational developments.

FIGURE 7
The Focus Areas of BIH



The Excellence Fund

The Excellence Fund sees all BIH project funding tools bundled together under one roof. This includes internal funding, such as project funds awarded in the Focus Areas, as well as project funds which are to be assigned on a national level. This pooling facilitates centralized control in terms of transparency and quality assurance. The relevant criteria and minimum standards required for all Excellence Fund projects are currently being defined together with BIH's faculty.

The aim of this dynamic instrument is to enable the integration of expertise not available on site, and to quickly and flexibly pilot particularly relevant concepts and technologies. In this way, high risk projects with high potential are given the opportunity to provide evidence of added medical value through temporary funding and to become viable for external funding.

The mandated BIH bodies – including the steering committees of the Focus Areas and the Translation Hubs as well as the selection committees of the Innovation Enablers and the BIH Research Council – remain fundamentally responsible **for internal BIH project funding**. Thus, funding decisions are based on science-led, quick and transparent processes.

All BIH scientists and future BIH fellows are eligible to apply for these project funds. When allocating funds to the Focus Areas and Translation Hubs, the expectation is that this will lay the foundations for additional third-party funds as these larger structures should be enabled, and encouraged, to strive to acquire external association funding.

The nationwide project funding of BIH adresses the following goals:

1. To bring missing expertise to BIH for specific goals;
2. To network BIH with national and international players in translational research;
3. To offer opportunities establishing Innovation Enablers with partners nationally, based on the experience of BIH;
4. To enable contract research for specific needs which cannot be met on site, neither scientifically nor economically.

Further perspectives can be an expansion of nationwide project funding – e.g. in the area of equal opportunities in translational research, nationwide funding of outstanding and innovative translational projects or junior translational research groups, each with a mainstay at BIH and their own facility. This is dependent upon the financial opportunities allocated to this nationwide funding instrument over time.

Success Criteria and Exploiting the Potential of BIH

As BIH's translational approach differs structurally from basic research institutes, it is essential to develop new criteria for evaluating the success of BIH that go well beyond the usual indicators, such as impact factors or third-party funding. The success of translational research cannot be measured in terms of the number of individual publications and, as a rule, cannot be assigned purely to individuals. Both specific criteria for translational projects and new evaluation principles for researchers working in translational research must therefore be defined.

Specific indicators must focus on BIH's mission, i.e. reflect the relevant medical benefits for patients. Direct parameters for this goal include:

- Introduction of new preventive, diagnostic and therapeutic procedures into the clinic
- Products and launches
- Changes to guidelines, treatment and therapy guidelines
- Returns from sales and licensing
- Social added value (virtual proceeds)
- PROMs (Patient Reported Outcome Measures)

The indicators above only emerge at the end of the successful translation and, therefore, with a considerable delay in the important preparatory steps. However, these contributions are indispensable and can also be measured at short notice. They also need to be assessed and incentivized:

- Proof of principle studies
- Manufacturing permits
- First-in-Human-studies and clinical studies based on own concepts (IIT)
- Ratio: from number of patents or patent applications to patents being used
- Licensing, spin-offs and corresponding cooperation

Essential elements to the success of BIH are the transmission of translational skills as well as the establishment of career paths that make research and clinical activities compatible. Indicators for this include:

- the recognition of translational competencies as medical competencies (professional policy impact)
- the establishment, recognition and nationwide scaling up of translational career paths
- the creation of new intersectoral career paths, e.g. for digital medicine

Parameters to assess quality and sustainability at all levels of translation are also relevant to the sustainable success of BIH and include:

- Open Access publications
- Open Data/Open Science
- Publication of negative results
- Confirmatory Studies

BIH QUEST Center has launched important initiatives for BIH and Charité in recent years in this area, which have led to a significant increase in open data publications and have been acknowledged both nationally and internationally.

