



GSCN

GermanStemCellNetwork

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of the GSCN

2025/26

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Stem Cells: Next-Generation Therapies

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*Fluorescence image of human ileal organoids. ZO-1 is labeled green,
and proliferating cells are labeled red.*

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Welcome Note

**Dear members of the
German Stem Cell Network,
dear reader,**

Stem cell research is a central foundation of modern biomedical research. It opens up new perspectives for understanding development processes, pathogenesis and regeneration, and forms the basis for innovative therapeutic approaches. For the Federal Ministry of Research, Technology and Space (BMFTR), stem cell research is a strategically important field where scientific excellence, technological innovativeness and social responsibility converge in a special way. The German Stem Cell Network (GSCN) has exemplified this aim for a great many years.

In the past year, German stem cell research has once again demonstrated what it can achieve. More fundamental mechanisms of embryonic development and cellular dormancy have been decoded at the molecular level. Reproducible brain organoids now enable detailed modeling of neurodegenerative diseases such as Huntington's and allow the identification of novel candidate drugs, for example against mitochondrial disorders. Significant progress has also been made in translational research: Prototype autologous cell therapies for Parkinson's patients are under development and iPS cell-based screening approaches have revealed new therapeutic options for rare diseases. These results show that German stem cell research strengthens both basic research and the bridge to clinical application.

With the National Strategy for Gene and Cell-based Therapies, the BMFTR has created a clear strategic framework to continue developing this dynamic field in a targeted and sustainable manner. The strategy aims to interlink research, clinical application, regulatory processes and industrial value creation coherently and thus to position Germany as a strong and reliable centre for gene and cell therapies. Through the establishment of the Berlin Center for Gene and Cell Therapies, powerful research and development infrastructures will be available in particular to start-ups, translational projects will be consolidated and clinical trials accelerated. This will create an environment in which scientific excellence can be transferred to medical practice more quickly and reliably – for the benefit of patients and to strengthen Germany's position as a centre for innovation.

