MDC
Technology Platforms
Advancing Molecular Medicine

HELMHOLTZ

MDC MAX DELBRÜCK CENTER FOR MOLECULAR MEDICINE IN THE HELMHOLTZ ASSOCIATION

Max Delbrück Center for Molecular Medicine

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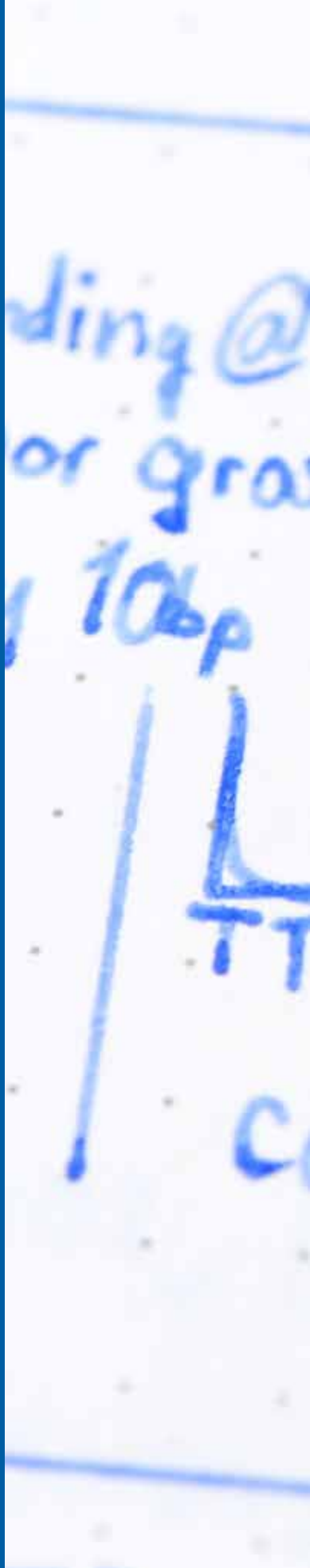

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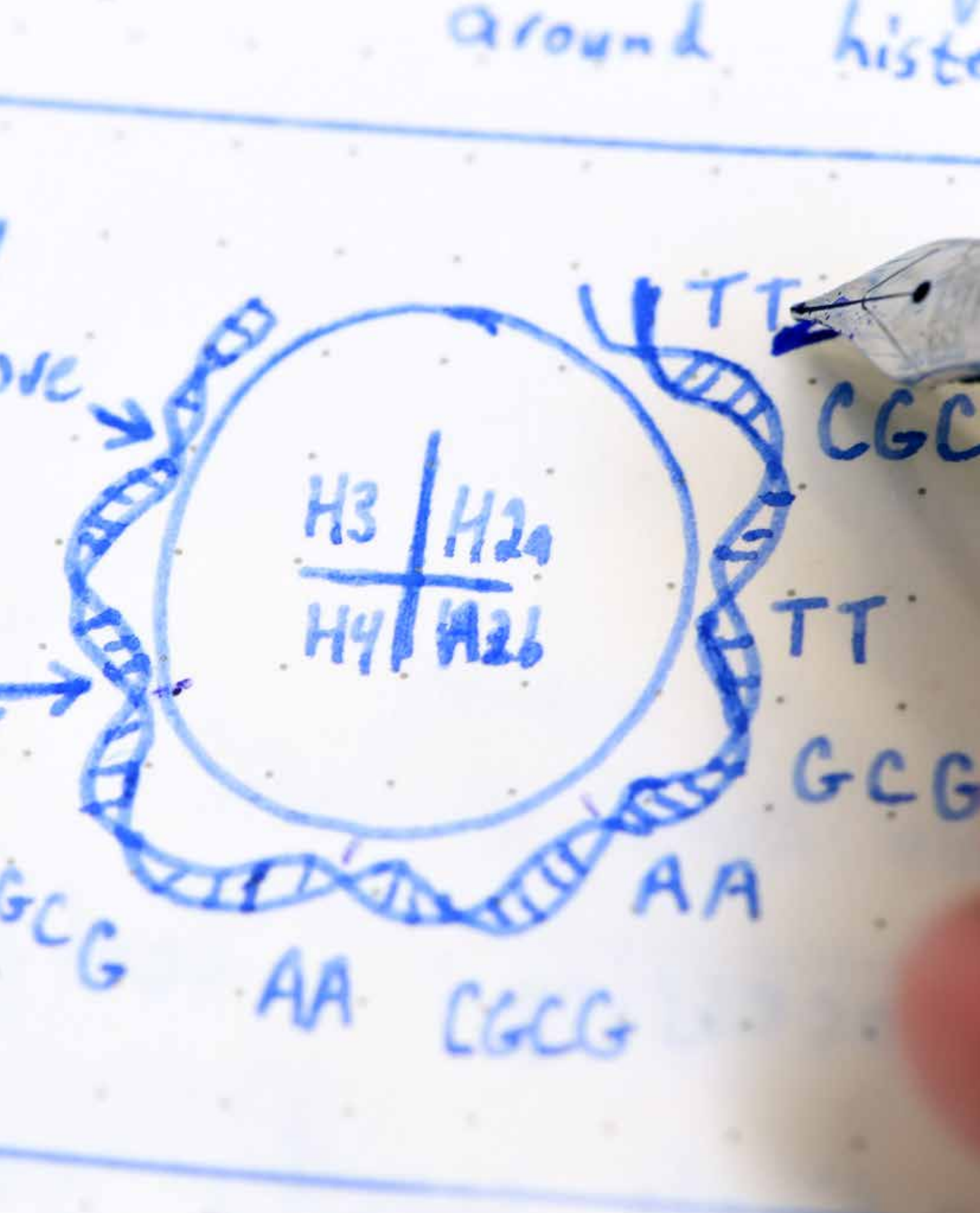


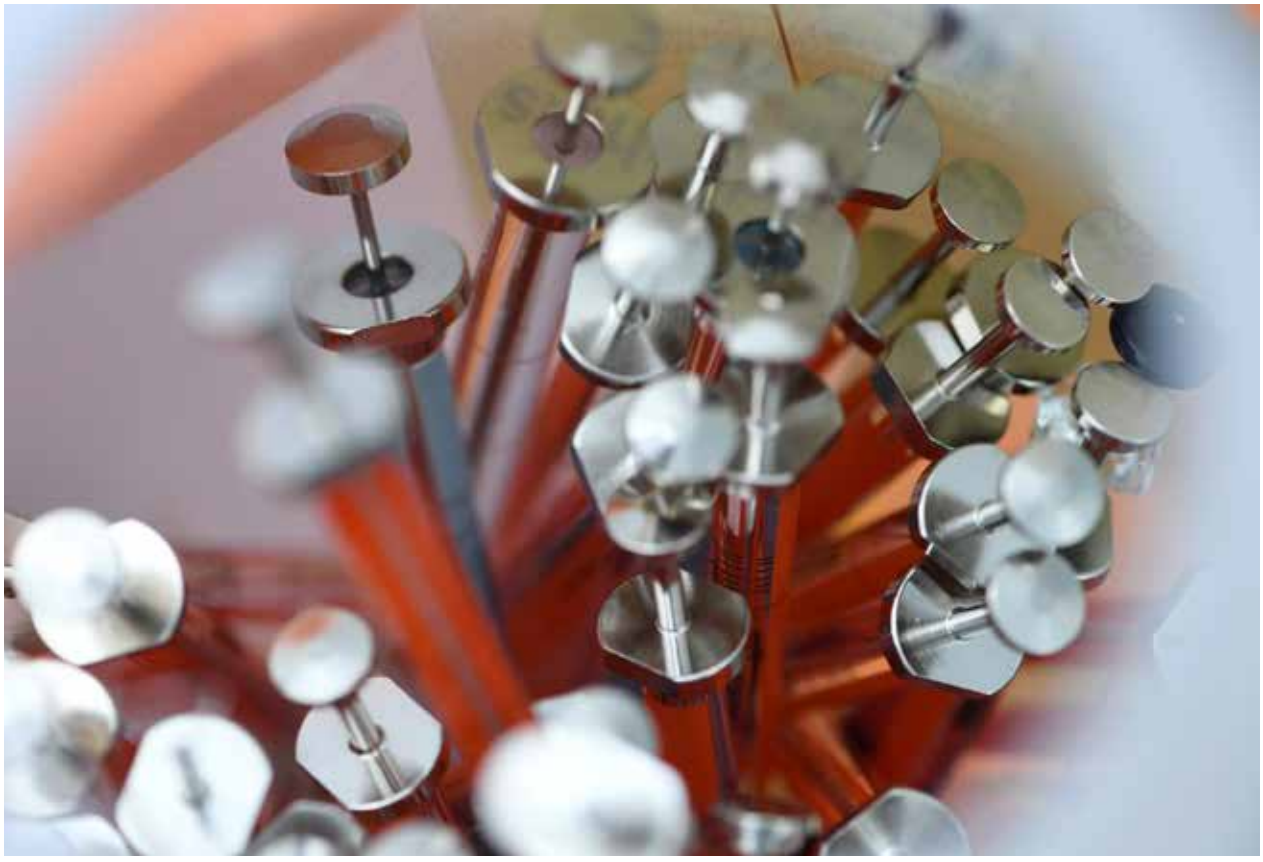
Advancing Molecular Medicine through Customized Technologies

Biomedical research is largely dependent on available technologies. When it comes to understanding the molecular basis of health and disease, researchers rely on high-performance instruments and methodological expertise. Approaches such as super-resolution light microscopy and cryo-electron microscopy; the elucidation of tissue, cell, and individual protein structures; and genome sequencing and editing techniques are all indispensable in answering major research questions.

TECHNOLOGIES OPEN UP NEW AREAS OF KNOWLEDGE

This brochure presents the research infrastructure of the Max Delbrück Center for Molecular Medicine in the Helmholtz Association (MDC). The Technology Platforms at the Berlin-Mitte and Berlin-Buch campuses, which are available to both MDC researchers and external project partners, range from imaging technologies and high-throughput analyses to bioinformatics computing, stem cell methods, and transgenic animal models. These customized approaches have been developed with established experts and enable competitive research to be carried out into issues such as systems-wide disease mechanisms.

The MDC's technology concept allows researchers to draw on a wealth of experience – particularly in imaging techniques, structure elucidation, animal models, and phenotyping. Another major factor behind its development was the establishment of systems biology as a research focus area. The launch of the Berlin Institute for Medical Systems Biology (BIMSB) prompted the expansion of the MDC's Omics and Data Analysis Technology Platforms that are now essential for all molecular medicine fields. The parallel analysis of thousands of genes (genomics), proteins (proteomics), and metabolites (metabolomics) is only possible with the help of high-throughput technologies and extensive data analysis. This array of scientific infrastructure is complemented by Technology Platforms that are geared towards translational research and managed and supported by the Berlin Institute of Health (BIH).

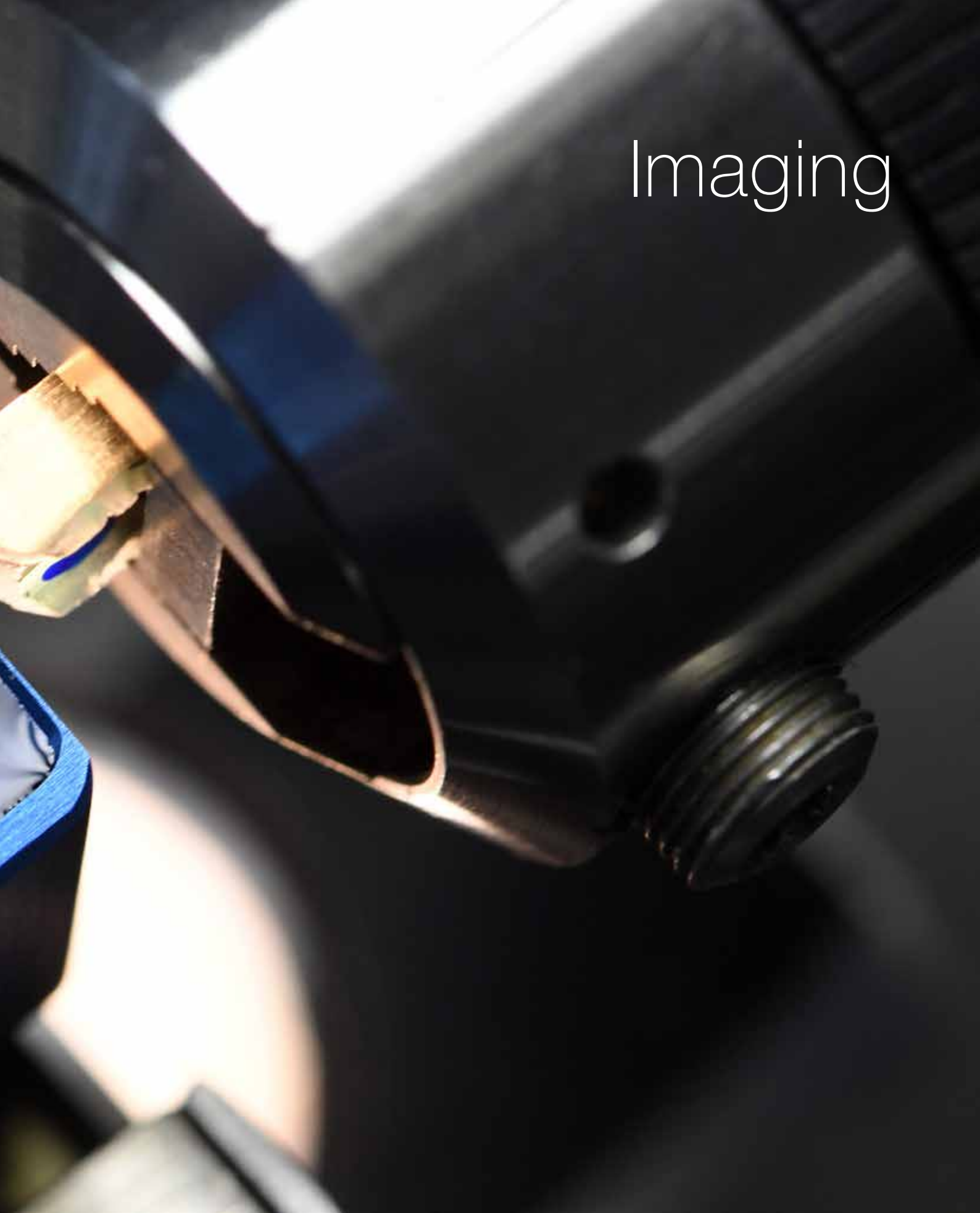


FOCUS ON LINKING SCIENTIFIC METHODS WITH RESEARCH TOPICS

A stand-out characteristic of the MDC's Technology Platforms is the integration of scientific methods and research topics. Methodical workflows are adapted and optimized, and technological approaches are continuously developed in order to best address the collaborating research team's project. The researchers heading up the platforms help to design the research projects and publish jointly alongside their partners. This means the technological teams are directly involved in the scientific process using state-of-the-art methods. All Technology Platforms are also supported by internal advisory bodies that help recognize trends (e.g., in single-cell analysis) and that pave the way for scientific developments through investments in staff or equipment.