In order to further develop structures and mechanisms for translation, BIH became the first continental European partner to cooperate with the Wellcome Trust in the UK in 2019. Within this context, parameters for measuring success and mechanisms to incentivize the different steps of translation – and the different areas and individuals in the Translational Ecosystem – are being developed and comparisons made with other international medical research centers, such as the National Institutes of Health (NIH) in the United States.

Structurally, BIH is a new type of scientific institution and, when integrated into Charité, becomes a prototype for direct federal funding of higher education institutions. The involvement in Charité enables BIH to strive for new standards on a structural level. That ranges from education – such as the promotion of young researchers into new translational career paths - to quality assurance and structural support in the processes of a research hospital in project selection, recruitment, and entrepreneurial support.

Appendix

The Innovation Enablers

BIH Academy

The BIH Academy focuses on strategic career and talent development within the biomedical sector and acts as a think tank in supporting the promotion of individuals through innovative career paths. Professional group-specific funding tools for research-oriented doctors (Clinician Scientists) and for scientists interested in clinically relevant questions (Medical Scientists) reflect the translational value chain from basic research to patient care. In addition, the Academy offers incentives for the successful development of translational careers. The Academy makes an essential contribution to the implementation of BIH's mission through early scouting of young talents who are comfortable in both clinical and scientific settings, creating a new generation of highly-skilled scientists interested in translation. The resulting community of several hundred fellows and alumni that has been created enables a cultural change in biomedicine that represents translation in practice.

BIH QUEST Center

The aim of BIH QUEST Center (Quality, Ethics, Open Science, Translation) is to develop and introduce new approaches to ensure quality, compliance with ethical standards, and the sustainability of research and development across all phases of the translational value chain. A wide range of services are available to BIH's community in the areas of open science, education and training, patient and stakeholder engagement, as well as the development of measures and incentives - for example, in making original data available (open data). Through meta-research, QUEST determines the potential for optimisation in research practice and generates scientific evidence for possible improvements. In addition, QUEST develops scientifically sound and practice-oriented recommendations on how the ethical requirements for research involving people, animals and sensitive data can best be implemented.
BIH QUEST is indispensable for the implementation of BIH's mission, increasing the quality and sustainability of biomedical research at BIH and its partners and enabling the effective translation of research results to cascade down to the patient.

BIH Translation Booster

BIH Translation Booster coordinates professional accelerator and incubator structures. A successful accelerator has already been established in the field of digital health and serves as a model for other structures, e.g. in the field of Regenerative Therapies. In close cooperation with BIH Innovations, scientific projects are evaluated early in terms of their scientific and translational potential, their possible marketing and the benefit they offer to patients. Projects rated positively gain access to the comprehensive portfolio of support offered by BIH, supporting research teams structurally and content-wise with skills in business development and approval issues on the journey to clinical application. Depending on the project level and need, additional scientific, technological, regulatory and commercial expertise can be added to the range of support. BIH Translation Booster also supports funding applications to public or private donors for the implementation of approval studies, the establishment of commercial partnerships or pitching to venture capitalists.

BIH Innovations

The joint technology transfer from BIH and Charité, BIH Innovations is responsible for ensuring that ideas are not only realised, but also reach the patient or are converted into commercial application. The implementation of knowledge gain in products and new jobs is the last step in a translational value creation system and an essential building block for the implementation of BIH's mission. BIH Innovations sees innovation management as a process that begins well before patenting (»early scouting«), and accompanies scientists from the systematic search and active selection of promising ideas through the development, validation and approval processes, and onward to utilization of a marketable product. BIH Innovations has two validation tools and is to be further developed in the areas of scouting and business development in the future.

The Translation Hubs

Digital Medicine

The Digital Medicine hub aims to build a leading digital medical infrastructure in Berlin to accelerate the translation process. With this aim, health data (from clinics, the laboratory, experiments, medical devices, Apps) are networked so as to be compatible with one another, and useable across different systems (interoperability). This health data is made available to patients, physicians and researchers compliant with all relevant legislation, e.g. data protection.