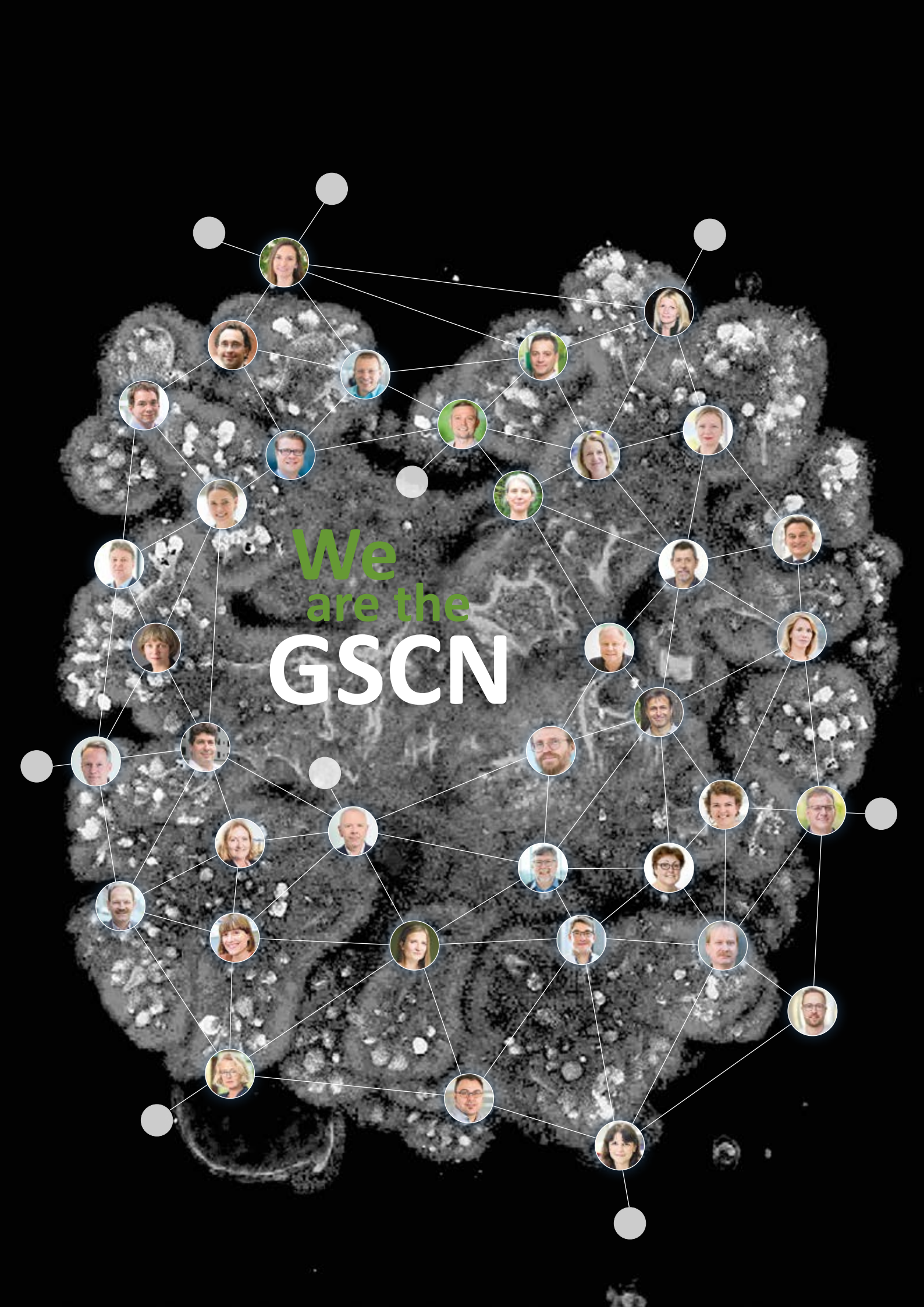


The GSCN assumes a key role in this context. As a national and international network, it strengthens scientific exchange, promotes young talent and supports interdisciplinary collaboration between basic research, clinical practice, ethics and law. In stem cell research in particular, such a network is a crucial prerequisite for quality, transparency and societal acceptance.

As Parliamentary State Secretary at the BMFTR, it is particularly important to me to actively support dialog between science, politics and society. Reliable funding structures, strong research infrastructures and a clear ethical and regulatory framework provide the basis for responsibly developing new gene and cell therapies and successfully bringing them into practice. The GSCN is an indispensable partner in this.

I thank all the scientists and other dedicated actors involved in the network for their excellent work and valuable input and impetus for the further development of stem cell research in Germany.

Matthias Hauer, MdB
*Parliamentary State Secretary
Federal Ministry of Research, Technology and Space*

The image features a network diagram overlaid on a grayscale brain scan. The network consists of approximately 30 circular nodes, each containing a portrait of a person. These nodes are interconnected by a web of thin white lines, representing relationships or collaborations. Some nodes are also connected to isolated gray circles. The background is a detailed brain scan showing various anatomical structures.

**We
are the
GSCN**

Foreword

The future of cell therapies is taking shape with increasing clarity—scientifically, technologically, and clinically. This issue of the GSCN Magazine therefore deliberately places this topic at its center. It opens with an in-depth interview on the significance of human embryonic stem cells (hESCs) and induced pluripotent stem cells (iPSCs), illustrating how fundamental biological insights are paving the way for novel therapeutic strategies. Complementing this is an article with a comprehensive overview of current clinical trials in Parkinson's disease, epilepsy, macular degeneration, diabetes, and the development of cardiac patches. Together, these contributions underscore the remarkable speed at which translation toward clinical application is advancing.

Another central feature explores hypoimmune cells - an area with the potential to fundamentally transform regenerative medicine. The prospect of universally applicable cell products represents a possible paradigm shift, opening new therapeutic avenues while simultaneously underscoring the need for clear and robust regulatory frameworks.

Translational research in Germany is gaining significant momentum. This progress is reflected in articles on the startup support program GeneNovate® and the **BIH Clinical Incubator**. Both initiatives actively facilitate the transition from concept to product, promote spin-offs, and integrate clinical expertise early in the development process. In doing so, they capture the dynamism of stem cell research within a young and innovation-driven biotech landscape.

At the same time, the reality of translation in Germany remains shaped by regulatory constraints. The scientific community operates within a complex framework of laws, approval procedures, and jurisdictions that often slow innovation. This discussion is essential—not only to identify barriers but to collaboratively develop responsible pathways that enable scientific progress while safeguarding patient safety. The contributions in this issue make clear how closely intertwined scientific vision and regulatory reality truly are.