It is precisely this blend of innovation and customization that makes the technological infrastructure of the MDC such a vital part of its research. The following pages provide insight into the fascinating opportunities, range of uses, and scientific scope of the individual methods and technologies.

Contents



Imaging

Advanced Light Microscopy

Fluorescence microscopy can reveal both structural and dynamic information about organs, tissues, cells, and even tiny molecular complexes. As such, the technique allows researchers to observe live molecular and cellular interactions in native biological environments.

Modern fluorescence-based microscopy technologies can image a wide variety of biological samples. These techniques use fluorescent molecules to generate images that provide not only structural information about the organization of cells, tissues and organs, but also about the interactions and dynamics of molecules and cells in live specimens. Thus, advanced light microscopy gives researchers the capability to quantitatively explore biological systems on a wide range of temporal and spatial scales.

Assembly of a chamber for holding the specimen during light-sheet microscopy.

FROM MILLIMETERS TO NANOMETERS

Our platform at the MDC campus in Berlin-Buch provides techniques that can image samples from nm scale (super-resolution microscopy), through µm scale (confocal and wide-field microscopy), and up to mm scale (multiphoton and light-sheet microscopy). In seminars and practical sessions, we help scientists to understand the theoretical principles of fluorescence microscopy and to use our microscopes independently. In addition, we offer advanced tools for quantitative image analysis and data processing as well as methodological support for research projects – including project planning, sample preparation, imaging workflows, and the establishment of new imaging methods.

A key technology is confocal microscopy, which can visualize the distribution, mobility, and interactions of molecules within intracellular compartments, tissues, and model organisms. Some fluorescent molecules indicate changes in the intracellular environment (e.g., changes in pH or ion concentration), revealing the heterogeneity of physiological responses to specific conditions in a cellular population. In addition, spinning disk microscopy (a variant of confocal microscopy) allows very quick dynamic processes to be imaged in living specimens.

Among the super-resolution techniques, total internal reflection fluorescence (TIRF) microscopy allows researchers to track single fluorescent molecules at the plasma membrane, while stimulated emission depletion (STED) microscopy provides detailed insight into the structure of cellular organelles.

The complex three-dimensional organization of cells within tissues and whole organs can be revealed using light-sheet microscopy. Also, multiphoton microscopy not only allows fixed tissue samples to be imaged, it can also track cells and observe cellular processes in living model organisms.

ADVANCED IMAGING TECHNIQUES AND DATA PROCESSING TOOLS

In recent years, we have collaborated with other research groups to establish a number of new imaging techniques. Specifically, our group has implemented data processing and analysis tools for light-sheet microscopy that keep pace with the rapidly increasing volumes of image data. We are now able to perform 3D morphological analyses of, for instance, mouse spinal cords and brains, zebrafish hearts, or even very large samples such as rat hearts.

In multiphoton microscopy, our group has implemented customized methods for intravital imaging in mice that enable researchers to study the interactions between nerve cells and inflammatory cells while simultaneously obtaining functional information on neuronal processes. We have adapted a multi-color excitation and detection technique to image color-coded ("confetti") mice expressing four different fluorescent proteins in their cells. Label-free imaging based on tissue auto-fluorescence has also been implemented.

OUR TOOLS

- Confocal laser scanning microscopy
- Multiphoton microscopy
- Light-sheet microscopy
- Total internal reflection fluorescence (TIRF) microscopy
- Stimulated emission depletion (STED) super-resolution microscopy
- In-vivo imaging
- Fluorescence live-time imaging
- Laser microdissection
- Image analysis and data processing

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Systems Biology Imaging

Light microscopy is uniquely suited to studying the structural organization of biological systems on a wide range of spatial scales. These methods allow researchers to not only see subcellular structures and molecular species, but also observe how they interact and organize into living organisms.

Light microscopy was the first technique to open a window into the invisible world. Through continuing technological advances, we now have the ability to visualize living systems at varying orders of magnitude. Light microscopy allows us to monitor the development of whole organisms, the structure and function of single cells, and the location and dynamics of individual molecules in model systems that systems biologists commonly use.

RECONSTRUCTING THE LIFE OF THE CELL

The Systems Biology Imaging Platform is part of the Berlin Institute for Medical Systems Biology (BIMSB) at the Max Delbrück Center and is located in the center of Berlin. It provides access to advanced microscopy methods as well as data processing and analysis tools for on-campus and visiting scientists. Our group is also working to increase the throughput of microscopy-based methods and fostering collaborations with industry partners to bring emerging imaging technologies to the MDC-campus in Berlin-Mitte.

The most widely utilized instrument within our platform is the confocal microscope. It measures fluorescence from a thin 2D slice inside a given sample. Assembling a large number of these "optical sections" allows for reconstruction of 3D volumes that indicate the abundance and distribution of fluorescently labeled molecules within a sample. For example, a protein that is of interest can be tagged with a fluorescent antibody and then visualized to explore subcellular structures, distinct cell types within complex tissue, or disease-related biomarkers.

We also offer a number of technologies that are optimized for live cell imaging. These include wide-field microscopy, light-sheet microscopy, and total internal reflection fluorescence microscopy as well as spinning disk confocal microscopy. Researchers often apply these tools to measure physiological processes in living samples, ranging from the biophysical properties of single receptors within the plasma membrane to cell division and lineage tracing in developing embryos.

In many microscopic investigations of living sytems, lab equipment like Petri dishes and pipettes are used in preliminary experiments.

MAKING SUPER-RESOLUTION A ROUTINE PRACTICE

Light microscopy has long been limited in resolution because of the nature of visible light. Recently, technologies have emerged that circumvent these limits and offer a much more fine-grained view of biological systems, with resolutions in the tens of nanometers range. In practice, however, the utility of these super-resolution methods is so far restricted by the relatively slow image acquisition and the small number of colors that can be detected simultaneously. Therefore, our group is currently developing an innovative microscope that will allow concurrent imaging of many molecules with different spectral properties over large sample areas, thus increasing the throughput of super-resolution approaches.

Moving forward, we will continue to focus on increasing the ease of microscopy-based assays through automation of instrumentation and image data processing and analysis. Our aim is to make light microscopy a high-throughput technology in which thorough molecular screenings of living systems are routine.

OUR TOOLS

- Laser scanning confocal microscopy
- Spinning disk confocal microscopy
- Light-sheet microscopy
- Total internal reflection fluorescence microscopy (TIRFM)
- 3D multicolor stochastic optical reconstruction microscopy (STORM)
- Live-cell wide-field microscopy

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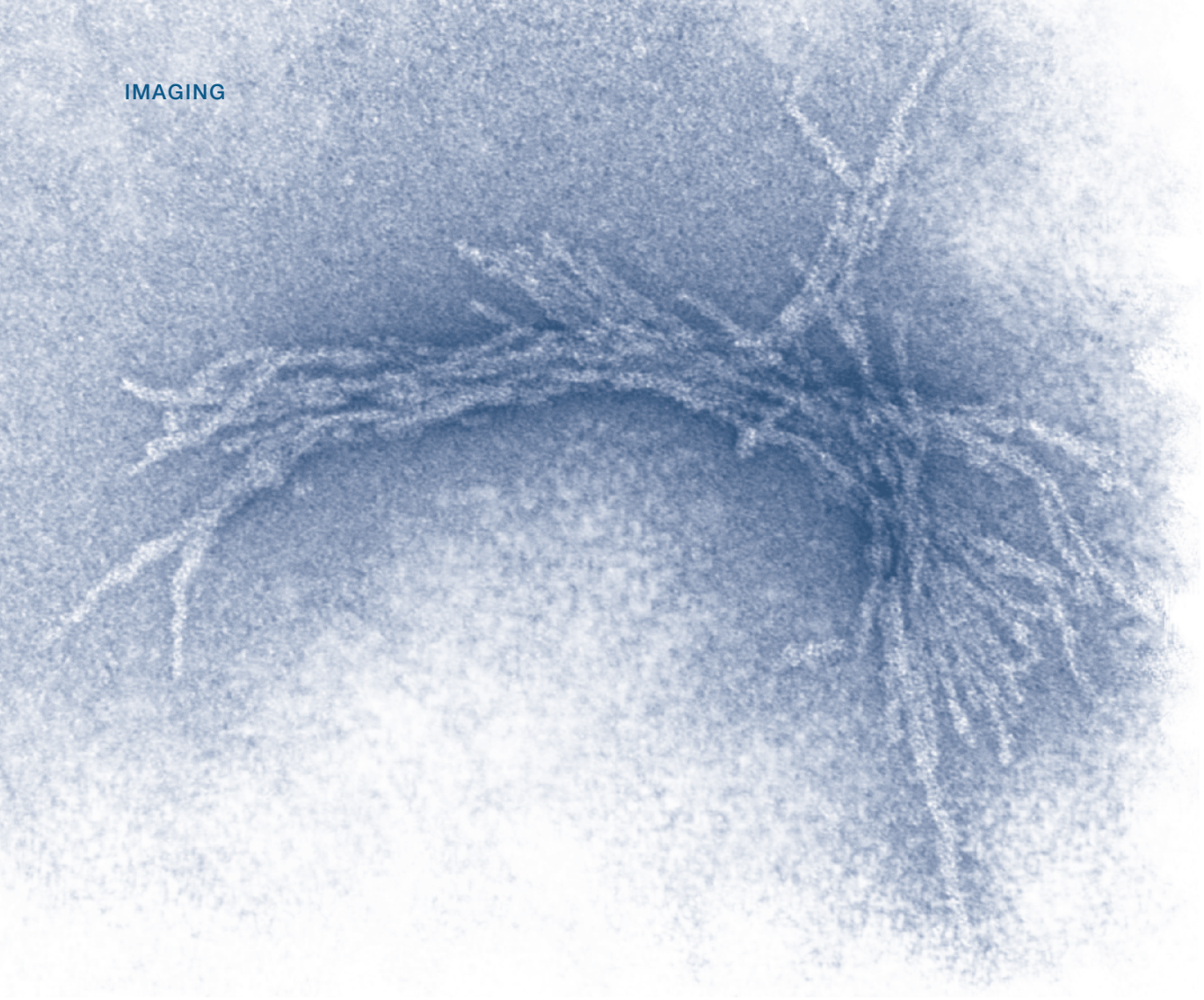
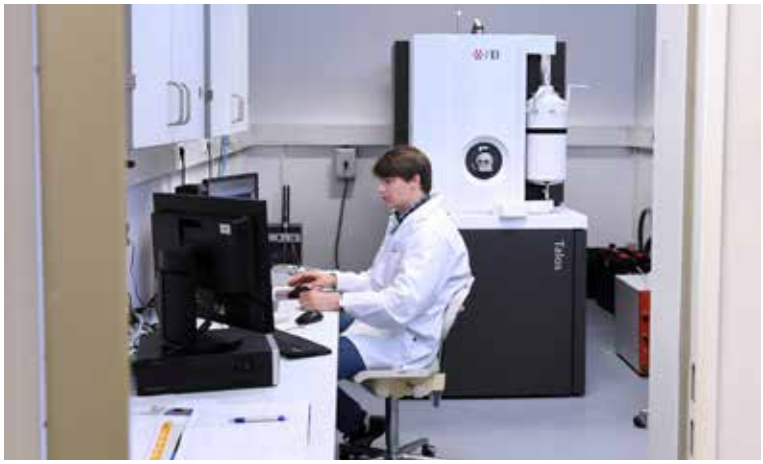


Electron Microscopy

With a resolution of less than one nanometer, electron microscopy allows researchers to peer deep into biological samples and even to explore the structure of molecular machines in the cell.

Electron microscopy is an indispensable tool in many fields of cell biology and medicine for studying subcellular structures in normal and diseased states. However, since the electron beam is only stable in a high vacuum (a vacuum with very low pressure), it is impossible to image living cells or tissues. Samples have to be chemically fixed and embedded, or immobilized through very low (cryogenic) temperatures – while retaining biological structures in a close-to-native state. Recent developments in cryo-electron microscopy in particular, such as highly sensitive electron detectors, allow visualizations at unprecedented resolution.

Electron microscopy even allows scientists to visualize individual protein structures, such as the fibrils that are involved in Huntington's disease (opposite page). A researcher operates a powerful new transmission electron microscope that is suitable for cryo-imaging (right).



DEPLOYING THE ELECTRON BEAM

Our group offers a range of electron microscopic methods to explore manifold specimens from humans and from model organisms, such as mice, zebrafish, and fruit flies. In many cases, immunolabeling of the sample with specific antibodies is required in order to identify the cellular structures that are of interest. Next, we usually deploy a routine preparation procedure known as the Tokuyasu cryosectioning technique, in combination with a special contrasting method developed in house. The approach allows researchers to clearly depict cellular membranes, and the inner structure of mitochondria, for example. Another important technique is the negative contrast, in which the background (instead of the target structure) is stained. Immunolabeling and negative contrast can also be combined.

Using these tools, our group has been investigating heart and muscle cell disorders, stem cells, and myelin defects in the brain. We have visualized neurodegenerative proteins as well as nanoparticles for drug development, and characterized various cell cultures. We also compared the well-known mouse model with the naked mole rat, a unique species, on an ultrastructural level. For many of the projects, available protocols had to be adapted or new sample preparation strategies developed. Recently, we started using a technique known as high pressure freezing, which is particularly suited for preserving the subcellular architecture. Our facility is available for all types of collaborations.

A 3D PLUNGE INSIDE THE CELL

Since 2017, we have a new transmission electron microscope (Talos L120C) at our disposal, opening the door to cryo-electron microscopy in the future. We have started optimizing sample preparation approaches and obtaining initial results in structural and cell biology. The device allows us to perform electron tomography in which detailed 3D structures are assembled from microscopic series. We will thus be able to visualize small cell compartments, such as vesicles and membrane structures, and even biological macromolecules in 3D. Additionally, we envisage close collaboration with the **Charité – Universitätsmedizin Berlin** to establish a new facility for high-end cryo-electron microscopy on the Berlin-Buch campus.