A prominent example of the hub's activities is the Health Data Platform (HDP), which brings together data from a variety of sources (clinic, laboratory, experiments). The HDP supports the process along the translational value chain from lab to practice with analyses of big data for the prognosis of active principles and interactions, as well as for the development of new hypotheses in the research context. The HDP thus represents a highly relevant link in the Translational Ecosystem and is a central instrument for realizing the potential of big data in medicine.

Multi-Omics

The Multi-Omics hub aims to make omics technologies usable for translational applications. These include the establishment of standardized pipelines for the preparation of samples and data, the development of computer-aided approaches for the integration, analysis and modelling of omics data, the continuous development of omics methods and technologies, as well as omics-based diagnostic analysis and therapeutic approaches.

The hub combines modern high-throughput technologies with bioinformatic methodology for the comprehensive analysis of genes, proteins and metabolic products as well as their interactions and phenotypical characteristics. The focus here is on the analysis of clinical samples using state-of-the-art omics technologies, which not only contribute to a better understanding of pathological mechanisms, but can also be used for the diagnosis and treatment of individual patients. In cooperation with the Clinical Translation hub, omics data can be correlated with external characteristics and clinical parameters, allowing a systems-medical understanding of disease-related mechanisms as well as the diagnostic and therapeutic options.

Organoids and Cell Engineering

The Organoids and Cell Engineering hub aims to harness new approaches in genetic engineering (e.g. CRISPR/Cas) or cell breeding, stem cell technology and bioprinting (e.g. organoids, human-on-a-chip models) to facilitate precision medicine through the development of new human models for preclinical research and the methodical development of cell-based therapies. This includes the use and improvement of new 2D and 3D cell culture models such as organoid, human-on-a-chip or mini-organ models. Human cells and their genetically edited forms can be examined under almost physiological conditions for a variety of enquiries, for example, regarding functional characteristics or processes of vascularization. For the analysis of these models, the hub uses a range of microscopy methods (e.g. light-sheet microscopy, high-content microscopy and quantitative image analysis) and single cell analyses in cooperation with the Multi-Omics hub and the Focus Area Single Cell Approaches for Personalized Medicine. On the other hand, the activities of the hub include the use of genome engineering methods (e.g. using CRISPR/Cas) and the further development of approaches to generate human CAR T cells for cancer immunotherapy or to correct mutations in patient cells (primary cells or adult stem cells).

Clinical Translation

The Clinical Translation hub aims to accelerate clinical innovation and optimise the quality of clinical trials. It occupies a unique position among BIH's Translation Hubs, since it acts as a central catalyst for clinical research and therapy development at BIH and Charité, developing the necessary infrastructure for them to translate innovative ideas into high-quality clinical studies. These infrastructures are extremely complex, ranging from the characterization of patients and their samples through to administration for quality assurance and data collection.

A prominent example of this structural support is the establishment of the Clinical Study Center, jointly supported by BIH and Charité. It acts as a single point of entry for all clinical studies and supports the entire process from study preparation, through to implementation and evaluation. In addition to staff in the classic supporting roles for clinical studies, the hub offers scientifically supervised phenotyping modules to record valuable data, e.g. on the immune, metabolic, mobility and cognitive status of the test subjects. By combining these results with data from the molecular analysis of biosamples, a comprehensive characterization can be carried out.

The Focus Areas

Regenerative Therapies

The focus of research of the area Regenerative Therapies is the stimulation of the body's own regeneration processes (endogenous regeneration) in patients with acute and chronic diseases.
The goal is a paradigm shift away from treating the symptoms to a restoration of the body function, i.e. a recovery. For this purpose, immune cells, biologically active factors and biomaterials (including so-called composite products) are used in situ, and specifically developed medicinal products for new types of therapy (Advanced Therapy Medicinal Products, ATMPs) are used.