On a personal note, the past year has been a special one for me, as my term as President of the GSCN draws to a close. The **GSCN Conference in Munich** was a particular highlight: scientifically outstanding, internationally connected, and sustained by a strong and committed community. It demonstrated how vibrant, creative, and collaborative stem cell research in Germany has become.

Looking ahead, I am eager for the upcoming **GSCN Conference in Berlin**, which will once again provide a forum for exchange, inspiration, and collaboration - while also marking the beginning of a new chapter in scientific partnership.

This Annual Magazine once more demonstrates how far we have come - and how much potential still lies ahead. For all of these developments, I would like to express my sincere gratitude to the GSCN community for its tireless dedication, its excellence, and its ongoing contribution to ensuring a strong future for stem cell research in Germany.

Heiko Lickert
Active GSCN President

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Conference Report 2025

The 13th GSCN Conference

15 – 17 October 2025 | Helmholtz Munich,
Conference Center Neuherberg

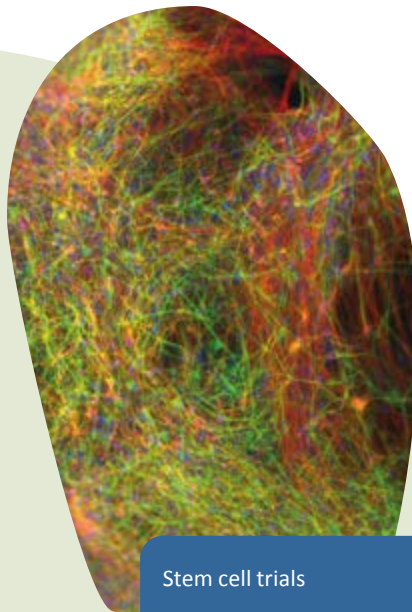
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The GeneNovate® Entrepreneurship Program

It takes a whole village to bring a medical product to patients

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**HI-STEM, the Heidelberg Institute for Stem Cell Technology and Experimental Medicine**

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The cell is not the problem – it's the law

Embryonic or induced Pluripotent Stem Cells – A defining question for the future

Which pluripotent stem cell sources—human embryonic stem cells (hESCs) or induced pluripotent stem cells (hiPSCs)—will prove decisive for future clinical applications? In light of rapid advances in ophthalmology, cardiac therapies, Parkinson's disease, and diabetes, the question of which cell types are best suited for clinical trials and eventual patient care has once again come to the forefront. The aim of this discussion is to capture diverse scientific, regulatory, and ethical perspectives on this defining question for the future.



OLIVER BRÜSTLE

tion (DFG). This step triggered a far-reaching debate at the time—covering ethical, regulatory, and, of course, scientific aspects. In the early 2000s, this led to the German Stem Cell Act, which in turn is based on the Embryo Protection Act of the early 1990s. Today, hESC lines can be used in Germany, but only as imports; their derivation within Germany is still prohibited. Since 2007, human induced pluripotent stem cells (hiPSCs) have also been available and increasingly established themselves as a potential alternative during the 2010s.

Against this background, how do you assess today the use of hESCs compared with hiPSCs in clinical development, particularly with regard to concrete therapeutic applications? What advantages and disadvantages do you see?

Oliver Brüstle: Looking back, it has become clear that the therapeutic approach using human pluripotent stem cells was the right one: both hESC- and hiPSC-based therapies have now reached clinical trials. This makes it all the more difficult to understand why German research continues to be restricted by the regulation of hESCs with the cut-off date.

This interview with **Oliver Brüstle** (Institute of Reconstructive Neurobiology, University Hospital Bonn, and founding president of the GSCN), **Wolfram-Hubertus Zimmermann** (Institute of Pharmacology and Toxicology, University Medical Center Göttingen), and **Heiko Lickert** (Institute of Diabetes and Regeneration Research, Helmholtz Munich) was conducted by **Daniel Besser** (Managing Director of the German Stem Cell Network, GSCN).