OUR TOOLS

- Transmission electron microscopes:
  - Talos L120 C (120 kV) with long duration dewar, 16M Ceta CMOS camera and 2 Gatan cryoholders (FEI)
  - Morgagni (80 kV) with 11M Morada CCD camera (FEI)
  - EM 910 (120 kV) with 11M Quemesa CCD camera (Zeiss)
- 4 ultramicrotomes, one with a cryochamber for Tokuyasu technique
- Freeze substitution device AFS2, grid plunger and grid stainer AC20 (Leica)
- Carbon coater, GloCube glow discharge system, trimming device and others

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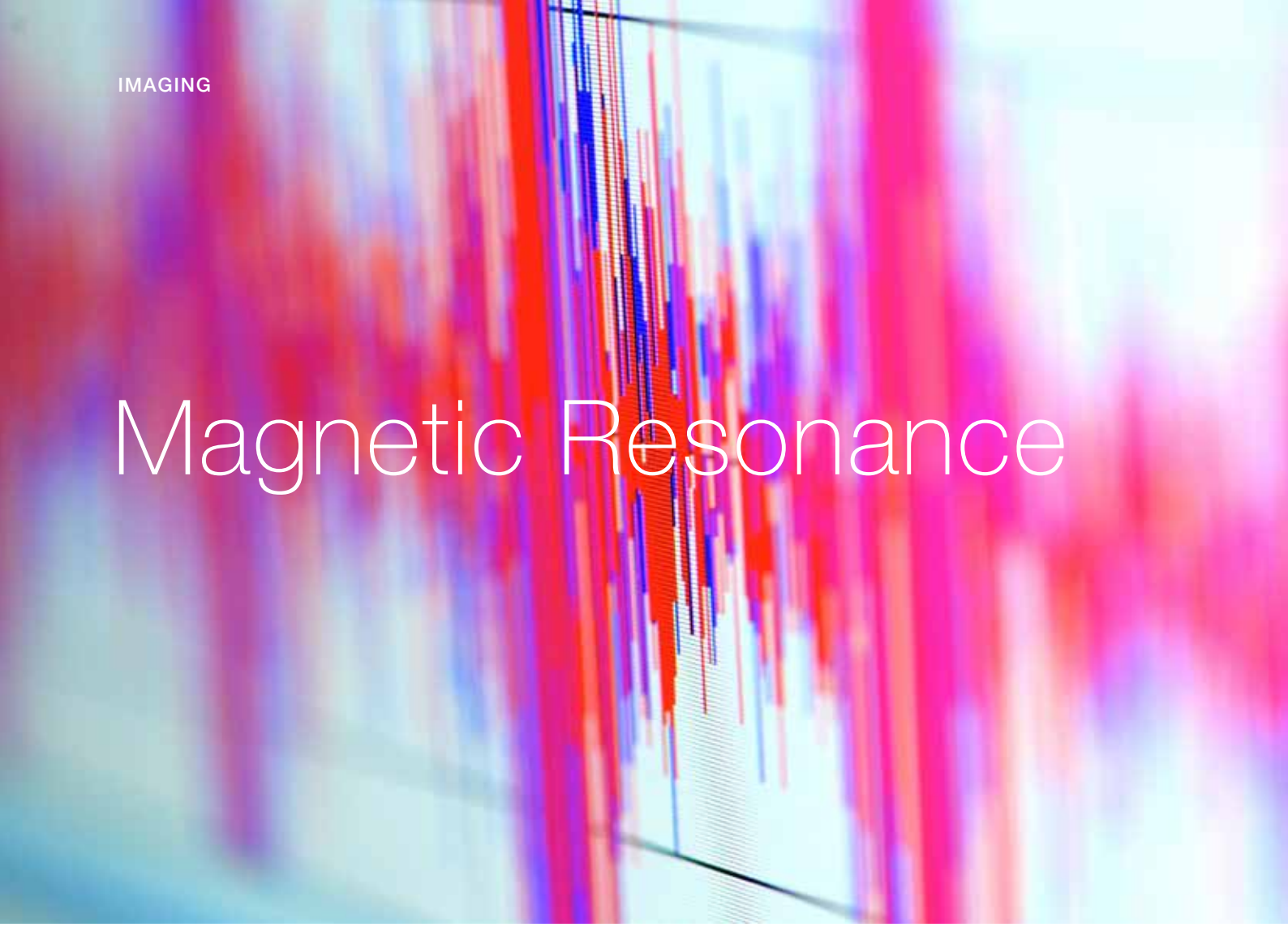


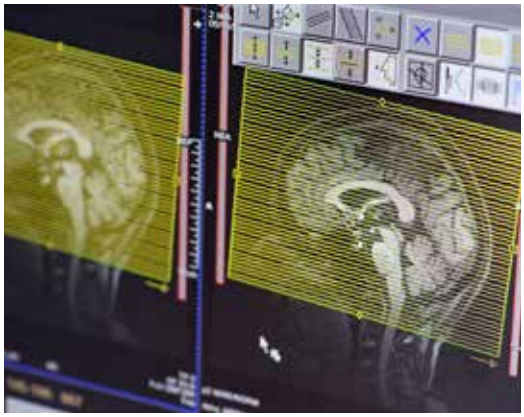
Magnetic Resonance

Our group carries out interdisciplinary imaging projects using small animal and whole-body human MR scanners with high and ultrahigh field strengths to explore organs and tissues in novel ways. One of our aims is to support new approaches to diagnosis and therapy.

Magnetic resonance imaging (MRI) is a crucial diagnostic tool in clinics worldwide. The approach uses magnetic fields and radio frequency (RF) signals to depict tissues and organs. Research applications are rapidly expanding thanks to constantly increasing magnetic field strengths, customized RF antenna arrays, and faster, smarter image processing. Higher spatial resolution combined with the capacity to image new substances noninvasively is providing new insights into healthy and pathological processes under in vivo conditions.

BRINGING MRI TO NANO-SCALE PROBES

The Berlin Ultrahigh Field Facility (B.U.F.F.) at the Max Delbrück Center provides advanced MRI capabilities for interdisciplinary research projects using small animal and whole-body human MR scanners. We carry out human MRI on 7-Tesla and 3-Tesla instruments, and animal MRI at 9.4 Tesla. Significant gains in field strengths are enabling us to image new substances and nano-scale probes. We are also expanding imaging to new organ and model systems by custom-designing novel types of MR detectors (RF antennae).



Clinical application of an in-house built radio-frequency coil array for investigating the heart at 7 Tesla (right). Examinations need to be carefully planned, as in the case of advanced brain imaging (above).

The facility has reception areas and changing rooms for volunteers, and all the technical prerequisites for clinical studies, including emergency equipment and extra patient monitoring units. This has allowed us to take on an important role in major research initiatives, including the Helmholtz Imaging and Curing Environmental Metabolic Diseases (ICEMED) Alliance, the German National Cohort, and a number of other national and international projects devoted to various health conditions.

MAPPING THE HEART AND KIDNEY IN NEW WAYS

B.U.F.F. is collaborating with other research groups to develop new methods for mapping anatomy, morphology, microstructure, function, physiology, and metabolism in animal and human subjects. By achieving new levels of spatiotemporal resolution, and imaging new substances such as sodium, we are able to conduct groundbreaking studies on organs such as the heart and kidney. We have begun a new thermal phenotyping project, supported by the European Research Council (ERC), to characterize the temperature profiles of various tissues, both healthy and diseased. One aim of the project is to use MRI to manipulate the temperature of tissues and utilize this parameter as a potential diagnostic and therapeutic tool.

OUR TOOLS

- Human MRI at 7 Tesla
- Human MRI at 3 Tesla
- Animal MRI at 9.4 Tesla

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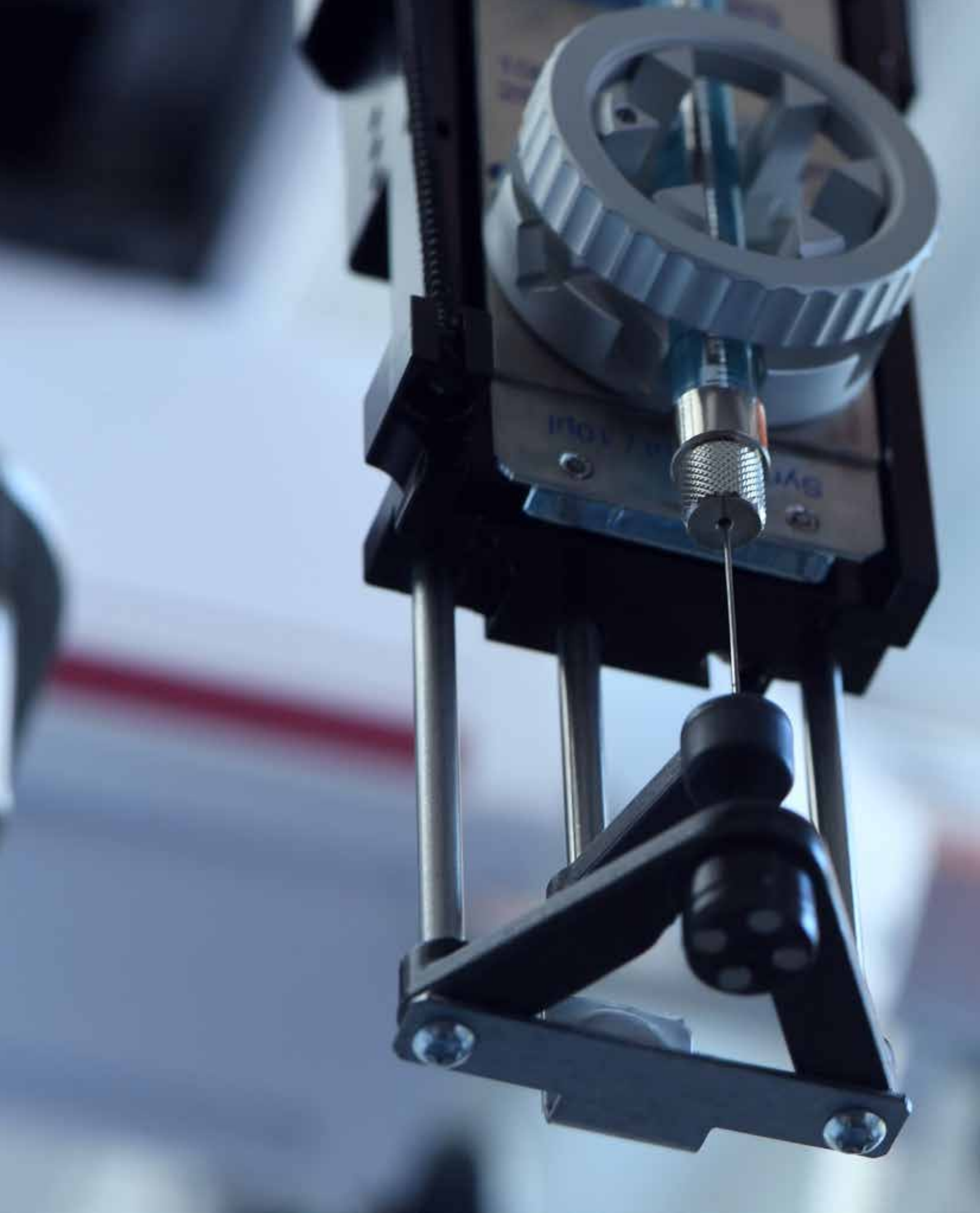
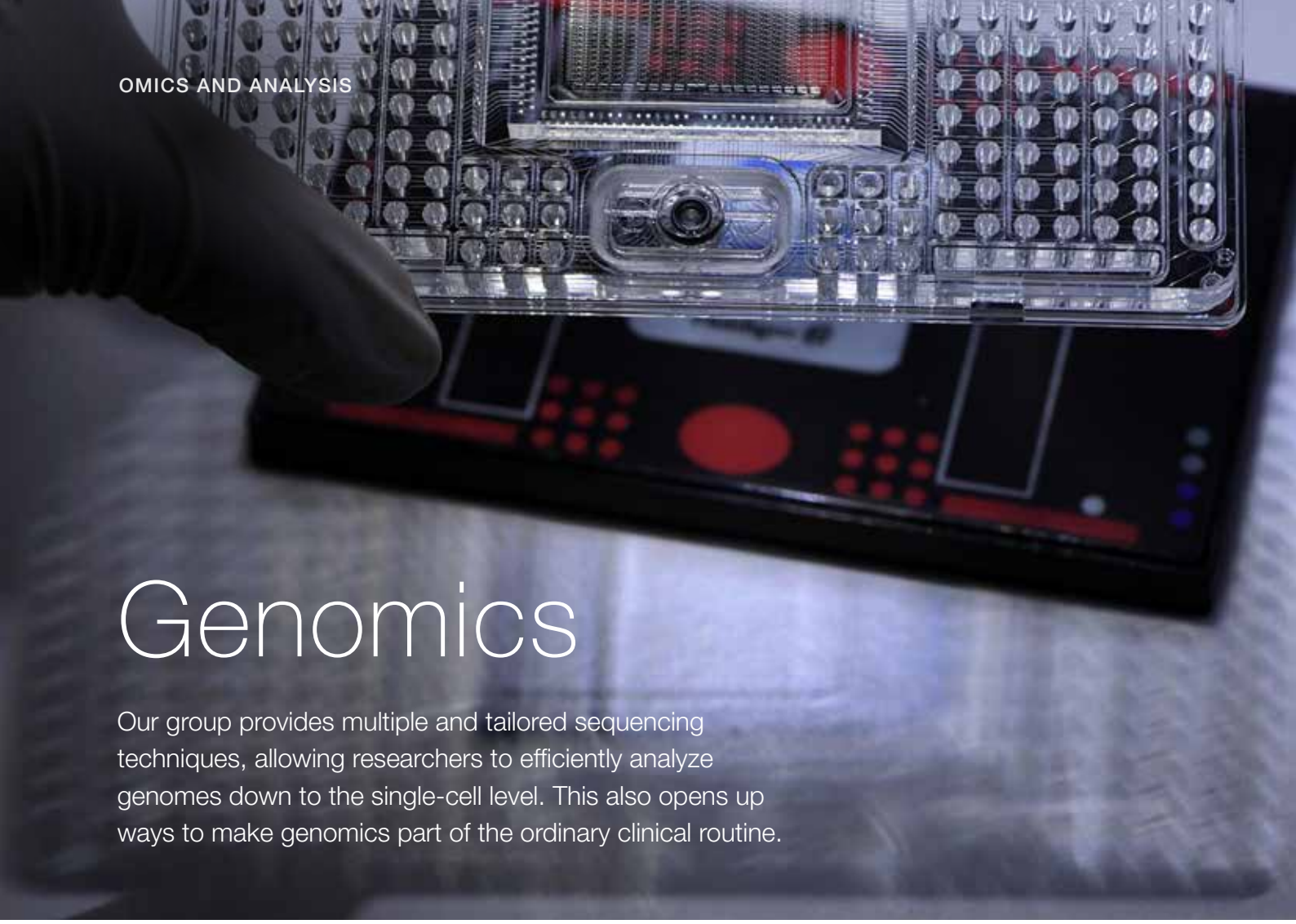


Omics and Analysis



Genomics

Our group provides multiple and tailored sequencing techniques, allowing researchers to efficiently analyze genomes down to the single-cell level. This also opens up ways to make genomics part of the ordinary clinical routine.

