



GermanStemCellNetwork

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The global stem cell economy

Annual magazine of the GSCN
2023/24

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Welcome note

Many diseases are still considered incurable, and often our understanding of their origins is limited. Stem cell research plays a central role in developing new therapies. It aids in uncovering the causes of diseases and developing new treatments based on these findings. Therefore, the Federal Ministry of Research supports the “German Stem Cell Network” (GSCN), an initiative that connects leading experts and forms a crucial link between science, politics, education, and society.

Recent scientific reports highlight the great potential of stem cell research. Globally, significant breakthroughs have been made, such as the approval by the U.S. Food and Drug Administration (FDA) of a therapy based on CRISPR/Cas9 for treating sickle cell disease. This treatment, which corrects faulty genes in hematopoietic stem cells in the bone marrow, was developed following the first successful clinical trial results in 2021 and moved into clinical application just two years later. Successes in stem cell research have laid the groundwork for this and other innovative therapies also for neurodegenerative diseases like multiple sclerosis and Parkinson’s disease.

The Federal Ministry of Education and Research (BMBF) has established an internationally leading German stem cell research landscape through long-term funding. Funded projects cover all application fields, including human-based model systems as alternatives to animal testing. For example, teams at the Philipps-University of Marburg and Justus Liebig University of Giessen are working on a platform to generate human lung organoids for lung cancer research. Researchers at the German Cancer Research Center (DKFZ) and the University Hospital Heidelberg are developing techniques to mature stem cells into functional neuronal cells for future treatment of Parkinson’s patients. Another project, Bio-Rescue, uses induced pluripotent stem cells from body cells of the nearly extinct Northern White Rhinoceros to create germ cells and embryos, thereby aiding in species preservation.

These research projects demonstrate the versatile applications of stem cell research. Future initiatives include a translation center in Berlin to promote gene and cell therapies and developing a national strategy in this field. The Berlin Institute of Health (BIH) is currently working with stakeholders across various sectors on a strategy paper, whose recommendations are expected to be implemented starting mid-2024. A network office for gene and cell therapy, which serves as a national hub, was established at BIH in October 2023, and comprehensive national project funding is planned for 2024.



Innovations in stem cell research are intended for medical application, necessitating the consideration of ethical, legal, and social aspects (ELSA). A specialist conference organized by the BMBF in October 2023 addressed research on human embryos, embryonic stem cells, and novel cell structures. Ethical and legal issues were intensely reflected upon, discussing potential adjustments to legal frameworks to advance research in a future-oriented manner. It is essential to continue these discussions to redefine research boundaries with current knowledge. I am ready to face this challenge.

The advancements in stem cell research and ongoing discussions give me hope for the future. I am pleased that the BMBF can support this important field of research. Stem cell research is a pivotal pillar of medical research and is crucial for improving medical care. It also plays a decisive role in strengthening Germany’s position as a research hub. The GSCN supports this through its role as a contact point for researchers and through transparent communication with the public. The current annual magazine impressively documents these developments. I wish the GSCN continued success!

A stylized, handwritten signature in blue ink, consisting of a large, flowing 'M' followed by a series of connected loops and a final horizontal stroke.

Mario Brandenburg
Parliamentary State Secretary
to the Federal Minister of Education and Research



We
are the
GSCN

Preface

The German Stem Cell Network (GSCN) unites stem cell researchers across Germany and actively promotes their networking and communication! This is done in various ways, and the involvement of young scientists is of great importance. A standout event is the annual GSCN Conference, and I am especially pleased to welcome the stem cell community to Jena this year!

To strengthen interactions and expand the network, the GSCN offers many additional events that take place in various parts of the country: I would like to mention the workshop on *New Developments in Disease Modeling and Drug Discovery* in Bonn in November 2023. The *Berlin Stem Cell Club*, a hybrid seminar series where two scientists each provide an overview of the current state of research in their fields, regularly attracts up to 100 participants – in person and in the virtual space. Besides these established formats, there is also *GSCN on Tour*, which organizes events in various cities and invites participants to hybrid lectures and discussions. The first GSCN stem cell days in Hamburg (February 2023) and Lübeck & Kiel (March 2023) were exciting scientific meetings attended by numerous colleagues who discussed data and deepened conversations over drinks and snacks. This excellent series continued in Dresden in 2024 and was well attended.

This issue of the GSCN Magazine focuses on a global atlas of the stem cell economy – an outstanding overview that provides a very good current impression of national strategies and key players worldwide. Regulations and laws in stem cell research are a highly topical issue. In the section on Germany, I would like to highlight the BMBF Symposium on Research on Embryonic Stem Cells as an example. Accordingly, the GSCN conducted a random survey among the population, to capture the opinion on research with human embryos and human embryonic stem cells (see article). We are extraordinarily pleased with the overwhelmingly positive attitude of the respondents, however the results also invite us to intensify communication with the public. This is done, for example, in our public events that regularly take place in the city of the GSCN Conference. This year, we will discuss fundamental and applied aspects of stem cell research on 27 September at the Volksbad Jena. Other events of science communication include the Unistem Day and the Long Night of Sciences in many German cities.

This year, the annual meeting of the International Society for Stem Cell Research (ISSCR) is in Hamburg. It is the first time ever that ISSCR will meet in Germany, and this event naturally brings the international stem cell community here – an honor that we are very pleased about! The GSCN will be organize many formats: a public event, the



WunderBar event, and a Meet-up Hub for networking with international colleagues, and together with the Berlin Institute of Health (BIH), a session on the translation of stem cell research into clinical practice.

The integration and support of young scientists are central interests of the GSCN. The GSCN Mentoring Program is after the second round an integral part of the GSCN. The feedback from the first cohorts of the Mentoring Program has been consistently positive (see article). I am particularly pleased that the value of this one-year program is recognized by both sides.

Locally, there have also been some changes! The GSCN Office is now in Berlin-Mitte. After the move, our office is much more accessible to everyone and welcomes visitors. Co-working spaces are also offered, and all members are cordially invited to visit at any time.

Stem cells remain a fascinating field of research, and applications with these cell types are increasingly moving into clinical practice. I am very glad and somewhat proud to be the president of the GSCN at this time and to announce this year's GSCN Annual Magazine for 2023/24.

With warm regards,

A blue ink handwritten signature, appearing to read 'C. Waskow'.

Claudia Waskow
Active President



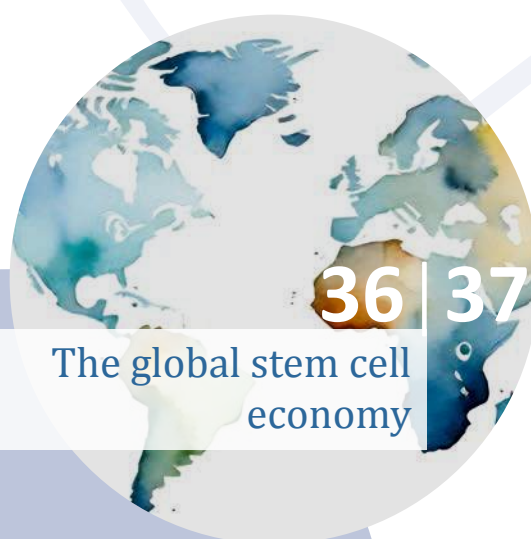
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Europe

A JOURNEY THROUGH THE EUROPEAN
LANDSCAPE OF STEM CELL RESEARCH
AND TRANSLATION



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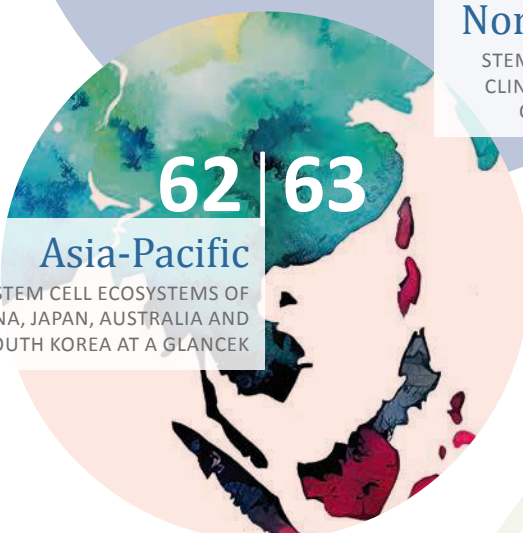
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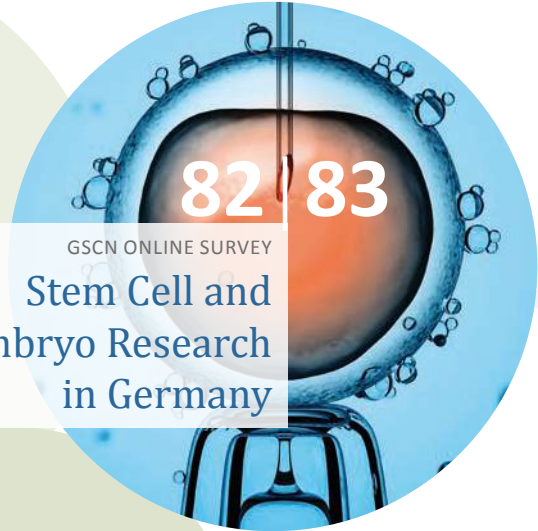
THE STEM CELL ECOSYSTEMS OF
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Leveraging bioengineering for
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GSCN MENTORING PROGRAM:

Fancy a career?
But which one?



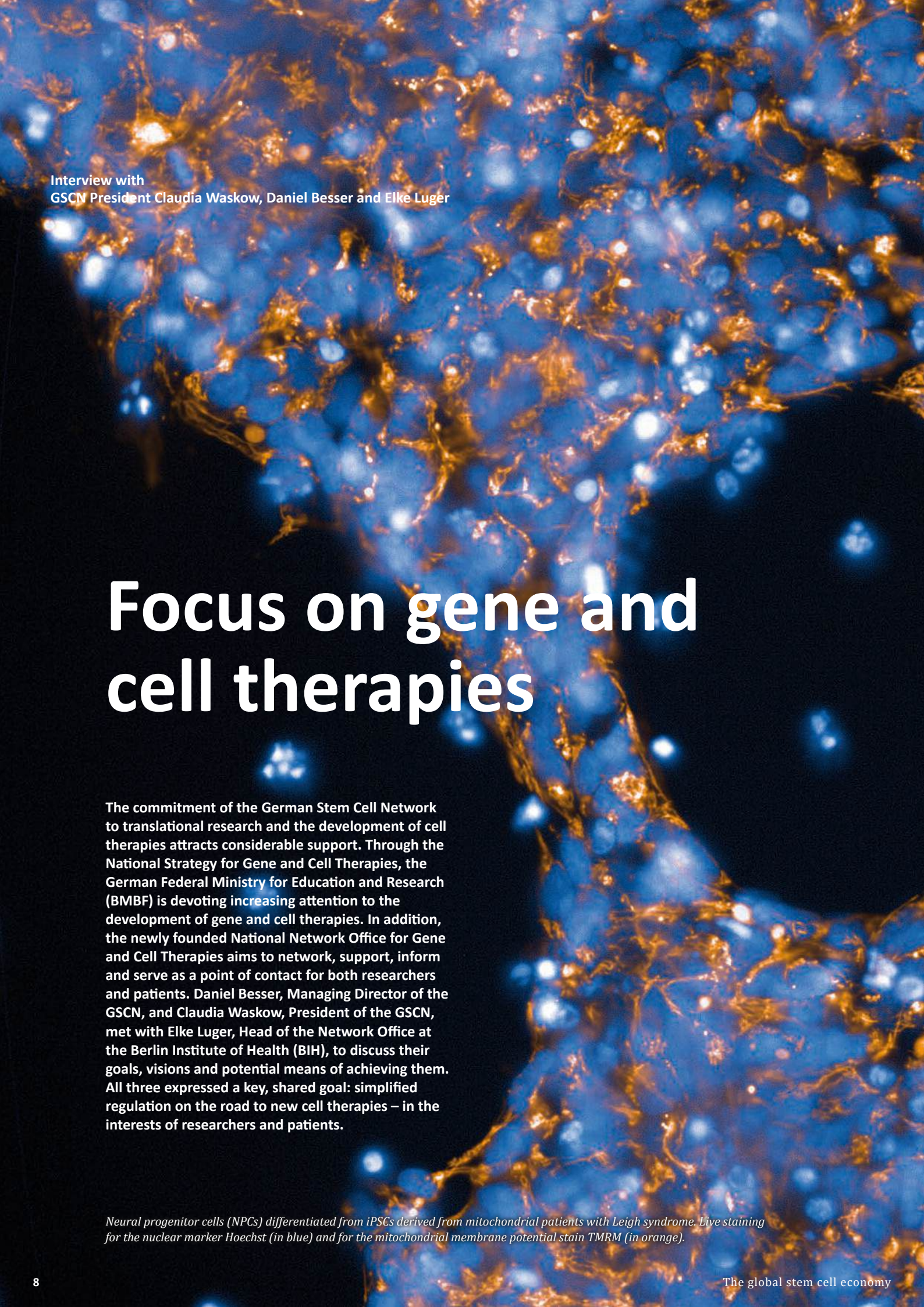
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WHITE RHINO: PREGNANCY IN A ROUNDABOUT WAY

Stem cell technologies – a backbone of
science-based species conservation



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Interview with
GSCN President Claudia Waskow, Daniel Besser and Elke Luger

Focus on gene and cell therapies

The commitment of the German Stem Cell Network to translational research and the development of cell therapies attracts considerable support. Through the National Strategy for Gene and Cell Therapies, the German Federal Ministry for Education and Research (BMBF) is devoting increasing attention to the development of gene and cell therapies. In addition, the newly founded National Network Office for Gene and Cell Therapies aims to network, support, inform and serve as a point of contact for both researchers and patients. Daniel Besser, Managing Director of the GSCN, and Claudia Waskow, President of the GSCN, met with Elke Luger, Head of the Network Office at the Berlin Institute of Health (BIH), to discuss their goals, visions and potential means of achieving them. All three expressed a key, shared goal: simplified regulation on the road to new cell therapies – in the interests of researchers and patients.

Neural progenitor cells (NPCs) differentiated from iPSCs derived from mitochondrial patients with Leigh syndrome. Live staining for the nuclear marker Hoechst (in blue) and for the mitochondrial membrane potential stain TMRM (in orange).

GSCN: The BIH has overseen the development of a National Strategy for Gene and Cell Therapies in Germany and simultaneously established the National Network Office for Gene and Cell Therapies. What is the thinking behind this?

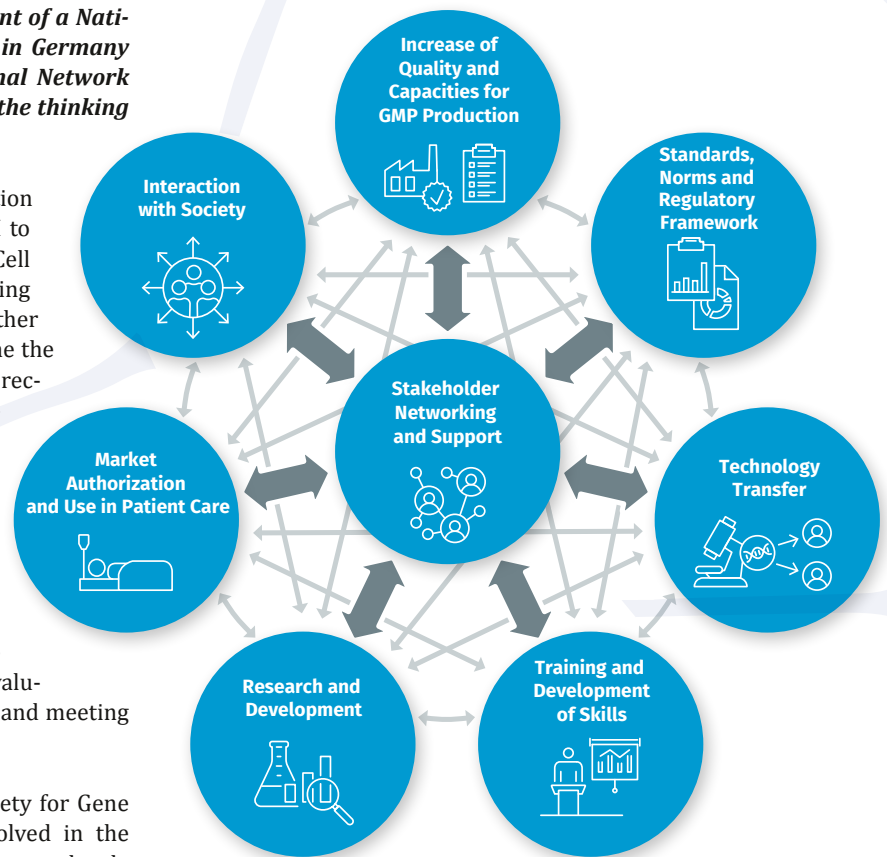
Elke Luger: The Federal Ministry of Education and Research (BMBF) commissioned the BIH to develop the National Strategy for Gene and Cell Therapies. The BIH was tasked with coordinating and moderating this process, bringing together experts from all over Germany to jointly define the topics of the eight fields of action and draw up recommendations for action. The resulting strategy paper is intended to define solutions and milestones to ensure that Germany remains internationally competitive and fully exploits the value chain in the field of gene and cell therapies (GCT). The National Network Office for Gene and Cell Therapies (Network Office for GCT) has the task of bringing stakeholders together, retaining the experts from individual working groups as valuable long-term contacts, and then identifying and meeting their needs.

Daniel Besser: There is also the German Society for Gene Therapies (DG-GT), which was heavily involved in the process of developing the strategy and will engage closely with the Network Office for GCT in the future. The strategy ultimately arose from the joint Charité-Universitätsmedizin-Bayer initiative in Berlin, which is to be put on a national footing. A long preliminary phase with several roundtables and various events has now produced the strategy paper.

GSCN: What are the interfaces between the German Stem Cell Network and these BIH gene and cell therapy projects?

Claudia Waskow: It is particularly important that the strategy development process and the projects pursued by the Network Office for GCT include close cooperation with the German Stem Cell Network (GSCN). After all, stem cells are cells used in gene and cell therapy. Hematopoietic cells are particularly important in this context because they have been extensively studied and are used in clinical settings. In many preclinical and clinical studies, researchers are examining treatments that involve genetic corrections of mainly monogenetic diseases. Close collaboration between our two networks and entities therefore make a lot of sense given the linked subject matter.

Daniel Besser: There is considerable crossover in the scientists who work in the two networks. However, as the GSCN, we have also already done a lot of groundwork in terms of engaging with society – through materials for schools, exhibitions and providing information online and at events.



We also have European partners, such as EuroGCT and the European Society for Gene and Cell Therapy, with whom links could be forged. I can also imagine joint white papers and a host of other excellent projects that could be added in the future.

Elke Luger: Referring to existing structures is crucial; this is also fundamental to the work of the Network Office for GCT. We will exploit synergies and avoid creating redundancies. As the network office for GCT, we want to build a GCT database for the community. Essentially, a central location to represent clinics, research institutions and contacts - for patients, students and researchers. In other words, a record of all the structures that exist and facilitation of effective national – and, in the long term, international – collaboration, as Daniel mentioned.

GSCN: What vision do the Network Office for GCT and the GSCN have for the future of the GCT research and therapy landscape in Germany?

Elke Luger: One of the visions for a potential future is the ability to fall back on joint protocols or joint GMP manufacturing sites to maximize the use of resources. We could close gaps where supply chains prove problematic. We could create a network, here in Germany, that extends from the developers to the users to the manufacturers. My aim is to keep this information up to date through regular exchanges with the community and to make it centrally accessible to everyone.

COMING
TOGETHER

Elke Luger



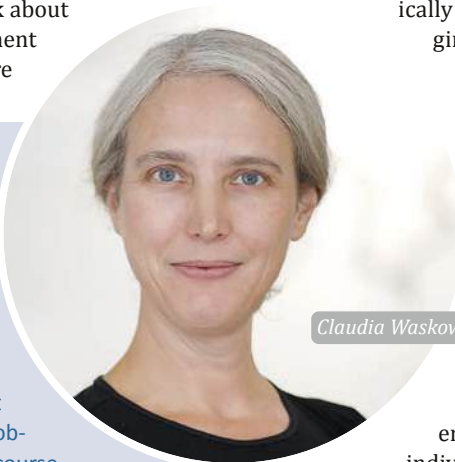
Daniel Besser: I think it's too narrow to think of cell therapies in the German context alone. There is a lot of work underway in Europe. There will have to be a give and take in development activities between different countries. I am also firmly convinced that we have to get to grips with the costs. At present, we have a structure that is ultimately geared towards the pharmaceutical industry with low-molecular substances in the regulatory process. This process is incredibly expensive. If I end up with a small molecule, i.e. a drug that I can produce centrally, then I can bear these costs of one to two billion euro for the entire clinical process. But if we don't bring these costs down in the future, I don't see how we'll be able to offer

VISION FOR THE FUTURE OF THERAPIES

such therapies to many patients with serious diseases, such as Parkinson's, diabetes and a variety of rare diseases, who are waiting for new gene and cell therapies.

This means that we will have to think about cost structures and reimbursement structures in the future. There are

Claudia Waskow has headed the Department of Immunology of Ageing at the Leibniz Institute on Ageing in Jena since 2017. Her scientific work focuses on age-related changes in hematopoietic stem cells and in the immune system, which are responsible for the fact that diseases that a young person survives without problems often take a life-threatening course in old age. She has generated innovative animal models to study human hematopoietic stem and immune cells and uses them to investigate mechanisms of functional regulation. Claudia Waskow received her doctorate from the Basel Institute of Immunology and the University of Basel in Switzerland. After a postdoctoral position at Rockefeller University in New York, USA, she took up a position as a junior researcher at the DFG Center for Regenerative Therapies in Dresden. She was appointed Professor of Immunology there in 2014 before moving to Jena in 2017.



Claudia Waskow

Elke Luger, who holds a doctorate in genetics, focused on strategic science management after her research career with positions at the University of Salzburg, the University of Maine, USA, Charité Berlin and the German Rheumatism Research Center Berlin (DRFZ). Most recently, she headed the office of the Leibniz ScienceCampus Chronic Inflammation at the DRFZ. Since fall 2023, she is managing director of the National Network Office for Gene and Cell Therapies.

over 10,000 diseases waiting for a cure. We have a lot of work ahead of us: beyond networking stakeholders and manufacturers, we must also make progress on national and European regulation, cost structures, and discussions with health insurance companies and the Federal Joint Committee (G-BA), working at both national and European levels.

Claudia Waskow: We must ensure that teams working in Germany are represented in all major international scientific initiatives in the future. This will require a coordinated flow of information, which the National Strategy can provide via the Network Office. There are large international consortia on gene and cell therapies that involve surprisingly few groups from Germany. Major centers in London, Paris and Milan are more strongly represented, so this requires urgent adjustment. Strategic collaboration should reduce the complexity

SIMPLE REGULATION

of regulatory requirements in Germany, specifically regarding regulations on genetic engineering.

GSCN: Looking at the situation internationally, what are the specific bureaucratic and regulatory disadvantages facing Germany?

Claudia Waskow: The implementation of European guidelines differs slightly in every country, which means that their interpretation also differs. In Germany, however, there are even differences between individual federal states, with regulations interpreted slightly differently. This soon leads to confusion.

Elke Luger: A straightforward regulatory framework is also crucial for international investors, who want to provide funding swiftly for these very current, technical procedures. If this process is so cumbersome in Germany, with such differences between the legislation of different federal states, it is easier to invest venture capital in France or Italy – where there is only one law in force nationwide.

Daniel Besser



GSCN: How can we change these regulations and bureaucratic processes in Germany?

Elke Luger: We obviously cannot abolish federalism. However, one aim of the National Strategy for Gene and Cell Therapies is to draw up guidelines upon which the individual German states can base their legislation.

Claudia Waskow: One approach would also be to cooperate with the relevant groups in the German Research Foundation (DFG).

Daniel Besser: The problem is more far-reaching: in Germany, companies must obtain authorization to manufacture cell and gene products from the state authorities and not just the Paul Ehrlich Institute (PEI) or the European Medicines Agency (EMA). The result is regulatory demands from two sides – the state authorities and the EMA – and these demands often do not coincide. We should strive to find common ideas and regulations.

GSCN: How will researchers benefit from the National Strategy for Cell and Gene Therapies? How can they get involved?

Elke Luger: They were invited to contribute to the development and drafting process, where the aim was to highlight deficits and propose solutions to move the whole topic forward. However, we want to continue to uphold and leverage this spirit of cooperation in the Network Office for GCT. We see ourselves as a platform for GCT-related communication, information, cooperation matching and events. We also want to provide information on how to secure funding and on future funding lines, both in Germany and across Europe. This is crucial for researchers; we see it as our duty. We also provide support in the scientific advice process. At present, we are setting up a regulatory support unit that will offer help with initial interactions with the Paul Ehrlich Institute.

Daniel Besser: For one thing, scientists are helping shape the strategy process, which is important. As soon as a financial structure for the strategy has been established, researchers who are already well informed will have a good chance of getting their projects funded, subject to a successful review. The distribution of funds must be – and will be – transparent. In terms of regulation, I think it is very important that start-ups and developers are supported and offered assistance

with less directly connected topics, such as human resources and intellectual property (IP). Where can I find the right people to facilitate certain things, such as GMP (Good Medical Practice) facilities? How should I protect my intellectual property? What support do I need when it comes to sponsors and legal matters? We have to offer support on these issues – nationwide!

Elke Luger: I agree. Researchers also need to broaden their horizons. To date, publications have been the currency of scientific impact.

Yet, if we see the goal of our research as providing treatments for patients, then the way we achieve that is by developing therapies. This idea of publishing less and dealing instead with the mechanisms of patent development and license development, is not yet anchored in any university curriculum. It is for precisely this reason that we need to develop a Germany-wide technology transfer program in the field of gene and cell therapies with partners in Munich and Mainz, where we are dealing with precisely these topics. How do I patent something? How do I secure a license? How do I launch a spin-off? We're trying to show that there are also intermediate forms between academic research careers and spin-offs. The program is called GeneNovate: Empowering Innovators and Entrepreneurs in Gene and Cell Therapies. In the future, we hope to work with partners to roll the program out at many other locations across Germany.

GSCN: How will the GSCN collaborate with the Network Office for GCT and contribute to its initiatives?

Claudia Waskow: I expect that the GSCN will benefit greatly from this new platform with its information and funding. The topics of gene and cell therapies are of interest to both of our members. Cooperation will yield benefits. We can do this in the GSCN Working Group on "Stem cells in regenerative therapies" and also at the GSCN Conference.

Elke Luger: We are delighted by the collaboration with the GSCN and see many interfaces – not only in terms of research and funding, but also in public outreach to groups of the population including patients, pupils and students.

Daniel Besser: We have positive experience of working together in the past; the collaboration between the GSCN and the Network Office for

GCT is an enriching one.

Interview by Stefanie Mahler

HOW DO I LAUNCH A SPIN-OFF?

GSCN News



GSCN Office in Berlin Mitte

At the beginning of 2024, the GSCN office with Daniel Besser, Antje Veldhues and Stefanie Mahler moved to the Rahel Hirsch Center in Berlin Mitte. With the move, the contact details also changed:

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GSCN Office: Luisenstr. 65 · 10117 Berlin

They are looking forward to your visit in the center of Berlin!

Gene and cell therapy 2.023



The GSCN contributed two chapters to the thematic volume “Gene and Cell Therapy 2.023 – Research, Clinical Application and Society” of the Gene Technology Report Working Group. The book provides an up-to-date overview of the state of gene and cell therapy in Germany and was produced with the support of the German Society for Gene Therapy (DG-GT) and the GSCN. It can be downloaded as a PDF or purchased as an e-book.

Link to purchase or download the book:

<https://library.open.org/handle/20.500.12657/87650>

GSCN: ATMP workshop in Potsdam

The GSCN organized the workshop “The Product is the Process – Is it?” Manufacturing and Translation of ATMPs and Tissue- & Cell-based products” together with the PEI and others on 23 Nov. 2023 in Potsdam. 140 participants learned about ATMPs in presentations from research, regulatory authorities, industry and translation and were enthusiastic about the workshop and the opportunity to exchange ideas.

GSCN Workshop “New developments in disease modeling and drug discovery”

On 16 and 17 Nov. 2023, the GSCN Working Group “Stem cells in disease modeling & drug development” organized a workshop in Bonn with the initiators Oliver Brüstle, Harald Stachelscheid, Bert Klebl and Karl-Ludwig Laugwitz as well as GSCN Managing Director Daniel Besser. The topic of the two-day meeting was new developments in disease modeling and drug discovery. Experts gave presentations at the workshop: Oliver Brüstle (Bonn), Jan Eickhoff (LDC Dortmund), Manuel Grundmann (Bayer AG, Wuppertal), Karl-Ludwig Laugwitz (TU Munich), Sandra Lubitz (Evotec AG, Hamburg), Florian Meier (Boehringer Ingelheim), Jutta Meyer (Bayer AG, Wuppertal), Ole Pless (Fraunhofer ITMP Hamburg, Discovery Research Screening Port), Henrik Renner (Evotec AG, Hamburg), Harald Stachelscheid (BIH/Charité Berlin), Johannes Wilbertz (Ksilink Strabourg, France) and promoted stimulating exchanges, discussions and networking.

It grows constantly: GSCN Mentoring Program

Every year, the group of GSCN mentees grows – and they are enthusiastic about their experiences (p. 88) The GSCN Mentoring Program offers a tandem program in which early career researchers are accompanied by mentors for a year. The mentors are available with advice and assessments for



good career decisions. The program also offers workshops and regular mentee club meetings with other alumni. The application deadline is 31 May 2024. More information on the website www.gscn.org/scientific-resources/gscn-mentoring-program.

Successful NonPI meeting in Ulm

16 early career researchers met at Ulm University for the 2023 Non-PI Meeting in the run-up to the GSCN conference. It was a very productive meeting with lots of interaction and exciting topics ranging from own research to problems in the lab and work environment. There is an increasing focus on career development at the non-PI meetings with invited guests – Hartmut Geiger and Birgit Stelzer from the University of Ulm advice and career considerations. In 2024, the non-PI meeting will take place



on 24.9.2024 in Jena. Registrations can be made via the GSCN Conference website (<https://gscn-conferences.org/gscn-conference-2024>)

Photo: GSCN

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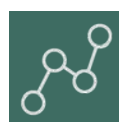
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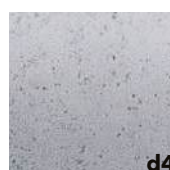
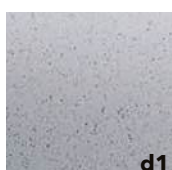


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GSCN Science Awards 2023

The “GSCN 2023 Young Investigator Award” goes to **Meike Hohwieler** from the Institute of Molecular Oncology and Stem Cell Biology at Ulm University Hospital.