GSCN: *Oliver Brüstle, around 25 years ago you were the first in Germany to propose conducting research with human embryonic stem cells (hESCs) derived from surplus embryos from IVF (in vitro fertilization) procedures, and you submitted a corresponding grant proposal to the German Research Founda-*

“Question about better cells for clinical trials remains unanswered”

Which cell source is “advantageous,” however, remains an open question. Using Parkinson's disease as an example, both hESC- and hiPSC-based studies have so far primarily demonstrated safety, without specific risks such as teratoma or tumor formation. Both cell types have successfully passed early clinical phases, and initial signals of efficacy are cautiously encouraging, even though statistically robust data are still lacking.



HEIKO LICKERT

The advantages and disadvantages discussed so far are largely theoretical: hESCs are considered genetically unmodified and therefore more “pristine,” whereas hiPSCs score points for easier availability, donor banks, and the principal option of autologous therapies. Which of these differences will ultimately prove clinically relevant cannot yet be reliably assessed due to the still limited patient numbers.

GSCN: *Wolfram Zimmermann, you are currently conducting the first clinical trial in Germany investigating the therapeutic use of stem cell–derived cardiomyocytes and stromal cells in the heart—the so-called BioVAT-HF study with cardiac patches, supported by the German Centre for Cardiovascular Research (DZHK)—using hiPSC as the starting material. What considerations at the time led to the decision to use hiPSCs?*

Wolfram-Hubertus Zimmermann: Our early work was based on hESCs, as hiPSCs did not yet exist at that time. It later became clear, however, that virtually all procedures could be transferred almost identically to hiPSC. The decisive question then became how such developments could be translated in Germany not only into clinical trials, but ultimately into routine patient care.

With hESCs, there is considerable uncertainty in this regard: it remains unclear whether products derived from these cell types would ever be permitted for routine clinical use in Germany. This makes clinical studies ethically problematic and financially risky, as investors require a realistic perspective for regulatory approval.

The decision therefore favored hiPSCs—not for scientific reasons, but for ethical, regulatory, and economic ones. As long as the cut-off date regulation and the associated legal risks persist, the translation of hESC-derived products into clinical practice is not realistically feasible.

GSCN: *How do you assess the international context in this regard? Could pressure from countries such as the United States or the United Kingdom eventually challenge Germany’s position? Is there a risk that Germany could fall behind because of its regulatory framework?*

Wolfram-Hubertus Zimmermann: I do not believe that the world closely aligns itself with German regulatory details, nor that other countries will allow their paths to be dictated. International pressure may increase, but relying on that alone would be a lengthy process. Globally, more than a hundred studies and over a thousand treated patients already point to an overall encouraging development—even though we are still in early clinical phases.

In Germany, however, the path to the clinic for domestically developed hESC-based products is hardly foreseeable, whereas hiPSCs offer significantly better prospects. That said, if a major pharmaceutical company were to generate convincing phase III data with hESC-derived products, approval would also have to be considered in Germany—legally, this would be possible via import from abroad. The disadvantage therefore lies less with patients than with researchers, companies, and Germany as a location for innovation: here, the development pathway for hESCs is effectively blocked, pushing research and investment abroad. Moreover, once a company has committed to a particular cell line, switching at a later stage is practically very difficult and also hard to justify from a medical perspective.

“There is considerable uncertainty surrounding human embryonic stem cells”

GSCN: *Heiko Lickert, in Munich a clinical trial is being planned using β -cells derived from pluripotent stem cells to treat type 1 diabetes. Which scientific, regulatory, and practical criteria guide the decision between using hESCs or hiPSCs in this context?*

The US-based company Vertex is pursuing an hESC-based approach to diabetes and is now also active in Dresden. Does this mean that β -cells derived from hESCs are already being used in Germany?



WOLFRAM-HUBERTUS ZIMMERMANN

Heiko Lickert: The question of whether hESCs or hiPSCs are the better source for clinical applications remains open. Numerous studies using both cell types are ongoing worldwide; hiPSCs tend to dominate in Asia and also in Europe, whereas hESC-based approaches are more prevalent in the United States, in part due to the availability of lines that meet Good Manufacturing Practice (GMP) standards. One key unresolved issue is whether the reprogramming process involved in generating hiPSCs could lead to clinically relevant mutations in the long term—so far, however, neither hESCs nor hiPSCs have shown typical risks such as teratoma or tumor formation.

In the field of diabetes, hESC-based studies, such as those conducted by Vertex, have shown promising signals of safety and efficacy, even though long-term data are still lacking. Autologous hiPSC-based approaches do exist, but so far they rely on very small patient numbers.

