MDC MAX DELBRÜCK CENTER FOR MOLECULAR MEDICINE IN THE HELMHOLTZ ASSOCIATION

BIH Berlin Institute of Health @Charité

CHARITÉ UNIVERSITÄTSMEDIZIN BERLIN

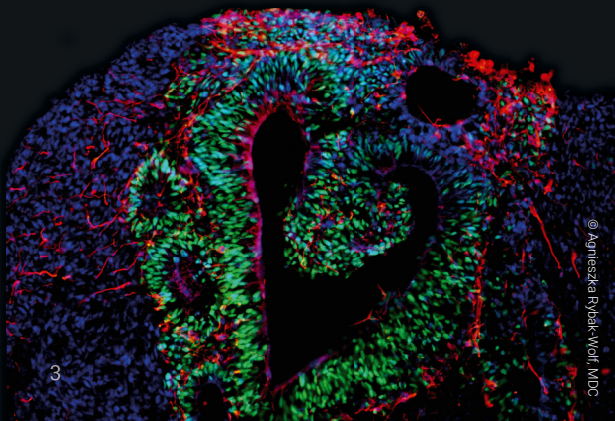
BIH, Charité, MDC Focus Area

SINGLE CELL
Approaches for Personalized Medicine

The individual cells isolated from the tissue are channeled into miniaturized chips for analysis.

SINGLE CELL goes clinical

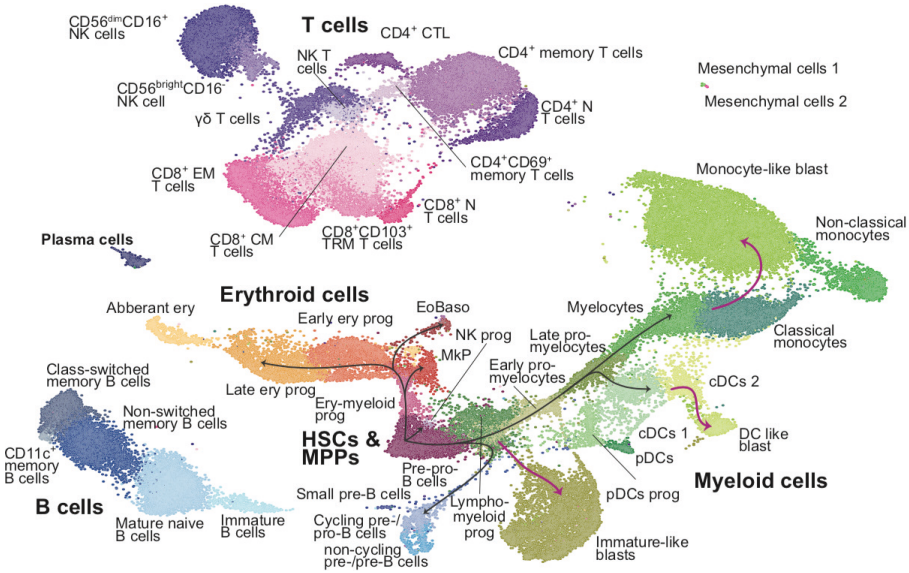
Single cell technologies are revolutionizing biomedical research by revealing molecular changes in individual cells, their interactions with neighbors and changes over time in previously unprecedented detail. They are the long sought doorway to precise diagnostics for early detection and prevention of numerous diseases, as well as reliable drug target identification for personalized treatments. To efficiently translate these groundbreaking technologies into clinical applications, new interdisciplinary and interinstitutional research strategies are essential. The rich Berlin research and health care environment provides ideal conditions to implement direct interfaces among technological and scientific experts, clinicians and data scientists to systematically diagnose, understand and monitor disease at the single cell level. The BIH, Charité and MDC took this unique and timely opportunity to establish the new joint **Focus Area *"Single Cell Approaches for Personalized Medicine"*** aiming to bring single cell discoveries to the bedside for patient benefit.