The “GSCN 2023 Hilde Mangold Award” goes to **Anne Grapin-Botton** from the Max Planck Institute of Molecular Cell Biology and Genetics (MPI-CBG) in Dresden.

The “GSCN 2023 Publication of the Year Award” goes to **Ruzhica Bogeska**, ... and **Michael D. Milsom** from the Department of Experimental Hematology, German Cancer Research Center (DKFZ) and HISTEM in Heidelberg, for the publication “Inflammatory exposure drives long-lived impairment of hematopoietic stem cell self-renewal activity and accelerated aging” in the journal *Cell Stem Cell*, Aug. 2022.



UniStem Days 2023 and 2024 in Germany

The UniStem Days are very well received as school days on stem cell research in Germany and Europe. In 2024, there was a noticeable increase in activities at various institutes: UniStem Days were held again in Munich

and in Heidelberg, in Jena there was a large number of participants, in Bavaria it was live for the first time and in Berlin and NRW the numbers were impressive. In total, 30,000 students were involved worldwide in 2024 in 13 countries and two continents.



New GSCN movie in German and English

The pancreas is his topic, he connects organoids and pig bladders. The GSCN has recorded a video about his research with Alex Kleger from Ulm University Hospital, on the occasion of the public event in Ulm on 15 Sept. 2023. It can be found in the GSCN media library and on the GSCN YouTube channel (<https://www.youtube.com/c/GscnOrg>).



Max Planck Institute for Molecular Genetics (MPIMG)

Research at the Max Planck Institute for Molecular Genetics (MPIMG) is focused on genome-wide analysis of humans and other model organisms. The overarching goal of the MPIMG's groups is to gain new insights into the origins of diseases at the molecular level, thereby contributing to the development of new medical precision treatments.

The work at the MPIMG revolves around genomics, developmental genetics, stem cell research, transgenic mouse models, human genetics, gene regulation, epigenetics, and computational biology. In particular, stem cell research and analysis of

cellular differentiation during embryonic development play a prominent role to explore mechanistic relationships. The interplay between all of these areas is crucial for progress in genome biology and their close coupling – especially between experimental and computational methods – is a major feature of all departments and research groups at the MPIMG.

Max Planck Institute for Molecular Genetics
 Ihnestraße 63-73 · 14195 Berlin
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Conference Report 2023

The 11th GSCN Conference

13 to 15 September 2023
University of Ulm, Ulm

The 11th GSCN conference took place in Ulm from 13 – 15 September 2023 and brought around 400 stem cell researchers to the university city in Southwest Germany. It was a conference of intensive exchange in 60 sessions and lectures as well as at 122 posters. The debates were lively and passionate. The conference was accompanied by an industry trade fair with 37 exhibitors. The industry also offered high-caliber presentations in its conference sessions.

Scientifically, the GSCN conference was outstanding: The keynotes by Margaret Goodell (Houston, US), Jan Lohmann (Heidelberg), Hiromitsu Nakauchi (Stanford, US), Nicolas Rivron (Vienna), Maike Sander (Berlin) and Fiona Watt (Heidelberg) were stimulating presentations, followed by lively discussions. The scientists were tirelessly engaged in a lively exchange. The presentations by the three GSCN award winners Meike Hohwieler (Ulm University Hospital), Anne Grapin-Botton (MPI-CBG, Dresden) and Ruzhica Bogeska and Michael D. Milson (Germany Cancer Research Center, DKFZ) provided important inspiration for discussion.

The GSCN conference was significant on many levels: At an ELSA symposium, scientists, philosophers, ethicists and lawyers discussed the development of the field with Nicolas Rivron, paying particular attention to developmental biology and the ethical evaluation of early embryonic cells. A successful non-PI meeting brought together young international scientists for an exchange of ideas. The GSCN Mentoring Program brought a new cohort of mentees and mentors on their common path.

The participants were greeted in Ulm by a dual leadership of the GSCN: Host Hartmut Geiger from the Ulm University had had to postpone the GSCN Conference as GSCN President (2020 & 2021) twice due to Corona

and was particularly pleased to welcome Germany's scientific community to Ulm. GSCN President Claudia Waskow emphasized the need to meet in real life and to promote scientific exchange. The Dean of the Faculty of Medicine, Thomas Wirth, welcomed the guests and impressed with his considerable expertise in stem cell research right at the start of the conference.



Hartmut
Geiger



Claudia
Waskow



Thomas
Wirth

Poster
122
GSCN Awards
3
Talks
60
National Highlight Talks
6
Sessions
11
International Highlight Talks
6

» The quality of the talks was high.«

SOURCE: GSCN ONLINE SURVEY

Public Event

at the Volkshochschule Ulm
on 15 September 2023

Panel discussion with short films and scientists

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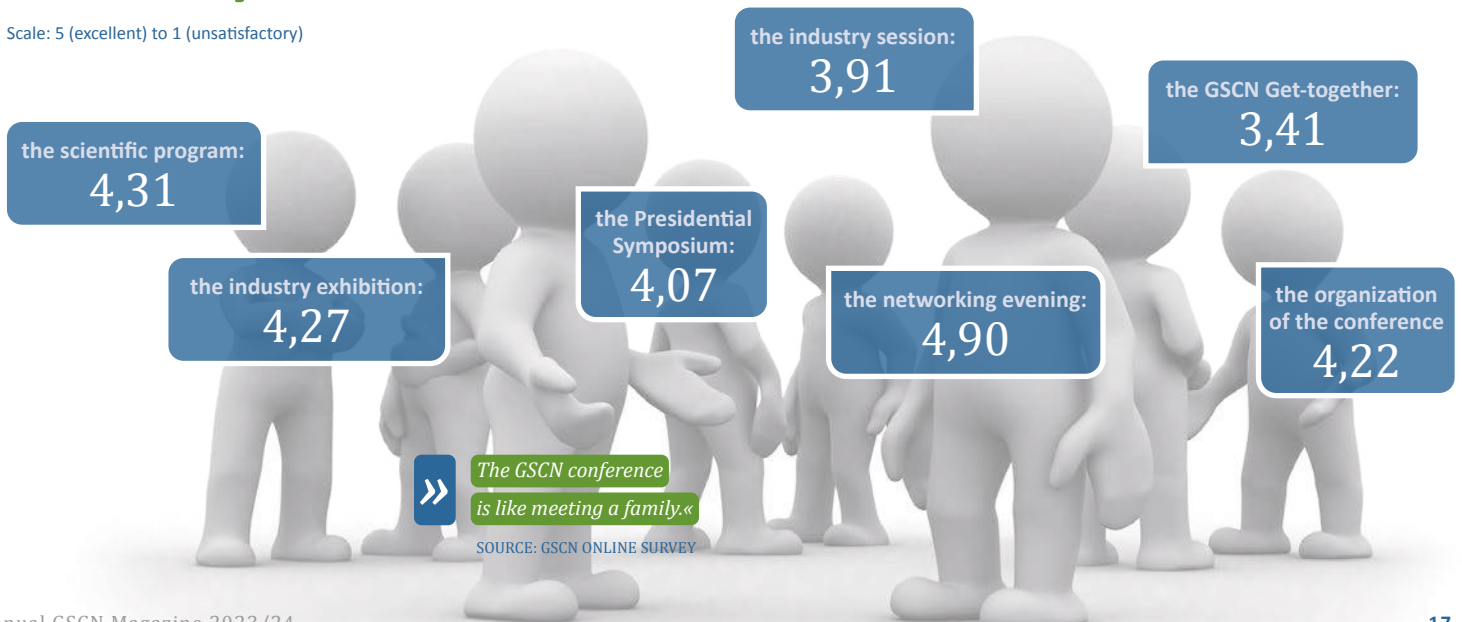
Prof. Dr. Hartmut Geiger, University of Ulm
Prof. Dr. Alexander Kleger, Ulm University Hospital
Prof. Dr. Ana Martin-Villalba, German Cancer Research Center DKFZ, Heidelberg
Prof. Dr. Katja Schenke-Layland, University of Tübingen
Moderation: Stefanie Seltmann



Evaluation of the 2023 online survey of participants (Ø)

How do you rate...

Scale: 5 (excellent) to 1 (unsatisfactory)



The international keynotes at the GSCN Conference 2023



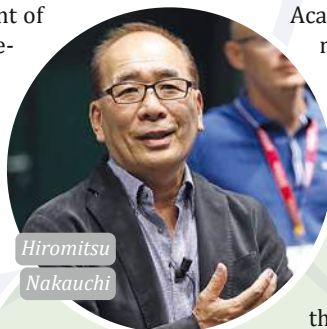
Margaret (“Peggy”) Goodell, director of the Stem Cells and Regenerative Medicine Center at Baylor College of Medicine, in Houston, Texas gave the opening keynote at the GSCN conference. She discussed three examples of somatic mosaicism in the blood, termed “clonal hematopoiesis”. Clonal hematopoiesis has recently emerged as a universal feature of normal aging. Clonal hematopoiesis is the consequence of life-long competition among stem cells in the bone marrow, such that the progeny of “winning” stem cells become over-represented in the blood. Around 20 genes have been observed to be recurrently mutated among the winners, indicating that certain genetic variants confer a competitive advantage over many years. The mechanisms through which these variant stem cells triumph is generally poorly understood. Goodell’s talk described three distinct mechanisms through which somatic mutations in humans impact stem cell function and lead to clonal hematopoiesis. Mutations in PPM1D are found in many individuals. In the context of ex-



Margaret Goodell

posure to a chemotherapeutic agent, PPM1D-mutant cells have a selective advantage and become overrepresented in the blood of people and mice. The mutations confer a minor improvement in resistance to cell death that leads to a significant survival advantage over time. Goodell also described her lab’s recent exploration of the gene SRCAP and its role in normal hematopoietic cells. SRCAP mutations are frequently found in humans exposed to certain stresses including bone marrow transplantation. Goodell modeled this mutation and described the mechanisms of advantage. Finally, Goodell touched on the role of the most common mutation in clonal hematopoiesis, in the DNMTA gene. Goodell described enhanced self-renewal offers stem cells a profound advantage over many years. Surprisingly, mutations in all genes studied so far differ slightly in their potency, the molecular mechanisms that confer fitness, and the conditions under which they are most likely to “win”. These mechanisms lend insight into the interplay between aging, clonal hematopoiesis, and leukemia development.

The second keynote of the GSCN Conference 2023 featured **Hiromitsu ("Hiro") Nakauchi** of Stanford University and Tokyo Medical and Dental University. The Nakauchi Laboratory consistently aims to translate fundamental scientific discoveries into clinical applications. One notable achievement is the development of a platform capable of generating platelets, crucial blood components for hemostasis, from both embryonic stem (ES) and induced pluripotent stem cells (iPSCs). This platform, later enhanced and expanded by former colleague Koji Eto, underwent a groundbreaking first-in-man study on iPSC cell-derived platelets in 2021. Another remarkable accomplishment involves the reprogramming of antigen-specific cytotoxic T cells into iPSC cells (T-iPSC), followed by redifferentiation into T cells from T-iPSCs. These rejuvenated T cells exhibit characteristics such as a naive T cell phenotype, extended telomeres, and heightened antigen-specific killing activity. Clinical trials for this innovative approach are expected to begin next year. Nakauchi's team has also achieved ex vivo expansion of mouse hematopoietic stem cells (HSCs) by refining the culture medium through the removal of impurities in bovine serum albumin (BSA) and its substitution with a polymer. Recently, the team successfully applied this concept to establish a culture platform for expanding human HSCs. However, the most challenging project described involves the generation of transplantable organs from one species within the body of another. This idea is derived from the experience of HSC transplantation, where it is necessary to prepare a "niche" for the engraftment of donor cells. While exogenous organ generation has been demonstrated between mice and rats, the team faced hurdles when attempting the same with human iPSCs injected into sheep, pigs, or mice embryos. Termed the "xenobARRIER," this phenomenon, likely attributed to evolutionary divergence, led to the early elimination of human iPSCs during embryogenesis. To overcome this obstacle, Nakauchi's team conducted gene editing on human iPSCs, resulting in their survival and co-development with mouse cells in some tissues and organs. Understanding and manipulating the xenobARRIER may hold the key to successfully generating human organs in live-stock animals.



Hiromitsu
Nakauchi

It is a well-established custom of the GSCN conferences that the evening of the first conference day is reserved for a keynote impinging on ethical, legal and social aspects of the research. In 2023 the ELSA keynote was given by **Nicolas Rivron** from the IMBA Institute of the Austrian

Academy of Science. He talked about how stem cell research has paved a new avenue for compre-

hending the early phases of animal and human development. This exploration commenced a decade ago using stem cells sourced from mice or humans, which, under specific conditions, spontaneously organized into structures resembling rudimentary early embryos within the initial two weeks of development. Different models were generated depending on the methodology employed, exhibiting varying degrees of completeness compared to embryos and representing distinct stages of development (such as preimplantation and postimplantation). However, even the most comprehensive mouse embryo models fail to generate newborn mice when transplanted into a mouse uterus, indicating that while these models are



Nicolas Rivron

not yet embryos, they also underscore our limited understanding of embryogenesis. Questions arise regarding what precisely is being replicated, the specific contributions these models can offer to science and medicine, and their legal status, including the possibility of future use for reproduction. Rivron's

lecture delved into various models, ranging from blastoids, including a more complete model developed in his laboratory, to gastruloids, and explored the potential scientific and medical breakthroughs as well as the ethical considerations they evoke.



The series of keynotes commenced on the third conference day on Friday, 15 Sept. 2023, by an exciting presentation from **Fiona Watt** from EMBL Heidelberg. Watt's team studies the stem cell compartment in adult mammalian epidermis. In her talk she covered two topics: the heterogeneity of stem cells in human epidermis and the process by which cells undergo dedifferentiation during wound healing in mouse epidermis. Using scRNAseq data from healthy human epidermis Watt's team was able to confirm predictions from in vitro experiments that the basal layer of the epidermis contains multiple cell populations. They were able to identify a potential hierarchy within the stem cell compartment, originating from a cluster of cells expressing the Notch ligand DLL1. They then used the scRNAseq data to identify the Fringe gene LFNG as a potential amplifier of DLL1 and confirm its effect in cultures of human epidermis. This work on dedifferentiation focuses on cells of the mouse sebaceous duct that express Gata6. During wound healing Gata6 lineage cells are able to dedifferentiate into stem cells. The dedifferentiation process appears to be a direct reversal of the differentiation pathway and is dependent on Myc and the actin cytoskeleton.

Fiona Watt



The closing keynote of the 2023 GSCN Conference was given by **Jan U. Lohmann** from the Center for Organismal Studies (COS) of the Heidelberg University with the title "Multilayer control of plant stem cell behavior". Lohmann's lab studies how the activity of plant stem cells is regulated by transcriptional, hormonal, and environmental signals. In contrast to most animals, plants maintain pluripotent stem cells over their entire life cycle. Stem cells are embedded in specialized tissues, called meristems, which provide the appropriate environment for this behavior. In the apical plant stem cell system, stem cells are only found in the central zone, whereas transient amplifying cells are found at the periphery, where they are exposed to differentiation signals. In his talk, Jan Lohmann presented recent results from his lab that demonstrate that plant stem cell control is based on a finely tuned network of complementing mechanisms. At the heart of this network is the stem cell inducing homeodomain transcription factor WUSCHEL, which is expressed in the niche, but moves via plasmodesmata to the adjacent stem cells. This mobility is highly regulated and by bringing together massive confocal imaging with computational quantification and mathematical modelling, the Lohmann lab has found that it is based on a tug of war between active transport of the WUSCHEL protein throughout the meristem and specific retention in niche cells. He furthermore showed that expression levels of WUSCHEL are dependent on light and energy availability and that both inputs depend on TOR kinase activity. Importantly, TOR controls WUSCHEL expression via translational regulation of enzymes that break down the phytohormone cytokinin, which stimulates WUSCHEL transcription. One of the central functions of WUSCHEL is to repress stem cell differentiation and this is brought about by the rheostatic control of cellular responses to another phytohormone by the name of auxin. Auxin triggers differentiation in the shoot and WUSCHEL acts to limit expression of a large fraction of the auxin signaling and response pathway. Finally, Jan Lohmann talked about unpublished work that shows that Nitric Oxide signaling defines transit amplifying cell fate at the periphery by repressing stem cell identity. Amazingly, this activity relies on the NO dependent interaction of WUSCHEL with ARGONAUTE4, a key regulator of the RNA directed DNA Methylation pathway, which is essential for transposon silencing.

Jan U. Lohmann



The Presidential Symposium: Lecture at the invitation of the President and the presentations of the GSCN Awards 2023

The Presidential Symposium 2023 featured yet again an impressive line-up of a lecture for the presidential invitee and three outstanding lectures from the GSCN awardees. GSCN president Claudia Waskow chaired the symposium and had invited Maike Sander from the Max Delbrück Center in Berlin to kick-off the session.

Over the last quarter-century, **Maike Sander** has investigated molecular mechanisms that control the formation, proper function, and survival of insulin-producing pancreatic beta cells in the pancreas. Her research group has been instrumental in laying the foundation for our understanding of the role played by transcription factors and signaling pathways in the acquisition and maintenance of

Maike Sander



pancreatic cell identity. Work by her group has elucidated the mechanisms through which the aberrant regulation of transcription factors contributes to the pathogenesis of diabetes. This foundational knowledge has been pivotal to develop methods for generating pancreatic islet cells from human pluripotent stem cells (hPSCs), currently undergoing clinical trials for diabetes treatment. Through the implementation of hPSC-based differentiation systems, she has uncovered fundamental insights into how chromatin state influences organ lineage commitment. Furthermore, her research has shed light on the intricate orchestration of human beta-cell differentiation by transcription factors and chromatin modifiers. Employing hPSCs, Sander's group has successfully modeled the effects



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of diabetes-associated genetic mutations and variants on beta-cell gene regulation, yielding novel insights into the underlying mechanisms of human diabetes. Collaborating with bioengineers, she has spearheaded the development of hPSC-derived multi-cellular vascularized islet organoids to provide a more accurate representation of how beta-cells are impacted in diabetes. Maike Sander's recent investigations into the connections between age, beta-cell intracellular metabolism, and adaptive responses of the beta-cell have significantly advanced our understanding of how environmental factors influence beta-cell function and regenerative capacity.

The *GSCN Young Investigator Award 2023* went to the Ulm-based scientist **Meike Hohwieler** from the Institute of Molecular Oncology and Stem Cell Biology at Ulm University Hospital. The stem cell biologist introduced work on establishing pancreatic organoids from human pluripotent stem cells and their use to dissect pancreatic progenitor heterogeneity, plasticity and early dysplasia.

First, she presented an optimized ductal differentiation approach, enabling the formation of pancreatic duct-like organoids, short "PDLOs", that resemble ductal morphology, functionality and expression profile. They could be applied as in vitro models for dysplasia and carcinogenesis by inducing expressing oncogenic *GNAS*, *KRAS*, or *KRAS* in *CDKN2A*-deficient cells. Each oncogene caused a specific growth, structural, and molecular phenotype in vitro. Moreover, she showed that after orthotopic transplantation into mice these PDLOs caused PDAC-like tumor or pancreatic cyst (IPMN) formation in response to the specific oncogene. In the second part of her talk, driven by the core interest of her group in studying exocrine pancreas disorders, Hohwieler focused on their recent success to engineer acinar cells from hPSCs. She explained how crucial it was to first generate true multipotent pancreatic progenitor cells without an endocrine lineage bias often observed

Meike Hohwieler



with current protocols. These MPCs are not only characterized and identified by expression of critical transcription factors like PDX1

and NKX6-1 but also by high levels of GP2. She showed that the research group's novel differentiation regimen induced high yields of GP2-positive PPs and reduced impurities. Using single-cell transcriptomic analysis, they were able to reveal profound heterogeneity and lineage fate commitment of subpopulations at the pancreatic progenitor stage. Importantly, she highlighted the capacity of trilineage differentiation from the same multipotent ancestor. This was proven in vitro by the generation of endocrine and ductal cells. Hohwieler demonstrated that only FACS-purified GP2^{high} PPs present a progenitor population that can also be challenged for differentiation into pancreatic acinar-like organoids. In conclusion, her findings serve as a basis for studying developmental processes and inherited disorders of the exocrine pancreas as well as deciphering early cancer formation in a cell type-specific context.



Center for Regenerative Therapies Dresden (CRTD)

Research Center of the TU Dresden

The Center for Regenerative Therapies Dresden (CRTD) of TU Dresden is an academic home for scientists from more than 30 nations. Their mission is to discover the principles of cell and tissue regeneration and leverage this for recognition, treatment, and reversal of diseases. The CRTD links the bench to the clinic, scientists to clinicians to pool expertise in stem cells, developmental biology, gene-editing, and regeneration towards innovative therapies for neurodegenerative diseases such as Alzheimer's and Parkinson's, haematological diseases such

as leukaemia, metabolic diseases such as diabetes, and retina and bone diseases. Through SaxoCell, the newly acquired transfer-oriented BMBF Cluster for Future, the CRTD will now expand its focus to cell and gene therapies.

The CRTD was founded in 2006 as a Research Center of the German Research Foundation (DFG) and until 2018 supported as a DFG Research Center, as well as a Cluster of Excellence. Since 2019, the CRTD is funded by the TU Dresden and the Free State of Saxony.



Center for Regenerative Therapies Dresden (CRTD)

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Anne Grapin-Botton received the *GSCN 2023 Hilde Mangold Award* for her significant contributions to the development of the organoid field and her contributions to understanding pancreas development. She started her talk reminding the audience of the importance of Hilde Mangold's work and a long tradition of grafting tissue to understand its commitment and signaling properties, a field to which she contributed as a PhD student, transplanting hindbrain rhombomeres to understand Hox code determination. Anne Grapin-Botton is particularly well known for the development of the first embryo-derived organoid model at the onset of the field and continuous work developing and exploiting stem-cell derived organoid models enabling to study human development. In her talk she showed how live imaging of organoids enables to observe processes that are normally hidden in the womb of mammals, notably collective movements and the dynam-



Anne
Grapin-Botton

ics of duct formation in the pancreas, as well as the timing of endocrine cell differentiation. She notably showed that endocrine differentiation is twice slower in human than in mouse and that the gene that triggers differentiation, Neurogenin 3 peaks at very heterogeneous levels of transcription and protein in different endocrine progenitors.

This heterogeneity may be due to heterogeneous Notch signaling inputs. However, even the low levels enabled endocrine differentiation, which may explain why endocrine differentiation in the pancreas is only affected by mutations that severely affect the function, while the enteroendocrine cells are more sensitive. On the technology side, she showed how statistically linking the dynamics of endocrine progenitor tracers in live imaging to single cell transcriptome analysis enables to identify new genes involved in endocrine progenitor motility. Similar methods could be applied to other systems. Complementing these mechanistic investigations focused on two proteins, she presented a screen enabling to follow multiple developmental events in parallel including cell identity, cell expansion and organoid size and shape. The small molecule screen based on four complementary analysis pipelines focusing on mean



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values, binning methods, network analysis and clustering analyses after dimensionality reduction of the 300 parameters measured. In summary, her talk showed the power of organoids combined with live imaging and quantitative image analysis to gain insights into mammalian and particularly human development.

The gradual dysfunction of regenerating tissues during the process of aging is widely thought to be caused by the so-called exhaustion of adult stem cells, which apparently contradicts the concept that these stem cells have extensive self-renewal capacity. In their 2022 publication, **Ruzhica Bogeska** and colleagues addressed this apparent paradox using the murine hematopoietic system as a model organ. As the recipient of the 2023 *GSCN Publication of the Year Award*, Bogeska presented this manuscript at the GSCN Conference, and explained how it impacts on our understanding of the role of adult stem cells in organismal aging. Following on from previous work that had shown that hematopoietic stem cells (HSCs) could be induced to exit from their predominantly quiescent state in response to inflammatory stress, Bogeska and colleagues from the laboratory of **Michael ("Mick") Milsom** were able to demonstrate that such instances of "emergency hematopoiesis" compromised the functional potency of the HSC pool. However, the key message of the manuscript was that the HSC compartment completely failed to regenerate following such challenge, even when mice were left to recover for up to one year. This finding could be faithfully recapitulated using a bacterial infection model. Together, these data suggest that temporally discrete rounds of challenge have a cumulative attrition effect

on the HSC pool, even if such exposures are separated by weeks, months or perhaps even years, thus providing a model for tissue aging. Indeed, to validate such a link, Bogeska and colleagues then went on to examine age-associated features of mice which had been exposed to inflammatory stimuli in early and middle age. They found extensive cellular and molecular evidence that the HSCs from such mice had undergone a process of accelerated aging compared to HSCs from control age-matched mice. Using a genetic mouse label retention model to capture in vivo HSC division events following inflammatory exposure, she was able to show that this accelerated aging phenotype was characterized by proliferation in the absence of self-renewal. Thus, while emergency hematopoiesis sustains the short-term demand for increased blood cell production following infection and inflammatory exposure, this comes at the expense of the functional potency of a small sub-fraction of the HSC pool. Such effects accumulate over a lifetime of exposures, eventually leading to the features of HSC dysfunction that we associate with aging, such as anemia and bone marrow hypocellularity.



Ruzhica
Bogeska

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- Helmholtz Centre for Infection Research Braunschweig
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The scientific GSCN sessions: Exciting projects from the scientific community

The GSCN conference in Ulm featured many projects from the stem cell community. In total 31 projects were presented as talks in the different sessions. Not all of the talks can be covered here but some exciting presentation are highlighted in the following text.

Caitlin MacCarthy (Max Planck Institute for Molecular Biomedicine, Münster) presented a project on engineering an enhanced Yamanaka cocktail by stabilizing Sox2/Oct4 dimerization in the session "Pluripotency and reprogramming" on the first conference day, Wednesday 13 Sept. Integrating structural elements from Sox17 into Sox2 yielded a chimeric super-SOX with



an increased ability to cooperate with Oct factors, which enhanced induction of pluripotency in five species. The work unveiled the mechanism of naive pluripotency: Oct4 alone binding stimulates proliferation and priming, while Sox2/Oct4 co-binding induces a highly developmentally potent naive state. Sox2/Oct4 dimerization declines upon transition from naive to primed pluripotent states, but the transient overexpression of super-SOX+Klf4 can reinvigorate this interaction, offering a universal naive reset technology applicable across species.

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In the session “Computational stem cell biology”, **Reyna Rosales Alvarez** (Würzburg Institute of Systems Immunology, Max Planck Research Group at the Julius-Maximilians-Universität Würzburg, Germany) introduced VarID2, a computational tool that allows to measure gene expression noise at single-cell resolution. VarID2 showed enhanced nuclear versus total cellular transcriptome noise across peripheral blood cells, and separated regulatory modes stratified by correlation between noise, expression, and chromatin accessibility. In murine hematopoietic stem cells (HSCs), noise levels are low and they increase upon both differentiation and aging. Differential noise between HSCs isolated from old and young mice reveals an emerging population of Dlk1+ HSCs in the bone marrow of ageing mice. These

Dlk1+ HSCs exhibit myeloid bias as well as enhanced quiescence and self-renewal capacity compared to Dlk1- HSCs. Overall, VarID2 elucidates key features of noise across cellular compartments, during stem cell differentiation and aging. It further enables the identification of distinct cellular sub-states which remain unresolved by conventional differential gene expression analysis or clustering.

In the session “Stem cells in disease modeling & drug development” on the second conference day, **Angelika Dannert** from the laboratory of Dominik Paquet (Institute for Stroke and Dementia Research, University Hospital LMU Munich) presented a novel model for Tau-related neurodegenerative diseases. To improve modeling of late-onset disease in iPSC-derived cortical neurons, multi-step CRISPR-editing was used to match the fetal-like Tau splicing pattern of iPSC-derived neurons to the Tau isoform ratios of adult human neurons. Upon insertion of dementia-related Tau mutations, neurons expressing adult Tau isoforms endogenously developed advanced Tau pathology, including Tau seeding, aggregation, and formation of neurofibrillary tangle-like structures. Neither the mutations nor adult Tau expression alone showed the same pathology. The presented model is the first to develop advanced Tau pathology exclusively from the endogenous human Tau locus. It, therefore, underscores the need to consider maturation-dependent differences for accurate modeling of late-onset neurodegenerative diseases using iPSCs.



Leibniz Institute on Aging – Fritz Lipmann Institute (FLI)

Research for better aging

The Leibniz Institute on Aging – Fritz Lipmann Institute (FLI) has dedicated to biomedical aging research since 2004. More than 350 employees from around 40 nations explore the molecular mechanisms underlying aging processes and age-associated diseases. The main aim of research at FLI is to delineate how aging leads to the development of tissue dysfunction and diseases in the elderly. If the understanding of the aging process contributes to the extension of healthy lifespan, the strains on society can be minimized and the society's future development

will be enriched by the wealth of knowledge and experience older people possess. As one of 97 independent research institutions of the Leibniz Association, the FLI is publicly funded by the German Federal Ministry of Education and Research (BMBF) and the State of Thuringia.

Leibniz Institute on Aging –
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In the “Stem cells in ageing & disease” session, **Alec Geßner**, PhD student at the laboratory of Michael Rieger (Department of Medicine 2, Hematology/Oncology, Goethe University Frankfurt), presented clonal dynamics and differentiation hierarchies in B-cell precursor acute lymphoblastic leukemia (BCP-ALL). Combining patient-derived B-ALL cells, lentiviral barcoding, and single cell sequencing, the in vivo subclonal architecture, organ distribution, and differentiation trajectories of BCP-ALL were presented. He showed that a few dominant clones exert strong local expansion, yet the clonal composition varies among recipient mice, indicating selective pressure from the microenvironment. Additionally, using the lineage barcode information together with single-cell CITE-Seq, subpopulations with prospective marker expression at various stages of BCP-ALL cell differentiation and distinct disease progression were demonstrated. This technique offers novel perspectives to investigate the hierarchical organization of BCP-ALL and the identification of potential new therapeutic targets in populations with leukemic stem cell potential.