Technologies for sequencing the genome have fundamentally changed our view on health and disease. Today, it is possible, for example, to analyze the complete DNA of a patient in a fraction of the time and at a fraction of the cost that would have been incurred just 10 or 15 years ago. Genomics – the systematic and quantitative study of genes and how they are regulated and transcribed – has thus become an everyday tool for biomedical research. Ongoing improvements in sequencing methods, often addressed as next-generation sequencing technologies, make genomics a vibrant scientific field.

UNDERSTANDING THE GENOME FROM A SYSTEMS PERSPECTIVE

The Scientific Genomics Platform combines resources and services of the Max Delbrück Center and the **Berlin Institute of Health (BIH)** and is committed to developing and implementing key sequencing technologies. Our portfolio encompasses diverse applications and approaches, such as high-throughput (massively parallel) sequencing and single-cell sequencing.

Single-cell genomics is a focus of our work. The approach aims at analyzing the genetic makeup of individual cells, which is of particular interest in tumor biology, for example. We also work to develop additional emerging gene perturbation approaches, where specific genes are perturbed to elucidate genetic functions and pathways. Our group also provides bioinformatics analyses of sequencing data.

Genomics transcends analysis of the genetic code. It also aims to explore modifying factors, such as the methylation of DNA, which are central to gene

Single-cell preparation for sequencing experiments requires tailored cell-biological and biochemical approaches as well as concentrated work (right). Modern lab equipment and automated systems (opposite page, below) ensure efficient workflows.

regulation. These modification patterns are known as epigenomes. The transcriptome – the set of RNA molecules in the cell necessary to transcribe genes into proteins – is also of interest to many researchers. Thus, we have established powerful platforms ranging from whole genome and targeted genome sequencing techniques, through various epigenomic profiling methods, to the many variants of transcriptome sequencing. The established technologies are available to all scientists at the Max Delbrück Center. In addition, we are actively collaborating with multiple external research groups.

TOWARDS PATIENT-SPECIFIC MOLECULAR PROFILING

Novel methods are of utmost importance in the advancement of science. We are currently developing highly sensitive genome-wide DNA methylation analysis procedures that can be applied down to the single-cell level. These methods are breaking new ground in our understanding of how basic transcriptional processes governing gene function are regulated. In combination with novel sequencing instruments (e.g. sequencers known as nanopore devices), these methods will allow fast and powerful diagnostic readouts of tumor cells, other cells, and even cell-free DNA circulating in the blood. This general approach to molecular profiling using simple blood samples (also called “liquid biopsies”) opens up new ways of understanding and monitoring disease development in individual patients and of tailoring therapy accordingly.

OUR TOOLS

- Illumina short-read sequencing
- Pacific Biosciences long-read sequencing
- Single-cell technologies (FACS, Fluidigm, Chromium, 1CellBio, ICELL8)
- Sequence data analyses

CONTACT

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Metabolomics

Metabolomics can tell complex stories about the interactions of small molecules – the metabolites – in cells and body fluids. This approach thus allows researchers to investigate diseases, their causes, and potential treatments in a new and in-depth manner.

A custom-built robot enables automatic sample handling in large metabolomics studies.

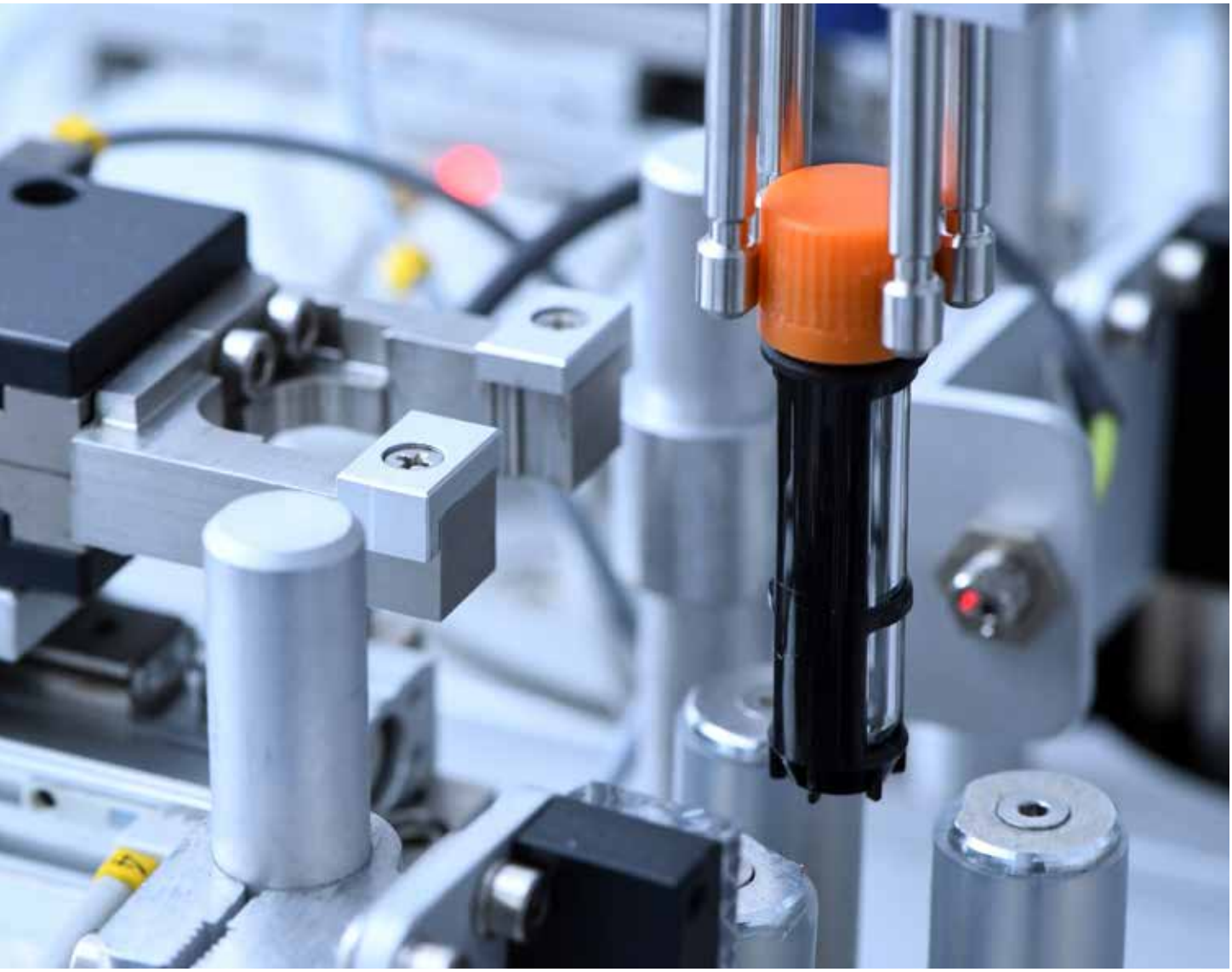
During the life of an organism, a myriad of small molecules arise as intermediates and products of metabolism. Metabolomics – the systematic study of these metabolites – aims at elucidating the chemical fingerprints that specific cellular states and processes leave behind, thus enabling a complex and in-depth understanding of health and disease. Metabolomics significantly relies upon mass spectrometry, an analytical technique that allows the molecular composition of a biological sample to be characterized by measuring hundreds of thousands of metabolites at the same time. Combined with statistical and modeling methods, it is thus possible to explore the organism's molecular response to disease, drugs, diet, and environmental factors.

MASS PROFILING OF BIOCHEMICAL SYSTEMS AND PATHWAYS

Our platform, part of the **Berlin Institute of Health (BIH)**, which is a joint undertaking of the Max Delbrück Center and Charité – Universitätsmedizin Berlin, provides a number of state-of-the-art mass spectrometry methods as well as bioinformatics and statistical support. Our tools are suited for both targeted and untargeted metabolomics approaches. Whereas untargeted approaches attempt to measure as many metabolites as possible in a single analysis in an unbiased way, targeted methods focus more specifically on pre-defined compounds, with analytical techniques being adapted to maximize their detection.

In principle, targeted approaches can be optimized for any group of metabolites. However, our group specializes in analyzing the metabolites of the central carbon metabolism, which includes analysis of the organism's core biochemical pathways for utilizing carbohydrates and generating energy. In addition, we support researchers who are interested in applying metabolomics approaches to lipid metabolism, a branch known as "lipidomics."

We have also recently added the capacity to use a specific tool (Biocrates P400 kit) that can perform analyses of up to 400 key compounds, offering a broad-brush approach to metabolic systems. This kit is particularly suitable where a general view of metabolism is required to verify or refine existing scientific hypotheses.



PICTURING CELLULAR AND SUBCELLULAR METABOLISM

Current challenges in the field of metabolomics include the need for better and more rapid identification of metabolites that are, as yet, unknown. In addition, there is increasing interest in metabolomics analyses of single cells, or even specialized subunits of the cell (organelles), such as mitochondria. These developments entail the need for new and refined approaches and protocols. In the longer term, we hope to develop and offer single-cell metabolic analyses for biomedical research. Moving forward, we are open for collaboration with other scientific groups that complement our research interests.

OUR TOOLS

- Gas chromatography mass spectrometry
- Liquid chromatography mass spectrometry
- Direct infusion mass spectrometry
- Liquid extraction surface analysis mass spectrometry (LESA-MS)
- Ultrahigh field asymmetric ion mobility spectrometry (Ultra-FAIMS)

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Proteomics

Our platform provides high-throughput techniques to study the basic function and regulation of proteins in health and disease. This helps to identify new candidates for novel diagnostic and therapeutic approaches.

Proteomics enables the global and targeted analysis of all proteins and their functional states. Proteins are central to most biological functions within an organism and frequently alter in their abundance and in their activation status in disease. Thus, proteins are routinely used as disease biomarkers as well as drug targets. To elucidate how proteins work, proteomics approaches make use of mass spectrometers. These high-throughput instruments allow proteins extracted from cells, tissues, and blood samples to be identified and quantified. In addition, it is possible to explore the binding partners of proteins, their localization in cells and tissues, and their functional activity.

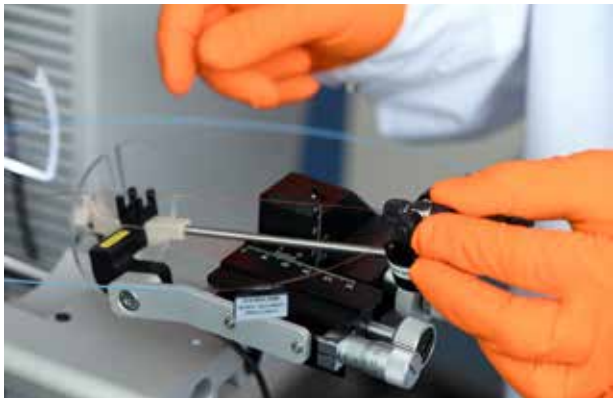
UNDERSTANDING HOW PROTEINS WORK

Our platform combines resources and services of the Max Delbrück Center and the **Berlin Institute of Health (BIH)**, develops mass spectrometry-driven proteomics methods and makes this technology available to partners at the Max Delbrück Center, Charité – Universitätsmedizin Berlin, and beyond. The most common application in our group is the generation of global quantitative inventories of all proteins in cell or tissue samples, with the highest possible coverage and throughput for various biological or clinical states. A special focus of our work is on improving multiplexing methods that enable us to analyze several samples at the same time, allowing us to either spend more time on an experiment and dig deeper into the proteome, or to analyze more samples at an even faster throughput.

We can also determine the activation status of the thousands of proteins we measure by detecting biochemical modifications, such as phosphorylation, ubiquitination, or acetylation groups in these proteins. Such modifiers act like molecular switches that turn functional states on and off.

Investigating proteins with sensitive and comprehensive methods (“deep coverage”) is crucial for connecting information about proteins with DNA-sequencing and RNA-sequencing information, since many genes that cause disease (and thus their protein products) occur at very low abundances. Reading out the consequences of genetic alterations on the protein level helps researchers to understand which mutations are possible drivers of disease and to identify potential drug targets.

For altered genes that have no known function in a certain context, it is also valuable to analyze the interaction partners of proteins. These may offer clues about specific roles in disease-causing processes. To validate initial discoveries, we employ targeted mass spectrometry methods that allow even higher throughput and could be used for biomarker analyses in future clinical studies.



This precision device, which couples liquid chromatography and mass spectrometry, is used to identify and quantify proteins.

CLOSING THE PERFORMANCE GAP

By augmenting throughput and coverage of proteomics approaches, we have contributed to closing the performance gap with regard to genomics techniques. Specifically, we have been able to demonstrate that proteomics analyses allow the reinforcement of findings from genomic sequencing studies (e.g. in cancer genomics), and enable researchers to gather additional information on precise disease mechanisms, such as how molecular signals and pathways are deregulated in a diseased state. A key task for the future will be to further increase the sensitivity of these techniques to make them applicable in routine clinical biopsy samples, possibly down to the single-cell level.