The Focus Area is represented by the BIH Center for Regenerative Therapies (BCRT), which developed out of an initiative to set up a Translation Centre for Regenerative Medicine, funded by the Federal Ministry of Education and Research and led by Charité and the Helmholtz Association.

A model was established in the BCRT as an example for translation in medicine, which depicts almost the entire translational value chain for novel therapies. This enables scientists, engineers and doctors to work together optimally in the research field of Regenerative Therapies. Transplant patients are currently being treated with genetically modified immune cells at the BCRT, which significantly reduces the risk of rejection of the new organ, and thereby the amount of immunosuppressants needed.

The Focus Area Regenerative Therapies will be significantly strengthened in the near future by the construction of the research building »The Simulated Man« (Si-M) at the Technical University of Berlin and Charité as well as the »Berlin Center for Advanced Therapies« (BeCAT). Their focus on 3D cell cultivation and the development of multi-organ chips and ATMP-based therapy perfectly complement the goals of the BCRT. This creates an interdisciplinary campus for the research and development of Regenerative Therapies, with the potential for rapid and revolutionary progress.

Single Cell Approaches for Personalized Medicine

Single cell technologies describe the investigation of individual cells using DNA and RNA sequencing, for example. They provide detailed insights into disease-related changes in cells. In order to make highly innovative single cell technologies practical for clinical use, BIH has established the clinical Focus Area Single Cell Approaches for Personalized Medicine in a jointly supported cooperation between BIH, Charité and MDC/BIMSB (Max Delbrück Center for Molecular Medicine/Berlin Institute for Medical Systems Biology). BIH and Charité bring clinical-related expertise (bioinformatics, imaging, machine learning, oncology, neurology, dermatology, biobanks, diagnostics and biomarkers), while MDC/BIMSB add technological and scientific expertise in single cell biology and gene regulation.

The Focus Area is based on two pillars:
In the first instance, four joint junior research groups by BIH, MDC/BIMSB and Charité are being established to bring single cell expertise into clinical use.
The leaders of these groups were recruited through a highly competitive selection process and all come from some of the world's leading research laboratories and institutes. The junior research groups are located at the BIMSB building at MDC, where they have access to state-of-the-art single cell technologies, machine learning and new concepts of molecular mechanisms, and are in close contact with top international researchers. At the same time, the groups are integrated into a clinic at Charité where they can identify clinically relevant topics and develop single cell approaches dealing with specific clinical questions and establishing technologies for clinical use. This bridge between basic research and clinic links BIMSB (with its internationally leading position in the field of single cell biology) with the clinical translational potential of BIH and Charité.

Secondly, a Clinical Single Cell Sequencing-pipeline will be set up, where a central bioportal for the collection, characterization and processing of patient samples will be found. The workflows for single cell genomics and bioinformatics services will be developed for participating clinics. While the pipeline will support junior research groups, it will also be accessible to the entire BIH faculty.

Vascular Biomedicine

Malfunction of the blood vessels plays a central role in many diseases. So far, research and therapy have mainly focused on the larger blood vessels, particularly the arteries. However, it is becoming increasingly clear that disorders in small blood vessels play a particularly important role in the development of disease and the resulting organ damage. Examples include vascular dementia, diastolic heart failure, kidney failure and angina pectoris. Recent findings also show the importance of (micro) vascular mechanisms in immune response and inflammation.

In order to address the deficit in translational approaches in this area, BIH, together with MDC, is expanding its research activities through targeted recruitment of leading international experts. Under the roof of a new BIH research building, the Käthe-Beutler-Haus on the Buch campus, a unique translational focus is being created under the joint control of basic researchers and clinicians. The aim is to decipher the local and systemic causes of vascular malfunctions so that clinical manifestations can be treated. Interdisciplinary teams work in a bottom-up approach on the central issues to address the most important clinical challenges in the personalized diagnosis and treatment of vascular disease. For this purpose, cohort studies, and research on humanized disease models, as well as computer-aided modelling approaches, are combined to develop new approaches for prevention, diagnosis and therapy.

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