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On Friday morning, 15 September 2023, the conference continued with the session “Stem cell in regenerative therapies”, and **Xuejun Yuan** (Max Planck Institute for heart and lung research, Bad Nauheim) presented her new findings on the interplay between metabolism and epigenetic mechanisms in regulating of muscle stem cell (MuSC) quiescence during muscle tissue homeostasis and regeneration. By applying knockout mouse models, she and her co-workers discovered that inhibition of fatty acid oxidation (FAO) resulted in loss of MuSC quiescence, premature MuSC activation/differentiation, and muscle hypoplasia following muscle injury. Mechanistically, they found that metabolic reprogramming after FAO inhibition prevents the nuclear translocation of metabolic enzymes, resulting in hypo-acetylation and suppression of genes related to signaling pathways required for quiescent maintenance. This study supports metabolic reprogramming of MuSC as a novel approach to intervene in muscle degenerative processes and diseases.

In the session “Hematopoietic stem cells”, **Jasmin Rettkowski** (from the Cabezas-Wallscheid laboratory at the Max Planck Institute for Immunobiology and Epigenetics in Freiburg) presented data on how myocardial infarction affects the molecular signatures and function of bone marrow hematopoietic stem cells. Specifically, she showed that hematopoietic stem cells molecularly shift toward a progenitor-like cell type, as demonstrated by population and single-cell RNA-seq analysis, and lose their self-renewal capacity, as evidenced by *in vitro* colony-forming assays and *in vivo* transplantation experiments. This work highlights the detrimental impact of myocardial infarction on hematopoietic stem cells and opens a novel therapeutic target for myocardial infarction patients.



The strategic GSCN meetings: common topics for all scientific fields

The session on “Clinical trials and regulatory affairs” was chaired by Zoltan Ivics (Paul Ehrlich Institute, Langen) and Torsten Tonn (DRK-Blutspendedienst Nord-Ost, Dresden). The first speaker of the session was **Christopher Baum**, chair of the Berlin Institute of Health (BIH) board of directors. He reported on a new initiative called the National Strategy for Gene and Cell Therapy (GCT), that is coordinated at the BIH. This initiative was fueled by recognizing a widening gap between the high-quality laboratory research and resulting high-impact publications in GCT by German scientists and the relatively inefficient translation of the preclinical findings. It is recognized that this trend needs to be stopped, or better reversed, in order to preserve German competitiveness in developing novel, innovative therapies. The initiative is aiming to close this gap by establishing a fully integrated network, or ecosystem, by linking and strengthening the conditions and the interactions between the various stakeholders in GCT. The mandate to launch this initiative is coming from the BMBF. A roadmap has been established by formulating working groups covering the different activity fields of GCT, including R&D, manufacturing, links to the society, educational activities, standards and regulatory conditions, technology transfer, market access and incorporation in medical care and others. Stakehold-

ers in Germany, including research networks, universities, the biotech sector and regulatory agencies delegated representatives to these working groups that together carry out a mapping exercise (identifying gaps) and formulating a recommendation (filling the gaps). The recommendation, collated from the different working groups, will be submitted to the BMBF so that steps for implementation can be considered and executed. The second speaker of the session was **Zoltan Ivics** (Paul Ehrlich Institute) who spoke on behalf of the German Society of Gene Therapy (DG-GT), as one of the stakeholder groups in GCT. The DG-GT is a scientific organization with a mission to promote basic research and translational development in GCT, to provide information to scientists at all stages of career development as well as to the lay public, to improve training and interactions between basic researchers and clinicians and to contribute to recommendations for regulatory and scientific processes and discussions. To support its activities, among other actions, the DG-GT has been organizing webinars to complement its annual conferences and has launched a paper prize to recognize young scientists for their outstanding publications. The DG-GT has published a position paper in the journal *Human Gene Therapy* in 2021, in which the society has formulated basic recommendations for improving



GCT in Germany. Recognizing that the numbers of ATMPs approved for market are expected to increase in the future, and that the market value of GCT is also projected to undergo a significant increase, the DG-GT has formulated recommendations for action that are in full alignment with the working plan of the National Strategy for GCT. The final speaker of the session was **Christoph Conrad** (BIH). As a former PEI employee with significant hands-on experience in regulatory aspects, he introduced the concept of setting up an advisory support service as an action that is linked to the National Strategy for GCT. He described the elaborate regulatory path from preclinical data sets to early phase clinical trials. Stemming from a recognition that academic developers of ATMPs very often lack the necessary background information, knowledge and especially the experience to guide a product through to approval of a clinical trial, he announced the foundation of a new office with a mission of offering early advice to such developers in the hope that through this support mechanism applicants to the PEI will be better prepared and therefore their applications accepted in a more streamlined fashion.



Christoph
Conrad

In this year's strategic session on "Career Development" chaired by Insa Schroeder (GSI Darmstadt) and Germán Camargo Ortega (ETH Zürich), **Karin Höhne** from the Berlin Institute of Health (BIH) at Charité presented data and led a discussion on *power abuse in academia*. Karin Höhne is head of the Equal Opportunities Department. Her work aims to boost innovation and high-quality scientific work at BIH by improving diversity, equality, and inclusion (DEI) and conditions for the compatibility of work and family. In her talk she convincingly described the nature of power abuse and its consequences to the individual but also to the research community in general. How the academic system might support power abuse and what could be done individually but also on an institutional level to counteract was part of the talk and a panel discussion, including Karin Höhne, **Marieke Essers** (DKFZ Heidelberg), and **Michael Rieger** (Frankfurt University). The audience's students and postdocs asked the panelists about their experience with power abuse in their research environment and vividly discussed several examples of known/reported cases of abuse in academia and how to deal with these properly. Valuable input was



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given by **Fiona Watt** (EMBL Heidelberg) sharing her perspective based on her experience of the research landscape in Great Britain, which was compared to that of Germany and the Netherlands. From the many questions from the audience and the lively discussion, it was clear that this is a red-hot topic that needs further open discussions.

In 2023, Andreas Bosio and Sebastian Diecke organized a session on “Technologies in Stem Cell Research,” with a new focus on “Multi-omics Applications in Stem Cell Research” at the GSCN Conference. This session was a part of the GSCN Working Group’s efforts to highlight the latest strides in stem cell technologies, particularly emphasizing how multi-omic approaches are revolutionizing our understanding and utility of stem cells. **Lars Velten** from the Centre for Genomic Regulation (CRG), Barcelona, Spain,

delivered the EMBO YIP Lecture, focusing on “Clonally resolved single-cell multi-omics of leukemic and hematopoietic stem cells”. His presentation showcased the power of multi-omics to unravel the complex genetic and epigenetic landscapes of leukemic and hematopoietic stem cells, shedding light on clonal evolution and its implications for therapy.

Ivano Legnini from the Human Technopole, Milano, Italy, spoke on “Spatio-temporal, optogenetic control of gene expression in stem cells and organoids”. He illustrated how integrating optogenetics with multi-omic data enables precise manipulation of stem cell fates and organoid development, paving the way for novel therapeutic strategies. **Johnny Kim** from TRON g GmbH, Mainz, presented his work on “The homeobox transcription factor Duxbl is required for totipotency exit in mice”, emphasizing the importance of the key transcription factors Duxbl on heart regeneration. His findings offer insights into the molecular mechanisms governing totipotency and differentiation, highlighting potential targets for regenerative medicine. The session underscored the transformative potential of multi-omic technologies in stem cell research. Discussions emphasized not only the advancements these technologies bring but also how the results from multi-omic studies can be functionally exploited to understand cellular processes, disease mechanisms, and therapeutic avenues.



ELSA-Symposium ‘What makes it (not) a human being?’

During the 2023 conference the session of the work group ‘ethical, legal, and social aspects’ discussed emerging topics on the artificial generation of embryo-like entities derived from pluripotent stem cells. Embedded in the key note series of the main meeting Nicolas Rivron presented a stunning overview of the recent advancement in modeling mouse and human development with stem cells. His talk comprehensively summarized novel findings in the field and his lab’s exciting contribution to the growing understanding of early post-implantation development.

During the following morning parallel session, the chairs Aljoscha Berve and Tobias Cantz interviewed Nicolas Rivron in order to revisit his definition of embryoids, blastoids, and self-assembled embryos. Together with the audience, they discussed intensively

why and how do these differences matter. All participants agreed that, as the current public discussion on the notion of ‘synthetic embryos’ shows, terminology matters and should be weighed responsibly by researchers. A particular emphasis was put on realistic expectations on advanced embryoid cultivation during the upcoming years and on the topic, how differing international regulations do affect current research activities.

The symposium was rounded-up by a presentation of Daniel Besser on the results of a Civey survey on embryo research regulation addressing issues on the perception of the German (internet) public the current regulation of embryo research and stem cell research regulation.





Poster prizes and travel grants

The GSCN congratulates the winners of the € 400 travel grants:

- Rajesh Vivekanandan, LEBAO, MH Hannover
- Esther Schickel, GSI Helmholtzzentrum für Schwerionenforschung GmbH, Darmstadt
- Thulaj Mehrarwade, Montreal Clinical Research Institute, Canada
- Sanjana Mathew-Schmitt, University of Würzburg

The poster prizes with € 500 were awarded to:

- Kim Krieg, Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, ScreeningPort Hamburg
Modeling metastatic cancer niches for drug discovery using human iPSC-derived brain organoids
Session: Stem cells in disease modeling & drug development
- Lennart Valentin Schneider, University Medical Center Göttingen
Neuro-vascular network co-development in a human innervated heart muscle model
Session: Stem cells in disease modeling & drug development
- Abdelrahman Mahmoud, Würzburg Institute of Systems Immunology
Cell-DRL: reconstructing causal disease trajectories by deep reinforcement Learning
Computational stem cell biology & systems biology
- Ismail Özcan, Institute of Cell and Systems Biology, University Hamburg
Genetic dissection of in vivo direct cellular reprogramming
Session: Somatic stem cells and development

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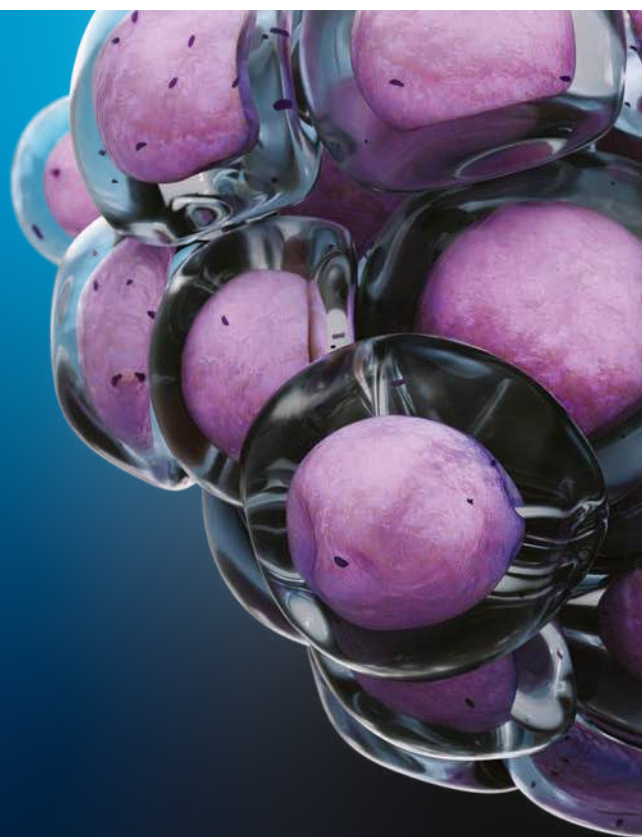
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The social highlights of the Ulm Conference 2023

The get-together was characterized by excellent Swabian specialties, which, however, were only accessible after a very detailed presentation and discussion by Nicolas Rivron. The conference participants were therefore well catered for in terms of food and content on the first day of the conference. The networking event on Thursday outdid itself in superlatives: Great food, an outstanding location in a former US casino Wiley Club with an original long bar and corresponding party atmosphere and later a DJ who ensured a lively atmosphere.



Public panel discussion

The public panel discussion at the Volkshochschule Ulm was one of the events of the final Ulm GSCN Conference and the GSCN Public Outreach. On Friday evening, **Hartmut Geiger** (Ulm), **Alexander Kleger** (Ulm), **Ana Martin-Villalba** (Heidelberg) and **Katja Schenke-Layland** (Tübingen / Reutlingen) discussed with moderator **Stefanie Seltmann** (Berlin) the status of current stem cell research and the application of existing stem cell-based therapies with a highly interested Ulm audience. It was an evening full of questions and discussions about ageing, pancreatic cancer, neuronal diseases, organoids and new technologies as well as visions for the future. The very stimulating discussion continued after the panel discussion between scientists and the audience in the foyer with pretzels and drinks.



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Impressions





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Hans Reimer Rodewald (Heidelberg, D)
Thomas Zwaka (New York, US)

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Abstract submission deadline for oral presentations: 21 June 2024

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- Hematopoietic stem cells
- Stem cells in aging and diseases
- Stem cells in regenerative therapies
- Stem cells in disease modeling and drug development
- Organoids: new models for diseases
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The global stem cell economy

Stem cell ecosystems: A global perspective

Innovation in stem cell research and stem cell-based regenerative medicine requires a global perspective paired with international exchange and cooperation. In this context, it is useful to have an understanding of the particular strengths and successful concepts of the world's leading regions and nations. The Atlas of Stem Cell Ecosystems provides a comprehensive overview of Europe, Asia-Pacific and North America – three regions where research and translation take place at the highest level.

In the summer of 2024, the world of stem cell research will gather at the ISSCR Annual Meeting in Hamburg. From July 10 to 13, the Congress Center Hamburg (CCH) will be transformed into a unique platform for the global research community to exchange the latest insights from basic and translational research and clinical development in the stem cell sciences.

Stem cell science and translation is a global endeavor. Nevertheless, different regions of the world have developed at different speeds and under different conditions.

So, which regions and nations have enjoyed particular success in driving forward developments in stem cell research and translation? How is research and regenerative medicine supported by national governments? Who are the key players in the fields of science, industry and administration? And what course is being set for the future?

The German Stem Cell Network (GSCN) has taken a closer look at the dynamic developments underway in three regions – Europe, North America and Asia-Pacific – and discussed its assessments with international stem cell experts. The result is a comprehensive collection: an Atlas of Stem Cell Ecosystems.

It defines innovation ecosystems in selected countries and macro-regions – areas in which stakeholders from science, business, politics and administration engage in transformative innovation processes in stem cell research and the translation of regenerative medicine.

A world map of stem cell legislation

Anyone seeking to understand why some countries have historically developed innovative stem cell ecosystems faster than others will find initial clues in the variety of legislation governing the use of human embryonic stem cells (ES cells). The register for human pluripotent stem cells, hPSCreg, uses a traffic light system to help users research its database of relevant legislation. Green indicates a permissive legislative framework, yellow a moderately permissive framework and red a restrictive framework. The hPSCreg team has compiled a concise world map for the GSCN (with information correct as of February 2023).

The Fraunhofer Institute for Biomedical Engineering IBMT



The development of new drugs and personalised diagnostic and therapeutic approaches are among the most promising topics of the future. The Fraunhofer IBMT is responding to this trend by developing innovative upscaling and cryopreservation strategies to optimise the efficiency and reproducibility of stem cell processes. Here, the most important criterion is the generation and cryopreservation of large quantities of stem cell solutions with consistently high quality.

Through the coordination of the IMI project EBiSC2 – The European Bank for iPS Cells – and the global stem cell registry hPSCreg, the Fraunhofer IBMT provides a unique infrastructure for the development of new cell models as well as drug and toxicity assays. In parallel, peripheral technologies in the field of intelligent sensors, digital stem cell technologies and ethics, bioinformatic data applications and cryobiotechnology are being developed.

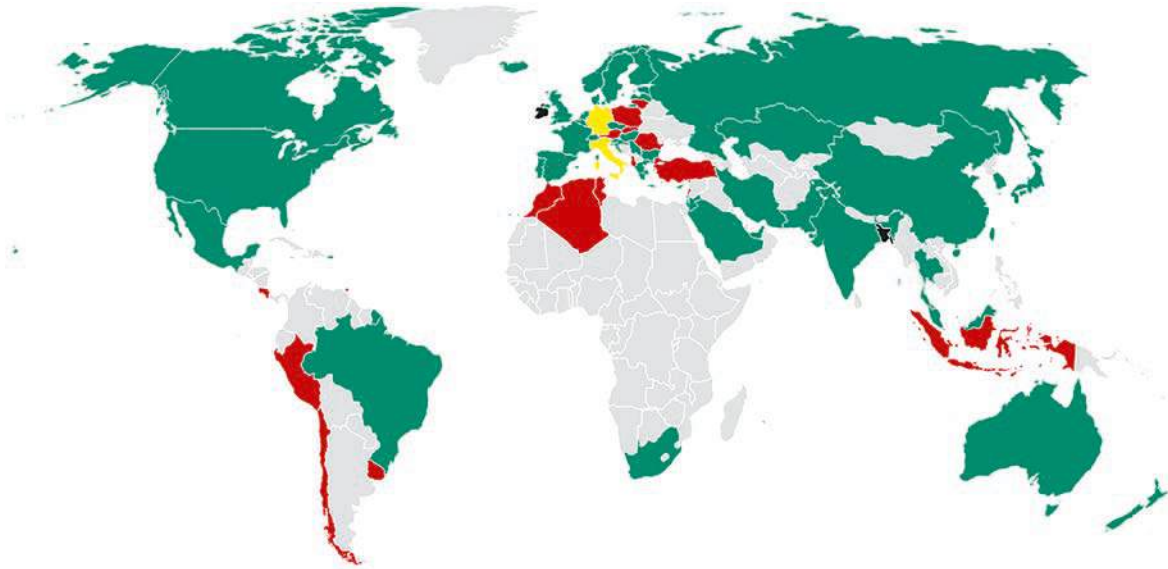


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World Map of Human Embryonic Stem Cell Policy

Legislation:

■ permissive
 ■ moderate
 ■ restricted
 ■ unclear
 ■ unregulated



National legislation on the research and production of human embryonic stem cells around the world.

As of: 21 February 2023; Data source: hPSCreg. Map generated with Data Wrapper. Research: Nancy Mah and Sabine Kobold (Fraunhofer IBMT)



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The legislative patchwork that still exists in European countries is striking. While most Western and Northern European countries such as Spain, Portugal, France, the UK, Denmark, Sweden and Finland have very few legal restrictions on embryonic stem cell research, some countries in Central and Eastern Europe – such as Germany, Austria, Poland and Romania – have restrictive legislation in place.

Against this backdrop, reprogramming technology has proven to be a game changer for global stem cell research and clinical translation. Shinya Yamanaka, the winner of the 2012 Nobel Prize in Physiology or Medicine, described the production of human induced pluripotent stem cells (iPS cells) in 2007. This practice is less ethically controversial and widely legally permissible. In addition, iPS technology allows the production of patient-specific cell preparations. Together with other technological breakthroughs such as genome editing, this has opened up huge opportunities and areas of application – both for disease research and drug discovery as well as for stem cell-based therapeutic approaches.

Cell therapies based on pluripotent stem cells

The hPSCreg registry has established a database of clinical studies around the world based on pluripotent stem cells. The hPSCreg team has also analyzed this data for the GSCN. This analysis makes it possible to see which nations are the most advanced in the clinical translation of stem cell-based approaches. As of February 2023, clinical trials based on human ES cells have been conducted or commenced in eleven countries. The USA tops the list on 23 trials, followed by China (12), the UK and Canada (both 7), South Korea (4), France and Israel (both 2), along with Belgium, Brazil, Japan and Sweden (1 each).

A slightly different pattern emerges when we consider past and present clinical trials conducted on the basis of induced pluripotent stem cells (iPS cells). As of February 2023, there were activities in this area in seven countries. While Japan clearly leads the way with 22 trials, it is closely followed by the USA (16) and China (12), with Australia (4), the UK, Germany and Iran (1 each) also in the rankings.

Stem cell-based gene therapies on the rise

Most of the clinical trials mentioned above are cell replacement therapies. However, immunotherapies based on pluripotent cell-derived natural killer cells (NK cells) are also increasingly being tested.

Dynamic developments are also evident in the pharmaceutical world in relation to tissue stem cells. This applies in particular to genome-edited blood stem cells, which are the basis for the Exa-cel gene therapy for the treatment of sickle cell anemia and beta-thalassemia. The US FDA, the UK Medicines and Healthcare products Regulatory Agency (MHRA) and the EMA have granted conditional approval for the product as the first marketable CRISPR-Cas drug – a true milestone for stem cell-based medicine.

Stem cell ecosystems at a glance

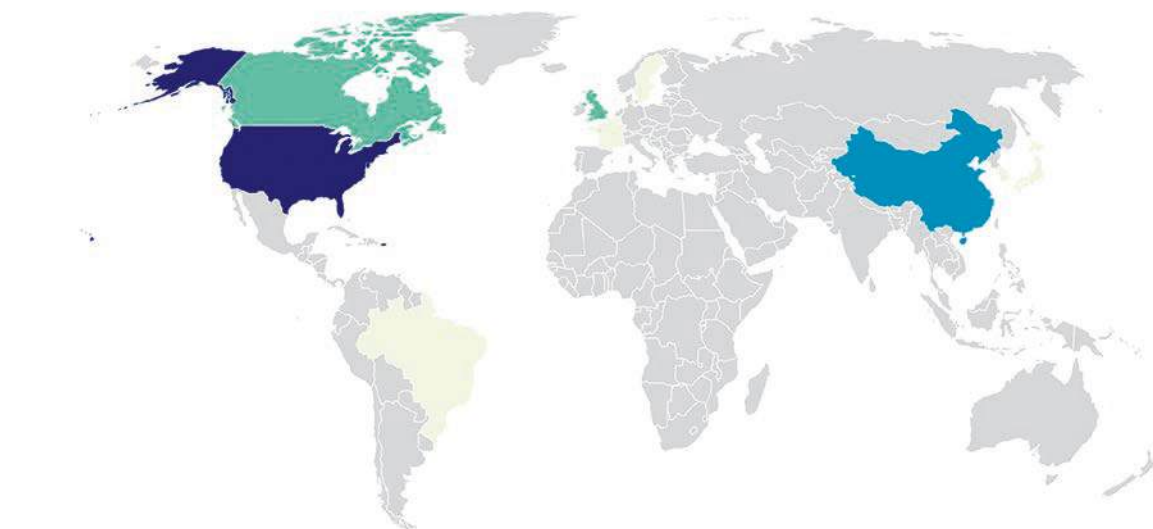
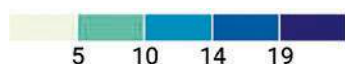
In this issue, the GSCN Annual Magazine provides a detailed overview of the science and medical translation of stem cell research in the world's leading regions and countries: an Atlas of Stem Cell Ecosystems.

- **Europe** (EU, the UK, Switzerland and Israel)
- **North America** (Canada and USA)
- **Asia-Pacific** (China, Japan, South Korea and Australia)

The result is a snapshot that reflects the different positions some countries have adopted in relation to basic and applied stem cell research, the priorities they have set, and the resources and capacities made available. This perspective provides a useful starting point for international exchange and cooperation.

Text: Philipp Graf

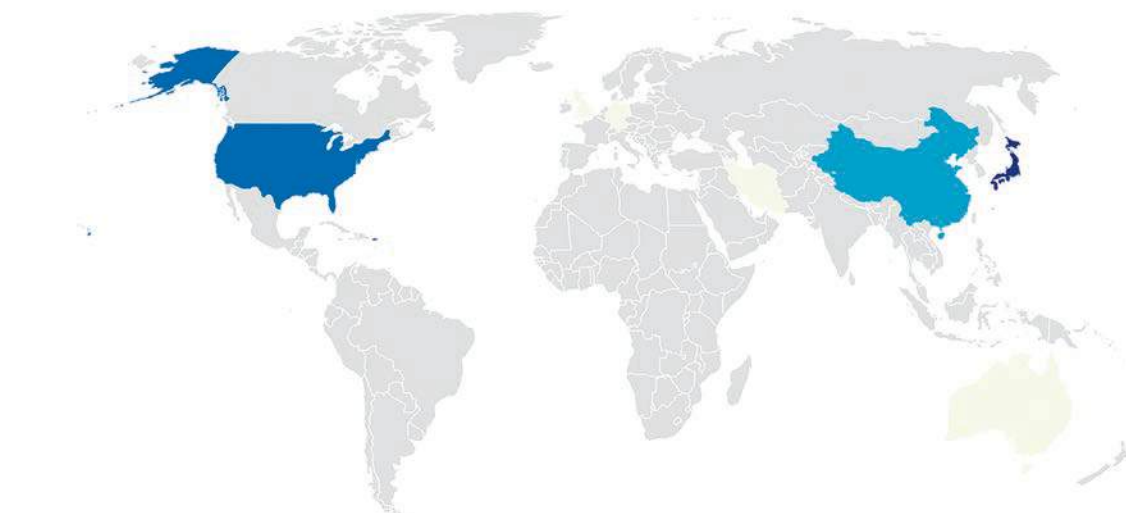
Human embryonic stem cell-based clinical studies



Countries in which clinical trials based on hESCs have been conducted or started as of 01/2023 (including long-term studies with patients from previous clinical trials).

As of: 17 February 2023; Data from various sources, e.g. clinicaltrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP). Map generated with Data Wrapper. Research: Anke Guhr and Peter Löser (Robert Koch Institute) as well as Sabine Kobold and Nancy Mah (Fraunhofer IBMT)

Human induced pluripotent stem cell-based clinical studies



Countries in which clinical trials based on hiPSCs have been conducted or started as of 01/2023 (including long-term studies with patients from previous clinical trials).

As of: 27 January 2023; Data from various sources, e.g. clinicaltrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP). Map generated with Data Wrapper. Research: Anke Guhr and Peter Löser (Robert Koch Institute) as well as Sabine Kobold and Nancy Mah (Fraunhofer IBMT)

Europe

A journey through the European landscape of stem cell research and translation



World-class research for stem cell medicine

Europe has an outstanding, highly diverse landscape of stem cell and regenerative medicine research, strongly supported by national governments and the European Commission. Innovative translational companies are harnessing stem cell-based approaches for pharmaceutical research and drug development. The global boom in cell and gene therapies has also sparked a great deal of dynamism in Europe – including pioneering clinical studies based on pluripotent stem cells.



France – Excellent research for health

The foray into hotspots of the European stem cell research landscape begins in France. One of the foremost centers of health research is the **Institut Pasteur** in Paris. The **I-Stem** at the Université d'Evry and the **SBRI** in Lyon exist under the umbrella of INSERM, the national non-university institution for health research. "Other places with excellent stem cell research include Montpellier, Nantes, Marseille, Lyon, Strasbourg and Toulouse," says Shahrugim Tajbakhsh, a stem cell researcher at the Institut Pasteur. He also coordinates the **Re-vive** stem cell consortium, which has been awarded government funding until 2024 as part of the Laboratoire d'Excellence program and consists of 28 partners. The Biotherapies program, which is funded by the government as part of the France 2030 plan, is also relevant to stem cell medicine.



Shahrugim
Tajbakhsh

Stem cell researchers in France have joined forces in the **French Society for Stem Cell Research (FSSCR)**, a major network organization. "Our annual conferences attract several hundred scientists," says Tajbakhsh. France also has a close-knit hospital network with highly advanced cancer medicine. "There is also a strong research and clinical sector in cell and gene therapy," says Tajbakhsh.

Germany: Top-level stem cell research



In Germany, the production of human embryonic stem cells (ES cells) is prohibited under the Embryo Protection Act (ESchG), though imports are permitted under the conditions set out in the Stem Cell Act (StZG). Despite this challenging legal environment, Germany has developed a stem cell research landscape at the highest international level.

In addition to numerous universities and excellent university hospitals, the primary hubs of stem cell research in Germany include the non-university research institutions of the **Max Planck Society** (e.g. MPIs in Münster, Bad Nauheim and Dresden), the **Fraunhofer Society** (e.g. Fraunhofer IBMT, ISC, IZI and ITMP), the **Helmholtz Association** (e.g. the German Cancer Research Center (DKFZ), the Max Delbrück Center and Helmholtz Munich) and the **Leibniz Association** (e.g. the Leibniz Institutes on Aging and for Zoo and Wildlife Research). In addition, the German Research Foundation (DFG) has given rise to Centers of Excellence in stem cell research and medicine, namely **REBIRTH** at the Hannover Medical School and the **Center for Regenerative Therapies (CRTD)** at the Technical University of Dresden, both of which are now funded by the respective state governments.

In recent years, the German government has invested heavily in expanding the infrastructure for better medical translation of regenerative medicine, including in translational centers for regenerative medicine and the German Centers for Health Research. In 2021, the **Berlin Institute of Health (BIH)** was integrated into Charité – Universitätsmedizin Berlin as the institution's third pillar. It represents the translational research area of Charité, while the Max Delbrück Center is a privileged partner of the BIH.

Since 2013, the research community has been organized in the **German Stem Cell Network (GSCN)**. The GSCN was initially funded by the Federal Ministry of Education and Research (BMBF) and has since formed the **Dialog Platform Stem Cell Research** with its cooperation partner, the BIH. Highlights of the network's work are the annual conferences, which are held in different locations and attract hundreds of participants. Another network is the **Stem Cell Network.NRW**, which is supported by the state government of North Rhine-Westphalia. Numerous German stakeholders are currently working on a National Strategy for Gene and Cell Therapies, which is due to be presented in 2024. In this context, a National Network Office for Gene and Cell Therapies has already been established.



Spain: Barcelona as a research stronghold

The Barcelona area has become the epicenter of stem cell research in Spain. For many years, the Center of Regenerative Medicine in Barcelona (CMRB) was one of the top non-university centers. Since 2019, it has been known as P-CMR[C] – the Program for advancing the Clinical Translation of Regenerative Medicine of Catalonia. P-CMR[C] is funded by the Catalan government and the EU, with research teams from the CMRB and the Bellvitge Biomedical Research Institute (IDIBELL) joining forces to maintain close ties with Bellvitge University Hospital. Research topics include regenerative approaches for the treatment of cardiac muscle weakness, neurodegenerative diseases, blood and eye diseases.

The **National Stem Cell Bank (BNCL)** is also based at the P-CMR[C], with additional locations in Valencia and Granada. Other relevant research institutions include the **Center for Genomic Regulation (CRG)** and the **Institute for Research in Biomedicine (IRB)**. **EMBL Barcelona** and **Pompeu Fabra University** are also involved in stem cell research. Activities are also underway in other parts of Spain:

the **Instituto de Biomedicina de Valencia (CSIC)**, for example, has a long tradition of research into neural stem cells. In Madrid, the **National Cancer Research Center (CNIO)**, the university and some clinics use stem cells for regenerative medicine purposes. In Seville, the **Andalusian Center for Developmental Biology** is one of several research institutions that deserve special mention. There is also an active **Spanish Cell Therapy Network (Ter-Cel)**.