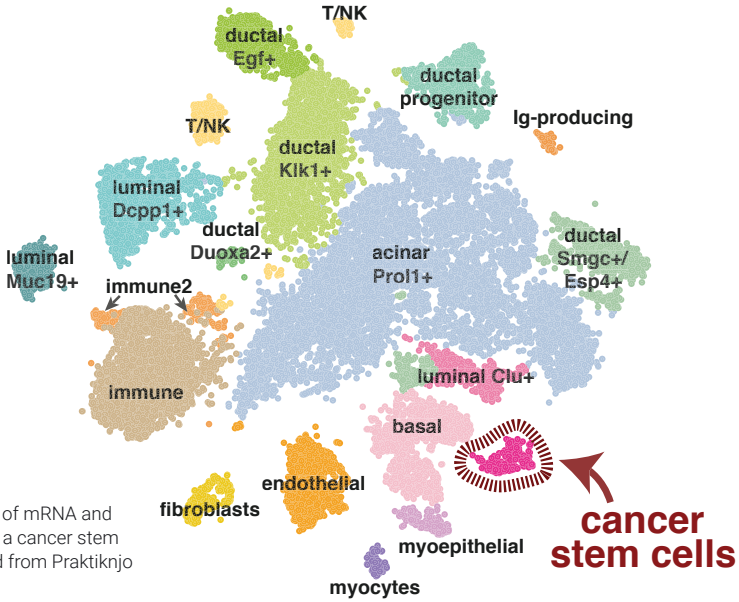
Section of an early stage cerebral brain organoid (~30 days). Red: neurons, green: neural progenitors, blue: nuclei.

The Berlin **SINGLE CELL** nucleus

Single cell technologies were named “the 2018 Breakthrough of the Year” by the renowned journal, *Science*, citing the work of researchers working at the “Berlin Institute for Medical Systems Biology” (BIMSB), part of MDC. It now became possible to break down entire organs into individual cells, measure their gene activity and – with the help of artificial intelligence – reassemble these individual cell data to visualize the entire organ or organism. Disease onset, development and progression can now be illuminated in unprecedented detail by combining these disruptive technologies with patient-derived models and artificial intelligence. In this way, suitable targets can be identified that will allow in future to intervene at an early stage, intercept disease and restore health.



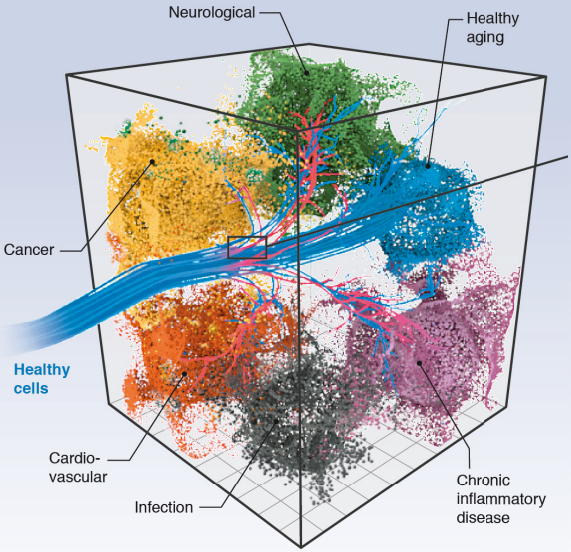
A comprehensive single-cell transcriptomic and surface proteomic map of bone marrow from healthy individuals and leukemia patients. Red arrows indicate leukemia development. (Adapted from Traiana et al., 2021, BioRxiv, under revision)



Simultaneous quantification of mRNA and cell surface proteins identify a cancer stem cell-like population. (Adapted from Praktiknjo et al., 2020, Nat. Commun.)