OUR TOOLS

- Proteomics of cell lines, tissues and plasma samples
- Label-free, TMT- and iTRAQ-based global protein quantification
- Targeted protein quantification
- Post-translational modification analysis
- Ultrahigh-pressure liquid chromatography
- High-resolution orbitrap mass spectrometry
- Multi-omic and proteogenomic approaches
- Pathway and signaling bioinformatics

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Proteomics and Metabolomics

We aim to use quantitative and time-resolved methods to help us understand the dynamics of biochemical pathways and networks at the molecular level. These studies will help us decipher the crosstalk between metabolism and gene regulation.

A team member does experimental lab work (right). The photo on the opposite page shows a temperature-controlled injection port, which is an important instrumental component for performing gas chromatographic analyses.

Interactions between genes, proteins, and metabolism are a key part of cellular processes. It is now possible to study the manifold molecular species and correlations in the cell at a systematic and quantitative level through large-scale analytical techniques such as mass spectrometry. Whereas proteomics (a term coined on the analogy of "genomics") aims at the large-scale study of proteins and their functional networks, metabolomics is concerned with the intermediates and products of metabolism. Investigating the intertwined molecular systems allows for a better and more complex understanding of metabolic regulation and its impact on basic processes such as cell differentiation and cancer formation.

CELLULAR CROSSTALK IN HEALTH AND DISEASE

The integrative proteomics and metabolomics research and technology platform is an integral part of the Berlin Institute for Medical Systems Biology (BIMSB). We are a team of biologists, engineers, chemists, pharmacologists, and bioinformaticians who have established a number of mass spectrometry-based proteomics and metabolomics methods that allow us to analyze the dynamics of metabolism under in vitro conditions and in living organisms.

For proteomics studies, we apply mass-spectrometric techniques that either use stable isotopes for labeling proteins or that are label-free. We have also developed and patented a specific workflow called pulsed stable isotope-resolved metabolomics (pSIRM) that provides dynamic, time-resolved quantitative measurements of the central metabolism in in vitro and in vivo investigations.

Specifically, our group is interested in the crosstalk between metabolism and gene regulation during cellular differentiation and cancer formation. We are focusing on central metabolism, a set of core biochemical pathways that is highly flexible and continuously adjusted to the physiological programming – and reprogramming – of the cell. Inversely, the metabolic state and metabolic modifications can influence how, for instance, potentially cancer-causing genes (oncogenes) are expressed.

PINPOINTING THE ROLE OF METABOLIC STRESS

Moving forward, we will intensify our efforts to explore this crosstalk between metabolism and gene regulation. For example, the protein MYC is an important regulator of gene expression that, if mutated, can promote tumor growth. We are deciphering, on a molecular level, how the production of MYC is itself controlled by metabolic stress. We also aim to further improve our methods and data integration workflows to allow us to apply proteomics and metabolomics techniques to interactions at the single-cell level in healthy and in cancerous tissues.

OUR TOOLS

- Gas chromatography mass spectrometry based metabolic profiling of cell lines and tissues
- Stable isotope resolved metabolomics analyses of cell lines
- Quantitative shot-gun proteomics analyses of cell lines and tissues

CONTACT
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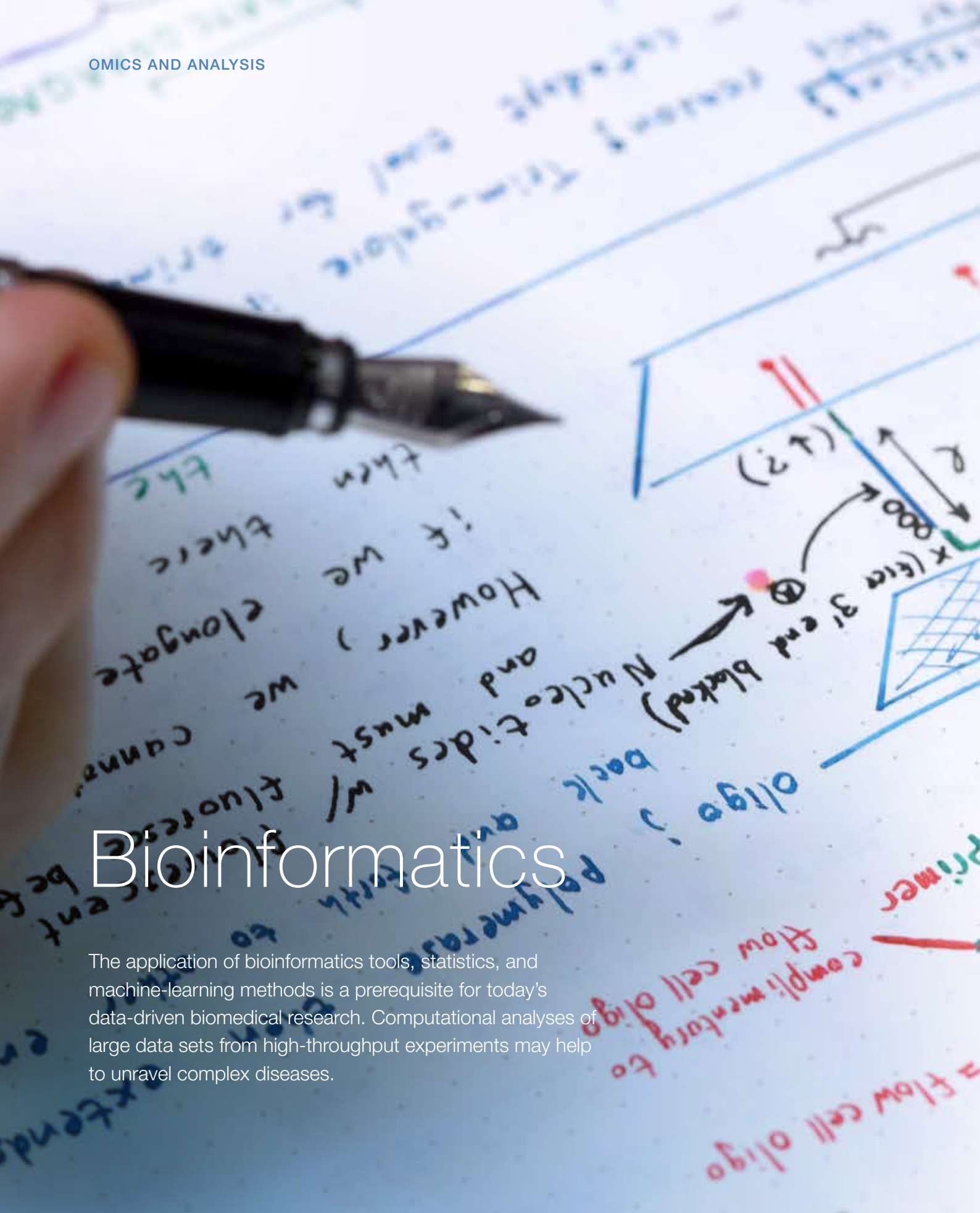

Bioinformatics

The application of bioinformatics tools, statistics, and machine-learning methods is a prerequisite for today's data-driven biomedical research. Computational analyses of large data sets from high-throughput experiments may help to unravel complex diseases.

Bioinformatics team members are discussing data analysis strategies. Handwritten notes and sketches can help clarify various processes.

High-throughput technologies in molecular medicine, such as next-generation genome sequencing, produce vast amounts of data that may help to characterize complex diseases. However, powerful bioinformatics tools for data analysis and interpretation are necessary to understand these high-volume data sets. The application of statistics and machine-learning methods to experimental results on a broad scale has thus become an essential part of biomedical research.

STUDYING BIOLOGICAL MECHANISMS WITH COMPUTATIONAL TOOLS

The Bioinformatics Platform is a research group within the Berlin Institute of Medical Systems Biology (BIMSB) at the Max Delbrück Center. The platform creates and maintains bioinformatics tools and databases. It studies molecular mechanisms using externally available and/or in-house techniques. In addition, the platform provides collaboration opportunities and support for MDC scientists.

Specifically, we supply infrastructure and expertise for the bioinformatics and scientific IT needs of researchers, providing hardware and software for research-oriented tasks. We have various web-based interactive tools at our disposal, e.g. a local copy of the UCSC (University of California, Santa Cruz) Genome Browser, Shiny Server for interactive analysis, and an internal Galaxy server. We also have access to bioinformatics software solutions such as methylKit, genomation, RCAS, netSmooth, and a GNU Guix bioinformatics software repository.

We provide additional specialized IT services geared towards bioinformatics end users as well as a mobile teaching system for scientists. In addition, we offer courses and consultation sessions on bioinformatics, IT skills, and programming.

UNRAVELING COMPLEX DISEASE

As a general principle, we aim at gaining an understanding of genetic and epigenetic control mechanisms of cellular differentiation and of complex diseases, such as cancer, by performing computational analyses of high-throughput data sets. These data are derived, for instance, from microarrays and next-generation sequencing experiments. Ultimately, we aim to uncover genomic and epigenomic anomalies and the interactions between them that lead to disease. In doing so, we strive to maintain state-of-the-art expertise in computational biology and data analysis, as well as to develop bioinformatics tools and techniques that are relevant, reproducible, and well documented.

OUR TOOLS

- Local copy of UCSC Genome Browser and track hubs to display genomics data (genome.mdc-berlin.de)
- Galaxy server for guided user interface for bioinformatics analysis (galaxy.mdc-berlin.net)
- Shiny Server for interactive analysis (shiny.mdc-berlin.de)
- R packages: methylKit; genomation; RCAS; netSmooth
- Reproducible bioinformatics software deployed at workstations and within the cluster via GNU Guix (guix.mdc-berlin.de)
- Virtual machines that can deploy publication-related web apps and databases such as DoRiNA and circBase

CONTACT

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Translational Bioinformatics

Our group provides bioinformatics expertise and workflows for turning large-scale biomolecular data sets into clinically relevant information. In close collaboration with researchers and clinicians, we thus aim to create knowledge and systems that lead to more patient-specific treatment regimens.

Sophisticated bioinformatics analysis plays a key role in understanding the molecular mechanisms of disease and in translating complex biological data into clinically relevant information. While bioinformatics in general has long been essential for handling extensive data sets from high-throughput (omics) experiments – such as genome sequencing or mass-spectrometric analysis of proteins and metabolites – the emerging science of translational bioinformatics focuses specifically on turning these data into actionable knowledge for clinical application. Translational bioinformatics thus aims to enhance human health and well-being as well as treatment outcomes through a range of computational methods.

FROM BENCH TO BEDSIDE

The Bioinformatics Core Unit provides bioinformatics and data analysis expertise for translational research projects. It is part of the **Berlin Institute of Health (BIH)**, which is a joint undertaking of the Max Delbrück Center and Charité – Universitätsmedizin Berlin. To achieve this, we combine a growing portfolio of standardized data processing workflows with project-specific bioinformatics solutions, exploratory statistics, visualization, data-mining methods, machine-learning algorithms, and customized data integration. We perform data analysis in close collaboration with researchers and clinicians. This enables us to refine intermediate results and to optimize

Discussing data analysis results and integration strategies forms an important part of the group's research and services.

data interpretation strategies in an iterative and incremental manner.

Established data analysis workflows cover a range of high-throughput sequencing technologies and allow the identification of relevant genetic variants in rare diseases. Our cancer genomics approaches provide rich annotations of variants that offer clinical intervention possibilities and aid researchers in defining immunological properties of cancer cells (neoepitope prediction, HLA typing). Workflows for RNA sequencing enable thorough statistical analyses and broad functional annotations for bulk as well as single-cell data.

We have built an omics data management system according to the internationally recognized FAIR Guiding Principles, whose aim is to make all research data Findable, Accessible, Interoperable, and Reusable. The system provides transparent long-term storage and enables cross-project data integration as well as efficient access to current analysis results. In addition, the Bioinformatics Core Unit organizes courses and workshops on high-performance computing, workflow management, and data analysis, while also advising on method selection, experimental design, and analysis planning.

TOWARDS PERSONALIZED CANCER DIAGNOSTICS AND TREATMENT

Our group provides a local instance of a web-based cancer genomics platform (cBioPortal) that supports the analysis and visualization of large-scale cancer genomic data sets. We are continuously working to develop extensions and add-ons in order to facilitate better identification and interpretation of somatic variants and pathway dysregulation. The system is used not only by researchers to better understand cancer biology, but is also a key tool for the molecular tumor board at the Charité Comprehensive Cancer Center, where oncologists, pathologists, and bioinformaticians work together to make optimal treatment decisions for individual cancer patients based on molecular data. Our methods have also helped to determine patient-specific neoepitopes for cancer immune therapy, to identify causative variants in genetic disorders, and to reveal the molecular processes underlying cardiovascular and neurodegenerative diseases.

OUR TOOLS

- Local instance of cBioPortal with extensions for clinically actionable variants (cbioportal.bihealth.org)
- Large collection of established workflows for next-generation sequencing
- Customized data analysis and cross-omics data integration
- Omics data management according to the FAIR Guiding Principles
- VCFPy: a Python library supporting reading and writing variant call format (VCF) files

CONTACT

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Disease Models

Pluripotent Stem Cells

Pluripotent stem cells, which are capable of self-renewal and can differentiate into many cell types, are unique tools for understanding complex disease mechanisms and investigating novel therapies. As such, the technology allows the gap to be closed between basic research and clinical use.

Human pluripotent stem cells have the potential for various clinical uses as well as for establishing laboratory models of disease that overcome the limitations of animal models. Pluripotent stem cells can be derived from patient-specific somatic cells through genetic reprogramming (human induced pluripotent stem cells, hiPSCs). These hiPSCs are capable of self-renewal and have the potential to differentiate into virtually any cell type, opening up ways to better understand certain disorders and to investigate regenerative therapies and novel drug candidates. As such, hiPSCs are unique tools for closing the gap between the identification of disease-causing mechanisms and the development of suitable therapeutic approaches.

Induced pluripotent stem cells normally grow on cell culture dishes, which are coated with special nutrient matrices.

SUPPORTING BASIC AND TRANSLATIONAL STEM CELL RESEARCH

The Stem Cell Core Facility is part of the **Berlin Institute of Health (BIH)**, a joint project of the Max Delbrück Center and Charité – Universitätsmedizin Berlin as well as the **Deutsches Zentrum für Herz-Kreislauf-Forschung (DZHK).**

We support basic and translational research by facilitating all aspects of hiPSC technology, including the derivation, differentiation, and distribution of human stem cell lines. Additionally, the platform provides scientists with state-of-the-art protocols and techniques for proper handling and manipulation of hiPSCs.