Belgium: A well-connected community

Alongside France and Germany, Belgium also has one of the most active network organizations for stem cell research in Europe: the **Belgian Society of Stem Cell Research (BeSSCR)**, which hosts annual specialist conferences. Stem cell research is carried out at the universities in Brussels (ULB, VUB), Leuven (KU Leuven), Liège, Antwerp, Ghent and Hasselt.



United Kingdom: A highly dynamic ecosystem for cell therapies

Stem cell research in the UK is in a class of its own, having developed from a strong tradition of basic research in developmental biology. Thanks to permissive legal regulations, researchers in the UK are pioneers in many fields, which is reflected in the first clinical trials in Europe based on derivatives from pluripotent cells for various diseases. The UK is also a world leader in embryo research.

The “golden triangle” of London-Oxford-Cambridge alone is home to numerous excellent research institutions, such as the **Francis Crick Institute**, the **Wellcome-MRC Cambridge Stem Cell Institute** and the **Oxford Stem Cell Institute**. **Imperial College London** places a strong focus on stem cell research and regenerative medicine, as does King's College London. The Future Targeted Healthcare Manufacturing Hub has been established at **University College London (UCL)**. There are also important players further north, including in Scotland. The **University of Edinburgh**, for example, is home to the Centre for Regenerative Medicine and the **Roslin Institute**, made famous by Dolly the cloned sheep.

The UK government is investing heavily in the life sciences and has published numerous strategies (including the Life Sciences Strategy and the Regenerative Medicine Strategy). There are also potent non-governmental sponsors of bio-



medical research, above all the Wellcome Trust as a private charitable foundation. In an effort to become the world's leading location for cell and gene therapies, the government has established the **Cell and Gene Therapy Catapult** as an important innovation center for the production of cell and gene therapy products. An Advanced Therapy Campus built around the Catapult's manufacturing center in Stevenage, not far from London, which is increasingly attracting players from the cell and gene therapy sector. The British Catapult initiative also includes the University of Sheffield's Advanced Manufacturing Research Centre (AMRC), where cell-based technologies also play a role.



Sweden: Making stem cell medicine a strategic priority

The Swedish research landscape is characterized by permissive legal regulations on research with stem cells, clear strategic funding support from the government and private foundations, along with world-class medical universities. These include the **Karolinska Institutet** near Stockholm and other excellent universities in Lund, Uppsala and Gothenburg. In 2008, the Swedish government designated "stem cell research and regenerative medicine" one of 24 strategic research areas. In addition, the Karolinska Institutet has defined stem cells and regenerative medicine (Stratregen) and neurosciences (StratNeuro) as strategic priorities. A world-class research facility has been established at the **Lund Stem Cell Center** at Lund University. Comprising 44 research groups, this center is funded by the Swedish government as part of its StemTherapy initiative.



Melissa Little

The Danish capital, Copenhagen, is an important location for stem cell research. Key players include the **University of Copenhagen**, clinical activities in Herlev and the Rigshospitalet, the cell therapy division of Novo Nordisk and the contract research organization Bioneer. Relevant research activities are also underway at the **University of Southern Denmark**, **Aarhus University** and **Aalborg University**.

The Novo Nordisk Foundation is an important sponsor of stem cell research. From 2011 to 2021, it established an international institute for basic research into stem cell and developmental biology with **DanStem**.

In 2022, parts of DanStem led to a unique global research consortium, the **Novo Nordisk Foundation Center for Stem Cell Medicine – reNEW**. It is based on a partnership between the University of Copenhagen, Leiden University in the Netherlands and the Murdoch Children's Research Institute in Melbourne, Australia. The foundation will invest €300 million in these three international locations by 2032. Its concept was developed by Australian stem cell researcher Prof. Melissa Little, who is now CEO of reNEW. The center is squarely focused on the translation of stem cell medicine.

Melissa Little explains: "Building on the stem cell research excellence that exists within all partners, reNEW aims to deliver outcomes across the breadth of stem cell medicine – new drugs based on human stem cell models, cell and tissue therapies, and new cell and gene therapies." The foundation is also investing up to €127 million in the construction of the **Novo Nordisk Foundation Cellerator**, a large

cell therapy development and manufacturing center at the Technical University of Denmark in Lyngby, which is scheduled to open in 2027.



Denmark: Significant investment from Novo Nordisk Foundation

Denmark also has its own specialist society for stem cell research, the **Danish Stem Cell Society (DSCS)**. The pharmaceutical company Novo Nordisk and the Novo Nordisk Foundation, one of the world's largest charitable foundations, are two financially powerful, internationally oriented players making strategic investments in stem cell-based medicine.

Austria, Switzerland and Italy

Directly adjacent to Germany, a small but high-caliber stem cell research community has developed in Austria, leading to the formation of the **Austrian Society for Stem Cell Research (ASSCR)** in 2018. Important locations for stem cell research include the capital city of Vienna – with the **Institute of Molecular**



Biotechnology Austria (IMBA) and the **Research Institute of Molecular Pathology (IMP)** – along with Innsbruck and Salzburg.

As a base for large pharmaceutical companies and contract manufacturers, many stem cell research activities in Switzerland focus on disease models and drug discovery. However, stem cell technologies and cell therapies are also developed here. The most important academic players are the universities and university hospitals in Basel, Fribourg, Bern, Geneva, Lausanne and Zurich. **ETH Zurich** and **EPFL in Lausanne** are true academic heavyweights in research into stem cell biology and technologies. Researchers have formed a network in the **Swiss Stem Cell Network (SSCN)**.

Stem cell research stakeholders in Italy have joined forces in the network organization **Stem Cell Research Italy**. The University of Modena and Reggio Emilia is a significant location of international renown and includes the **Centre for Regenerative Medicine “Stefano Ferrari” (CMR)**, an important cell therapy research and production center. Its achievements include Holoclar, the first stem cell-based drug for the treatment of corneal damage.

Another leading location for gene and cell therapies is the **San Raffaele Telethon Institute for Gene Therapy** in Milan. It was the development location for Strimvelis, a gene therapy approved for use in the EU since 2016. In addition, genetically modified blood stem cells are used to treat the immunodeficiency disease ADA-SCID. This gene therapy is now provided by the Fondazione Telethon, one of Italy’s most prominent biomedical foundations.



Netherlands: Leading clusters in Leiden and Utrecht

Leiden University and the **Leiden University Medical Center (LUMC)** in particular have a long tradition of performing organ transplants and developing stem cell-based disease models and therapies. The LUMC therefore plays a leading role in regenerative medicine in the Netherlands. It is also one of the three sites of the Novo Nordisk Foundation Center for Stem Cell Medicine, reNEW. In addition, the **Leiden Academic Center for Drug Research (LACDR)** is based at the university. **NecstGen**, a large development and GMP manufacturing center for gene and cell therapies, has also been established at LUMC.

Another important research cluster has been established in Utrecht. The most important

facilities are the **University Medical Center Utrecht** and the **Hubrecht Institute**. The latter is part of the Royal Netherlands Academy of Arts and Sciences (KNAW) and home to 20 research groups examining developmental and stem cell biology. The Hubrecht Institute stands for pioneering research activities on organoid technology, shaped by Hans Clevers. There are also research teams investigating stem cells in Amsterdam, Rotterdam, Groningen and Nijmegen. They meet at the regular conferences of the **Dutch Society for Stem Cell Research (DSSCR)**.

Israel: Close links to the European Research Area

Highly innovative stem cell research in Israel is closely linked to the European research area. Since 2006, the stem cell community has been networked together in the **Israel Stem Cell Society**. There are relevant stem cell activities at the **Hebrew University of Jerusalem**, Tel Aviv University, the Tel Aviv Sourasky Medical Center, the Weizmann Institute of Science in Rehovot, the **Technion** – Israel Institute of Technology in Haifa, and the Ben Gurion University of the Negev. A dynamic and innovative industrial landscape has also emerged.

Substantial funding from the European Union and private foundations

The European Union offers a wide range of funding opportunities for stem cell research and regenerative medicine. This section provides only a brief outline.

The EU’s key funding programs for research and innovation (FP7, Horizon 2020 and Horizon Europe) have provided and continue to



Supporters Funding instruments	Formats	Project examples including stem cell approaches
EU Horizon Europe (2021–2027)		
Joint projects	Research consortia, cooperation projects	HEAL, ISLET, DREAMS, IMPACT, hPSCreg registry
European Research Council (ERC)	Starting Grants, Advanced Grants, Consolidator Grants, Synergy Grants, Proof of Concept Grants	iPYRO; immSC-AgingFate; InteractOmics; DOR CODE; RESTART
European Innovation Council (EIC)	EIC Pathfinder EIC Transition EIC Accelerator	AiPSC; Pan3DP; HyperTargIPS-NK; ACHILLEUS
Marie Skłodowska-Curie Actions (MSCA)	Postdoctoral Fellowships Doctoral Networks Staff exchanges etc.	various
Innovative Health Initiative (IHI), previously IMI	Public-private research consortia	European Stem Cell Bank EBISC; EBISC2, FAIRplus
IPCEI Health	Research consortia	Gene and cell therapies
EMBO	Postdoc Fellowships, Collaboration Grants,	various
Wellcome Trust	Early Career Awards, Discovery Awards, Translation Fund, Research Centers	Discovery Research Platform for Tissue Scale Biology Wellcome-MRC Cambridge Stem Cell Institute
Novo Nordisk Foundation	Grants in open competition; institutional funding	renew, Cellerator
Human Frontier Science Program Organization (HFSPO)	Collaborative research grants Program Grants Early Career Grants	various

provide substantial resources. As the European Commission's Directorate-General for Research & Innovation determined in response to a request from the GSCN, a total of 570 projects involving stem cells received funding through Horizon 2020 alone (from 2014 to 2020). This amounted to €893 million of EU funding.

The **European Research Council (ERC)** played a significant role in this support. In Horizon 2020 (2014 to 2020), it provided around €461 million for 236 projects relevant to stem cell research. When looking at this data, it is important to bear in mind that the ERC, like the **Marie Skłodowska-Curie Actions**, are exclusively bottom-up funding programs with no predefined topics. Between 2014 and 2020, the ERC supported a total of 6,707 research projects with combined funding of €13.3 billion.



Daniel
Besser

Other funding providers include the **European Molecular Biology Organization (EMBO)** alongside private foundations such as the Wellcome Trust and the **Novo Nordisk Foundation**. The Strasbourg-based **Human Frontier Science Program Organization (HFSPO)** also supports stem cell research.

“EU and national funding is very important and should be sustainably expanded to enable the successful translation of stem cell research in Europe,” says Daniel Besser, Head of the German Stem Cell Network (GSCN). “However, it is also important that we remove regulatory and bureaucratic hurdles in the clinical development of therapeutic approaches with stem cells.” Jointly developing strategies for the use of stem cells and ensuring a close link between basic and applied research could prove beneficial.

ATMP regulations with accelerated approval pathways

The European Union has had a regulatory framework for cell-based medicinal products that have undergone biotechnological processing during their manufacture since 2008. These products are legally classified as “**Advanced Therapy Medicinal Products (ATMPs)**”. The **European Medicines Agency (EMA)**, based in Amsterdam, is responsible for central marketing authorization. When assessing ATMPs, regulatory authorities such as the EMA follow a flexible, knowledge-based approach. Each stem cell product is individually assessed on the basis of its risk profile. New formats, such as the **PRiority Medicines (PRIME)** program, have been created in the EU to accelerate patients’ access to experimental ATMPs.



Sandra
Lubitz

One of the major challenges for ATMP developers is the fragmented European market, which requires them to clarify the market access and reimbursement in each EU member state. High development costs are therefore accompanied by high approval costs.

Of the 26 ATMPs approved in the EU to date, seven have already been withdrawn from the market due to economic difficulties, and only a few are stem cell-based, including Holoclar for corneal tissue regeneration. In the UK, the **Medicines and Healthcare Products Regu-**

latory Agency (MHRA) has been the leading regulatory authority for ATMPs since Brexit. **ILAP** presents a further pathway for accelerated approvals. By January 2024, 23 ATMPs were approved in the UK.

The corporate landscape for translation

A growing number of companies in Europe have specialized in stem cell-based innovations and technologies, and are driving medical translation forward. This article highlights only a small selection of the relevant players and activities.

The Hamburg-based biotechnology company **Evotec** relies on iPS technology in two fields of application: early drug discovery and the development of regenerative therapies. “We have established an industrialized iPS infrastructure at our sites in Hamburg, Göttin-

gen and Modena, which represents one of the largest and most complex iPS cell platforms in the industry,” says Sandra Lubitz, Senior Vice President iPSC Drug Discovery at Evotec. Collaborations exist with numerous academic partners and pharmaceutical developers. From the large pipeline of the iPSC Drug Discovery platform, one identified drug candidate – BMS-986419 – has already progressed to clinical trials. Another mainstay is allogeneic, iPS-derived cell therapies. These include a beta cell replacement therapy for the treatment of

Photo: Evotec

Heidelberg Institute for Stem Cell Technology and Experimental Medicine (HI-STEM)

HI-STEM gGmbH is a non-profit public-private partnership between the German Cancer Research Center (DKFZ) and the Dietmar Hopp Foundation (DHS). Located within the DKFZ in Heidelberg, HI-STEM performs cutting-edge research on stem cells and translates these results into novel clinical applications. This includes the development of novel diagnostic tools and innovative therapies to monitor and target leukemic and solid tumor stem cells as well as metastatic disease. Professor Dr. Andreas Trumpp and seven Research Group Leaders direct an international research team of more than fifty

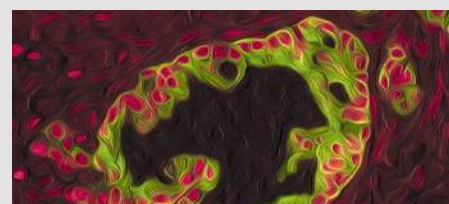
employees. The HI-STEM Research Groups:

- Hematopoietic and Leukemic Stem Cells (A. Trumpp)
- Stem cells at the interface of hematopoiesis, immunity and cancer (Simon Haas)
- Pattern Recognition and Digital Medicine (Daniel Hübschmann)
- Experimental Hematology (Mick Milsom)
- Stress induced activation of HSCs (Marieke Essers)
- Cancer Stem Cells and Metastasis (Martin Sprick & A. Trumpp)
- Neural Reprogramming and Clinical Translation (M. Thier)
- Cancer Progression and Metastasis (Rene Jackstadt)



HI-STEM

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FOR STEM CELL TECHNOLOGY
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HI-STEM gGmbH within the
German Cancer Research Center (DKFZ)
Im Neuenheimer Feld 280 · 69120 Heidelberg
www.hi-stem.de

diabetes, which is to be tested in clinical trials with the company's Canadian partner, Sernova, at the end of 2025. Evotec also has a state-of-the-art cGMP cell therapy manufacturing center in Modena.

One contract manufacturer with a strong European foothold is the US company **Catalent**. In 2021, the company acquired the Düsseldorf-based iPS cell specialist Rheincell Therapeutics. This facility develops, manufactures and stores GMP cell lines for use in stem cell-based therapies. In February 2024, it was announced that Novo Holdings had agreed a USD 16.5 billion takeover deal for Catalent. The Bordeaux-based biotech company **TreeFrog Therapeutics** specializes in the mass production of iPS-based cell types for use in cell replacement therapies.

One of the largest German biotech companies, **Miltenyi Biotec**, is among the leading European players in the cell and gene therapy sector. As a technology provider with international operations, the Bergisch Gladbach-based company specializes in cell sorting systems for research and clinical applications, such as blood stem cell transplants. It recently became a developer of cell and gene therapies (in particular CAR-T) through a new subsidiary, Miltenyi Biomedicine.

The pharmaceutical company **Roche** recently established the **Institute of Human Biology (IHB)** in Basel to research primarily human model systems for pharmaceutical research and drug development. Stem cell-based organ models and organoid technology are a focal point. Researchers also hope to develop the next generation of human model systems at a Berlin research center, **Der Simulierte**

Mensch (Si-M) – which literally translates to “the simulated human”. Si-M is run by Technische Universität Berlin and Charité – Universitätsmedizin, with a new building for the center currently under construction.

The Bonn-based translational company **LIFE & BRAIN**, situated close to the University of Bonn, offers stem cell-based products and services for pharma, biotech and academic institutions. It is also a partner in **KSILINK**, a Franco-German translation center based in Strasbourg. Partners from academic research and industry use patient-based disease models for drug discovery in the treatment of muscular and neurological diseases as well as cancer. Modern AI technologies are also used for image analysis.

ISAR Bioscience is a center for translational biomedicine in the Munich area that relies on iPS-derived model systems for drug development. Major European players with iPS-based platforms for drug discovery and development include **Ncardia** (Leiden) and **Axol Bioscience** (Cambridge).

Institute of Reconstructive Neurobiology

From disease modeling to stem cell therapies

The Institute of Reconstructive Neurobiology at the University of Bonn Medical Faculty focuses on the use of pluripotent stem cells for the study and treatment of neurological and psychiatric disorders.

Based on a broad technology portfolio including cell reprogramming, neural differentiation, direct cell fate conversion, stem cell industrialization and neurotransplantation, the Institute develops stem cell-based model systems for disease-related research and drug development

as well as novel cell therapy regimens. It closely interacts with LIFE & BRAIN GmbH, a translational hub of the University of Bonn Medical Faculty providing stem cell products and services for pharma, biotech and academia.

Institute of Reconstructive Neurobiology

University of Bonn Medical Faculty

Venusberg-Campus 1, Geb. 76 · 53127 Bonn

www.stemcells.uni-bonn.de

Institute of Reconstructive Neurobiology



Innovative cell therapy approaches in clinical trials

One major life science company that has focused on stem cell-based therapies for many years is the Danish pharmaceutical company **Novo Nordisk**. Perhaps best known for its diabetes medication, the company is cooperating with academic research projects including **STEM-PD**. In this project, a team from Lund University and researchers from Cambridge in the UK are testing dopaminergic neurons derived from hES cells as a cell replacement therapy for the treatment of Parkinson's disease in a Phase I clinical trial. Novo Nordisk is also exploring the potential of stem cell-based therapies for other diseases. A research collaboration with researchers at Hannover Medical School is also exploring the potential of iPS-based macrophages against bacterial lung infections.

Europe's first clinical trial with cell replacement products derived from iPS cells started in Germany in 2021 at the University Medical Center in Göttingen. The **BioVAT-HF-DZHK20** study, which is largely financed by public funds, involves implanting "heart tissue patches" in patients with heart muscle weakness.

The Israeli company Kadimastem in Rehovot is testing hES-based astrocytes for the treatment of amyotrophic lateral sclerosis (ALS) in a clinical phase I/II study and is working on the development of hES-based beta cells for the regeneration of type I diabetes. **Pluri**

Biotech from Haifa, Israel, is testing mesenchymal stromal cells from placental tissue in numerous clinical programs. The Berlin stem cell technology start-up **MyoPax** is also working with adult stem cells: the spin-off from Berlin's Charité and the Max Delbrück Center is currently preparing a clinical trial to test genome-edited muscle stem cells as a therapeutic agent for the treatment of specific muscular dystrophies.

Boom in ATMP translation centers

The boom in cell and gene therapies has triggered a number of investments in translational infrastructures. A translation center for cell and gene therapies is under construction on Bayer's Berlin campus and will be largely financed by public funds. A major manufacturing center, NecstGen, has been established in the Dutch city of Leiden. Meanwhile, the Karolinska Institutet in Stockholm and the Karolinska University Hospital are building the Karolinska ATMP Centre. In addition, the Novo Nordisk Foundation Cellerator in Lyngby, Denmark, is due to open its doors in 2027.

For Joachim Fruebis, Head of Cell Therapy R&D at Novo Nordisk, these are extremely promising signs of an industry on the rise: "All these activities illustrate that cell therapies can also flourish in Europe – and have the ability to attract great talent."

Text: Philipp Graf





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North America

Stem cell research and clinical
translation in Canada and the USA



Canada: Driving commercialization in regenerative medicine



Canada is one of the leading nations in stem cell research, with key players networked in the government-supported Stem Cell Network. Work is currently underway to massively expand production capacities for gene and cell therapies.

Canada has a long tradition in stem cell research and regenerative medicine and is one of the world's leading nations in this field. In the early 1960s, Ernest McCulloch and James Till from the University of Toronto's Ontario Cancer Institute identified hematopoietic stem cells in the bone marrow of mice for the first time. These stem cell pioneers, who were later awarded the Lasker Prize and other accolades, had an enormous influence on the development of stem cell research in Canada.

The top centers for stem cell research and regenerative medicine include the University of British Columbia with its main campus in **Vancouver**, McGill University in **Montreal**, the McEwen Stem Cell Institute – part of the University Health Network (UHN) – in **Toronto**, and the **Ottawa** Hospital Research Institute.

Regenerative medicine as a national priority

The Canadian government recognized and promoted the potential of stem cell research at an early stage. The **Stem Cell Network (SCN)** was founded back in 2001 and has been awarded long-term public funding for research support and community building (see info box). Cate Murray, CEO and President of the SCN, emphasizes that the government considers regenerative medicine to be one of the nation's strengths, mentioning the field in the same breath as artificial intelligence, quantum computing and other cutting-edge technologies. "A key is that the government invests for the long term. That way, the SCN can play an important role as an enabling factor," says Murray.



Cate
Murray

Canada's stem cell legislation is classified as moderate. **Health Canada** is the central authority for the country's regulatory framework and conducts its own regulatory reviews, often in alignment with the FDA. In Canada, cell and gene therapy products are generally regulated through frameworks developed for traditional pharmaceutical drugs. This can create complications as cell and gene therapies are complex to assess, especially when they have been extensively manipulated. Health Canada is currently looking to modernize its regulations and consider how best to regulate cell and gene therapies for the future.

The key to success for the stem cell ecosystem in Canada is seen by Murray as the country's very strong collaborative spirit, with interdisciplinary cooperation taken as given. Mentoring and training of talented researchers in the centers of excellence are also beneficial. Cate Murray believes that one of the major challenges facing both academia and the growing Canadian regenerative medicine industry in the future is attracting and retaining talent.

Driving commercialization in regenerative medicine

In 2021, in response to the COVID-19 pandemic, the government adopted its **Biomanufacturing and Life Sciences Strategy**. This CAD 2.2 billion (€1.5 billion) package is designed to support biomedical research and the biopharma industry, particularly in relation to industrial biomanufacturing manufacturing capabilities. The field of gene and cell therapies certainly stands to benefit. A further CAD 1.2 billion (€820 million) will go towards rebuilding vaccine manufacturing capacity.

In the spring of 2022, the Ontario published its own **Life Sciences Strategy** with the aim of establishing the province as a global hub for life sciences and manufacturing. It focuses

on commercial output from the Life Sciences system rather than research input. Two other provinces, British Columbia and Quebec, also have their own life science strategies. Collectively, these strategies demonstrate a clear recognition that the life sciences is a strategic sector for Canada – in terms of both improving public health and boosting economic productivity.

Other Canadian organizations complement the SCN and play a key role in translating and scaling the work performed within Canada's stem cell ecosystem.

The **Centre for Commercialization of Regenerative Medicine (CCRM)** is a public-private partnership established with seed funding provided by the Government of Canada, the Province of Ontario and partners from academia and industry. Focusing on gene and cell therapies, CCRM has supported the development of more than a dozen start-ups. At present, CCRM has 200 employees along with a facility at the MaRS Centre in Toronto with GMP rooms for the production of cells and viral vectors.

A subsidiary of CCRM, **OmniaBio Inc.**, is set to become Canada's largest contract development and manufacturing organization (CDMO) for the manufacture of cell and gene therapies, from the pre-clinical phase through to commercialization. Supported by the government of Ontario, OmniaBio is built upon leadership in iPS cells, immunotherapy and LVVs. Omnia's commercial biomanufacturing center is under construction at McMaster Innovation Park in Hamilton, Ontario, with one of two sites is set to open in 2024. In the first phase of construction, OmniaBio is building a 7,000 m²

facility equipped with 15 clean rooms and staffed by 500 employees. With a second building (30,000 m²) in the pipeline, OmniaBio and CCRM will soon have more than 50 clean rooms and over 1,000 employees.

The **Canadian Advanced Therapies Training Institute (CATTI)** has a clear vision: to build a skilled biomanufacturing workforce in Canada for the emerging cell and gene therapy sector. Launched in 2021, CATTI is developing and scaling e-learning and on-site GMP training programs, including at its recently opened training facility at the University of Guelph. OmniaBio will be one of CATTI's major strategic customers.

Bavarian research association ForInter

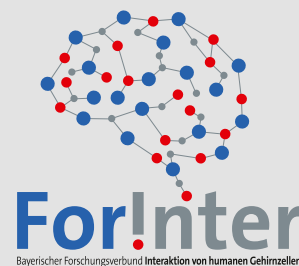
Human brain cell interaction

The research group ForInter aims to investigate the complex cell and molecular biological interactions of different cell types in the human brain in multidimensional, highly innovative cell culture systems. Our consortium is unique in Bavaria as an interdisciplinary research network of this kind. Under the leadership of the Friedrich-Alexander-Universität Erlangen-Nürnberg, scientists with basic biological and translational expertise in neurobiology and neurology, neuropathology, bioinformatics as well as legal and ethical aspects of genetic

engineering lay a foundation for application-oriented research of the human brain.

ForInter's new platform for functional analysis of the brain is intended to contribute in the long term to intervention strategies and therapies for diseases of the nervous system.

Funded by:
Bavarian State Ministry of Science and the Arts



Bavarian research association ForInter
Universitätsklinikum Erlangen
Department of Stem Cell Biology
Glückstr. 6 · 91054 Erlangen
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Key industry players

Key industry players include Canada's largest biotechnology company, Vancouver-based **STEMCELL Technologies**. Founded over 30 years ago by stem cell researcher and founder of the Terry Fox Laboratory, Allen C. Eaves, the laboratory equipment supplier manufactures culture media and reagents, particularly for cell cultures, as well as technologies for cell isolation. The company is currently building a biologics plant in Burnaby (British Columbia) for CAD 138 million (€94.4 million), of which CAD 45 million (€30.6 million) is from public funds.

Aspect Biosystems, a spin-off from the University of British Columbia, combines stem cell technologies and microfluidics with the development of innovative therapies. In 2023, the start-up secured a USD 2.6 billion (€2.3 billion) partnership with Novo Nordisk to develop bioprinted tissue therapeutics for diabetes and obesity.

Another important player is **BlueRock Therapeutics**, an independent subsidiary of Bayer specializing in cell replacement therapies from pluripotent stem cells. Headquartered in Boston, Massachusetts, the company has more than 110 employees in Toronto and has set up shop on a 30,000 m² site in the MaRS Discovery District, part of the University Health Network (UHN). In 2020, BlueRock received the go-ahead for a Phase I clinical trial on Parkinson's disease. The University of Toronto is a center for the trial alongside other locations in the USA (see also our portrait of the USA). The scientific co-founder and advisor of BlueRock is Gordon Keller, Director of the McEwen Stem Cell Institute at the University Health Network in Toronto. Michael Laflamme, a specialist in heart muscle cells from the Toronto General Hospital Research Institute, is also a member of the scientific advisory group.

Strengthening Canadian companies

There is considerable enthusiasm in the Canadian ecosystem about BlueRock. "It is a validation of the quality of Canadian science," says Cate Murray. The other side of the coin – as Murray also notes – is that IP funded with Canadian dollars and generated in Canada is now held by a global big pharma company rather than a Canadian entity. The long-term goal for Canada, Murray says, is to strengthen Canadian companies' participation in later components of the value chain. Murray's colleague Gordon McCauley, President and CEO

of adMare BioInnovations, argues that Canada needs to build anchor companies to support its domestic life sciences industry.

The boom in cell and gene therapies is also currently impacting the availability of venture capital. In addition to a growing appetite of investors from abroad, the Canadian venture capital market is also on the move: Lumira Ventures raised USD 220 million (€200 million) for a Canadian life science fund in 2021. However, it remains challenging for Canadian venture capitalists to make the big bets on the future and take risks on Canadian innovations.

Text: Philipp Graf

Spotlight: Stem Cell Network (SCN) of Canada

The Canadian Stem Cell Network (SCN) is one of the world's oldest and best-funded national network organizations for stem cell research and regenerative medicine. It has been funded by the Canadian government since its foundation in 2001. Its budget was recently more than doubled: in the 2022–2025 funding period, the SCN has CAD 45 million (€31 million) at its disposal, around CAD 15 million (€10 million) annually. Its funding has also been extended until 2029. In strategic terms, the SCN is aligning itself more strongly in the direction of applied stem cell research and regenerative medicine. It has a team of 17 staff and is officially headquartered in Ottawa. The President and CEO of the Canadian Stem Cell Network is Cate Murray, who has a background in research administration, public policy and external relations.

The work of the SCN is based on three pillars:

- Research funding to support scientific endeavors across the research pipeline, including early-stage clinical trials
- Training to enhance the skills and knowledge of graduate students, postdocs, and early career researchers
- Knowledge mobilization to ensure that the results of research can be used for policy making, public education and further scientific and commercial advancements (community outreach and engagement).

Two thirds of the SCN budget is invested in research. There is also a Biotechnology Partnership Program, which supports collaboration between researchers and small biotechnology companies. The SCN has already invested more than CAD 148 million (approx. €100 million) in strategic funding, with 279 research groups, over 6,400 trainees, 30 clinical trials and 25 biotech start-ups benefiting from this support. Highlights of SCN's work include its annual conference, known as the Till and McCulloch Meetings, which brings together over 500 experts from around the world to learn, network and collaborate.

www.stemcellnetwork.ca

USA: An innovative powerhouse for research and translation



The United States is the undisputed world leader in stem cell research and regenerative medicine. A high density of excellent universities, clinical and biomedical research institutions and biotechnology clusters form the foundation for this, as does the diversity of public and private funding sources.

The most important state sponsor of biomedical research is the **National Institutes of Health (NIH)**. The same applies to stem cell research, with the NIH investing more than USD 2 billion (approx. €1.8 billion) directly in stem cell research every year. Figures from the NIH show a steady increase in this investment in recent years (from USD 1.4 billion in 2015 to around USD 2.3 billion in 2023).

Competition for coveted NIH funding remains fierce: for example, the success rate for an R01 grant – the most important NIH funding project format for basic researchers – is 22% (2022). Overall, biomedical research funding in the United States will benefit from the Biden administration's substantial increase in the NIH budget by USD 2.2 billion (approx. €2 billion) in 2022. The budget for

the **National Science Foundation (NSF)** has also been increased.