In Germany, the main obstacle lies less in the science than in regulation and funding: research and translation involving hESCs are subject to strict legal restrictions and are, in practice, scarcely eligible for funding. As a result, realistic perspectives for clinical development and investment are lacking, prompting many projects to shift toward hiPSCs. Without adjustments to the legal framework, Germany therefore risks losing international competitiveness.

GSCN: *Germany's position has a strong impact on European funding instruments, and this stance in turn directly influences the private sector. Professor Zimmermann, you have already noted that it becomes difficult to bring private investors or companies on board when the overall environment is effectively opposed to hESC-based approaches. Is this a central problem?*

Wolfram-Hubertus Zimmermann: In Germany, funding for hESC-based translation is practically impossible. Private investment in biomedical research is already significantly lower in Germany than in the Anglo-American world, and legal restrictions effectively exclude an entire field from funding. US investors would also tie their engagement to relocating development activities abroad—a clear disadvantage for Germany as a research and innovation location. For this reason as well, the current regulation with a cut-off date should be reconsidered.



GSCN: *It is becoming increasingly clear that Germany needs to adapt its regulatory and legal framework to the international dynamics. Professor Brüstle, how do you see this? This was essentially one of your core demands many years ago. Has this need become even more urgent in light of current clinical developments?*

Oliver Brüstle: In Germany, two political guiding principles essentially stand in opposition in the field of stem cell research: on the one hand, a very high ethical and moral standard, particularly regarding the handling of embryos; on the other hand, a clear commitment not to deny patients potentially effective therapies. German legislation has attempted to strike a compromise between these two demands. As a result, the medical use of hESCs has not been completely excluded, but the innovation and production perspective has been hampered by excessive restric-

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.

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Institut für Rekonstruktive
Neurobiologie



tions. This is particularly evident in the cut-off date regulation of the Stem Cell Act: cell lines that were generated abroad in the past may be imported and used for research in Germany, even if their derivation would be legally prohibited domestically. Politically, this is convenient, as it allows one to argue that therapeutic research is being enabled while ethically controversial steps are shifted abroad. At the same time, however, this construction also means that economic value creation, production expertise, and industrial development take place outside Germany.

A second key factor is the investment and reimbursement perspective. Cell therapies based on human pluripotent stem cells—especially hESCs—will be very expensive. As long as there is no clear evidence of clinical superiority over established therapies, it remains uncertain whether and to what extent such treatments will later be reimbursed. This uncertainty deters investors. At present, science can only outline cautious scenarios, but cannot provide robust forecasts. The result is a kind of pincer movement: on the one hand, a political environment that avoids ethically sensitive debates and unduly restricts the legal space for such future technologies; on the other hand, an economic environment that remains hesitant due to regulatory uncertainty and the lack of clear reimbursement frameworks.

When major industry players such as Novo Nordisk or Takeda recently withdraw from the field of stem cell-based therapies or relocate their activities abroad, this effect is further reinforced. Policymakers interpret this as a sign of insufficient maturity of the field, which in turn encourages further hesitation. Thus, a downward spiral emerges, driven by political caution, investment reluctance, and a lack of industrial momentum.

A real impetus for change will therefore likely come from outside—through convincing international clinical successes that are so compelling that German policymakers can no longer avoid addressing the issue. At that point, market-ready “off-the-shelf” products derived from hESCs could establish facts and increase pressure to act. Especially in such a phase, however, it would be important for Germany to regain confidence in its own scientific expertise and to make a clear political commitment not merely to be a user of these technologies, but an active shaper and innovation hub in this field.

GSCN: *With the new hypoimmune approaches (see article p. 37), a fundamentally new scenario is emerging: pluripotent stem cell lines could be modified in such a way that they become universally applicable—for example by knocking out HLA genes and additionally expressing protective signals (“don’t-kill-me” mechanisms) such as CD47. Such cells could potentially be used broadly without immunosuppression. With only a few standardized cell lines, a large number of patients with different diseases could be treated—an approach that would be highly attractive not only medically, but also economically.*

This raises a strategic question: should these hypoimmune products be developed on the basis of hiPSCs, or should already GMP-certified hESC lines be used to generate a small number of genetically adapted “off-the-shelf” variants? At the same time, these approaches bring a new dimension of genetic modification into focus—and with it the question of how we should address this from a regulatory and ethical perspective.