We interact closely with international stem cell facilities to address the constant innovations in the field of reprogramming, differentiation, and genome editing. In recent years, our group has established a feeder-free cultivation system of hiPSCs that does not require foreign feeder cells and instead uses chemically defined culture media. In collaboration with other teams at the Max Delbrück Center, we also developed neuronal, cardiac, endothelial, and muscle cell differentiation protocols. In addition, the facility has performed multiple genome engineering experiments on hiPSCs, and we were able to reprogram various disease-specific and non-disease-specific cells from patient samples.

The Stem Cell Core Facility also organizes regular training courses on stem-cell culture techniques, as these methodologies are distinct from those used in other mammalian cell cultures and require a profound depth of knowledge and hands-on expertise. The training courses are intended for researchers and technicians who plan projects using hiPSCs.

SCALING UP STEM CELL PRODUCTION FOR CLINICAL USE

We are currently collaborating with Harvard Medical School to set up a stem-cell engineering course for scientists on how to genetically manipulate pluripotent stem cells. One big problem is the maturation of the differentiated stem cells, which we are trying to address using 3D and suspension culture systems. Moreover, we are working to find ways, and are testing suitable machines, to allow for the automated, high-throughput functional analysis of differentiated stem cells. We are also interested in developing good manufacturing practices for producing stem cell lines for future clinical applications and in establishing a certified lab for quality-controlled hiPSCs.

OUR TOOLS

- Isolation of primary cells from patient samples
- Reprogramming of cells into human induced pluripotent stem cells (hiPSCs)
- Gene editing and cell labeling
- Provision of hiPSC reference lines and banking
- Provision of hiPSC-derived differentiated cells
- Derivation of organoids

CONTACT

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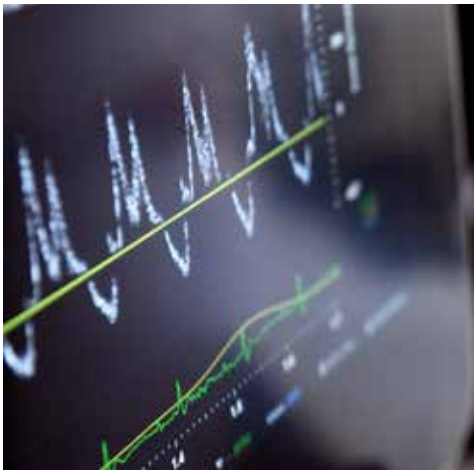


Mouse and rat hearts can be investigated with ultrasound (top left) as well as high-resolution micro-CT imaging (right). Bar-coded chips (bottom left) enable automated blood testing.

Animal Phenotyping

Our platform provides a large set of validated approaches for investigating physiological and morphological characteristics in mice and rats and sensitively screening for phenotypic variations. This gives researchers an important resource for studying animal disease models.

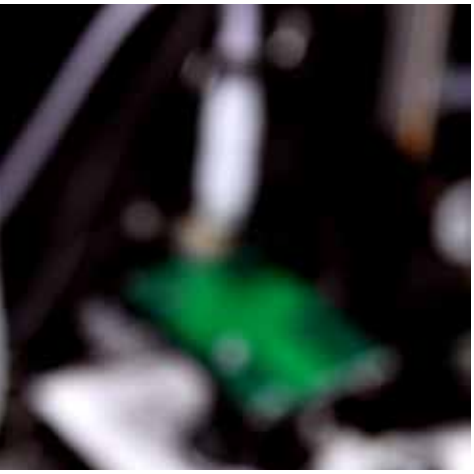
Despite numerous advances in research techniques such as in vitro methods and advanced computer modeling that avoid the use of animals, there is still a need in preclinical research to study the morphological, physiological, metabolic or behavioral characteristics – the phenotype – of animals. Such a whole-system approach to health and disease provides data that would otherwise not be available. Specifically, animal phenotyping allows researchers to gain a better understanding of the complex interactions between the cardiovascular, respiratory, and central nervous systems, which is critical for the development of many human pharmaceuticals and therapies.

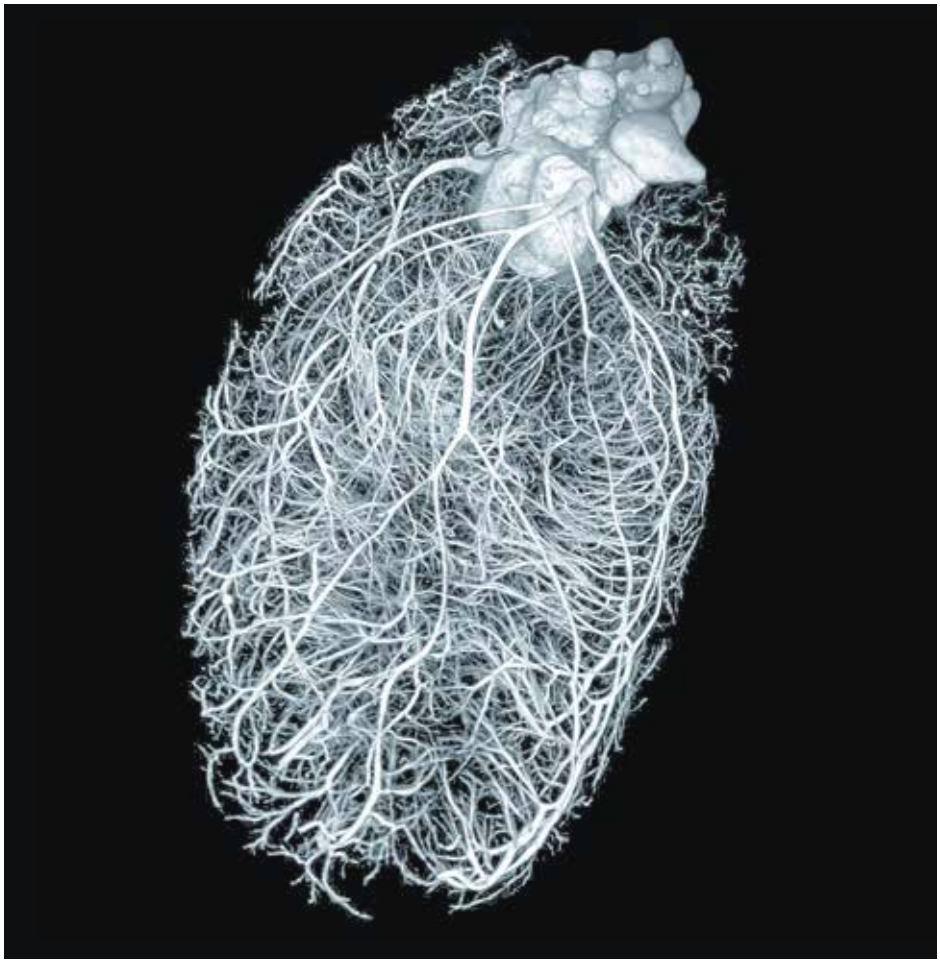
STUDYING MODEL ANIMALS IN NON-INVASIVE WAYS

The Animal Phenotyping Platform at the Max Delbrück Center houses a comprehensive collection of tools for the physiological and morphological assessment of experimental mice and rats. We focus on techniques that minimize animal use and enable researchers to obtain comparable levels of information from fewer animals or to obtain more information from the same number of animals.

Using a wide variety of preclinical imaging techniques – such as high-frequency ultrasound, photoacoustic imaging, micro-computed tomography, quantitative bioluminescence and fluorescence imaging, and time-domain nuclear magnetic resonance imaging – allows researchers to characterize disease progression and ascertain therapeutic effects throughout the entire experimental period.

Additionally, we use various non-invasive in vivo examinations that allow physiological, metabolic, and bioelectrical variables to be monitored in conscious animals (e.g., blood pressure and heart rate measurements, electrocardiography, and respiratory analysis). We provide state-of-the-art services, innovative techniques, and helpful advice on pathophysiological questions to both experienced and novice investigators.





A WHOLE-ORGANISM APPROACH TO FUNCTIONAL GENOMICS

The Max Delbrück Center is currently building a dedicated facility for in vivo pathophysiology experiments (the In Vivo Pathophysiology Laboratory) to promote preclinical translational research and functional genomics. Our platform will pool and further improve well-established phenotyping approaches, ensuring the highest technological and quality standards. We will give investigators the capacity to accurately assess developmental, behavioral, cardiovascular, and metabolic characteristics in rodent disease models over long periods of time and to sensitively screen for phenotypic variations. The planned laboratory is expected to have multiple benefits for researchers at the Max Delbrück Center and for collaborating external scientists.

OUR TOOLS

- High-frequency ultrasound
- Photoacoustic imaging
- Micro-computed tomography
- Bioluminescence and fluorescence imaging
- Clinical chemistry
- Hematology
- Metabolic phenotyping
- Body composition analysis
- Electrocardiography (ECG)
- Blood pressure measurements
- Respiratory analysis

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Transgenics

Our group provides services for engineering the mouse genome, creating “knock-out” and “knock-in” mice. A powerful molecular tool – the enzymatic CRISPR-Cas9 system – enables highly precise gene editing in a single-step procedure.

The mouse is the most important model organism for analyzing human genetic disease. Engineering the mouse genome is thus a key technology in biomedical research. In “knock-out” mice, genes become inactivated, which allows their essential function to be tested. In “knock-in” mice, on the other hand, gene sequences are replaced or inserted, enabling researchers to mimic human disease mutations or study how specific genes are expressed in the cell.

TARGETING MOUSE GENES TO ELUCIDATE HUMAN DISEASE PROCESSES

We use a powerful enzymatic technique, known as CRISPR-Cas9, to generate new, genetically modified mouse lines. The approach was named “2015 Breakthrough of the Year” by *Science* magazine. The CRISPR-Cas9 method allows the genome to be easily cut and altered at highly specific locations. To achieve this, CRISPR-Cas9 reagents are injected into single-cell mouse embryos, and gene editing is then achieved

Team members perform microinjections on mouse embryos using micromanipulators equipped with micropipettes.

through natural DNA repair mechanisms, leading either to gene inactivation (with loss of short genetic sequences) or to precise sequence modifications (with an artificially constructed DNA molecule serving as a template for repair).

The Transgenic Core Facility offers advice on the preparation of suitable CRISPR-Cas reagents, and performs the embryo isolation and microinjection as well as their transfer into foster females. Of the pups derived from single-cell embryos microinjected with CRISPR-Cas9 reagents, we usually achieve success rates of about 50 percent for sequence deletions and of about 15 percent for sequence replacements.

Our services also include reproductive techniques for the preservation of precious mouse lines. One important approach is the cryopreservation of sperm and embryos in liquid nitrogen. This helps to save animal housing resources when strains are not actively being used for research. It also prevents gene drifting and excludes loss of colonies in case of infection. When required, thawed sperm samples can be used for in vitro fertilization of mouse eggs, with the resulting single-cell embryos being transferred into foster females. The same in vitro technique, which enables hygienic rederivation of specific strains, is also deployed for the pathogen-free import of mouse lines from external repositories.

ENGINEERING A UNIVERSAL TRANSGENIC CONSTRUCT

Many mouse genes are active only in some specialized cells, organs, or developmental stages. A notable exception is a genetic locus (a specific location on a chromosome) known as Rosa26, which is active in all tissues, whatever the subject's age. Transgenic constructs integrated into Rosa26 are universally active too, which makes it highly valuable for medical research. More than 500 Rosa26 knock-in mouse lines have been generated so far. The Transgenic Core Facility, in collaboration with another group at the Max Delbrück Center, was first to demonstrate the insertion of transgenes into Rosa26 using the CRISPR-Cas9 technology. The resulting strain facilitated gene editing in somatic cells, thereby aiding the analysis of somatic cell disorders. Today, this transgenic mouse line (known as C57BL/6) is distributed via the Jackson Laboratory, a nonprofit biomedical research institution in the United States, which is one of the largest sources of genetically defined mice.

OUR TOOLS

- Microinjection of single-cell embryos
- Microinjection of embryonic stem cells into blastocysts
- Embryo transfer
- Sperm freezing
- Embryo freezing
- In vitro fertilization

CONTACT

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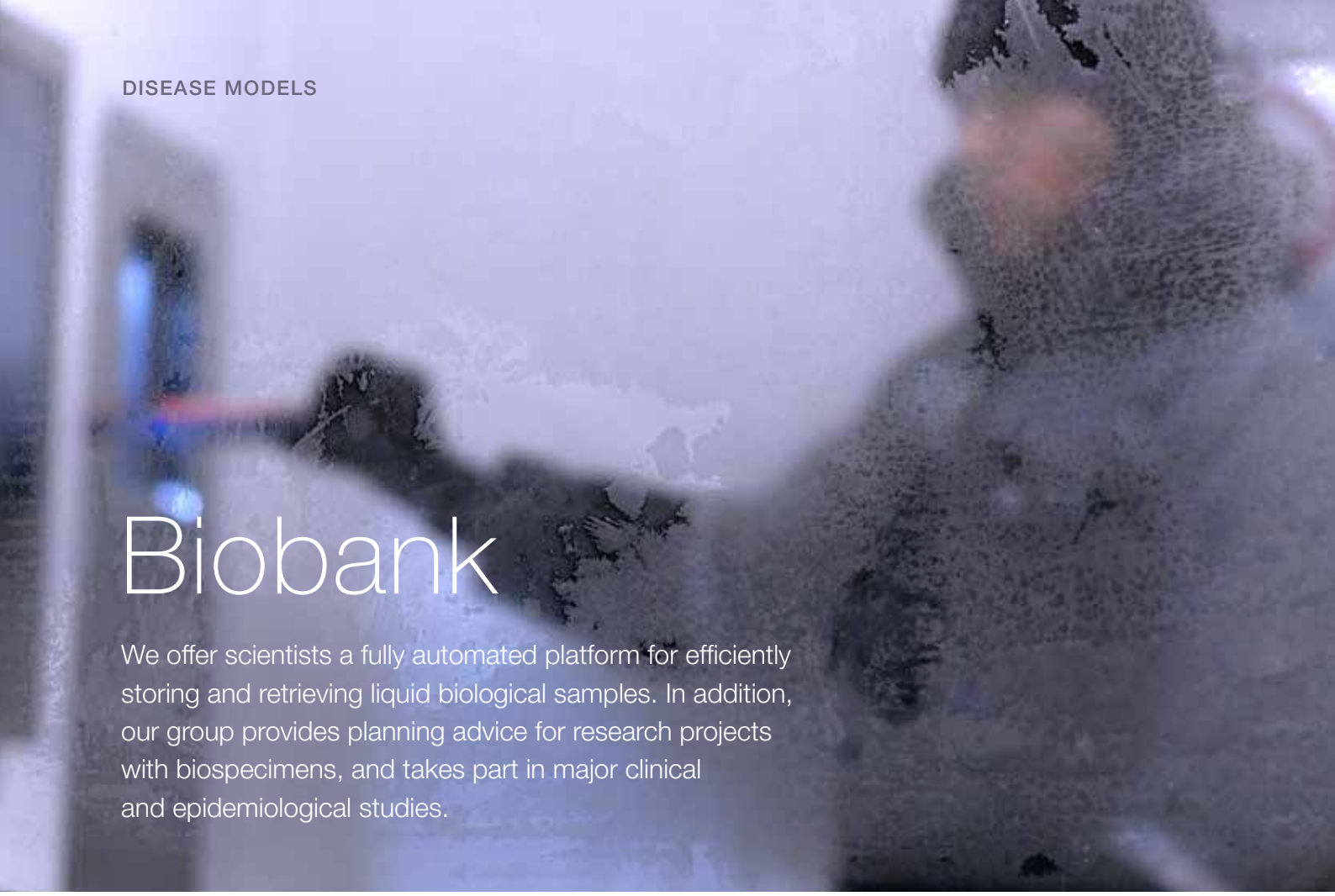

Biobank

We offer scientists a fully automated platform for efficiently storing and retrieving liquid biological samples. In addition, our group provides planning advice for research projects with biospecimens, and takes part in major clinical and epidemiological studies.