The Biden administration has launched a new innovation funding agency for biomedical research, the **Advanced Research Projects Agency for Health (ARPA-H)**. It is being set up as part of the NIH and will operate along the lines of the Defense Advanced Research Projects Agency (DARPA). Funding will be provided for transformative high-risk research

that has the potential to produce breakthroughs in biomedicine and health research. The benefits to the stem cell community have already been demonstrated by the award of the first Industry Grant: worth USD 37 million (€34 million), it was awarded to Thymune Therapeutics, a company developing iPS-based cell therapies for the thymus.



Maike
Sander

Challenges in biomedical research

Nevertheless, observers consider biomedical research in the USA to be in "crisis". In an interview in the newspaper "Tagesspiegel" (5.12.2022), stem cell researcher Maike Sander – who moved from San Diego to head

Photo: GSCN

Max Delbrück Center

Excellent stem cell research at the Max Delbrück Center in Berlin



The Max Delbrück Center is one of the world's leading biomedical research institutes. Many of the scientific teams at its two Berlin locations are using stem cells and organoids in their research. For example, they modify muscle stem cells using CRISPR-Cas to develop therapies for previously incurable muscle-wasting conditions. They are using human pluripotent stem cells to produce pancreatic islet organoids. They are also attempting to cultivate egg cells from reprogrammed skin

cells of the northern white rhino in a bit to save the endangered species.

One technology platform provides expertise on iPS cell lines, another on organoids. „Our excellent infrastructure supports state-of-the-art biomedical research,“ says Professor Maike Sander, Scientific Director of the Max Delbrück Center. „Our organoid platform, for example, pools expertise and opens up new avenues to study the development and function of organs.“



Photo: Katharina Böhm/MDC

Max Delbrück Center
Robert-Rössle-Str. 10 · 13125 Berlin
www.mdc-berlin.de

While federal funding is theoretically open to all US researchers, it is the initiatives of individual US states that are currently shaping the funding and research landscape for stem cells. Federal funding programs were a response to the restrictions on the use of human embryonic stem cells under the Bush administration (2000 to 2008). Six states – California, Connecticut, Illinois, Maryland, New Jersey and New York – launched their own initiatives from 2006 onwards.

up the Helmholtz Association's Max Delbrück Center in Berlin-Buch in November 2022 – named a number of structural problems in the US research system. These include a lack of long-term funding beyond four-year terms and issues attracting young talent to biomedical research. On the one hand, this is due to the many job offers from the biotech and pharmaceutical industry in the USA. "On the other hand, talented young researchers from countries such as China are staying away because the entry and residence regulations were tightened under President Trump and remain in place," says Sander.

According to industry expert Joachim Fruebis, there are no noticeable restrictions on NIH funding for the clinical development or commercialization of cell therapies under the Biden administration. Fruebis has been Head of Cell Therapy R&D at the Danish pharmaceutical company Novo Nordisk since 2023. He was previously responsible for clinical development at the Bayer subsidiary BlueRock Therapeutics.

For Fruebis, heavy investment in stem cell-based therapeutic approaches is key to the success of regenerative therapies. In the US,

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Data demonstrating the exceptional performance of CTS HiFi Cas9 Protein can be found at thermofisher.com/ctscas9. We will also have an application note available shortly comparing the performance of CTS HiFi Cas9 Protein to other suppliers as well as the performance in a CAR-T cell therapy workflow at both small research scale and large manufacturing scale.

Please let us know if you have any initial questions or if you'd like more details on how to sample CTS HiFi Cas9 Protein in your workflow: katja.hufschmid@thermofisher.com or tim.wessel@thermofisher.com

he feels there is a greater push for cell therapies to address unmet medical needs than in Europe. “It takes a supportive environment with money, time and creative space to address the challenges in the industry,” says Fruebis.

California’s CIRM: Billions for stem cell research

The **California Institute for Regenerative Medicine (CIRM)** stands out as a state funding agency. After receiving USD 3 billion (€2.7 billion) in funding under Proposition 71 (2004 to 2017), California’s stem cell research funding agency was awarded funding of USD 5.5 billion (€5 billion) for a further ten years from 2020 under Proposition 14. Investments will be made in stem cell projects relevant to basic research, translational research and clinical research, as well as in education and research infrastructure. However, the massive investment of Californian taxpayers’ money has also increased the pressure on politicians to justify their actions and to meet public expectations for the rapid development of regenerative therapies. This is another reason why the focus of funded projects has increasingly shifted towards clinical studies, which has attracted criticism the research community.

The CIRM has created a remarkable ecosystem that aims to decisively advance the translation of stem cell research into the clinic. It supports universities and other research institutions,



Joachim

Fruebis

as well as companies that develop and produce stem cell therapies. Over 2,700 projects and more than 90 clinical studies have been funded by CIRM. A network of clinics for regenerative therapies has been established (Alpha Stem Cell Clinic Network). More than 50 start-ups have their roots in the CIRM environment.

Biotech companies that have benefited from CIRM funding and are currently

in clinical development with various programs include **Lineage Cell Therapeutics** (with two preparations in Phase II, including a partnership with Genentech for the treatment of macular degeneration with RPE cells) and **Aspen Neuroscience** (Parkinson’s therapy, pipeline so far preclinical).

Setback for stem cell researchers in New York

New York has also long been a hotspot for stem cell research funding: the **Empire State Stem Cell Program (NYSTEM)** was launched in 2007 with an initial budget of USD 600 million (€549 million) until 2018. Since 2016, however, there have been irregularities in funding activities. In 2021, it was officially decided to end and phase out the program. This was seen as a major setback by stem cell researchers. Ten start-ups emerged on the basis of NYSTEM funding, including BlueRock Therapeutics (Parkinson’s therapy by Lorenz Studer), Oscine Therapeutics and Luxa Biotechnology.

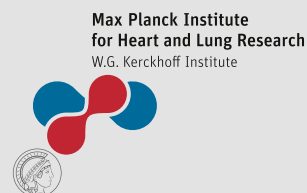
Photo: Privat

Max Planck Institute for Heart and Lung Research (MPI-HLR)

The Max Planck Institute for Heart and Lung Research, located in Bad Nauheim, investigates developmental processes of organs in the cardiovascular system and the lung. A second focus is molecular and cellular processes during the formation of diseases in heart, blood vessels and lung, including remodeling processes in these organs. Scientists at the institute search for new approaches to support repair and regeneration of the affected organs.

The MPI closely cooperates with universities in Frankfurt, Gießen and Marburg. It is a major part of various federal and state excellence initiatives and contributes to two “Gesundheitsforschungszentren”.

Max Planck Institute for Heart and Lung Research
W.G. Kerckhoff Institute
 Ludwigstr. 43
 61231 Bad Nauheim
www.mpi-hlr.de



Philanthropic foundations

The USA also has numerous private philanthropic foundations that invest in stem cell research, such as the **New York Stem Cell Foundation (NYSCF)**. While NYSCF maintains its own research institute, it also awards highly endowed grants to researchers worldwide (including alumni based in Europe) and demonstrates particular commitment to women in science. One focus is stem cell-based approaches in neuroscience, neurology and diabetes. In 2020, the NYSCF opened its own GMP facility and licensed a technology for the production of iPS-based RPE cells (iRPE). The cells are to be used to treat patients with macular degeneration. A Phase I/IIa clinical trial started in 2022.

Product-based regulations with FDA as approval authority

Gene and cell therapies are classified as biologics in the USA. The legal basis is the Federal Food, Drug, and Cosmetic Act (FFDCA), in addition to the regulations and guidelines of the **Food and Drug Administration (FDA)** as the central approval authority. US regulations are product-based rather than process-oriented. The FDA program primarily used for the approval of cell therapies is the **Regenerative Medicine Advanced Therapy (RMAT)** designation. It is the equivalent of an ATMP approval in the European Union and allows innovators to accelerate development. Nevertheless, caution and risk assessment are the maxim for approval: "Risk-benefit trade-offs are difficult to fully assess with cell replacement therapies and remain a major challenge," says Joachim Fruebis. This is why cell therapy developers are in constant communication with the regulatory authorities.

Compared to T-cell therapies, however, cell replacement therapies have different prerequisites: they are living cells that are applied once, integrate into the body and are not designed to disappear. "The envisioned lasting health benefit, of course, comes with a potential lifelong health risk that has yet to be fully understood," says Fruebis.

Manufacturing of cell preparations

According to Joachim Fruebis, the manufacture of safe cell preparations in large quantities for use in clinical practice is the bottleneck of the cell therapy industry.

He points to the example of Canada – which launched an ambitious life sciences and manufacturing initiative in response to a lack of manufacturing capacity during the COVID pandemic – to show how a supportive environment and framework conditions can create a spirit of optimism here.

"Setting up large cell therapy factories is a significant risk for a company," says Fruebis. One concept that could mitigate the risk, he says, is to not only produce the company's own preparations in a manufacturing plant, but also offer cell production as a service. "Since the global demand for cell products is huge, suppliers of first-class products can also call up high prices here. Overcapacity in production can thus help offset the risk of investing in the facilities."

Publicly funded manufacturing facilities can also be a solution to drive forward developments in regenerative medicine. Examples include **City of Hope** in California – a renowned academic cGMP manufacturing facility for gene and cell therapies. The facility has benefited

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greatly from CIRM funding and expanded its capacity. Another notable facility is the **Stanford University Center for Definitive and Curative Medicine (CDCM)**, the translational arm of the Institute for Stem Cell Biology and Regenerative Medicine. Thanks to significant investment, Stanford has become an academic leader in the field of cell and gene therapies.

Cell therapy industry

Hotspots for cell and gene therapy include the large biotech clusters in California and the Boston/Cambridge area of Massachusetts. However, dynamic developments are also evident in the Seattle area and North Carolina. In the Philadelphia area, where CAR-T technology was developed, an ecosystem with a high density of CGT companies has also developed – dubbed “Cellicon Valley”. The USA remains the world’s strongest venture capital market: the biotechnology sector alone raised more than USD 15 billion (€14 billion) in VC capital in 2023. The US government hopes to consolidate its leading global position with its biotechnology agenda (Executive Order 2022; Bold Goals).

The United States is also a global leader in clinical research: it is the site of most clinical trials based on pluripotent stem cells. According to research by the Human Pluripotent Stem Cell Registry (hPSCreg), in the period from 2018 to 2022 alone, there were 14 clinical trials financed by academia and government funds, along with 18 financed by companies.

One of the major pharmaceutical players in the development of stem cell-based therapies in the USA is **BlueRock Therapeutics/Bayer** (based in New York City, Cambridge, Toronto and, since 2023, Berlin). The company start-

ed the first clinical Phase I trial based on hES cell-derived dopaminergic neurons for the treatment of Parkinson’s disease (Bemdaneprocet BRT-DA01) in 2021. Following promising results, a Phase II trial is planned from 2024. Research and development activities focused on cell preparation production is underway at several sites in Toronto. With an investment of USD 250 million (€237 billion), Bayer and technology supplier Cytiva have built a facility in Berkeley, California, designed for the commercial production of allogeneic stem cell therapies and will open in fall 2023.

Novo Nordisk is developing cell replacement therapies based on pluripotent stem cells for the indications of chronic heart failure, Parkinson’s disease and type 1 diabetes. The pharmaceutical company operates GMP manufacturing centers in Fremont, California, and West Lebanon, New Hampshire, where cell preparations for clinical trials are produced.

In recent years, Boston-based **Vertex Pharmaceuticals** has acquired Semma Therapeutics (based in Cambridge) and ViaCyte (San Diego), two leading companies in beta cell replacement therapy for the treatment of patients with type 1 diabetes, and is now advancing this therapy based on human ES cells in clinical trial programs. The pharmaceutical company **Eli Lilly** (Indianapolis) is also developing a beta cell replacement therapy. **Fate Therapeutics** produces cell preparations from iPS cells for the treatment of cancer and diseases of the immune system. **Sana Biotechnology** (Seattle/Cambridge/Rochester) develops T-cell therapies as well as islet cell therapies and therapies with glial precursor cells for the treatment of neurodegenerative diseases such as MS or Huntington’s disease.

ISAR Bioscience GmbH

ISAR Bioscience is a translational company developing technologies and new therapies for degenerative diseases. We work closely with research institutions and companies from the biotechnology and pharmaceutical industries. We act as a bridge builder between these institutions, creating a direct link between basic research and new therapies and products. Our focus is on the pathological loss of function of organs as a result of aging, insufficient blood flow or due to a misdirected immune system.

In the case of degenerative diseases (e.g. Alzheimer’s disease, chronic cardiac insufficiency after surviving a heart attack), the natural ability of the organs to regenerate from their own stem cells is no longer sufficient. This leads to the loss of cells and ultimately to the loss of organ function. In most societies, they represent the greatest burden of disease and are the leading causes of death. If degenerative diseases can be reversed, the vision of healthy aging will be within reach. ISAR Bioscience GmbH is initially supported with € 20 million by the Free State of Bavaria.

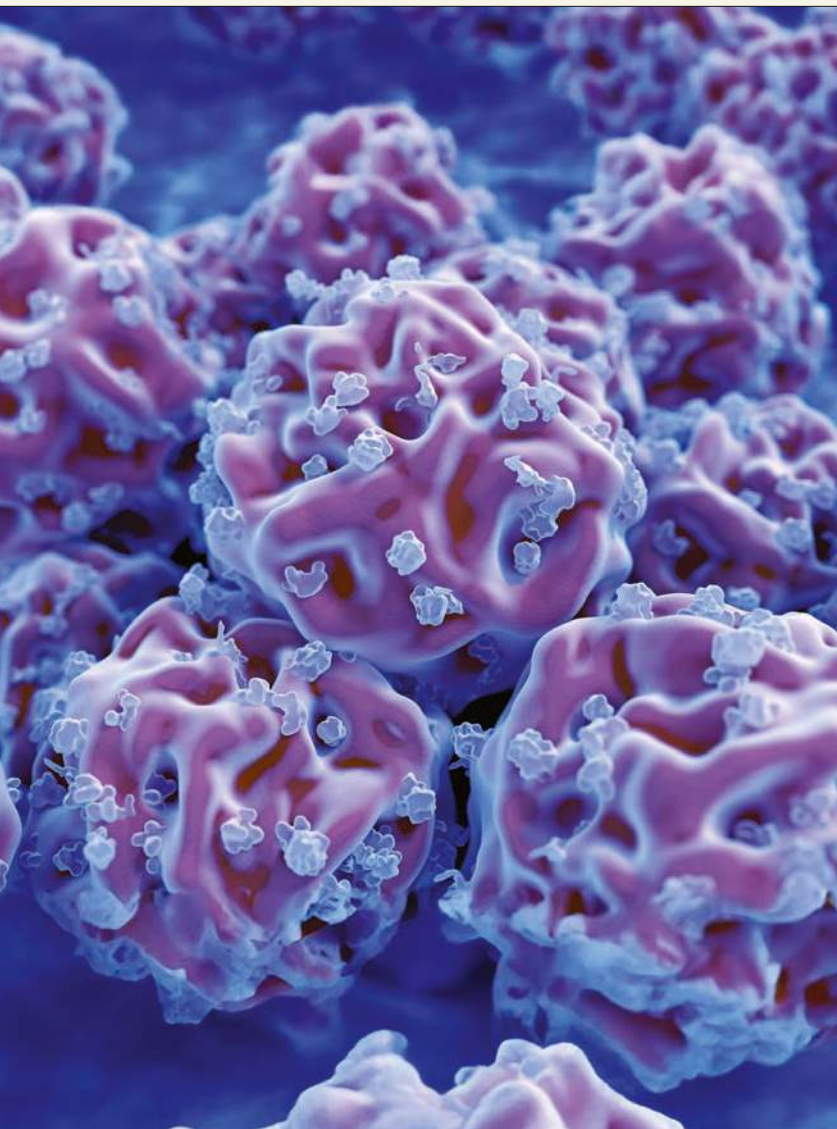


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FUJIFILM Cellular Dynamics (FCDI) (Madison/Wisconsin) is one of the world's largest developers and manufacturers of iPSC-based technologies and therapies. The company not only develops its own cell therapy pipeline, but also enters into strategic partnerships with other companies (e.g. **Opis Therapeutics**). FCDI is also active as a contract development and manufacturing organization (CDMO). In Madison, WiCell is a non-profit organization that offers services related to stem cell technologies and stem cell lines from its own cell bank.

Recursion (Salt Lake City) is a biotechnology company specializing in drug discovery using digital tools. Stem cell technologies are also used in the assays. Last but not least, the boom in T-cell immunotherapies in the USA has led to numerous talented people switching to the biotech and pharmaceutical sector. Competition for the best minds has intensified, with public biomedical research at universities and research institutes now struggling to keep up.

Text: Philipp Graf



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Asia-Pacific

The stem cell ecosystems of China, Japan,
Australia and South Korea at a glance



China: A vast and vibrant ecosystem



China has developed into a leading nation in stem cell research. The dynamic research community regularly produces pioneering developments in cell reprogramming. The Chinese government attaches great importance to the expansion of research infrastructure and the commercialization of cell-based therapies and technologies, as evidenced by enormous funding increases.

There are top academic centers for stem cell research in the capital **Beijing** (Institute of Zoology of the Chinese Academy of Sciences (CAS), Peking University and Tsinghua University), in **Shanghai** (Fudan University, Shanghai Jiao Tong University), in neighboring **Hangzhou** (Westlake University, Zhejiang University) and in **Guangzhou** in southern China (Sun Yat-sen University), not forgetting **Hong Kong** and **Macau**.

“There is a vibrant stem cell research community in all these major centers,” says Duanqing Pei, Professor of Regenerative Biology at Westlake University in Hangzhou. Pei, who heads up the Cell Fate Control Laboratory at Westlake, is a long-time expert on the Chinese stem cell ecosystem. Following a career in the USA, he has been involved in setting up the Guangzhou Institutes of Biomedicine and Health and the Hong Kong Center for Regenerative Medicine and Health since 2002.



Duanqing
Pei

Contribution to 82 high-ranking publications in the life sciences), surpassing the USA for the first time. In this regard, China is now the world's leading scientific nation.

The publication output in stem cell research is also high. There are high-ranking contributions on topics including developmental biology and the further development of iPS technology. “The topic of chemical reprogramming is typically Chinese. There is a very active community here that works closely together,” says Pei. “We are very proud of that.” In 2022, a team led by Hongkui Deng reported in the journal *Nature* on a cocktail of small molecules that can be used to bring cells not only into a pluripotent state, but also into a totipotent state.

“Recreating the conditions for totipotency in the laboratory, and making it possible to study them, is a holy grail of stem cell research,” says German stem cell researcher Prof. Ralf Jauch of the University of Hong Kong. Numerous Chinese researchers have played a leading role in this field and published ground-

breaking work, such as Pengtao Liu, Sheng Ding, Miguel Esteban and Jichang Wang. These techniques are seen as groundbreaking for the clinical translation of stem cell-based therapeutic approaches.

Returning talents and top publications

Duanqing Pei returned to China of his own accord to further his career. Over the past 20 years, China has continued to make considerable efforts to attract Chinese talent from overseas to return – such as the **Thousand Talents Program** launched in 2008.

China has significantly increased its scientific performance in recent years. The proportion of Chinese publications published in high-ranking and highly cited journals has risen sharply. In 2022, China had the highest share in the Nature Index (a country's contri-

Strategically important field of technology

The Chinese government attaches great importance to stem cell research and regenerative medicine and has invested heavily in this field of technology, particularly in the 2000s. Duanqing Pei describes the funding situation as good and expects funding for stem cell research will be significantly expanded once again in the coming years. National funding tends to focus on basic research, while local and regional funding is geared towards translation.

The **Ministry of Science and Technology (MOST)** is by far the most important source of funding for stem cell research. The Medium and Long-Term Plan for the Development of Science and Technology in the years 2006–2020 had a far-reaching strategic influence and helped to launch several initiatives for stem cell research.

Since the restructuring of the Chinese research funding system in 2015, the **National Key R&D Program of China** is currently the most relevant research funding program. As a mission-oriented program, it focuses primarily on national technology goals, including stem cell technologies and regenerative medicine. The “Developmental programming and its metabolic regulation” initiative was launched in 2018, followed by the “Stem cell research and organ repair” initiative in 2021. Since 2006, the MOST has invested more than 6 billion RMB yuan (approx. €816 million)* in the aforementioned initiatives, which primarily promote collaborative projects. The Chinese Academy of Sciences (CAS) has also launched its own strategic research program, from which many researchers benefit.

The **National Natural Science Foundation of China (NSFC)** also promotes basic research. “However, the NSFC grants are smaller and mostly aimed at individual laboratories, similar to the NIH’s R01 grants in the USA,” says Pei. Further exploratory pioneering research is to receive strategic funding in the coming years. In addition to state funding programs, there are relevant funding programs at regional level in China, while universities and industry also have their own programs.

Key topics in the current five-year plan

With its innovation-driven development strategy, China has changed tack in the science and technology system, setting course for qualitative growth based on its own research, development and innovation. It is placing a special focus on basic research with the aim of achieving greater independence in science and technology. This is also reflected in the Five-Year Plans. The current 14th Five-Year Plan (2021–2025) lists a number of technology sectors and subject areas that will be the focus of funding in the coming years. These include “Genes and Biotechnology” and “Clinical Medicine and Health”, which are relevant to stem cell research and regenerative medicine.

Research infrastructures expanded

One of the central government’s key approaches to Chinese innovation policy is the establishment of platforms for the collection, coordination and access to knowledge and resources for stakeholders in the innovation system. These include national clinical research centers and national priority laboratories, most of which are located at universities or CAS institutes. In the 14th Five-Year Plan, the

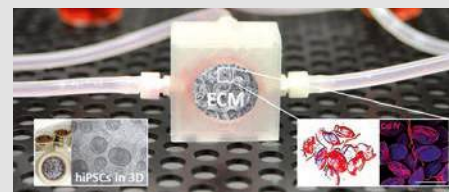
Chair of Tissue Engineering and Regenerative Medicine

Human organ models meets stem cell process engineering

The Chair Tissue Engineering & Regenerative Medicine, University Hospital Würzburg is working closely together with the Translational Center Regenerative Therapies, Fraunhofer Institute for Silicate Research Würzburg. Our research focuses on human organ models that find their application as alternative test systems to animal experiments. Basis of our models are either synthetic or biological carrier structures combined with primary- or iPSC-derived cells. Culturing of our models in specific bioreactors mimics *in vivo*-like microenvironmental

conditions *in vitro*. Since January 2021, we collaborate with the Fraunhofer Project Center for Stem Cell Process Engineering Würzburg, whose core institutes (Fraunhofer Institute for Biomedical Engineering IBMT and the Fraunhofer Institute for Silicate Research ISC) form a competence center in the field of stem cell process engineering. Our common goal is to transfer stem cell processes through automation solutions to an industrial scale and to improve the fields of cell expansion, differentiation and cryopreservation using novel materials.

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National Laboratories play a key role in building the country's scientific and technological strength and are to be further expanded. One of the most important is the **State Key Laboratory of Stem Cell and Reproductive Biology** at the Institute of Zoology of the CAS in Beijing. Another relevant key laboratory is the **State Key Laboratory in Reproductive Medicine** in Nanjing.

Another important piece of research infrastructure for the biobanking of stem cells is the **National Stem Cell Resources Center (NSCRC)** in Beijing, which was set up as a stem cell bank for the Institute of Zoology at CAS and works with partner organizations in Guangzhou and Shanghai. All human pluripotent stem cells from MOST-funded projects are registered here. This includes more than 600 human pluripotent stem cell lines, both ES cells and iPS cells. The NSCRC plays a leading role in the development of biobanking and bioprocessing standards. In 2019, a National Alliance of Stem Cell Resource Centers was also established to network the most important stem cell banks in China.

International research collaborations

There are strong international ties in stem cell research, particularly between China and the USA. The coronavirus pandemic, rising geopolitical tensions and rivalries between systems have led to a significant decline in Sino-American cooperation.

Europe has thus become an even stronger focus for research cooperation. The NSCRC is well networked internationally. "There is a close partnership with the EU-funded hPSCreg database," says the British stem cell application expert Glyn Stacey, who has

been advising the CAS and the NSCRC for many years as part of an International Fellowship for Special Experts Grant (PIFI) and has assisted them in setting up the International Stem Cell Alliance (ISCA) with Chinese support. The aim of the ISCA program is to harmonize processes and procedures and to facilitate international communication on stem cell data.



Ralf
Jauch



China is also a member of the International Stem Cell Forum (stemcellforum.org) and a partner of the International Stem Cell Banking Initiative (www.iscibi.org).

The first Max Planck Center in China was founded in 2016: the **Max Planck-GIBH Joint Center for Regenerative Biomedicine in Guangzhou**, headed by Hans Schöler and Duanqing Pei. Ralf Jauch headed a research group here as a German scientist. Until the end of funding in 2021, the Max Planck Center brought together researchers from two German Max Planck Institutes in Münster and Bad Nauheim with scientists from the Guangzhou Institute of Biomedicine and Health (GIBH), the Chinese Academy of Sciences, the University of Hong Kong (HKU) and the CUHK. "One achievement of this cooperation was the development of artificial Yamanaka factors, which allow the production of neuronal and pluripotent stem cells of higher quality and with better efficiency," says Jauch.



Glyn
Stacey

Legislation and translation of stem cell-based approaches

Stem cell researchers in China benefit from less restrictive legislation. However, studies involving human genes or embryos have been regulated by the Civil Code since 2020. The regulatory framework for the clinical application of stem cells and cell-based therapies in China

has been significantly revised in recent years and adapted to international standards.

The Administrative Measures on Stem Cell Clinical Research (AMSCCR) published in 2015 is decisive for the current regulations. The **National Health Commission (NHC)** and the **Chinese Food and Drug Administration (CFDA)** are responsible for this. "We now have stringent regula-

tion that I consider adequate," says Duanqing Pei. "All players who act responsibly in China comply with it," he says.

"More than 20 clinical trials with preparations based on pluripotent stem cells are currently underway in China," says Glyn Stacey. Significant interest from the venture capital market has created a booming sector for gene and cell therapies in China.

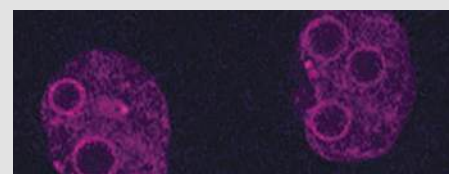
Photo: ISCBI

Helmholtz Zentrum München

German Research Center for Environmental Health

The Institute of Epigenetics and Stem Cells (IES) is part of the Stem Cell Center at Helmholtz Munich, the German Center for Environmental Health. Researchers at the IES are on the mission to understand how a cell can remember its function and identity to reset its memory so far that it once again takes on the identity of a totipotent cell. Understanding cell identity, therefore, has huge potential to revolutionize future regenerative therapies. Under the leadership of Maria-Elena Torres-Padilla, the research fellows from 25 different

nationalities are devoted to exploring the mechanisms underlying (stem) cell identity and to uncovering the processes behind cell reprogramming and genome stability by studying how cells package their genome, how they protect their chromosomes and how they acquire fitness to be able to generate cells that can make any cell type in the organism. The IES consists of five research groups and a Microscopy Core that follow original and complementary research lines to enable pioneering discoveries at IES.



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Stem Cell Center, Helmholtz Munich
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Germany
www.helmholtz-munich.de/ies

Academic research is also gearing up for translation. One example is the **Center for Translational Stem Cell Biology (CTSCB)**, a spin-off from Hong Kong University, where stem cells with proximity to totipotency are being used for translational applications in drug development and ageing research.

A number of Chinese start-ups are focusing on iPS-based approaches for the production of NK cells for tumor immunotherapy. These include **iCamuno Biotherapeutics** based in Suzhou, **CytoLynx Therapeutics** and **Neukio Biotherapeutics** (both Shanghai) and **Cell Origin Biotech** (Hangzhou). The start-ups are still in the preclinical stage with their development candidates.

iRegene Therapeutics is using iPS-based cells to develop a Parkinson's therapy, as is **Xellsmart Biomedical**. **Allife Medicine** and **Hopstem Biotechnology** are addressing the indications of strokes. **Nuwacell Biotechnologies** is testing iPS-based mesenchymal stromal cells (iMSCs) for the treatment of arthritis in the knee.

In early 2023, Nanjing-based **HELP Therapeutics** received approval for a Phase I clinical trial of the use of iPS-based cardiomyocytes for the treatment of heart failure.

Text: Philipp Graf

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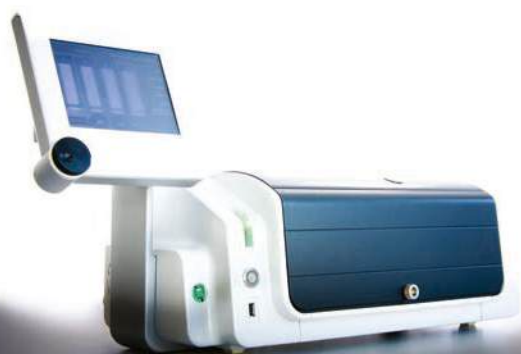


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Japan: Mission iPS-based regenerative medicine



By discovering iPS cell technology and receiving the Nobel Prize, Shinya Yamanaka has sparked a sense of euphoria regarding stem cell research and regenerative medicine in his home country unlike anything else around the world. Japan is also the country with the most clinical trials based on iPS cells to date.

The year 2006 marked a milestone in stem cell research: developmental biologist Shinya Yamanaka reported for the first time on his revolutionary reprogramming technique, which can transform somatic cells into induced pluripotent stem cells (iPS cells). In 2012, the Japanese researcher was awarded the Nobel Prize for his work. Since then, the Japanese government has invested heavily in research and application of iPS technology.

Academic hotspots

The **Kyoto Center for iPS Cell Research and Application (CiRA)**, of which Yamanaka was the founding director, is the leading center for iPS research in Japan. It holds a large number of patents in this area. In addition, an important iPS cell biobank (iPS Cell Stock Project) for the Japanese and international stem cell ecosystem is being established at the facility. It also stores clinically applicable cell lines from HLA-homozygous cell donors and can therefore supply large parts of a population with immunologically compatible transplantable cell types.

In addition, **Kobe** (RIKEN Center for Biosystems Dynamics Research), **Tokyo** (Keio University, Tokyo University) and **Osaka** (Osaka University) are important academic centers for iPS cell research. Shinya Yamanaka started the work that secured his Nobel Prize at the Nara Institute of Science and Technology (NAIST), which is located near **Kyoto**.