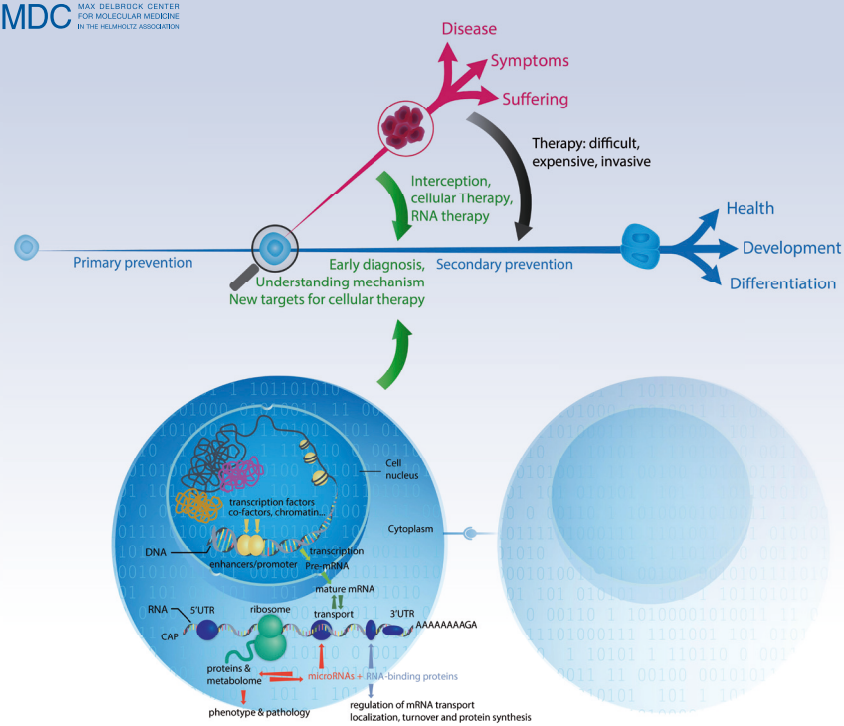
To transform this **vision of cell-based interceptive medicine** into reality, four outstanding and internationally recognized single cell technology experts were recruited to the BIH and MDC to directly partner with Charité Heads of Department in this shared endeavor. The highly competitive recruitment process attracted scientists coming from the world's leading life science institutions. The novel bridge concept optimally combines the internationally leading position of the BIMSB/MDC in the development of single cell technologies with the high potential of BIH/Charité for medical innovations. Dr. Leif Ludwig and Dr. Simon Haas are probing hematological diseases by mitochondrial genomics and spatial multi-omics single cell applications in direct collaboration with Prof. Lars Bullinger and Prof. Ulrich Keller, the Heads of Charité's Department of Hematology, Oncology and Cancer Immunology at Campus Virchow-Klinikum and Campus Benjamin Franklin, respectively. Dr. Stefanie Grosswendt will investigate together with Prof. Angelika Eggert, Head of Charité's Department of Pediatric Oncology and Hematology, the embryonal origin of the childhood tumor neuroblastoma. Dr. Ashley Sanders in cooperation with Prof. Britta Siegmund, Head of Charité's Department of Gastroenterology, Infectious Diseases and Rheumatology, will apply single cell genomics to better understand autoimmune diseases. Prof. Nikolaus Rajewsky (MDC) and Prof. Angelika Eggert (Charité) are the speakers of the new Focus Area. They also oversee the setup of the *Clinical Single Cell Sequencing Pipeline* to apply these innovative technologies to relevant patient cohorts and ensure the transfer of single cell studies to the clinic.

Early disease detection and interception by understanding and targeting cellular trajectories through time. (Adapted from Rajewsky et al., Nature, 2020)



The Berlin CELL HOSPITAL

The nucleus of the Single Cell Focus Area will be developed and extended towards the vision of the Berlin Cell Hospital (BCH) in coming years. The BCH will realize the medical vision of the pan-European *LifeTime* consortium (https://lifetime-initiative.eu/), to track, understand and target single human cells during the onset and progression of complex diseases and monitor their responses to therapy. Combining breakthrough single cell and imaging technologies with artificial intelligence and personalized disease models will allow us to predict onset and clinical courses of diseases in individual patients and select the most effective therapies for each patient. We



Integration of different levels of gene regulation to understand their connection to disease onset. This is key for the implementation of cell-based interceptive therapies, before irreparable damage occurs (BIMSB mission figure)

coined the term ***cell-based interceptive medicine*** for this innovative concept (Rajewsky et al., 2020, Nature). The ability to intercept diseases at an early stage before irreparable damage occurs will substantially improve outlook for many patients. To reach this ambitious goal, we will foster close ties among scientists working at the forefront of experimental single cell technologies, experts in data science and artificial intelligence and experienced clinicians under one roof. We will explore new avenues of cross-discipline education and training alongside new intense cooperation strategies with industry to transform technological and scientific innovations into patient benefit.

From left to right: Dr. Ashley Sanders, Prof. Dr. Angelika Eggert, Dr. Stefanie Grosswendt, Prof. Dr. Nikolaus Rajewsky, Dr. Leif Ludwig, Dr. Simon Haas.

CONTACTS

Core Single Cell Research Groups (all are Tri-Institutional (BIH, Charité, MDC) and housed at BIMSB):

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Clinical Single Cell Sequencing (CSCS) Pipeline:

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Janine Altmüller	BIH

Steering committee:

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Norbert Hübner	MDC
Jan Philipp Junker	MDC
Ulrich Keilholz	Charité
Ana Pombo	MDC
Frank Tacke	Charité

Speaker: Nikolaus Rajewsky, MDC

Co-Speaker: Angelika Eggert, Charité

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