Many medical research projects make use of biological specimens such as blood, urine, tissue samples, cells, or DNA, which have to be stored over time. For example, clinical and epidemiological studies may aim at exploring long-term correlations between specific genetic and metabolic characteristics (biomarkers) and the development of disease. This requires an infrastructure – a biobank – to reliably preserve and retrieve probes when necessary. Biobanks allow researchers to archive biological information for planned as well as unforeseen future use.

HIGH-QUALITY STORAGE AT ULTRALOW TEMPERATURES

The biobank, part of the **Berlin Institute of Health (BIH)**, which is a joint undertaking of the Max Delbrück Center and Charité – Universitätsmedizin Berlin, can support any type of research study that requires state-of-the-art storage of liquid biological samples. This includes cohort studies and clinical trials, but also experimental research projects involving, for instance, stem cells. Specimens are stored at temperatures below –160°C in the vapor phase of liquid nitrogen in a fully automated robotic system. This allows high-quality storage as well as swift identification and efficient retrieval of samples for analysis.

Our platform currently encompasses two large-dimension liquid nitrogen tanks with a capacity for 2.5 million 250-µL tubes as well as tubes of 700 µL, 1000 µL, and 2 ml. The handling procedures guarantee that the cold chain is not interrupted when transferring samples into the biobank. A laboratory information management system provides full documentation, including sample characteristics, storage conditions, project information, and analysis results.

In addition, our group offers advice for research projects using biosamples when it comes to study design, standard operating procedures, data protection, and ethical issues. We also offer DNA or RNA extraction.

This storage rack contains automation-friendly sample tubes with unique bar-codes (right). The continuous cooling of samples is also guaranteed during manual handling by using a cryo-workbench (below).

IDENTIFYING BIOMARKERS OF HUMAN DISEASE

Currently, the biobank stores samples from 30,000 individuals in Berlin and Brandenburg who are taking part in the German National Cohort, a large nationwide epidemiological study. The project aims at elucidating the mechanisms of major chronic diseases, with several assessments of clinical and biological data to be performed in the years up to 2023, thus enabling researchers to explore the associations between biomarkers and the risk of incident health problems. Our group is also participating in a study to identify biomarkers for postoperative cognitive impairment in elderly patients. The study is supported by the research framework program of the European Union. The platform also supports the various research studies and trials of the Berlin Institute of Health.

OUR TOOLS

- Cryo-workbench for manually handling and scanning samples at -80°C
- Fully automated storage in the vapor phase of liquid nitrogen
- Laboratory information management system for sample tracking, history, and data connection

CONTACT

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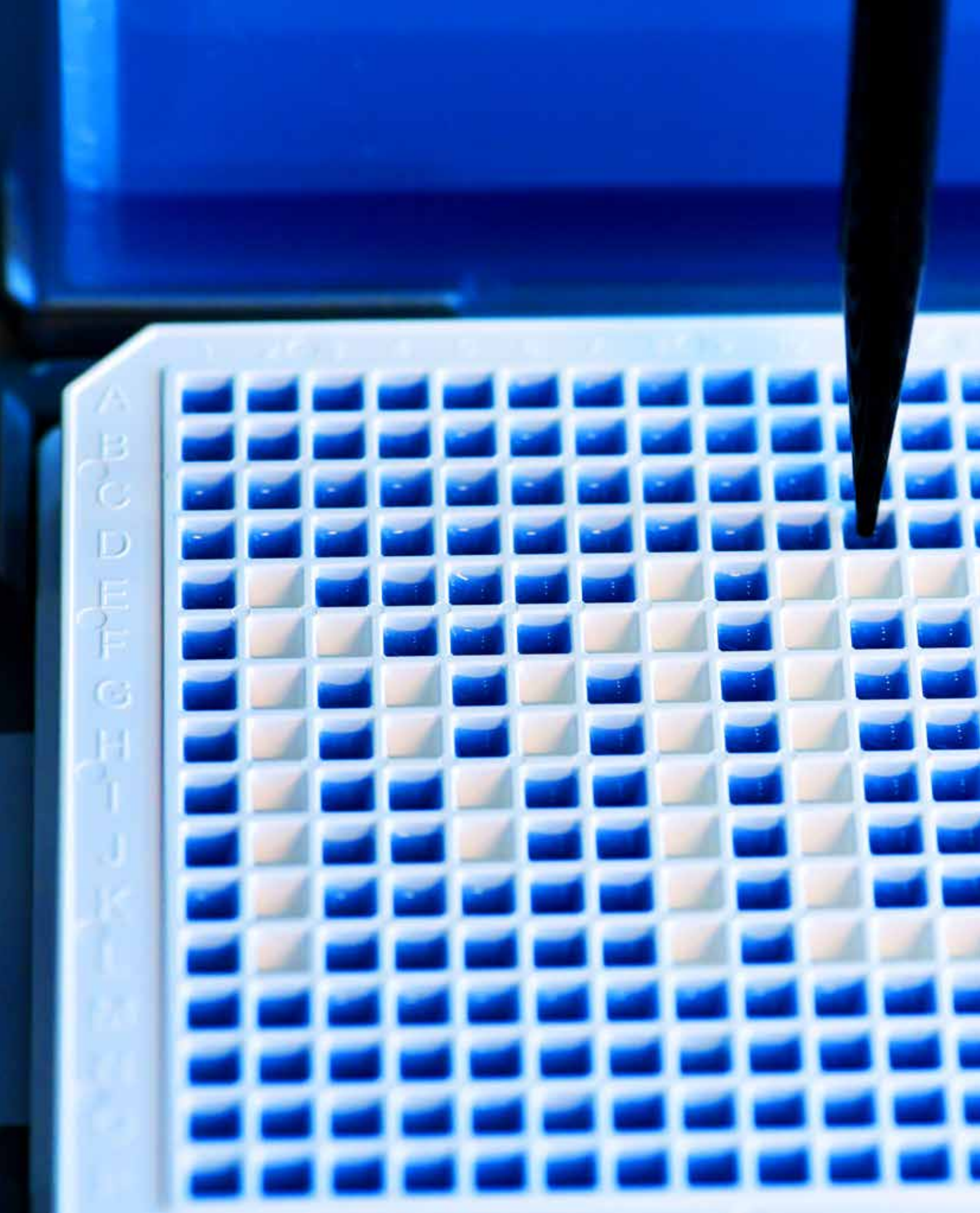
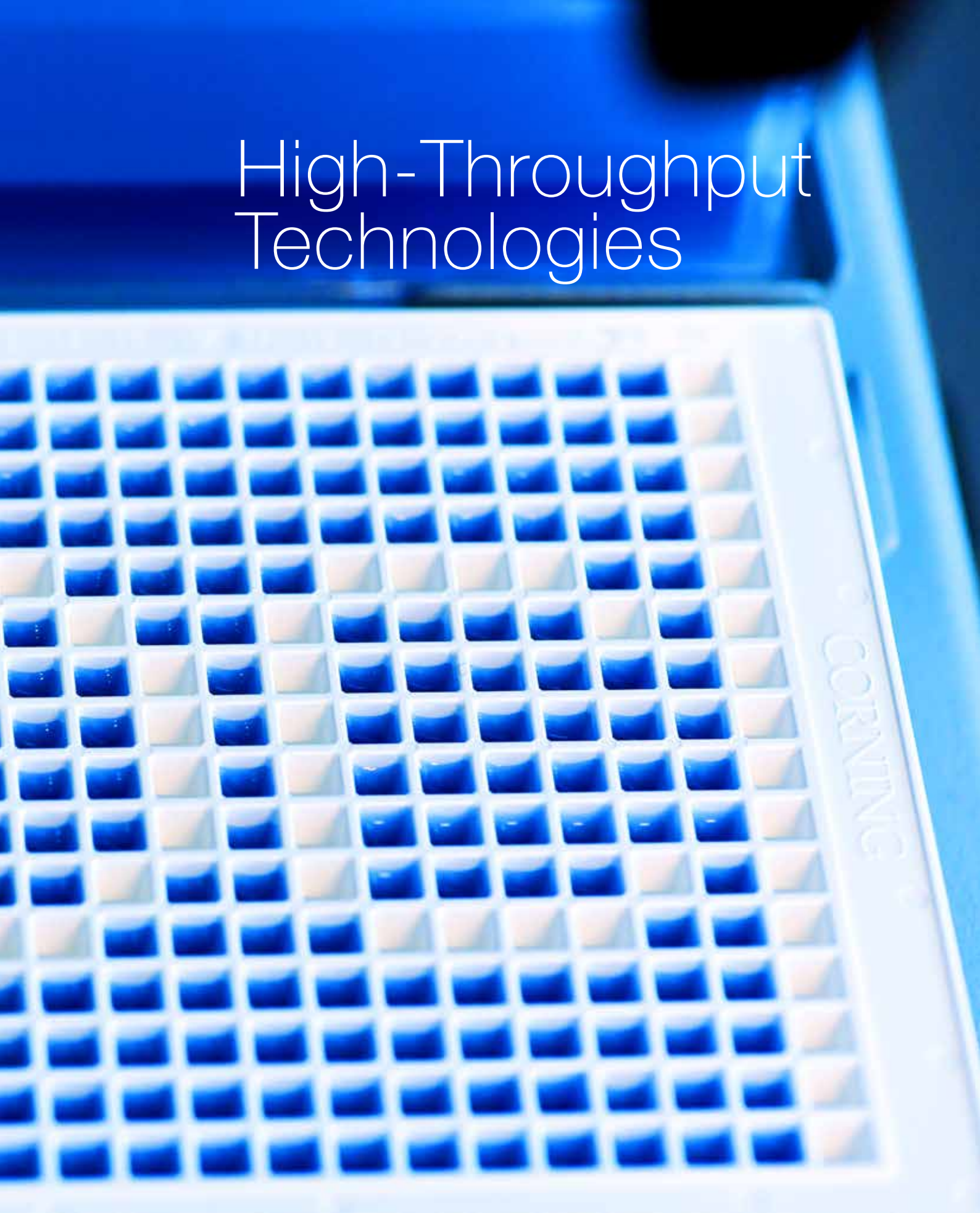
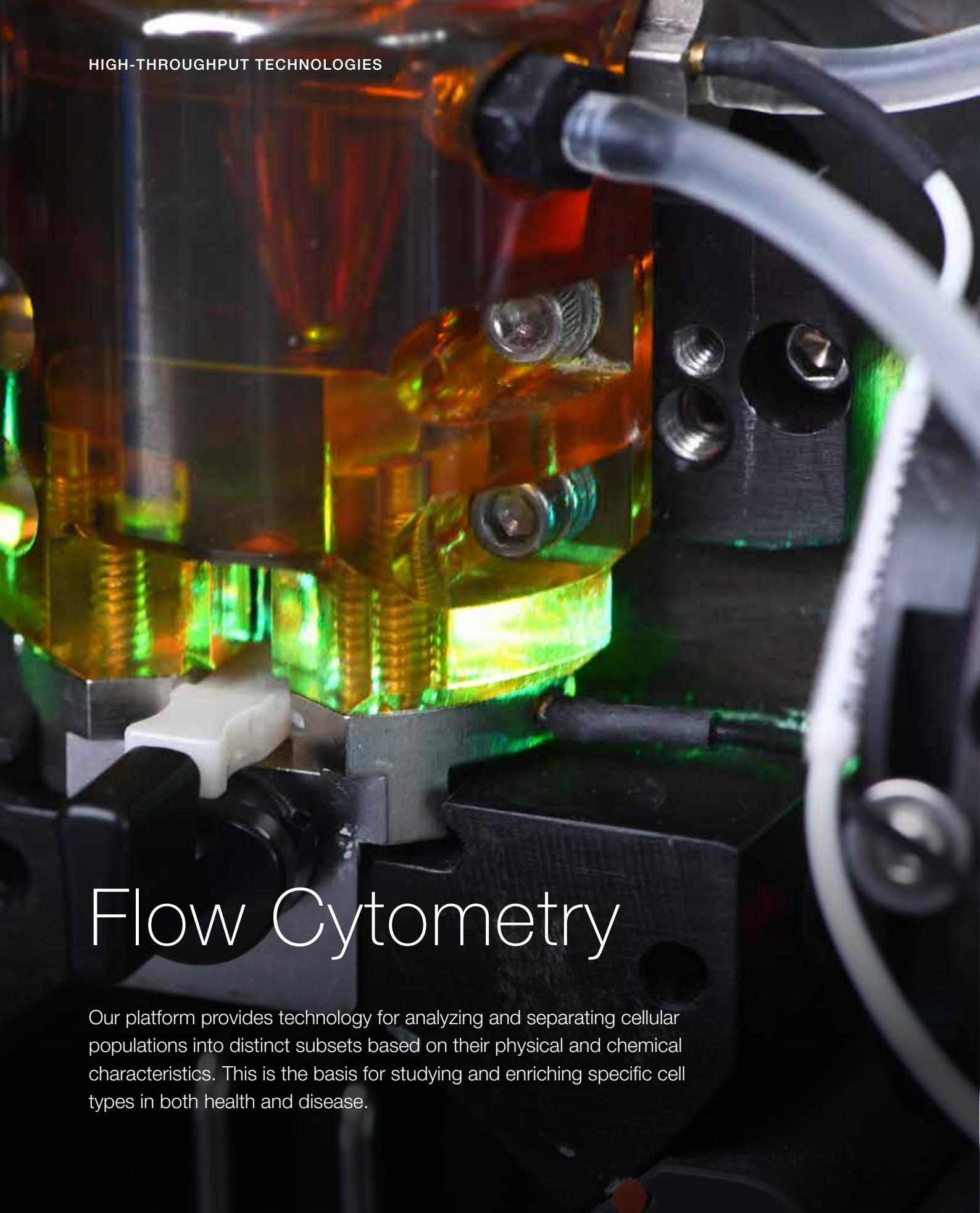