Further development of iPS technology is underway for both basic research and clinical application. Japanese researchers have even succeeded in producing germ cells using the reprogramming technique. Stem cell biologist Katsuhiko Hayashi from Osaka University reported in the journal *Nature* in 2023 that his team had succeeded in transforming somatic cells from a male mouse into functional mouse oocytes using iPS technology.

Political tailwind and generous research funding

The Nobel Prize for Shinya Yamanaka also marked the beginning of a new era for Japanese research and innovation policy: the LDP-led government in office in 2012 saw iPS cell applications as one of the most important growth drivers for the Japanese economy moving forwards. It placed particular emphasis on medical translation: Japan was to become an international hub and pioneer for iPS-based regenerative medicine.

From 2008 to 2013, the Japanese government funded iPS cell research with a total of 50 billion yen (€380 million). In 2013, the new government provided around 115 billion yen (€920 million) of funding for research into iPS cells over the next ten years. From 2014, an iPS cell initiative was also launched: 9 billion yen (€72 million) will be available annually over ten years.

Given the strong government commitment to funding in this area, there are growing expectations and mounting pressure on biomedical scientists to translate their findings from iPS cell technologies into functioning therapies.

“The hype surrounding iPS cells has given way to normal enthusiasm,” says Masayo Takahashi. In 2014, the ophthalmologist from Kobe and her team became the first in the world to implant iPS-based cells into a patient’s retina. In 2019, the stem cell pioneer founded Vision Care, a gene and cell therapy company, to advance her cell replacement therapies. She now manages the start-up, which has more than 60 employees.

After the national euphoria, Takahashi believes that many people are now somewhat skeptical as to why, following ten years of development, effective therapies are not yet available. Even with small molecules as an active ingredient class, it has taken 20 years to reach market maturity. Patience and a wealth of experience are therefore required before complex cell replacement therapies become part of clinical routine.

“We now really have to show that our cell replacement therapies work and are a real

treatment option for patients. We are making good progress here," says Takahashi. She expects government investment in the promotion of iPS technology and translation to continue in the coming decade, albeit at a lower level.

Regulatory framework geared towards acceleration

Amendments to the relevant pharmaceutical laws, the **Pharmaceuticals and Medical Devices (PMD Act)** and the **Act on Safety of Regenerative Medicine (ASRM)**, which came into force at the end of 2014, are regarded as crucial regulatory changes. These laws are helping to simplify regulations, remove hurdles to translation and significantly shorten the approval process for cell therapies. The



Masayo
Takahashi

Sakigake Designation System allows developers of cell-based therapies to obtain "early conditional approvals" and submit data on the efficacy of their therapies through confirmatory studies.

The **Agency for Medical Research and Development (AMED)** has been established as an authority pooling the relevant budgets of three ministries in order to accelerate health research and

its administrative processing. According to a recent analysis published in the journal *Nature Biotechnology*, 17 gene and cell therapies had been approved in Japan by the end of 2022, including nine cell-based products and eight gene therapy products. Only two of the 17 products were based on randomized clinical trials.

Photo: Vision Care

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Large number of clinical iPS-based cell therapy studies

Riding the tailwind provided by the national funding programs, more than 20 clinical trials based on iPS cells have been launched in recent years. These trials have been funded in particular by academia and the government. Industrial sponsors have only appeared on the scene in the last five years. The studies have generally demonstrated a good safety profile, but the data on the efficacy of cell replacement therapies is still thin on the ground.

In 2014, Masayo Takahashi started the world's first clinical trial to transplant iPS cell-derived retinal pigment epithelium (RPE) cells for the treatment of retinal diseases such as age-related macular degeneration (AMD). The cells survived the transplantation and the disease did not progress in the test subjects. "We have improved our treatment approach twice," says Takahashi. A major advantage is that only a small amount of cell material is required and the RPE represents a single cell layer. In future, **Vision Care** will pursue both autologous and allogeneic strategies. In the meantime, Takahashi's team has also developed iPS-based photoreceptors and is conducting a clinical study on the subject. Vision Care is currently running a total of four clinical trials.

The Tokyo-based company **Healios K.K.** is also conducting research into iPS-based RPE cells. The company's portfolio also includes iPS-based immune cells (NK cells) and liver cells.

Koji Nishida's group reported promising results in 2022. The Osaka University-based team implanted iPS-based corneal tissue into several patients and proved the method to be safe and effective, with improvements the test subjects' vision.

In 2018, the group led by CiRA Director Jun Takahashi started a Phase I clinical trial with iPS-based dopaminergic neurons for the treatment of Parkinson's disease. The clinical trial is now being funded by **Sumitomo Pharma**. At the end of 2023, the developers received approval to conduct clinical trials in the USA.

Koji Eto's group has succeeded in mass-producing blood platelets (thrombocytes) from iPS cells. The first clinical study on the use of autologous platelets from iPS cells has already been carried out. **Megakaryon**, a biotech com-

pany from Osaka, became a subsidiary of the Japanese diagnostics giant Sysmex Corporation in December 2023. It has established a technology platform for the mass production of iPS-based platelets and is aiming to commercialize these preparations for regenerative therapies.

The Japanese company **Heartseed** (founded by Keiichi Fukuda, a researcher at Keio University) has been testing the injection of iPS-derived cardiac muscle cells in a Phase I clinical trial since 2023. In 2021, the Danish company Novo Nordisk acquired the development and commercialization rights for the program.

More and more clinicians are founding companies

Masayo Takahashi reports that at least five of her research colleagues in Kyoto and Osaka have founded their own companies in recent years – motivated in part by the impending cuts to national research budgets – in order to put their treatment approaches into clinical practice in the future. "This is a real trend," says the President of Vision Care. As an entrepreneur, she only aims to attract investors with an understanding of the tremendous balancing act between cost and effectiveness in regenerative medicine.

However, iPS-based regenerative medicine in Japan is not limited to cell replacement therapy approaches. Other applications include drug discovery, toxicity studies and disease modeling.

An important public-private partnership in this regard is **T-CiRA**, a research alliance between the pharmaceutical company **Takeda** and CiRA: "We have access to all Takeda resources," reported Yamanaka at the annual conference of the German Stem Cell Network in Münster in September 2022. Takeda has been investing around 20 billion yen (€143 million) in the partnership as part of a ten-year plan launched in 2016. This has resulted in a promising drug repurposing project: the leukemia drug bosutinib proved to be effective in an iPS-based disease model. A Phase II clinical trial (iDreAM) started in April 2022. There are also similar drug repurposing studies for Alzheimer's disease.

Text: Philipp Graf

Australia: Bridging gaps in translation



Excellent stem cell research in Australia enjoys strong government support. However, the sector Down Under has some catching up to do when it comes to translation, venture capital funding and production capacities for regenerative therapies.

“Stem cell research is one of the strengths of biomedical research in Australia,” says Melissa Little. “We have a substantial stem cell community for our size.” Little is a Professor at the Murdoch Children’s Research Institute in Melbourne. Previously the Program Coordinator of the Stem Cells Australia initiative championed by the Australian government, she is also a former President of the ISSCR and is currently CEO of the Novo Nordisk Foundation Center for Stem Cell Medicine (reNEW) in Copenhagen, Denmark.

Melbourne as an academic hotspot

The stem cell community has self-organized in the **Australasian Society for Stem Cell Research (ASSCR)**. According to Little, excellent stem cell research is now underway in most Australian states. The academic hotspot for stem cell research is **Melbourne**, with further centers in **Brisbane, Sydney, Adelaide** and **Perth**. “There is high quality research on stem cell biology in Australia,” says Little. “But there are also major challenges around investment and genuine development of the biotechnology industry within the country.”

Massive government funding for health research

Biomedical research is massively supported by national funding programs. The most important funding bodies for basic scientific research are the **Australian Research Council (ACR)** and the **National Health and Medical Research Council (NHMRC)**. The **Medical Research Future Fund (MRFF)** is the most significant research framework program. The second edition of the MRFF has made AUD 6.3 billion (€4 billion) available for health research between 2022/2023 and 2031/2032.

A number of distinct stem cell initiatives have been launched as part of the MRFF in recent years, including

- **Stem Cells Australia** (2011 to 2019): Under this initiative, the government provided AUD 24 million (€15 million) to support more than 300 researchers from 14 Australian universities.
- **MRFF Stem Cells Therapies Mission** (2019 to 2028): This funding program will invest AUD 150 million (€96 million) over nine years in support of innovative, safe and effective stem cell-based therapies.

Foundations are also funding research, such as the **National Stem Cell Foundation Australia**. Some states have also set up their own initiatives, such as the **NSW Stem Cell Network** in New South Wales. Other important sources of capital for developers of cell-based therapies with government involvement include the **Biomedical Translation Fund** and the **BTF co-investment program**.

A significant investment in Australian stem cell research and medicine is the **Novo Nordisk Foundation Center for Stem Cell Medicine (reNEW)**. The Novo Nordisk Foundation is investing a record €300 million over ten years in this research consortium. The Murdoch Children’s Research Institute in Melbourne is an important pillar of reNEW, alongside the University of Copenhagen in Denmark and Leiden University Medical Center in the Netherlands.

A sought-after location for clinical trials

Australia is characterized by an excellent infrastructure and capacities for clinical trials. This has seen Australia develop into an important and dynamic international location for clinical trials in recent years. The Australian government is making an important contribution to this with its **R&D Tax Incentive** program. Research project and clinical trial expenditure is eligible for a 38.5% tax refund. This incentive is paid directly to newly founded companies in the early stages that do not yet have taxable profits.

Biotechnology drives weakening pharmaceutical sector

By contrast, low levels of venture capital investment, geographical isolation from investors and gaps along the translation and innovation pathway have long caused difficulties for the Australian life sciences ecosystem in transferring research results into application. “We simply don’t have a vibrant pharmaceutical sector in Australia,” says Little. Several large pharmaceutical companies have recently scaled back their production capacities in recent years – including Pfizer, Johnson & Johnson, Roche and GSK.

The biotechnology sector is developing very dynamically against this trend, with massive support from the government as part of a long-term **Biotechnology in Australia Plan**. Major investments are being made in areas such as vaccine research and manufacturing. Moderna is set to complete construction of an RNA vaccine production facility in Melbourne in 2024, while BioNTech has announced the establishment of an mRNA research and innovation center in Melbourne.

Few manufacturers of clinical cell products

The two largest biotech companies in Australia in the field of regenerative medicine are **CSL** (founded in 1916 as Commonwealth Serum Laboratories) and **Mesoblast**. “We have hardly any manufacturers of cell products in the country. Venture investments in this area have also been low so far,” says Melissa Little. As she explains, Mesoblast bases its production and clinical trials abroad. CSL is a global company specializing in the production of blood products and vaccines, with subsidiaries in dozens of countries, including Germany (CSL Behring in Marburg).

In addition to the difficult financing of translation, there is also the geographical challenge of long distances involved in the implementation of regenerative therapies. CAR-T therapy, for example, requires many thawing and freezing cycles – because parts have to be processed outside Australia. Even for Phase I clinical trials, capacities are still low. “For many developers, it is currently still easier to produce abroad,” says Little.

Cell Therapies Pty Ltd. is an important contract manufacturer for cell therapy products based in Melbourne. The company recently opened a GMP manufacturing center. In Western Australia, Cell and Tissue Therapies WA (CTTWA) at the Royal Perth Hospital (RPH) manufactures cell products for clinical trials.

Regulation and translation

The **Therapeutic Goods Administration (TGA)** is the national regulatory authority for medicines. “The TGA is smaller and less experienced in dealing with biologics than, for example, the FDA in the USA,” says Little. In 2019, the TGA enacted a new set of rules to maintain patient access to established and approved stem cell therapies and protect them from untested therapies.

Cyto Therapeutics is one of the key players in the development of stem cell-based cell therapies. In 2017, the company launched a clinical trial in which hESC-based dopaminergic cells are being tested for the treatment of Parkinson’s disease. Based on allogeneic mesenchymal cells derived from iPS cells, **Cynata Therapeutics** is testing a treatment for graft-versus-host disease in a Phase I clinical trial. Regeneus is testing mesenchymal stromal cells (MSC) from adipose tissue for the treatment of osteoarthritis.

Investment in infrastructure for research and development

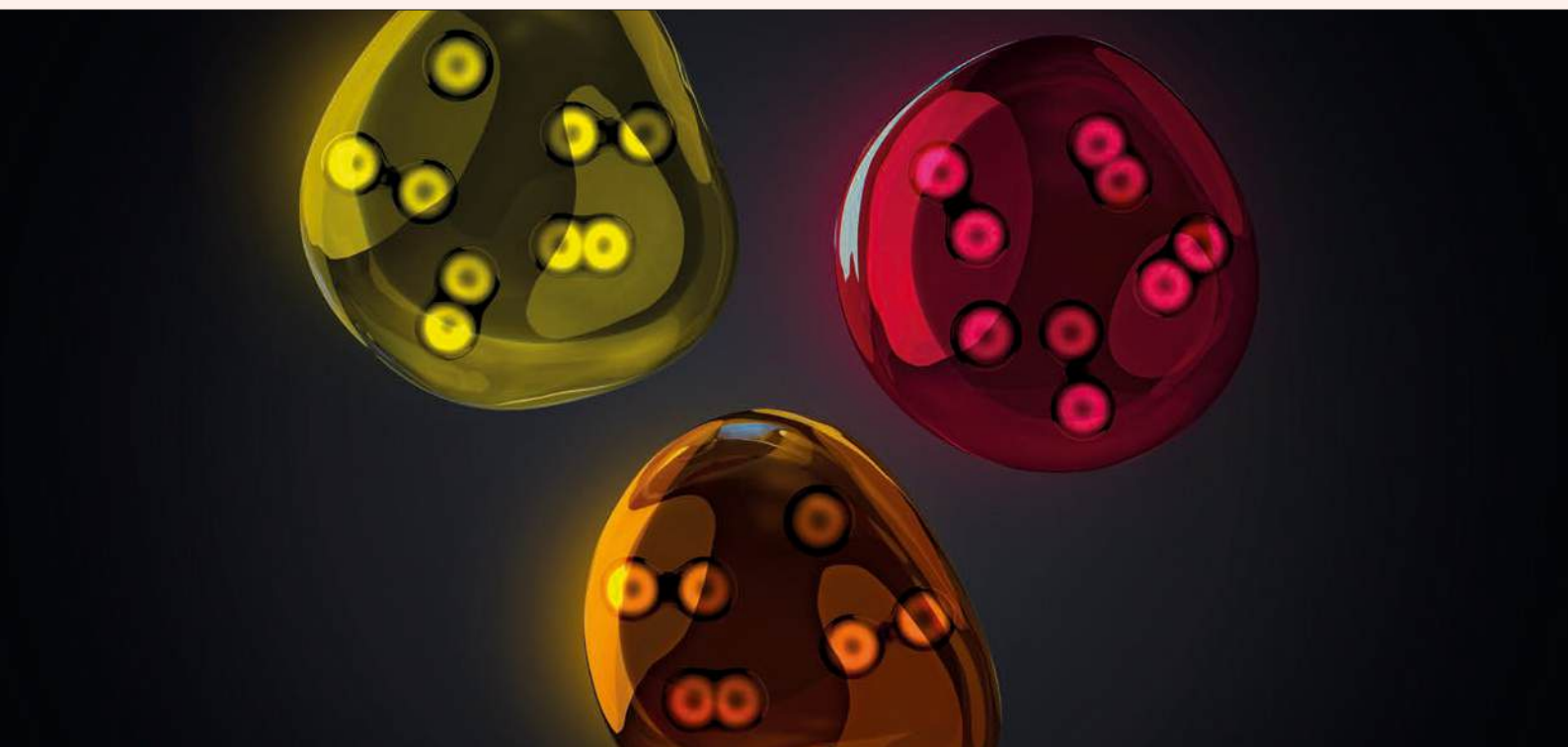
The translation of stem cell-based therapies will also benefit from recent investments in the construction of new, large-scale research laboratories in the vicinity of well-funded universities. Under the **University Research Commercialization Package**, the federal government will provide more than AUD 2.2 billion (€1.4 billion) over 11 years to support various initiatives, including incentives to commercialize research results and university-business partnerships.

Important incubators for biomedical translation are also being established in Australia, such as the Biomedical Precinct in Melbourne, the Biomedical Accelerator in Sydney and the Translational Science Hub in Brisbane.

The government's AUD 1.3 billion (€820 million) **Modern Manufacturing Initiative** sees health and medical devices as a key growth area. It aims to support Australian manufacturers in increasing their competitiveness through funding rounds in the areas of translation, integration and collaboration.

CCRM Australia, an offshoot of the Canadian public-private partnership **Centre for Commercialization of Regenerative Medicine (CCRM)**, is a catalyst in the Australian RegMed scene. In 2021, the Regenerative Medicine Catalyst Project Consortium developed a road-map for regenerative medicine in Australia. Its primary focuses are how to increase manufacturing capacities for cell-based therapies and make regenerative medicine more attractive for investors, both domestically and internationally.

Text: Philipp Graf



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South Korea: Cell-based medicine as a growth driver



As a dynamic field of biotechnology, the research and translation of stem cell-based approaches is a high priority in South Korea. The Korean government provides massive support for research and development in regenerative medicine.

As a high-tech country with a rapidly growing biotechnology sector, South Korea has developed into a dynamic hub for stem cell research and regenerative medicine.

The academic strongholds of stem cell research include research institutions in the **Seoul** region, including Seoul National University (SNU), Konkuk University, Korea University and the Catholic University of Korea. In **Daejeon**, there is the Korea Advanced Institute of Science and Technology (KAIST) and the Stem Cell Research Center (SCRC) at the Korea Research Institute of Bioscience & Biotechnology (KRIBB). Elsewhere in the country, leading institutions include Ajou University in **Suwon**, CHA University in **Pocheon** and the **Ulsan** National Institute of Science and Technology (UNIST) in the southeast. Stem cell research is also carried out at the Institute for Basic Science (IBS), which has established basic research centers similar to the Max Planck Institutes in Germany. These include the IBS Center for Genome Engineering in Daejeon. The Korea National Institute of Health (KNIH) near **Cheongju** is home to the national stem cell bank.

Important organizations in the stem cell ecosystem

Stem cell researchers are connected by the **Korean Society for Stem Cell Research (KSSCR)**. Other relevant associations include the Korean Tissue Engineering and Regenerative Medicine Society (**KTERMS**) and the **Organoid Society**. The **Regenerative Medicine Acceleration Foundation (RMAF)** is a non-profit organization that sees itself as a catalyst for the regenerative medicine ecosystem in Korea.

Government funding

The **Ministry of Science and ICT – MSIT** is responsible for research and innovation funding. The most important source of funding for universities is the **National Research Foundation (NRF)**. The stem cell community benefits from high government spending on research and development activities in biotechnology and the bio-health industry in recent years.

The Korean government is investing heavily in basic research and development in the field of regenerative medicine, while also facilitating clinical research and early-stage commercial clinical trials. It regards innovation in manufacturing technology as a critical factor in reducing costs. The Ministry of Trade, Industry and Energy, the Ministry of Health and Welfare and the MFDS are therefore preparing a new national R&D fund for innovations in manufacturing technology.

Funding allocated to research and development will fall by a total of 8% in the 2024 budget to the equivalent of around USD 22 billion (approx. €20.3 billion). The Ministry of Health will receive almost USD 37 million to set up a funding agency modeled on the US Advanced Research Projects Agency for Health (ARPA-H).

New regulations for regenerative medicine

In 2020, the **Act on the Safety and Support for Advanced Regenerative Medicine and Advanced Biological Products** introduced a set of regulations that enables accelerated translation and faster review processes for cell-based therapies via conditional approvals. This legislation has since been amended in February 2024. The authority responsible for drug approvals is the **Korean Ministry of Food and Drug Safety (MFDS)**. Hospitals and clinicians of other facilities wishing to conduct clinical research in regenerative medicine must be certified as an Advanced Regenerative Medicine Institution. The Regenerative Medicine Acceleration Foundation supports this process to promote the development of a cell and gene therapy ecosystem.



International cooperation

Internationalization of the domestic research and development landscape is a high priority in Korean innovation policy and is considered an essential part of catching up with top international research.

There is strong international cooperation with the country's closest neighbors: stem cell researchers from Korea have founded the Korea-China-Japan Trilateral Federation of Stem Cells and Regenerative Medicine (AASCRM) and also work closely with the Stem Cell Society Singapore (SCSS).

In addition to the partners from the Asia-Pacific region, there is also a close exchange with European researchers. Looking at the example of Germany, in 2010, the Ulsan National Institute of Science and Technology (UNIST) even named a new stem cell institute after the German stem cell researcher and Münster-based Max Planck Director Hans Schöler (Hans Schöler Stem Cell Research Center – HSSCRC). The Max Planck Institute for Molecular Biomedicine in Münster also worked closely with a partner group at Konkuk University, led by Dong Wook Han. The newly launched **Boston-Korea project** strongly supports collaborations with institutions in the Boston biotech ecosystem.

Translation and corporate landscape

The cell and gene therapy sector is experiencing dynamic growth. In recent years, investments and strategic partnerships have increasingly focused on biotechnology companies advancing cell and gene therapies. Although initially hesitant, large domestic companies such as Samsung Biologics, LG and SK Bioscience have also recently decided to invest in this area.

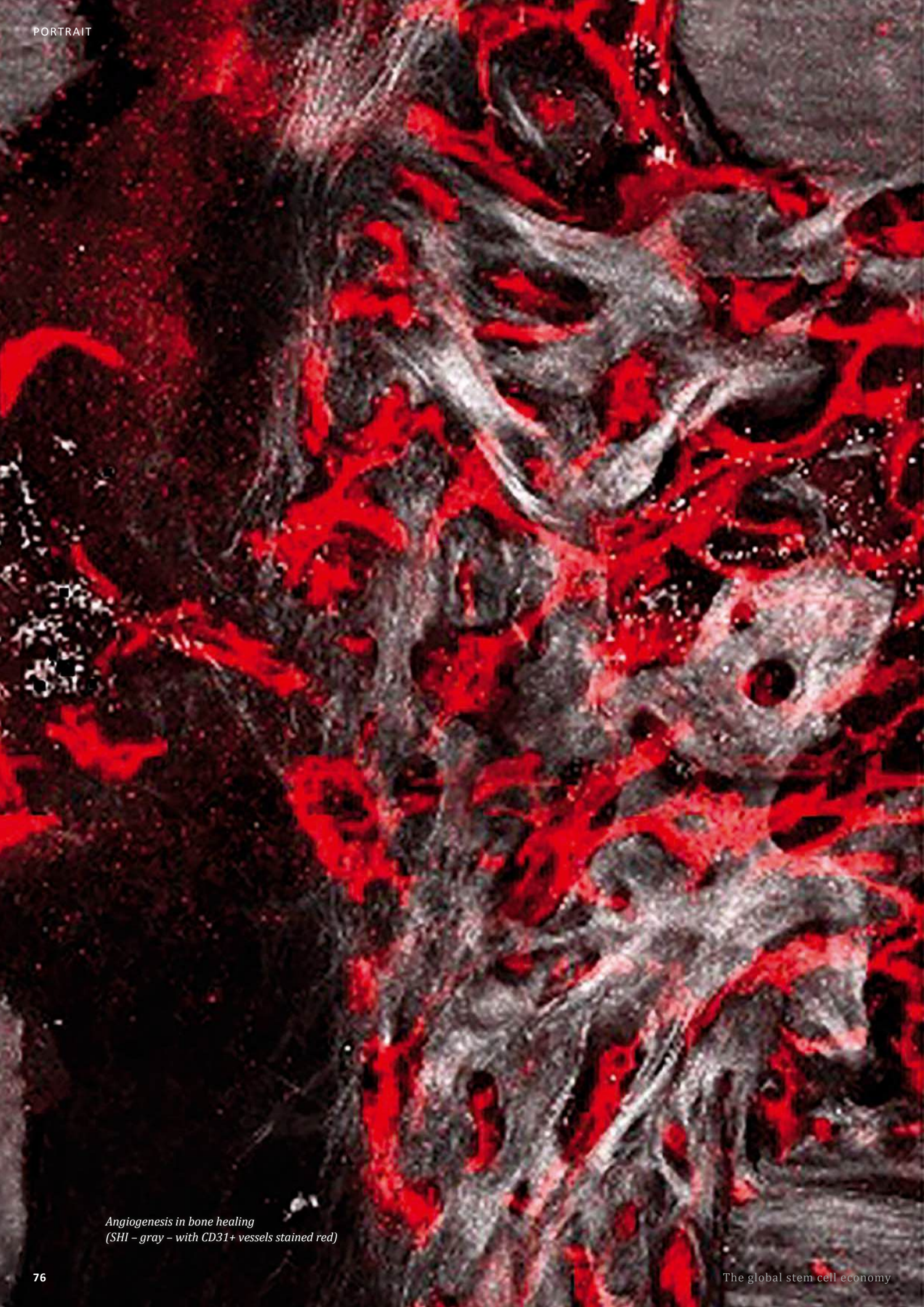
Probably the largest company in the development of cell therapies is **CHA Biotech**. It can draw on an entire ecosystem of universities (CHA Medical University), research institutes (CHA Advanced Research Institute) and hospitals (CHA Hospitals) for research and development. The company relies on preparations derived from ES cells or adult stem cells. ES-derived RPE cells are being tested in clinical trials, including for the treatment of macular degeneration (in-licensed from the US company Astellas). **Pharmicell** attracted attention with its mesenchymal stem cell-based therapy Hearticellgram-AMI, which became the world's first approved stem cell-based therapy worldwide in 2011. **Anterogen** received approval for two stem cell-based preparations in 2012.

Seoul-based **Kangstem Biotech** specializes in therapeutic approaches using mesenchymal stromal cells from umbilical cord blood and is testing these in clinical trials for the treatment of dermatitis and other inflammatory diseases.

The biotechnology company **YIPSCCELL**, a spin-off of the Catholic University of Korea, is developing various diagnostic and therapeutic programs based on iPS technology. Preparations are underway for clinical trials, including for a cell replacement therapy to treat osteoarthritis with iPS-based chondrocytes.

The start-up **OrganFactory** is developing organoid-based, patient-specific disease models for drug discovery for neurodegenerative and other diseases using reprogramming technologies. **NEXEL**, a spin-off from Korea University in Seoul, specializes in ES and iPS technology and uses these cell lines for drug discovery and toxicity testing. **StemLab** in Seoul combines cell reprogramming with medical imaging technology. The portfolio for therapeutic applications includes skin cells, hair follicle cells and the central nervous system. **StemExOne** is a biotechnology company that offers technological solutions for the production of extracellular vesicles.

Text: Philipp Graf



*Angiogenesis in bone healing
(SHI – gray – with CD31+ vessels stained red)*

A Portrait: Georg Duda

Leveraging bioengineering for advanced and sustainable medicine

Since November 2020, Professor Georg Duda has held a tenured W3 Professorship for Engineering Regenerative Therapies at the Berlin Institute of Health (BIH) and at Charité – Universitätsmedizin Berlin. Duda, an expert in biomechanics and regenerative medicine, is particularly interested in how biology and mechanics interact in tissues like bone and muscle, including how such tissues respond differently to mechanical and physical stimuli. The European Research Council (ERC) awarded him an ERC Advanced Grant in 2022 to support his research on immunomechanics.



Georg Duda

Finding a suitable therapy requires us get to the bottom of healing problems. It usually makes sense to look at the problems from various perspectives, employing strategies and approaches from different disciplines.” Duda, who originally trained as an engineer, is still driven in his work by the interplay between biology and mechanics. “Even though these two fields were treated separately when I was in school and later in university lectures, they are closely linked in nature and in the human organism.”

Persistently asking questions is the key to finding answers. That is Georg Duda’s motto. He does not accept the first answers that come up. After all, a potential therapeutic strategy can be just as complex as the disease pattern itself. The 57-year-old Berliner is Professor of Engineering Regenerative Therapies at the Berlin Institute of Health (BIH) and at Charité – Universitätsmedizin Berlin. He is particularly interested in the special ability of tissues of the musculoskeletal system to heal on their own, taking into account that the healing of bones and muscles proceeds quite differently and is regulated by mechanical and physical stimuli. “If we want to help patients, we have to understand them as holistically as possible,” he explains. “Many patients nowadays have complex disease patterns. A simple fracture may heal quickly, but it’s a different story for older patients with diabetes or autoimmune diseases.

This interplay provides the intellectual underpinnings of Charité’s Julius Wolff Institute for Biomechanics and Musculoskeletal Regeneration, of which Duda is founding director. “Wolff was the first professor of orthopedics at Charité and the original founder of the ‘form follows function’ rule,” explains Duda. “He coined Wolff’s law, which states that the shape of a bone corresponds precisely to its load.” Wolff’s principles are central to research at the Julius Wolff Institute and its partner division, the Center for Musculoskeletal Surgery. These principles are incorporated into their work with patients in the jointly run translational unit BeMoveD (Berlin Movement Diagnostics). “Here we analyze the movement of patients with osteoarthritis or back pain and correct their movement patterns, giving them detailed advice and recommendations,” explains Duda. He believes that not only physicians

Photo: Julia Ginkel, BCRT

BIH Center for Regenerative Therapies (BCRT)

The BCRT was established as an interdisciplinary translational center to enable the development of cell-, gene- and biomaterial-based therapies to enable and foster endogenous regeneration. Here, clinicians and researchers are working closely together on developing personalized medicine of the future: targeted, advanced therapy development based on profound and in-depth characterization of the patients’ medical need and individual healing capability. The primary focus of the BCRT is on diseases in four clinical indication fields and organ systems,

respectively infection & immunotherapy system, musculoskeletal system and cardiovascular system and metabolism and the field of hepatology. The main clinical fields are connected through cross-sectional topics that are shared across all such as (epi)genetic & cell differentiation; inflammation; stem cells, cell engineering, organoids cell-based therapies and matrix & biophysics. To boost our translational efforts, we are tightly co-developing therapies with various sized commercial entities or own start-ups, are in an open dialogue with health care providers and regulatory authorities.