Wolfram-Hubertus Zimmermann: The key question is whether hypoimmune cell products can truly function without immunosuppression—so far, there are no robust data to support this. The approach is promising, but important tools for reliable clinical translation are still lacking, such as robust methods to monitor graft survival. As a result, initial studies using hypoimmune cells will likely still need to be conducted under immunosuppression.

Experience from xenotransplantation also shows that even extensively genetically modified cells do not reliably prevent rejection responses. In parallel, the potentially increased tumor risk of such cell lines must be considered. Overall, we are still at a very early stage: any reduction in immunosuppression would already represent a major advance, but complete avoidance cannot currently be predicted. What matters is a stepwise, clinically sound approach without exaggerated promises.

“Innovation prospects are being held back in Germany”

Heiko Lickert: A good example is the approach pursued by Sana Biotechnology in Seattle, USA. There, primary islet cells obtained post mortem were rendered immune-evasive through knockout of MHC class I and II molecules and insertion of the CD47 signal. These modified islets were transplanted into a patient with type 1 diabetes and, according to reports, were neither allogeneically nor autoimmunely rejected for one year despite the absence of immunosuppression—an impressive result.

Sana is not yet working with hESCs, but plans future Investigational New Drug (IND) application studies to transfer this concept to pluripotent stem cells and to generate β -cells as well as hypoimmune off-the-shelf CAR-T and CAR-NK products. Century Therapeutics in Philadelphia is pursuing similar strategies based on hiPSCs. Overall, the most dynamic translation is currently taking place in the field of genetically modified immune and stem cell therapies.

A true clinical breakthrough, however, will only be achieved if immunosuppression can be significantly reduced or avoided altogether. Studies such as those by Vertex show promising effects, but effectively remain “rescue therapies” as long as patients require lifelong immunosuppression—problematic from a clinical, economic, and reimbursement perspective. Without convincing additional benefit, there is a risk of a second valley of death after market entry.

This is precisely why hypoimmune concepts are so attractive. At the same time, extensive genetic modifications naturally increase the potential risk of tumor formation and the danger of immunological “invisibility” of transformed cells. Safety mechanisms such as so-called suicide genes will therefore be essential. The trend is clearly moving toward combined gene and cell therapies with multiple built-in safety layers. In the long term, the development of a broad and economically highly attractive market for cell replacement therapies could be significantly advanced through the use of hypoimmune yet safe off-the-shelf solutions.

Oliver Brüstle: With regard to immunosuppression in neural cells, I would like to add that we are dealing with a special case here: due to the blood–brain barrier, the central nervous system is considered an immune-privileged organ. It has been shown, for example, that transplanted allogeneic dopaminergic neurons can survive in the brains of patients with Parkinson’s disease for more than twenty years—even after discontinuation of initial immunosuppression. Nevertheless, immunological matching or genetically optimized, immunologically “invisible” cells would be desirable, particularly when transplanting non-neuronal cell types into the brain.

“A downward spiral of political skepticism, reluctance to invest, and a lack of industrial momentum”

GSCN: *How do you assess potential issues of ownership, patents, and informed consent in the comparison between hESCs and hiPSCs? For example, what happens if an hiPSC line is derived from the tissue of a living donor who later demands financial participation or seeks to prohibit its use—analogue to the case of the HeLa (Henrietta Lacks) cells?*

Oliver Brüstle: One must distinguish between patents and freedom to operate (FTO). A patent is a time-limited monopoly right that protects inventors and investors from unfair competitors who might otherwise copy and commercially exploit developments that have required many years and substantial financial investment. FTO exists when no third-party patent claims stand in the way of one’s own invention and market strategy.

The patentability of products and processes based on hESCs remains controversial. Years ago, we filed a patent for the differentiation of ESCs into neural cells. This process did not concern the derivation of hESCs but started from already

existing hESC lines. However, because hESCs were originally derived from surplus fertilized oocytes—biologically speaking, an early embryo—the European Court of Justice rejected patentability, arguing that a human embryo in the broadest sense could form the basis of a therapy with economic value. In my view, this was an ultra-restrictive decision.