High-Throughput Technologies

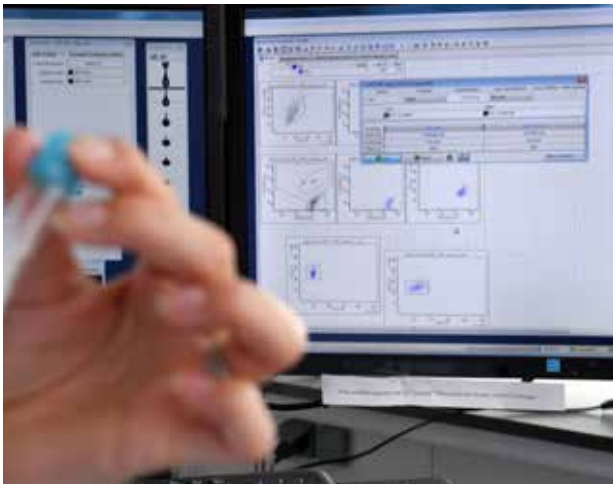




Flow Cytometry

Our platform provides technology for analyzing and separating cellular populations into distinct subsets based on their physical and chemical characteristics. This is the basis for studying and enriching specific cell types in both health and disease.

This software (BD FACS Diva) controls the fluorescence-activated cell sorting and records the experiments.



In multiple areas of molecular medicine, researchers are interested in finding out the specific properties of cells based on their genetic make-up, surface proteins, or other markers. These kinds of experiments can be performed by using flow cytometry to sort cell populations. Modern flow cytometers continuously analyze thousands of cells per second in a liquid stream, based on light scattering and cell surface characteristics. In particular, an advanced laser-based technology known as fluorescence-activated cell sorting (FACS, a BD trademark) allows the enrichment of highly specific cells of interest for subsequent investigations.

PROVIDING TECHNOLOGIES TO SORT AND ANALYZE CELLS

Our platform primarily enables researchers to access and operate cell sorters that are based on the FACS technology. These sorters can isolate up to 20,000 cells per second for large-scale cell isolation and even allow for single cell sorting, in which individual cells are precisely spotted into the well of a microtiter plate for analytical purposes. Our group assists in the design and setup of specialized and sophisticated experiments that use additional analytical cytometers or large numbers of fluorescent labeling compounds (fluorochromes), with up to 15 different colors possible. The facility has two flow cytometry analyzers and four high-capacity digital cell sorters.

The specific analytical software of flow cytometers allows researchers to tackle general research questions relating to programmed cell death (apoptosis) and cell viability, cellular signal transduction, cell cycle analysis, cellular protein production, and the efficiencies of gene modification experiments. Sorted cells are routinely prepared for gene expression analyses. In addition, isolated cells may be prepared for genome editing, DNA sequencing, live-cell imaging, or transfer into animal models of disease.

The Flow Cytometry Platform is a multi-user facility. Numerous groups from the Max Delbrück Center and partner institutions have used the platform for various research projects over the past few years.

ENABLING GENOME EDITING

The possibility to specifically alter and edit the genome with a powerful enzymatic technique (CRISPR-Cas9) has revolutionized the field of genetics, and FACS is an essential tool in utilizing the full potential of this technology. CRISPR-Cas9 allows targeted gene inactivation ("knock-out") or insertion ("knock-in") in virtually every cell type. However, the efficiency of these manipulations varies dramatically between experimental setups. FACS-based cell sorting is therefore used to separate mutated and non-mutated cells. Mutated cells can be tracked by detecting cell surface proteins or the fluorescent dyes that mark manipulated cells. In this way, FACS allows us to create purified mutated cell populations, which is a prerequisite for studying the impact of these mutations on health and disease.

OUR TOOLS

Flow cytometry analyzers and cell sorters:

- LSR II (6 violet – 6 blue – 3 red)
- Fortessa (2 ultraviolet – 6 violet – 2 blue – 5 yellow green – 3 red)
- Aria 1 (2 violet – 5 blue – 2 red)
- Aria 2 (3 violet – 2 blue – 5 yellow green – 3 red)
- Aria 3 (3 violet – 2 blue – 5 yellow green – 3 red)
- Aria F (6 violet – 2 blue – 5 yellow green – 3 red)

CONTACT

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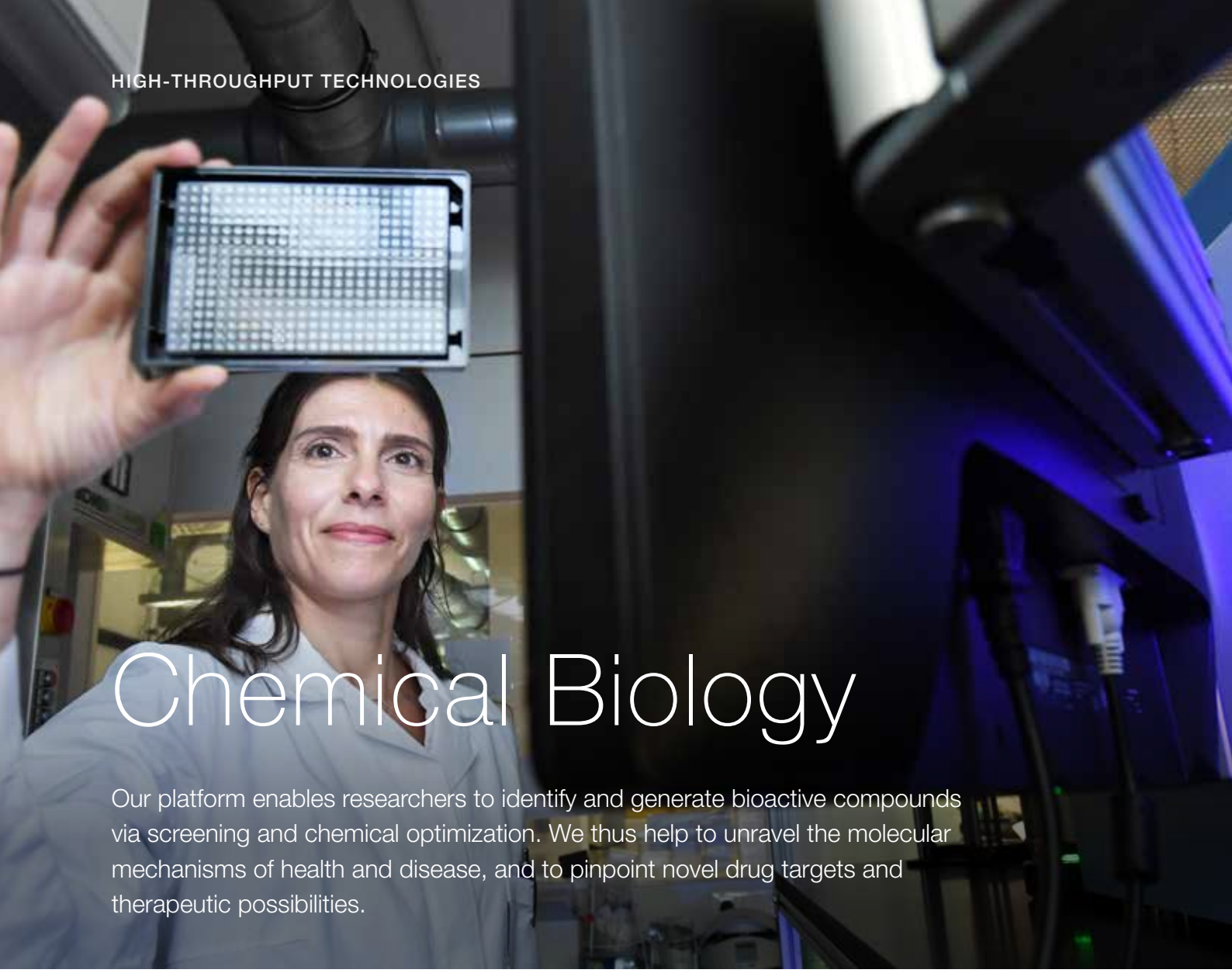


Chemical Biology

Our platform enables researchers to identify and generate bioactive compounds via screening and chemical optimization. We thus help to unravel the molecular mechanisms of health and disease, and to pinpoint novel drug targets and therapeutic possibilities.

Most therapeutic drugs are small molecules – chemical compounds with a small size and a low molecular weight – that help regulate a biological process. To drive medical progress forward, there is an ongoing need to identify and chemically optimize small molecules that influence cellular target structures in a specific and stable manner. In addition, analysis is needed into exactly how and where such compounds are active, to allow researchers to unravel the molecular mechanisms of health and disease. Today, such investigations in the field of chemical biology deploy various high-throughput approaches as well as computational and modeling techniques, enabling researchers to map the activity of small molecules, even at the level of a single cell.

IDENTIFYING DRUG CANDIDATES AND MOLECULES FOR RESEARCH USE

The Chemical Biology Platform is part of the Infrastructure of the neighboring Institute, the **Leibniz-Forschungsinstitut für Molekulare Pharmakologie (FMP).** Based on a collaboration agreement, the platform offers screening technologies for novel drug candidates as well as possibilities of influencing gene expression through RNA molecules (RNA interference) also to MDC researchers. In addition, our platform is working to generate and optimize chemical compounds as molecular tools for scientific research.

For systematic screening, we have established a broad portfolio of high-throughput approaches that allow researchers to explore the cellular effects of specific molecules. These approaches include high-content screening, high-speed kinetic imaging, impedance measurement, and fluorescence-activated cell sorting. Our platform supports all kinds of fluorescence and luminescence measurements. It also offers methods for studying the binding properties of specific substances (surface plasmon resonance) as well as protein interactions (capillary electrophoresis). Data documentation and analysis have been automated to allow for effective process control.

Using medicinal chemistry approaches, potential drug candidates identified during screening ("primary hits") can be further explored and optimized, for example, through systematic chemical alterations. Also, chemical probes can be developed for diagnostic means. Our small molecule drug-like screening collection of around 67,000 compounds contains about 3,300 substances that are approved by the U.S. Food and Drug Administration (FDA) and lend themselves to drug repurposing approaches. Additionally, we have at our disposal 44,000 compounds derived from the World Drug Index, and 20,000 natural products.

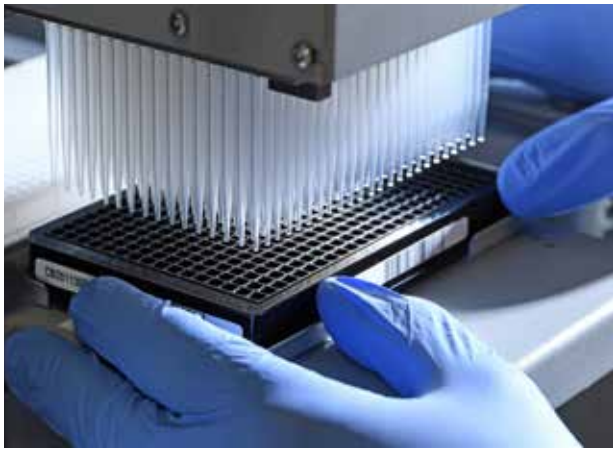
Not least, the platform also includes support from computational methods, such as virtual ("in silico") screening, similarity searches in existing substance libraries, modeling approaches, and molecular simulations.

TARGETING TUMORS

Using this set of powerful tools, we have been able to identify various drug candidates that interfere with tumor development and metastasis as well as the malformation of blood vessels in a rare disease. Some projects are already in an advanced stage, with substances being evaluated in preclinical studies or even ready to enter clinical trials. In the future, we will also integrate microscopic methods, such as confocal microscopy, into our high-throughput screening protocols, thereby responding to the evolving methodological demands of other research groups.

OUR TOOLS

- High content screening
- High-speed kinetic imaging
- Fluorescence-activated cell scanning
- Capillary electrophoresis
- Surface plasmon resonance spectrometry
- 300 MHz NMR spectrometry
- Liquid chromatography – mass spectrometry
- Automated compound store with 67,000 small molecules



Four 384-tip pipetting systems enable us to test up to 160,000 compounds per day for their biological effects.

CONTACT

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Background Information

The MDC's 16 scientific Technology Platforms are led by established experts and employ approximately 100 people in total. They are supported by internal advisory bodies that help recognize trends (e.g., in single-cell analysis) and that pave the way for scientific developments through investments in staff or equipment. Dr. Jutta Steinkötter is executive manager of the Technology Platforms, while the scientific strategy is overseen by the Scientific Infrastructure Board, members of which include Prof. Holger Gerhardt, Prof. Matthias Selbach, and Prof. Markus Landthaler.

The Technology Platforms primarily support the work of MDC researchers, but also maintain numerous collaborations with scientific partners in Berlin and beyond – particularly under the umbrella of the Berlin Institute for Health (BIH) and in cooperation with Charité – Universitätsmedizin Berlin, the Leibniz-Forschungsinstitut für Molekulare Pharmakologie (FMP), and the German Center for Cardiovascular Research (DZHK). Further collaborations are currently being established, for example, in cryo-electron microscopy and in connection with enhancements to super-resolution light microscopy.

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This brochure features 16 overviews that introduce the scientific-technological infrastructure of the Max Delbrück Center for Molecular Medicine in the Helmholtz Association (MDC). The methodological platforms, available to both MDC researchers and external project partners, range from imaging technologies and molecular high-throughput analyses to bioinformatics computing, stem cell methods, and transgenic animal models. These customized approaches have been developed with established experts and enable competitive research into molecular medicine.

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