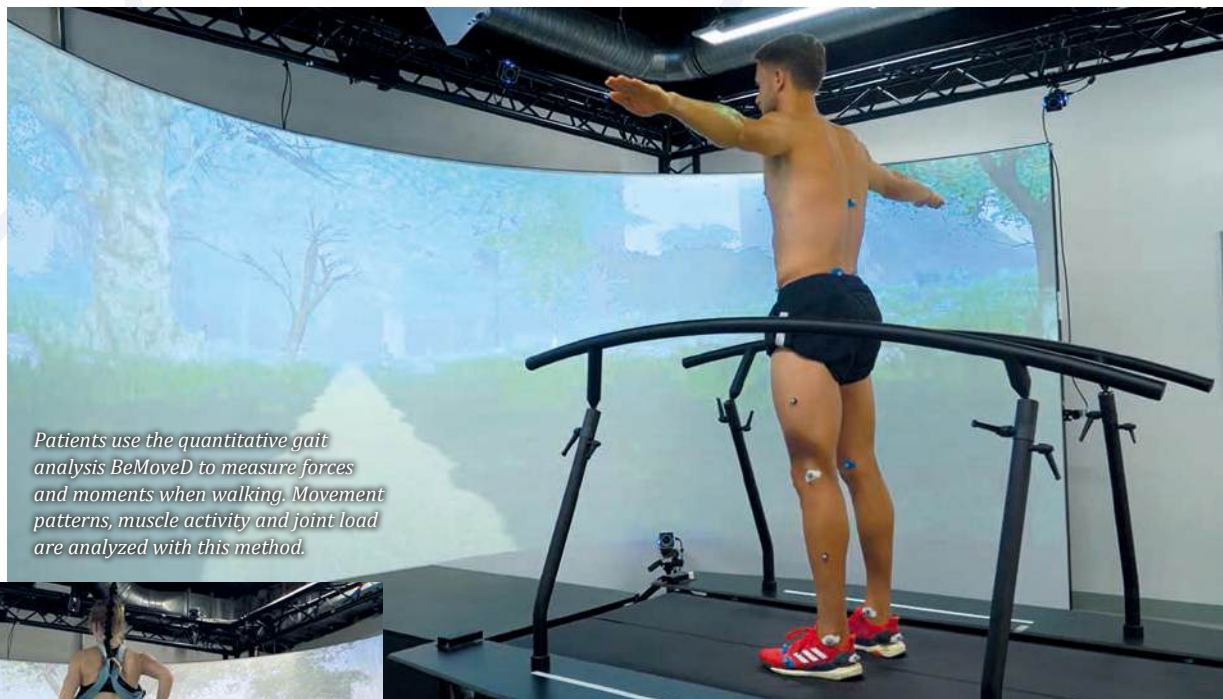
BIH Regeneration

BIH Center for Regenerative Therapies (BCRT)



BIH Center for Regenerative Therapies BCRT
Charité – Universitätsmedizin Berlin
Augustenburger Platz 1 · 13353 Berlin
www.bihealth.org/de/regeneration

Photo: Peer Schröder



Patients use the quantitative gait analysis BeMoveD to measure forces and moments when walking. Movement patterns, muscle activity and joint load are analyzed with this method.



but also researchers should focus on the patient, a conviction that he brought back with him from his years in the United States: “During my studies I found some lectures – even on biomechanics topics – rather outdated. Then I went abroad after graduating and worked at the Mayo Clinic. What truly fascinated me was how it put patients at the center of attention – even in scientific research – and viewed them holistically and not from the perspective of

a single medical discipline. Plus, there were case discussions every week. I thought that was cool, it really inspired me. In my eyes, it was the perfect combination of basic research and applied medicine, with surgeons and researchers working together to formulate scientific questions based on patients’ medical problems.”

Advanced therapies offer new approaches in regenerative medicine

In his study of the interaction between bones and muscles, Duda investigates biomechanical influences and their effects on both the intact and injured musculoskeletal system, such as the load on joints and bones at rest and during movement sequences. He seeks to understand the body’s own regeneration and healing processes and – if necessary – to specifically stimulate them in order to enable natural

Photos: Julia Ginkel, BCRT

German Cancer Research Center (DKFZ)

Research for a life without cancer

The German Cancer Research Center (DKFZ) in Heidelberg, a member of the Helmholtz Association, is the largest biomedical research institution in Germany.

More than 1,000 scientists investigate how cancer develops, identify risk factors and develop new methods for the prevention, diagnosis and therapy of cancer. Several research groups focus on normal stem cells, cancer stem cells or the stem cell niche. The goal is to identify the initial cells of tumors and metastases and to find ways to specifically eliminate them.

Jointly with the Dietmar Hopp Foundation, the DKFZ is a shareholder of the Heidelberg Stem Cell Institute HI-STEM gGmbH. HI-STEM investigates normal and malignant stem cells with the aim of developing novel approaches for the diagnosis and therapy of tumors based on the results.

The DKFZ maintains translational partnerships with university medicine at twelve locations in Germany with the aim of transferring the results from cancer and stem cell research to the clinic.



German Cancer Research Center
Im Neuenheimer Feld 280, 69120 Heidelberg
www.dkfz.de

regeneration even in difficult healing situations. His team pays particular attention to the role of inflammation in healing and how this also influences the regeneration of muscles, tendons and bones under mechanical stress. Bone is one of two organ systems that can heal without scarring. The aim is to understand the principles behind these regenerative abilities and apply them to other tissues that lack such properties. His conclusion: a certain degree of mechanical stimulation as well as well-controlled inflammation are essential for uncomplicated healing, while too much or too little load or no inflammation or inflammation that lasts too long can delay healing.

“Bone has a remarkable endogenous regenerative capacity that enables scarless healing and restoration of its prior mechanical function, even under challenging conditions such as advanced age and metabolic or immunological degenerative diseases,” says Duda. “Yet, despite much knowledge, there are still situations today where seemingly simple fractures fail to heal. Going forward, we want to identify these problems very early on and prevent patients from suffering from such injuries for a long time.”

Through its basic research on stress and strain in human joints, the team of researchers at the Julius Wolff Insti-

tute has laid the foundation for many of the standards used today worldwide for the approval of joint replacement technologies. They have used their understanding of mechanobiological interactions to redesign implants for fracture treatment and to fundamentally change treatment strategies. This has led to the perfection of implants for fracture treatment and joint replacement which have found their way into current clinical practice worldwide.

“It’s always important that questions come from the clinic”

“The exciting part about medicine is coming up with good, fundamental questions and then testing them in the clinic – such as shedding light on what makes a therapy work in almost all patients, but not in some patients. Such observations often lead to new relevant questions and ultimately to the development of even better therapies,” says Duda. “Therein lies the special advantage of German university medical centers – the close integration of basic biological research, technology development and clinical scientific medicine. This enables insights to be gained directly from patients, while at the same time using basic research to improve new therapeutic approaches.”



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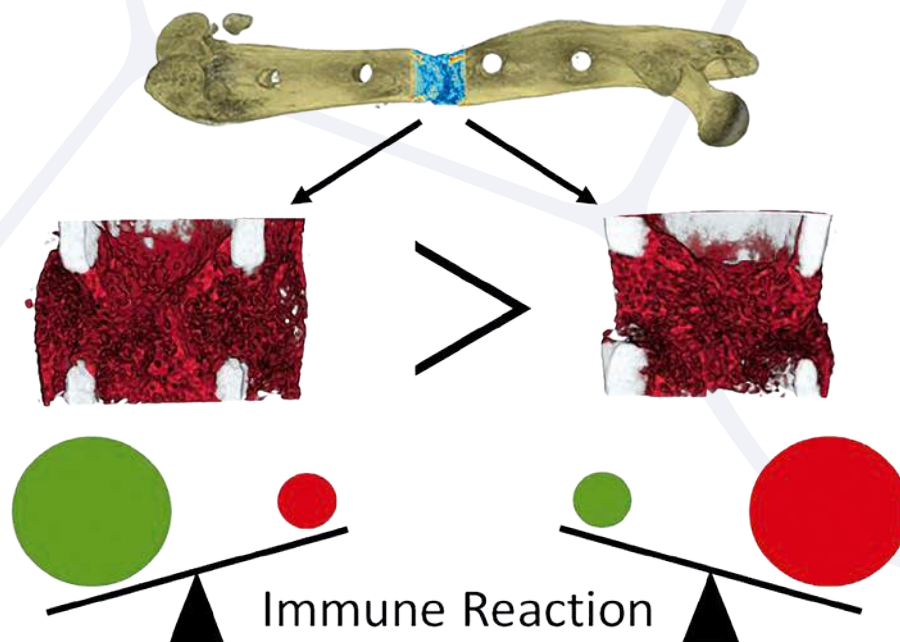
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The role of the immune experience influences the speed of healing: Rapid bone healing with a predominantly naive immune system (green circle, left) and delayed healing with a predominantly experienced immune system with a longer inflammatory phase (red circle, right).

Together with other institutes and several clinics, the Berlin-Brandenburg Center for Regenerative Therapies (BCRT) was founded at Charité in 2006, initially as a collaboration between Charité and the Helmholtz Association. Today, the BCRT is an essential part of the BIH and enables the faster development of advanced therapies – i.e., cell, gene and combination therapies – for clinical use in cardiovascular diseases, liver regeneration, organ transplantation, infections, cancer and musculoskeletal diseases. “At the BCRT, clinicians, scientists and engineers are working together to better understand the body’s own regenerative processes and to figure out where they fail, using this knowledge to develop new therapies that can cure patients,” says Duda. “We have established an infrastructure at the BCRT that allows clinically active researchers and scientists from basic research and technology development to become involved in the translation of therapies at an early stage and to provide support in what is often a long and complex process.”

Bringing advanced therapies to patients

Duda is currently part of a research group that is investigating new ways of treating damaged muscles more quickly and without scarring. “To date, we lack a truly satisfactory therapeutic approach for damaged muscles,” says Duda. His team has also been collaborating with orthopedist Tobias Winkler, stem cell researcher Sven Geissler, immunologist Hans-Dieter Volk and with a small start-up on the development of a novel therapeutic approach. This advanced therapy aims to reduce scarring in the regenerating muscle so that muscle function can be restored more quickly after an operation. Stromal cells, which have already proven themselves in other clinical studies, are obtained from placentas. Using a special process, these cells are prepared in such a way that they reduce local inflammation in the tissue and stimulate angiogenesis, while also spurring muscle regeneration through their signaling. The results of a successful phase I/IIa tri-

ILL: BCRT

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al have been confirmed in a phase III trial, although the cell system needs to be further optimized before broader therapeutic use is possible.

In the medium term, Duda aims to demonstrate, especially in the non-oncological domain of medicine, that such novel therapeutic approaches, so-called advanced therapies, can really bring about healing, thus taking a step closer to sustainable medicine while changing direction away from the chronic treatment of symptoms toward a true restoration of tissue structure and function in patients. "We are currently working to translate the discoveries into breakthroughs in other major fields, such as osteoarthritis. Examples from rheumatology and hepatology also show that such approaches to sustainable therapy are possible. Today, it is less about prolonging life by treating symptoms and more about increasing so-called quality-adjusted life years (QALYs) – in other words, enabling people to grow older in better health. To do this, we need to move away from the chronic treatment of symptoms and achieve a 'real' cure."

Text: Katharina Kalhoff

Georg Duda studied precision engineering and biomedical engineering in the 1980s at Technische Universität Berlin. After completing his degree there, Duda moved to Minnesota in the United States to work in the Biomechanics Lab of the renowned Mayo Clinic. He went on to do his Ph.D. at the Hamburg University of Technology (TUHH) before working as a postdoc in trauma research and biomechanics at Ulm University. The Berlin native joined Charité in 1997 to head a research lab at the Center for Musculoskeletal Surgery. Duda and his team successfully applied to the German Research Foundation (DFG) for the establishment of a clinical research group, which led to him being appointed to a Professorship in Biomechanics and Biology of Bone Healing in 2002. Together with Georg Bergmann, Duda founded the Julius Wolff Institute for Biomechanics and Musculoskeletal Regeneration at Charité in 2008. He is also an Associate Faculty member at Harvard's Wyss Institute for Biologically Inspired Engineering and holds a Visiting Professorship in Regenerative Therapies at Oxford University.



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Stem Cell and Embryo Research in Germany

Stem cell and embryo research has been intensely discussed in Germany for years, both in public and scientific circles. These areas of research raise ethical, legal, and social questions that test the limits of what is technologically possible and morally permissible. From 3 to 7 August 2023, the German Stem Cell Network (GSCN), in collaboration with the Berlin-based startup Civey, conducted an online survey in which 2,500 people participated. The aim of the survey was to capture the opinion of the German population to better understand societal acceptance and concerns regarding these research areas. Since participants had to register with Civey, the samples cannot be considered completely random. Therefore, the results of this survey are primarily seen as a reflection of sentiment and not as absolutely representative. This reflects the challenge of how surveys with relatively small samples can generally be considered “representative.” To avoid suggesting false precision, this article does not include decimal numbers for the percentage values.

Background

Stem cells have the extraordinary potential to develop into any cell type of the human body, making them an invaluable tool for regenerative medicine and understanding human developmental processes. Particularly, embryonic stem cells, which are derived from human embryos, are at the center of scientific and ethical debates. In Germany, the handling of embryonic stem cells is strictly regulated by the Embryo Protection Act (ESchG) and the Stem Cell Act (StZG). These laws provide strict guidelines for the research with human embryos and the use of embryonic stem cells to comply with ethical principles.

Survey Objective

The survey conducted by the GSCN aims to capture a sentiment snapshot of various aspects of stem cell and embryo research among a specific group of the German population who have registered online with Civey. Registration allows for the inclusion of personal data such as age and gender, as well as social (e.g., regional environment) and political information (such as voting intentions) in the analysis. Additionally, a preliminary survey on the interest and engagement of respondents in the life sciences identified a specific target group of about 200 people (approximately 8% of the total respondents). The insights from this target group enable a more detailed examination of the impact of in-depth information on opinions about the topic.

Methodology

To create a comprehensive sentiment picture within the population, a wide-ranging online survey was conducted to gather quantitative data. However, it should be noted that deeper insights into individual beliefs and ethical considerations of respondents are usually achieved through focused interviews or discussion groups, which were not feasible in the context of this survey. The following questions were of interest in the survey:

Fraunhofer Institute for Translational Medicine and Pharmacology ITMP

Fraunhofer is the largest application-oriented research organization in Europe with over 30,000 employees and operates 76 institutes and research facilities in Germany. ScreeningPort is a department of the Fraunhofer Institute for Translational Medicine and Pharmacology ITMP located in Frankfurt, Hamburg, Göttingen, Munich and Berlin. Fraunhofer ITMP conducts health research in line with the Fraunhofer 4D concept (Drugs, Diagnostics, Devices, Data), which aims to optimize inter- and transdiscipli-

nary health research in order to improve patient treatment qualitatively and economically. One focus of ITMP ScreeningPort is on assay development for biochemical and cell-based formats, on development and application of efficacy and toxicity assays based on human pluripotent stem cells, on assay miniturization, high-throughput and high-content screening, and on chemi- and bioinformatics. The indication focus is on infectious and immune-related diseases.

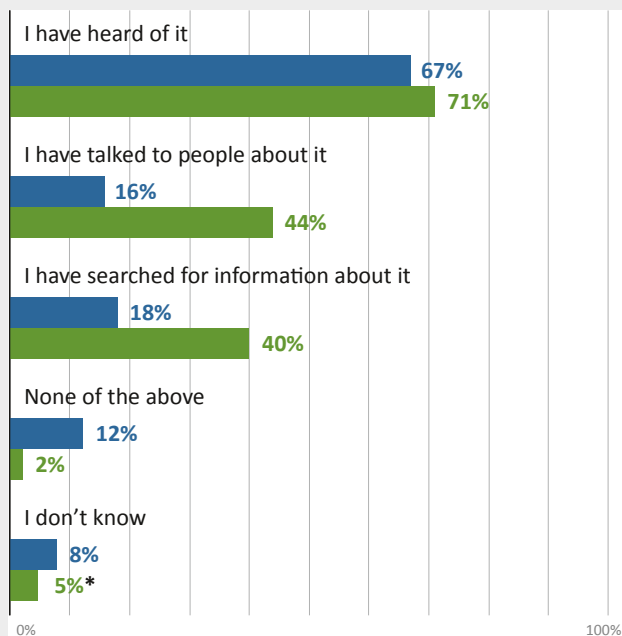
Fraunhofer
ITPM



Fraunhofer Institute ITMP ScreeningPort
Schnackenburgallee 114 · 22525 Hamburg
www.itmp.fraunhofer.de

Which of these statements regarding stem cell research apply to you? (multiple answers possible)*

- I have heard of it
Overall result: **67%** · Target group (TG): **71%**
- I have talked to people about it
16% · TG: **44%**
- I have searched for information about it
18% · TG: **40%**
- None of the above
12% · TG: **2%**
- I don't know
8% · TG: **5%***



■ Overall result ■ Target group

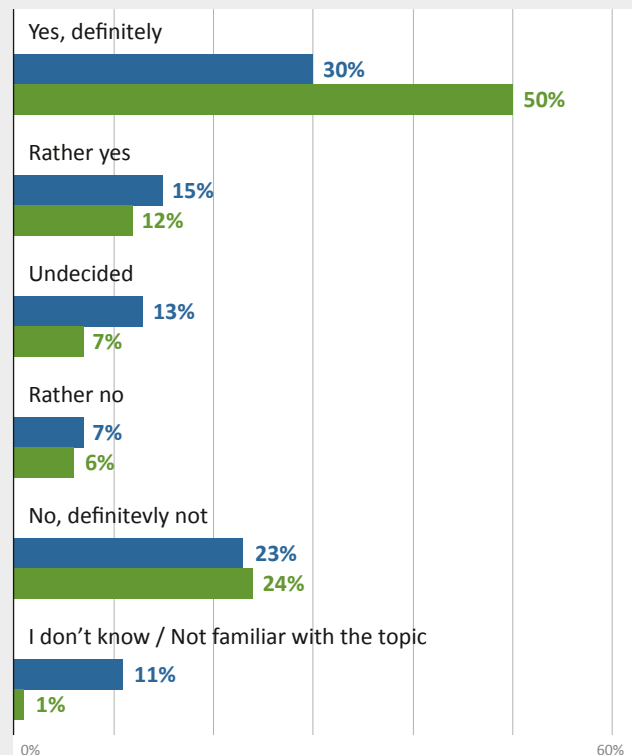
* The totals do not add up to 100% as multiple answers are possible.

Should research on artificially created embryo-like structures that cannot develop into a human be allowed in Germany, in your opinion?

- Yes, definitely
Overall result: **34%** · Target group (TG): **61%**
- Rather yes
14% · TG: **10%**
- Undecided
12% · TG: **4%**
- Rather no
5% · TG: **2%**
- No, definitely not
24% · TG: **20%**
- I don't know / Not familiar with the topic
12% · TG: **3%**

Should research on embryos that are no longer needed for in vitro fertilization be allowed in Germany, in your opinion?

- Yes, definitely
Overall result: **30%** · Target group (TG): **50%**
- Rather yes
15% · TG: **12%**
- Undecided
13% · TG: **7%**
- Rather no
7% · TG: **6%**
- No, definitely not
23% · TG: **24%**
- I don't know / Not familiar with the topic
11% · TG: **1%**



Human embryonic stem cell production is prohibited in Germany, but importation from abroad for certain research purposes is allowed. Which legal regulation do you support?

- Prohibit both production and import
Overall result: **26%** · Target group (TG): **29%**
- Prohibit production but allow import
4% · TG: **4%**
- Allow both production and import
46% · TG: **65%**
- I don't know / Not familiar with the topic
24% · TG: **2%**

How important do you think the research on human embryonic stem cells is for the development of future therapies for severe diseases?

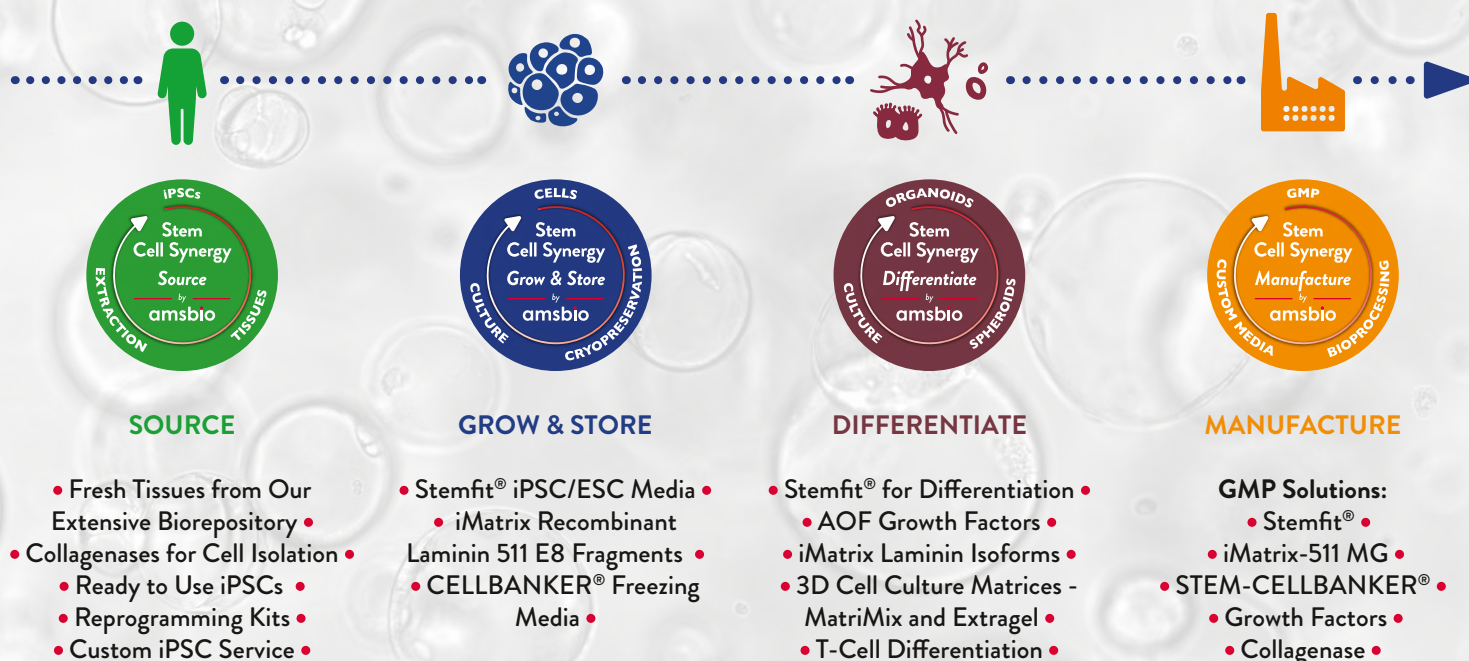
- Very high
Overall result: **39%** · Target group (TG): **47%**
- Rather high
26% · TG: **22%**
- Rather low
9% · TG: **12%**
- No significance
7% · TG: **12%**
- I don't know / Not familiar with the topic
20% · TG: **7%**

Should the use of human embryonic stem cells be allowed in Germany for research and application of therapies, in your opinion?

- Yes, definitely
Overall result: **40%** · Target group (TG): **54%**
- Rather yes
14% · TG: **14%**
- Undecided
13% · TG: **10%**
- Rather no
6% · TG: **3%**
- No, definitely not
16% · TG: **17%**
- I don't know / Not familiar with the topic
13% · TG: **3%**

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On a scale from 0 to 10 (0 = not relevant at all), what relevance does research with human embryonic stem cells have for you personally?

- Low relevance:
 - 0 (Overall result: **31%** · Target group (TG): **31%**)
 - 1 (**10%**; **10%**)
 - 2 (**7%**; **8%**)
 - 3 (**6%**; **5%**)
 - 4 (**4%**; **0%**)
 - Overall unimportant (58%; **54%**)
- 5 (**15%**; **9%**)
- High relevance:
 - 6 (**5%**; **9%**)
 - 7 (**5%**; **7%**)
 - 8 (**8%**; **15%**)
 - 9 (**3%**; **2%**)
 - 10 (**7%**; **5%**)
 - Overall important (**27%**; **37%**)

To what extent do you agree with the statement: “The Embryo Protection Law should be changed to reflect current developments in reproductive medicine (e.g., egg donation or surrogacy)”?

- Strongly agree
 - Overall result: **28%** · Target group (TG): **38%**
- Somewhat agree
 - 16%** · TG: **16%**
- Undecided
 - 16%** · TG: **8%**
- Somewhat disagree
 - 6%** · TG: **10%**
- Strongly disagree
 - 19%** · TG: **25%**
- I don't know / Not familiar with the topic
 - 16%** · TG: **3%**

To what extent do you agree with the following: “The Stem Cell Act (which, among other things, regulates the import of embryonic stem cells) should be changed to give science internationally equivalent opportunities”?

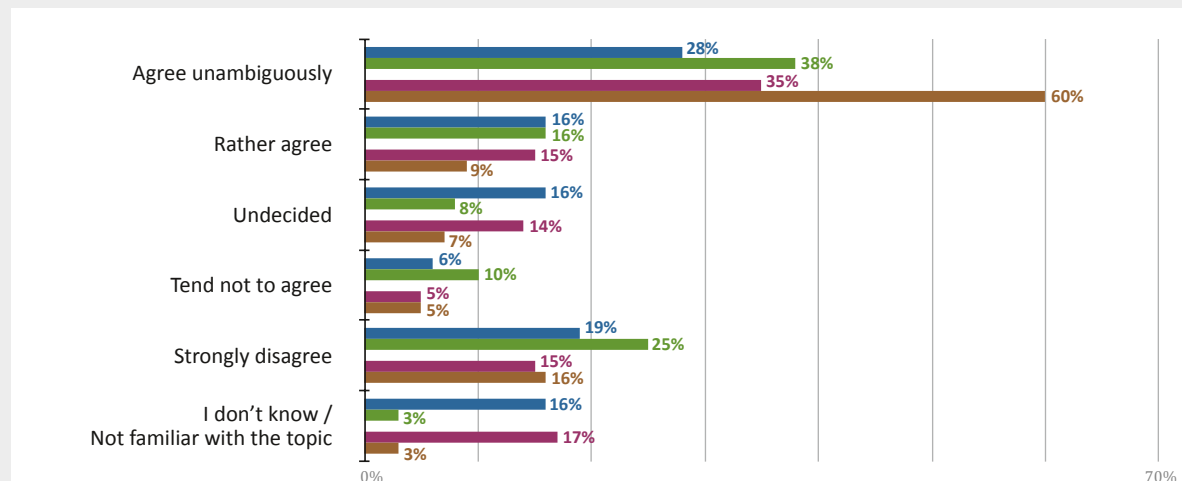
- Strongly agree
 - Overall result: **35%** · Target group (TG): **60%**
- Somewhat agree
 - 15%** · TG: **9%**
- Undecided
 - 14%** · TG: **7%**
- Somewhat disagree
 - 5%** · TG: **5%**
- Strongly disagree
 - 15%** · TG: **16%**
- I don't know / Not familiar with the topic
 - 17%** · TG: **3%**

Results

The survey results offer insights into the sentiment in Germany regarding stem cell and embryo research, though a detailed discussion of the entire results is not possible at this point. In summary, the majority of respondents support research on embryos and embryonic stem cells, although there is always a 20-30% opposition. This opposition does not change significantly even among the specially interested target group in the life sciences, although approval rates are higher due to less indecision. It appears that while more information increases approval, it does not necessarily reduce skepticism. However, a very large group of people overall expects embryonic stem cell research to be highly significant for the development of therapies for serious diseases (65% in the entire group and 69% in the specific target group).

■ Total result ESchG ■ Specific target group ESchG
■ Total result StZG ■ Specific target group StZG

To what extent do you agree with the statement: “The Embryo Protection Act (ESchG) resp. the Stem Cell Act (StZG) should be amended to reflect current developments”?



Regarding demographic differences, the results show that men are more positive towards research with human embryos than women (52% to 39%) and are more likely to favor loosening the legal regulations of the Stem Cell Act (53% to 45%). People from East Germany are more open to research and legal changes than those from the West (49% to 44% and 52% to 49%, respectively). Interestingly, potential voters for the FDP and The Greens are more positive about the research (around 53%) compared to voters for the SPD, Die Linke (about 48%), CDU/CSU (about 45%), and AfD (36%), with the latter predominantly opposing the research at 42%.

The current legal regulations that prohibit the production of embryonic stem cells but allow imports are considered adequate by only about 3-4% of respondents. A clear majority (46% and 64% in the specific target group) supports both the production and import of these cells. About 26% and 29% oppose both.

A majority also advocates for a change in legislation, both for the Embryo Protection Act (44:25% overall or 56:35% in the specific target group) and the Stem Cell Act (50:20% overall or 69:21% in the cross-sectional group). Detailed demographic breakdowns of the results by age, gender, educational level, and other factors can be viewed on the GSCN website under the URL: <https://www.gscn.org/public-resources/gscn-umfrage-survey-2023> in the Excel document GSCN_EmbryonaleStammzellforschung_DE_EN_0823.xlsx and the graphical representation GSCN_EmbryonaleStammzellforschung_0823.pdf.

Conclusion

The survey on stem cell and embryo research in Germany has provided significant insights into public opinion on this controversial topic for the GSCN. The results contribute to enhancing the exchange between science, politics, and society, and provide a solid foundation for informed decisions and future regulations in this area of research.

Text: Daniel Besser



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Photo: GSCN / Arne Sattler

GSCN Mentoring Program:

Fancy a career? But which one?

Do you know how your professional career will continue? Do you have a firm plan - or rather some ideas and a lot of uncertainties? The GSCN offers an annual mentoring program dedicated to supporting and advising career development. Experienced scientists make their expertise available to young scientists in order to jointly develop solutions and perspectives. In addition to meetings with the mentor, there are workshops/trainings on career development paths and meetings with other and former mentees.

The GSCN Mentoring Program has been in place since 2021 and the experience reports are very positive. Not only for the mentees, by the way.

MENTEES



Nina Graffmann

I was keen to take part in the GSCN mentoring for two reasons. Firstly, I hoped that the discussions with my mentor would give me more clarity about my career path and show me how to set up my own research group. On the other hand, this was a unique opportunity for me to exchange ideas and experiences with other young scientists from the stem cell field and to establish a network within the GSCN.

The discussions with my mentor were always very helpful for me. She shared her experience of setting up a research group and the distinct roles within this group with me and she was able to give me valuable tips on setting priorities and developing strategies. Through her questions and comments, I have become more aware of my goals so that I can now work more systematically towards them.

We met three times online and talked for about an hour. The workload was manageable for me. The topics we discussed generally kept me busy all the time, so our meetings were welcome occasions to organize my thoughts. I kept a short log after each meeting so that I didn't lose sight of our results.

Overall, the year was very successful for me, even if my long-term goal is still a long way off. It motivated me during this time to know from my mentor's feedback that I am on the right track or how to get there.

The meetings of the Mentee Club were also an enrichment for me. We meet online every 6-8 weeks with mentees from all years to discuss problems and progress. A senior scientist from the GSCN is also invited to each meeting to report on his/her career path. This, as well as the mid-year workshop, has shown me how much everyone struggles with difficulties that can eventually be overcome if you trust yourself and know where to look for support.

I very much hope that the network of the mentee club will continue to grow in the future and that we can regularly exchange ideas online and at the conferences.

I can only recommend mentoring to everyone and think that it is a good support, especially at the end of the doctoral period or at the beginning of the postdoc phase.



Katia Mattis

After having successfully obtained a PhD from the University of Oxford in 2019 and gained valuable postdoctoral research experience in both biotech and academic environments, I had reached a point in early 2022 where I had to make a key decision regarding my future career. Back then, the GSCN mentoring program came at exactly the right time. The Career Development Team helped me a lot in choosing my mentors; in the end, I even had the privilege of working with two mentors from an international biotechnology company. Even though our quarterly meetings mainly took place online, I always experienced the time with my mentors as extremely productive and motivating. With their support, I redefined my scientific goals and dared to try something new professionally: At the beginning of 2023, I moved from stem cell research in academia to a federal institute where I now perform risk assessments of food. Without the support of my mentors, this step would have certainly not been so easy for me. The openness of my mentors, the mutual appreciation, the commitment and confidentiality, the motivating and encouraging words as well as the impulses, ideas and their feedback have made our mentor-mentee relationship something special for me. I am also very grateful for the many enriching contacts I have made during the mentoring program. I am already looking forward to expanding this network in the future.

In conclusion, I enjoyed the mentoring year so much that I have already applied for a new mentoring program at my current institute. Therefore, to everyone who has the opportunity, take it and participate in the GSCN mentoring program.



MENTORS



Sina Bartfeld

I enjoy being a mentor. For me, being a mentor means that your mentee can come to you with problems, curiosities, and questions, of course in full confidentiality, and we can try together to find solutions that fit for the mentee. Often, this will of course entail that I share my experiences, but not necessarily, we mainly try to find out what is best for the mentee. Does she want to be a group leader, a professor, or lead in an industry position? What are the different paths to being a group leader in Germany? What is the difference in being at a University, Max Planck, Fraunhofer, Leibnitz or Helmholtz Institute? What are the most important assets and skills needed for which path? How will I be evaluated when I apply? What are funding schemes in which I could apply for a grant? But also, personal problems can be a topic. Work-life balance? How does one manage a family and a career in science? Or maybe there is trouble in the team or an issue with the supervisor. With every mentee, there are new topics to discuss. I enjoy being a mentor for three reasons. First, it is simply fantastic to be able to help. Second, the reflection makes me learn and grow as well, knowing the problems, maybe I can contribute better to improving the system. Third, it is payback to my mentors – without them I would not be where I am.



Claudia Waskow

It was a great pleasure to be able to accompany and support a doctoral student over the course of a year in a non-scientific capacity! In the last year of the doctorate, many decisions have to be made: how do I write my thesis, which experiments will be included in the doctoral thesis to make a concrete scientific statement, but also - and of course this is the primary focus of the GSCN mentoring program - what comes next, how can I prepare for it, how and when do I apply, where do I want to go in my career? Dealing with these questions made me aware of their urgency for scientists at this career stage and has (hopefully) led to improved mentoring of the scientists in my department. At the same time, I became more aware of the weaknesses of the life sciences career path in academia, and this led to reflections on how it can be improved at laboratory, institute, national and international levels. I very much hope that my mentoring has helped the doctoral student in important decision-making processes. For me, a learning process has taken place that I would not want to miss. I would be delighted to mentor other scientists in a non-scientific capacity in the future and support their careers.

The one-year GSCN mentoring program is preferably available to GSCN members and BIH scientists who are active in stem cell research and could become members of the GSCN.

Application deadline:	annually end of May
The application includes:	– a letter of motivation – a curriculum vitae – a brief description of your research project – Selection of a mentor from the GSCN mentor list (online) and justification of their choice
Information on acceptance:	early July
Program start:	GSCN Conference
End of program:	GSCN Conference the following year
Any questions?	Mail to stefanie.mahler@bih-charite.de



White rhino: Pregnancy in a roundabout way

Stem cell technologies – a backbone of science-based species conservation



Thomas Hildebrandt speaks of an emotional, overwhelming moment when he announces a milestone for the BioRescue project in front of a group of journalists, supporters, sponsors and consortium members on January 24, 2024. For the first time in the world, he and his team had succeeded in creating a pregnancy in a rhinoceros via a detour: immature egg cells (called oocytes) were retrieved from a southern white rhinoceros in the Belgian zoo "Pairi Daiza" and sperm from a male animal in Salzburg. In the laboratory, the consortium's specialists fertilized the egg with a single sperm using the ICSI method, creating an embryo "in a test tube". This embryo was cryopreserved and months later – freshly thawed –

implanted into a surrogate mother, a southern white rhino in the Ol Pejeta Conservancy in Kenya. "This embryo transfer is completely new territory for rhinos," says Hildebrandt, who developed, tested and refined the necessary methods, veterinary protocols and all the technical equipment for this procedure with many colleagues. What has long been common

practice for humans and is also well established for breeding horses or cows is now also an option for rhinos. „A milestone for species conservation“, says Hildebrandt.

The significance of this breakthrough is huge for the conservation of species on the brink of extinction – or even beyond it. In this case, the already almost extinct northern white rhinoceros: hundreds of thousands of these charismatic and ecologically highly significant her-

bivores once grazed in the savannahs of Central Africa, separated from their southern relatives by the African Rift Valley. Poaching, destruction of their habitat and bloody wars caused the extinction of the northern white rhino in

”

**This embryo transfer
is completely
new territory for rhinos.**

“

the wild. Only two specimens in human care have survived to this day: the female rhino Najin and her daughter Fatu. Two females, some cryopreserved sperm and preserved cell cultures from a dozen individuals are all that remains for science and conservation. The path to salvation is inevitably a detour – via the test tube.



The last two females of the northern white rhino: Najin and Fatu



In order to achieve the long-term goal of the survival of the northern white rhinoceros, Hildebrandt and his colleagues must manage to produce offspring and maximize the genetic diversity of the newly growing population in the long term. To achieve this, they are pursuing three complementary strategies. In the first phase, natural oocytes and sperm are used to create embryos that can then be transferred to surrogate mothers and carried to term. However, the number of oocytes and sperm donors is limited. BioRescue scientists at the Max Delbrück Center in Berlin and Osaka University in Japan are therefore working on developing pluripotent stem cells from preserved tissue samples and obtaining “artificial” oocytes and sperm from these. If successful, this would more than double the number of founder animals in the new population. The scientists have already achieved their first successes at the “cutting edge” of stem cell research: They have been able to generate so-called primordial germ cells from the northern white rhino. The next step is to turn them into oocytes and sperm, which would replenish BioRescue’s dwindling supply.

However, pluripotent stem cells also play an essential role in the third pillar of the ambitious program: together with ancient DNA specialists from Colossal BioSciences, BioRescue is compiling a register of northern white rhino exhibits in natural history museums worldwide. Genetic material can be extracted from these and compared with the alleles in key regions of the genetic material of the stem cells. If museum specimens offer added value in terms of genetic diversity, the pluripotent stem cells will be enriched using gene editing, thereby significantly increasing the diversity and viability of the northern white rhino population.



Vera Zywitzka at the microscope
at the Max Delbrück Center

Leibniz Institute for Zoo and Wildlife Research (IZW) in the Forschungsverbund Berlin e.V.

Evolutionary wildlife research for conservation

The Leibniz Institute for Zoo & Wildlife Research (IZW) is an internationally renowned research institute of the Leibniz Association. With the mission of „understanding and improving adaptability“ it examines evolutionary adaptations of wildlife and its resilience to global change, and develops new concepts and measures for conservation. To achieve this, the IZW uses its broad interdisciplinary expertise in evolutionary ecology and genetics, wildlife diseases, reproductive biology and management

in a close dialogue with stakeholders and the public. The Department of Reproduction Management, headed by Prof Dr Thomas B Hildebrandt, develops cellular techniques for conservation. This new approach is an essential, promising option for highly endangered wildlife. For this purpose, the IZW builds up international networks on „cellular techniques“, including international expert meetings of the world’s leading scientists in the field of „cellular techniques“, and develops new methods of securing and preserving wildlife tissue samples.



Leibniz Institute for Zoo and Wildlife Research
Alfred-Kowalle-Straße 17 · 10315 Berlin
www.leibniz-izw.de



Thomas Hildebrandt is convinced that stem cell-associated technologies form a backbone for the future of the northern white rhino. Without these technologies, it may be possible to yield offspring sporadically, but a permanently viable population would be impossible to achieve. At the same time, stem cell technologies cannot replace all steps of the mission, Hildebrandt concludes. He is looking forward to the moment when the team does not have to laboriously remove each oocyte from Fatu under general anaesthesia. However, the embryo transfer back into a surrogate mother will still be without alternative even when using stem cells to create the embryo. "To have achieved a pregnancy in this way, to have proven that it is possible after years of development and many setbacks, cannot be considered significant enough," says the vet. There it is again, the emotional and overwhelming January 24, 2024, which will mark a turning point in the history of the northern white rhino.

Text: Jan Zwilling



”

To have achieved a pregnancy in this way, to have proven that it is possible after years of development and many setbacks, cannot be considered significant enough.

“

Thomas Hildebrandt



GSCN Annual Report



Board members

Executive Board

According to § 8 paragraph 1 of the statutes of the German Stem Cell Network (GSCN) e.V., the Executive Board (Presidium) consists of the Acting President (Chairwoman), the Senior President (1st Vice Chairman), the President-elect (2nd Vice Chairman), the Treasurer and the Assessor. In the current association year (Sept. 2022 – Sept. 2023), the Executive Board is made up of the following persons:

Acting President (Chairwoman)

Claudia Waskow
(Leibniz Institute on Aging, Jena)
claudia.waskow@leibniz-fli.de

Senior President (1st vice chair)

Hans Schöler (MPI for mol. Biomed.)
h.schoeler@mpi-muenster.mpg.de

Designated President (2nd vice chair)

Heiko Lickert (Helmholtz Zentrum München)
heiko.lickert@helmholtz-muenchen.de

Treasurer

Michael Cross (University of Leipzig)
michael.cross@medizin.uni-leipzig.de

Assessor

Andreas Trumpp (DKFZ Heidelberg)
a.trumpp@dkfz.de



Members of the GSCN Boards (from left): Daniel Besser, Heiko Lickert, Uli Martin, Hans Schöler, Claudia Waskow, Hartmut Geiger, Sina Bartfeld, Michael Cross, Mina Gouti, Ingmar Glauche, Robert Zweigerdt

Extended Board

In the reporting period, the following persons were members of the extended Executive Board, § 9 point 1 of the GSCN e.V. Articles of Association:

Sina Bartfeld (TU Berlin)
sina.bartfeld@tu-berlin.de

Oliver Brüstle (University of Bonn)
r.neuro@uni-bonn.de

Nina Cabezas Wallscheid (MPI Immunobiology and Epigenetics, Freiburg)
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Marieke Essers (DKFZ Heidelberg)
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Michaela Frye (DKFZ Heidelberg)
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Hartmut Geiger (University of Ulm)
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Ingmar Glauche (TU Dresden)
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Mina Gouti (MDC Berlin)
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Anne Grapin-Botton (MPI of Molecular Cell Biology and Genetics)
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Meritxell Huch (MPI of Molecular Cell Biology and Genetics)
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Nico Lachmann (MH Hanover)
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Ulrich Martin (MH Hanover)
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Ana Martin-Villalba (DKFZ Heidelberg)
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Helen Morrison (Leibniz Institute on Aging, Jena)
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Robert Zweigerdt (MH Hanover)
zweigerdt.robert@mh-hannover.de

Ingmar Glauche was elected to the Extended Board. Mina Gouti and Ana Martin-Villalba were re-elected to the Extended Board.

Working group initiators

Scientific working groups

Pluripotency and reprogramming

Micha Drukker (Uni. Leiden)
m.drukker@lacdr.leidenuniv.nl
Hans Schöler
Mathias Treier
mathias.treier@mdc-berlin.de

Somatic stem cells and developmental biology

Thomas Braun (MPI Bad Nauheim)
thomas.braun@mpi-bn.mpg.de
Federico Calegari (CRTD Dresden)
federico.calegari@crt-dresden.de
Ana Martin-Villalba
Elly Tanaka (IMP Vienna)
elly.tanaka@imp.ac.at

Basic, translational, and applied hematopoiesis

Nina Cabezas-Wallscheid (MPI Freiburg)
Timm Schroeder (ETH Zurich, Basel)
tim.schroeder@bsse.ethz.ch
Claudia Waskow

Stem cells in ageing and diseases

Thomas Brabletz (University of Erlangen Nuremberg)
thomas.brabletz@fau.de
Hartmut Geiger (University of Ulm)
Michael Rieger (Goethe University Frankfurt)
m.rieger@em.uni-frankfurt.de
Andreas Trumpp

Stem cells in regenerative therapies	Michael Cross Ulrich Martin Wolfgang Wagner wwagner@ukaachen.de
Stem cells in disease modeling & drug development	Oliver Brüstle Bert Klebl (Lead Discovery Center, Dortmund) klebl@lead-discovery.de Karl-Ludwig Laugwitz (Klinikum r.d.I. TU Munich) klaugwitz@med1.med.tum.de Harald Stachelscheid (Berlin Institute of Health (BIH) at Charité, Berlin) harald.stachelscheid@bih-charite.de
Computational stem cell biology	Georg Füllen (IBIMA Rostock) fuellen@uni-rostock.de Carsten Marr (Helmholtz Zentrum München) carsten.marr@helmholtz-muenchen.de Ingo Roeder (TU Dresden) ingo.roeder@tu-dresden.de
Strategic working groups	
Funding programs and policies	Ulrich Martin N.N.
Career development	Germán Camargo Ortega (ETH Zurich, Basel) german.camargo@bsse.ethz.ch Karin Höhne (Berlin Institute of Health (BIH) at Charité.) karin.hoehne@bih-charite.de Marieke Essers Insa Schröder (GSI Helmholtzz. f. Schwerion.forsch.) i.schroeder@gsi.de
Clinical studies and regulatory affairs	Andreas Kurtz (BCRT Berlin) andreas.kurtz@charite.de Torsten Tonn (Inst. f. Transfus.med. Dresden) t.tonn@blutspende.de Hans-Dieter Volk (BCRT Berlin) hans-dieter.volk@charite.de Zoltán Ivics (Paul-Ehrlich-Institut Langen) zoltan.ivics@pei.de
Public engagement and outreach activities	Tobias Cantz cantz.tobias@mh-hannover.de Ira Herrmann iherrmann@lifeandbrain.com
Ethical, legal and societal aspects – ELSA	Tobias Cantz Sara Gerke (Penn State Dickson Law, Carlisle, US) sgerke@psu.edu Aljoscha Berve (Stem Cell Network.NRW) berve@stammzellen.nrw.de
Patient information (e.g. stem cell therapies)	Ira Herrmann Richard Schäfer (Freiburg University Medical Center, Institute for Transfusion Medicine and Gene Therapy) richard.schaefer@uniklinik-freiburg.de
Technologies in stem cell research	Andreas Bosio (Miltenyi GmbH, Bergisch Gladbach) andreas.bosio@miltenyibiotec.de Sebastian Diecke (Max Delbrück Center, Berlin) sebastian.diecke@mdc-berlin.de

Facts and figures

Meetings

Meetings of the Executive Board

The Executive Board of the GSCN e.V. meets at regular intervals and holds video conferences. The meetings are coordinated and organized by the Central office. In 2023, the following meetings of the Executive Board took place, some of them online:

- 3 Jan. 2023
- 12 Sep. 2023

Meeting of the Extended Board with the Executive Board

- 12 Sep. 2023

General meeting

- 13 Sep. 2023 in Ulm

Overview of members 2023

Total members		452
Natural persons	Full members	282
	Junior members	128
Legal entities	Research institutes	18
	Company > 20 full-time employees	7
	Company < 20 employees full-time	16
	Partner companies	1
Terminations of members in 2023		52
Exclusion of members in 2023		1
Members of the specialist groups		
Scientific working groups	Pluripotency and reprogramming	220
	Somatic stem cells and developmental biology	183
	Basic, translational, and applied hematopoiesis	97
	Stem cells in aging and diseases	187
	Stem cells in disease modeling & drug development	224
	Stem cells in regenerative therapies	231
	Computational stem cell biology	66
Strategic working groups	Funding programs and policies	166
	Career development	170
	Clinical studies and regulatory affairs	136
	Public engagement and outreach activities	76
	Patient information (e.g. stem cell therapies)	36
	Ethical, legal and societal aspects – ELSA	45
Technologies in stem cell research		267

Status 12/31/2023

Member institutes

- Bavarian Research Association ForInter – BayFOR
- BIH Regeneration – BIH Center for Regenerative Therapies (BCRT), Berlin
- Center for Regenerative Therapies Dresden (CRTD)
- German Cancer Research Center (DKFZ), Heidelberg
- Fraunhofer Institute for Biomedical Engineering IBMT, Sulzbach
- Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Hamburg
- Fraunhofer Institute for Production Technology IPT, Aachen
- Fraunhofer Translational Center for Regenerative Therapies (TERM, Würzburg)
- Helmholtz Zentrum München, German Research Center for Environmental Health
- Institute for Reconstructive Neurobiology, University of Bonn
- ISAR Bioscience, Munich
- Leibniz Institute on Aging/Fritz Lipmann Institute (FLI) e.V., Jena
- Leibniz Institute for Zoo and Wildlife Research in the Berlin Research Network
- Max Delbrück Center (MDC), Berlin-Buch
- Max Planck Institute for Heart and Lung Research (MPI-HLR), Bad Nauheim
- Max Planck Institute for Molecular Genetics (MPIMG), Berlin
- REBIRTH Cluster of Excellence, Hannover Medical School (MHH)
- TRON – Translational Oncology at the University Medical Center of the Johannes Gutenberg University

Member companies

- Active Bioscience GmbH
- AMSBIO
- Biolamina
- bio-techne GmbH
- bit.bio
- BlueRock Therapeutics
- Catalent Düsseldorf GmbH
- denovoMATRIX
- Eppendorf AG
- HI-STEM gGmbH
- iota Sciences
- Miltenyi Biotec B.V. & Co KG
- NIPPON Genetics EUROPE GmbH
- OLS - OMNI Life Science GmbH & Co. KG
- PELOBiotech GmbH
- PeproTech GmbH
- Proteintech Europe
- Sartorius
- STEMCELL Technologies
- Stem Genomics
- Takara Bio Europe SAS
- Thermo Fisher Scientific – LSG
- Vita 34 AG

Partner companies

- German Society for Transfusion Medicine and Immunohematology (DGTI) e.V.

General Meeting of the GSCN

On 13 September 2023, the GSCN General Assembly 2023 took place as part of the 11th GSCN Conference with 82 participants. The minutes and the presentation of the General Assembly are available on the GSCN Intranet HumHub in the Membership Documents folder.



Activities 2023/2024

The network

GSCN Conference 2023

The 11th GSCN conference took place in Ulm with 376 participants and was characterized by intensive scientific exchange. From 13 to 15 Sept. 2023, the GSCN met at the University of Ulm with an industry fair with 37 exhibitors, 122 posters, 11 sessions and six international keynotes.

Non-PI Meeting 2023

On 12 Sept. 2023, 14 young scientists met at the Institute of Molecular Biomedicine in Ulm for the non-PI Meeting. In addition to discussing their own scientific work and problems in their day-to-day work, the participants discussed career paths with invited PIs. The organizers Germán Ortega Camargo (Basel), Mona Vogel (Ulm) and Gülce Percin (Jena) had organized the meeting independently and excellently, the GSCN financed an overnight stay and a dinner together in the evening.

Science prizes GSCN Awards 2023

- The [GSCN 2023 Young Investigator Award](#) goes to **Meike Hohwieler** from the Institute of Molecular Oncology and Stem Cell Biology at Ulm University Hospital.
- The [GSCN 2023 Hilde Mangold Award](#) goes to **Anne Grapin-Botton** from the Max Planck Institute of Molecular Cell Biology and Genetics (MPI-CBG) in Dresden.
- The [GSCN 2023 Publication of the Year Award](#) goes to **Ruzhica Bogeska**, ... and **Michael D. Milsom** from the Department of Experimental Hematology, German Cancer Research Center (DKFZ) and HISTEM in Heidelberg, for the publication "Inflammatory exposure drives long-lived impairment of hematopoietic stem cell self-renewal activity and accelerated aging" in the journal *Cell Stem Cell*, Aug. 2022.

Visited worldwide: the hybrid Berlin Stem Cell Club

The Berlin Stem Cell Club (BSCC) is a format of the Dialog Platform for Stem Cell Research since 2022. It is an on-site lecture with an external speaker and a speaker from Berlin from the field of stem cell research, which is also offered as a hybrid lecture. In Berlin, the two talks are followed by a social get-together with drinks and finger food to promote networking on site. The event has also established itself globally: Worldwide participants are interested in the monthly meeting and join online. The line-up of speakers is impressive (see details on the website) and the discussions are also excellent in hybrid form.

The GSCN participated in many successful online and on-site events in 2023 with sessions, public events and financial support:

GSCN at the ISSCR Annual Meeting 2023

The GSCN was very present at the ISSCR Meeting from 14 to 17 June 2023 in Boston. On the one hand, it successfully organized the GSCN Hub on 15 June 2023 in the meeting's exhibition hall as a meeting point for German scientists and other interested colleagues. As a traditional "WunderBar" event, the GSCN invited the German stem cell scientists and friends to a Mexican restaurant for drinks and finger food on 16 June in the evening to continue the networking of the ISSCR – a Wunderbar evening full of successful encounters.

IGDL Conference 2023

The conference of the GSCN partner organization Interdisciplinary Group for Laboratory and Flow Cytometry (IGDL) took place from 22 to 24 March 2023 in Frankfurt. The GSCN participated with a joint session.

DGTI Annual Congress 2023

The GSCN financially supported the annual meeting of the Society for Blood, Cells & Tissues (DGTI) from 21 to 23 Sept. 2022 in Mannheim. Top-class scientists were involved in the Joint Session of the GSCN on Friday, 23 Sept. 2023. The session, chaired by Karen Bieback (Mannheim) and Daniel Besser (Berlin), started with a presentation by Toni Cathomen (Freiburg), followed by Wolfgang Wagner (Aachen), Rabea Dettmer (Hannover) and Jessica Thiel (Dresden).

EuroGCT Workshop 2023 in Copenhagen

The EuroGCT workshop for science communication on 21 Nov. 2023 in Copenhagen was attended by Stefanie Mahler (Communication GSCN). Together with other European partners, she exchanged views on public outreach formats. Particular attention was paid to the topic of how patients in clinical trials and museum exhibitions can succeed better in science communication. In 2023, in addition to a monthly online training course on science communication, there was a series of online meetings on the European programme EuroGCT (Gene and Cell Therapy, <https://www.eurogct.org>), which succeeds the EuroStemCell programme with 47 European partner organizations. EuroGCT deals with the broad field of gene and cell therapy and information material on the subject for patients, relatives and the interested public.

Public scientific event 2023

GSCN Workshop “New developments in disease modeling and drug discovery”

On 16 and 17 Nov. 2023, the GSCN Working Group “Stem cells in disease modeling & drug development” organized a workshop in Bonn with the initiators Oliver Brüstle, Harald Stachelscheid, Bert Klebl and Karl-Ludwig Laugwitz as well as GSCN Managing Director Daniel Besser. The topic of the two-day meeting was new developments in disease modeling and drug discovery. These experts gave presentations at the workshop: Oliver Brüstle (Bonn), Jan Eickhoff (LDC Dortmund), Manuel Grundmann (Bayer AG, Wuppertal), Karl-Ludwig Laugwitz (TU Munich), Sandra Lubitz (Evotec AG, Hamburg), Florian Meier (Boehringer Ingelheim), Jutta Meyer (Bayer AG, Wuppertal), Ole Pless (Fraunhofer ITMP Hamburg, Discovery Research Screening Port), Henrik Renner (Evotec AG, Hamburg), Harald Stachelscheid (BIH/Charité Berlin), Johannes Wilbertz (Ksilink Strabourg, France) and promoted stimulating exchanges, discussions and networking.

PEI-GSCN workshop “The Product is the Process – Is it?”

On 8 Dec. 2023, the GSCN and its partners bbb e.V., Paul Ehrlich Institut (PEI), the German ZLG, Health Capital – Cluster Healthcare Industries Berlin Brandenburg & Berlin Partner organized the one-day workshop “The Product is the Process – Is it?” in Potsdam: Driven by remarkable research successes, innovative therapy and product concepts for advanced therapy medicinal products (ATMPs) were increasingly the focus of interest.

GSCN@BMBF ELSA Symposium

From 9 to 10 Oct. 2023, the BMBF organized a symposium on the topic “Human embryos in medical research: Taboo?-Justifiable? Opportunity? Daniel Besser was involved in the preparation of the symposium and gave a presentation followed by a discussion.

GSCN travel grants 2023

• EMBO workshop: Gene regulation in neural fate decision

07 – 10 September 2023, Alicante Spain
Katherina Tavernini (IMBA, Vienna, Austria)

• ISEH 2023 New York City

17 – 20 August, 2023
Germán Camargo Ortega (ETH Zurich, BSSE Basel)
Nina Henning (Leibniz Institute on Aging / FLI, Jena)
Marius Kulp (Goethe University Hospital, Frankfurt)

• XVI European Meeting GLIA 2023, Berlin

08 – 11 July 2023
Catarina Fernandes (University of Mainz)

• ISSCR 2023, Boston

14 – 17 June 2023
Lika Drakhlis (MH Hanover)
Fawaz Saleh (MH Hanover)
Johanna Siehler (Helmholtz Center Munich)
Marcel Tisch (University of Innsbruck)

• Gordon Research Seminar & Conference: Myogenesis, Renaissance Tuscany II Ciocco, Italy

10 – 16 June 2023
Xhem Qabrati (ETH Zurich)

• Gordon Research Conference: Pancreatic Diseases, Renaissance Tuscany II Ciocco, Italy

30 April – 5 May 2023
Andrea Ruiz Sarvari (DKFZ Heidelberg)

Science communication

Public relations and public outreach present the tasks and work of an organization as targeted information for various groups. In the case of stem cell research, for the GSCN these are political decision-makers, students, patients and the interested public.

UniStem Day 2023

UniStem Day in Germany took place in 13 cities on 10 March 2023. The focus was on NRW with 10 cities and 17 institutes as well as Berlin, Dresden, Bavaria and Jena. The Stem Cell Day for schoolchildren is dedicated to communicating current stem cell research, meeting scientists and discussing life sciences, ethics and various careers in research.

Ulm 2023 public event

On 15 Sept. 2023, the GSCN organized a public event at the Ulm Adult Education Centre with short videos and a panel discussion on the topic of “Responsible for growth, diseases and new therapies: Stem cells – the all-rounders among cells”. Hartmut Geiger (University of Ulm, specialist in stem cells and ageing), Alexander Kleger (Ulm University Hospital, specialist in organoids and pancreatic stem cells), Ana Martin-Villalba (German Cancer Research Center DKFZ, Heidelberg, specialist in neural stem cells) and Katja Schenke-Layland (University of Tübingen, specialist in the development of tissue engineering / biomaterials) took part in the panel discussion. The moderator was Stefanie Seltmann.

Collaboration in the thematic volume “Gene and Cell Therapy 2.023 – Research, Clinical Application and Society”

In autumn 2023, Daniel Besser organized and edited two chapters of the thematic volume “Gene and Cell Therapy 2.023 – Research, Clinical Application and Society” of the AG Gentechnologiebericht. The book provides an up-to-date overview of the state of gene and cell therapy in Germany and was produced with the support of the German Society for Gene Therapy (DG-GT) and the GSCN.

Poster exhibition “Cells for life”

The modular and interactive poster exhibition “Cells for Life” or “Stem Cells for Life” with its digital “information rooms” was used on various occasions and at various locations and institutes in 2023.

GSCN teaching material “Stammzellen-verstehen.de” and “Understanding-stemcell.info”

The GSCN's teaching material is available in both languages for the general public. They are particularly popular with teachers and biology teacher training courses.

GSCN video about pancreatic organoids

In 2022, the GSCN produced a video with Alexander Kleger from Ulm University Hospital about pancreatic cancer, pancreatic organoids and the question of what these organoids can find on a pig's bladder. The film is available to the general public both on the GSCN website and on the GSCN YouTube channel.

Outstanding journalist contacts

In 2023, the GSCN continued to be requested by journalists for interviews and background discussions throughout the year. Daniel Besser was a sought-after interview partner both on television (RBB, Deutsche Welle) and for newspaper articles – but especially for background discussions for journalists as a classification of stem cell research in relation to scientific and ethical issues.

Further GSCN events

- Event on stem cells for medical students at the Charité on 8 June 2023, 3 Nov. 2023 and 14 Dec. 2023.
- Lecture to schoolchildren on 9 Jan. 2024 at the Planetarium Berlin

Social Media GSCN

The GSCN uses many channels for its communication: The GSCN reaches its members and interested followers via the Humhub membership platform, the newsletter and the SM channels Twitter, LinkedIn, the GSCN website and Facebook. Patients also get in touch all year round and seek assessments of clinical trials and the prospects of stem cell therapies.

On our own behalf

The office of the German Stem Cell Network moved from its location at the MDC in Berlin-Buch in mid-January 2024. Managing Director Daniel Besser, Project Manager Antje Veldhues and Communication Officer Stefanie Mahler have moved into the new offices in the Rahel-Hirsch-Center in Berlin Mitte.

Their new contact details are:

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Finances

The GSCN is a non-profit association and was financed in 2023 by **membership fees and the joint dialog platform for stem cell research at the Berlin Institute of Health (BIH) at Charité**. According to § 4 of the GSCN statutes, the amount of the membership fees is regulated in a membership fee regulation issued by the General Assembly. The membership fees are listed on the GSCN membership form.

The financial year is the calendar year. Membership fees are due at the beginning of the financial year. The Executive Board is responsible for preparing the annual financial statements of the association and presenting them to the General Meeting. The detailed **presentation of the finances** takes place at the general meetings.

It should be noted at this point that GSCN membership can be terminated simply and informally by sending an email to the GSCN office (office@gscn.org). The letter must be received by November 30 of the year in order to cancel membership for the next financial year (from January 1).



GSCN

GermanStemCellNetwork