The legal situation is different for hiPSCs. Here, critical questions concern potential participation claims or withdrawal demands by donors, but these can be addressed through clear informed consent procedures at the time of donor recruitment. One ongoing challenge is that, due to increasingly detailed genetic characterization of cell lines, it is becoming more difficult to guarantee permanent donor anonymity. However, this is not specific to hiPSCs, but applies to anonymous cell donations more generally.

The situation becomes complex again in patent law: in Europe, new procedures often have to be limited to hiPSCs, since claims referring to hESCs are difficult to enforce. Internationally, this leads to a fragmented protection landscape—with patent protection available outside Europe but restricted claims within the EU.

GSCN: *There would certainly be much more to discuss, but as key points we have highlighted that the strict legal regulation in Germany restricts both the scientific field and the willingness to invest economically to an extent that is already having negative effects, both now and in the long term. How policy-makers can be motivated to intervene in a timely manner and to advance the necessary legislative changes remains a major challenge—also for us as researchers.*

And which cell lines—hESCs or hiPSCs—will ultimately prove decisive in Germany is less a scientific question than a political and economic one.

Thank you all for this stimulating discussion.

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)



Foto: Peer Schröder

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GSCN News 2025/26

GSCN Stem Cell Club (GSCC) – a growing hybrid forum

The GSCN Stem Cell Club (GSCC) continues to thrive. The hybrid format - two on-site lectures at TU Berlin followed by a get-together, combined with live online streaming of the talks and discussion - has been very well received. On the first Thursday of each month (with occasional exceptions), lively discussions and meaningful exchange take place, with strong international participation from the online audience. Stay tuned and join us - either in person or virtually - because GSCC meets every first Thursday of the month. Announcements, speakers, and the Zoom link are always available on the [GSCN website](#).



GSCN on Tour in Leipzig, Hannover, Cologne/Bonn, and Aachen

In 2025, GSCN was actively on the road across Germany. Daniel Besser (Managing Director) and Stefanie Mahler (Communications Manager) initiated four local stem cell symposia:

- 31 March 2025: Leipzig, with Michael Cross, Ulrike Köhl, Zoltan Ivics, and many additional presentations
- 2 April 2025: Hannover, with Ulrich Martin and other outstanding speakers
- 24 Nov. 2025: Cologne/Bonn, featuring 12 thematically diverse presentations from both cities, chaired by Kurt Pfannkuche and Oliver Brüstle
- 26 Nov. 2025: Aachen, chaired by Wolfgang Wagner, with a series of exciting scientific studies

The “GSCN on Tour” symposia follow a consistent concept: bringing together the local stem cell community for a full day, including participation from a GSCN industry partner. A get-together and speakers’ dinner provide ample opportunity for networking and discussion. The shared conclusion from all four symposia: it is both valuable and refreshing for local researchers to connect and exchange ideas—and many are surprised to discover colleagues working on related topics right in their own cities, outside the spotlight of major conferences. GSCN continues to advance networking at every level.

GSCN ATMP Workshop in Potsdam in November 2025

ov. 2025, GSCN co-hosted the workshop “The Product is the Process – Is It? Manufacturing and Translation of ATMPs and Tissue- & Cell-Based Products” in Potsdam. In collaboration with the Paul-Ehrlich-Institut (PEI) and other partners, GSCN organized an informative day for approximately 150 participants. The program included a keynote lecture by Heiko Lickert (Munich) on stem cell therapy for diabetes, along with additional presentations from academia, regulatory authorities, industry, and translational research focused on advanced therapy medicinal products (ATMPs). Under the leadership of Ralf Sanzenbacher (PEI), the workshop will become a permanent fixture in the GSCN calendar. The next [ATMP Workshop](#) in Potsdam will take place on 02 Dec. 2026.

Computational GSCN Workshop in Berlin and Munich

Within the GSCN workshop series, the “Computational Stem Cell Biology” working group organized two outstanding workshops titled “Computational Single-Cell Genomics for Stem Cell Biologists.” From 7 - 9 April 2025, Sara Jiménez and Tim Treis from the laboratory of Fabian Theis at Helmholtz Munich provided beginners and advanced participants in Berlin with in-depth training in data analysis and quality control, dimensionality reduction, cell type annotation, trajectory analysis, and multimodal integration using both R and Python.

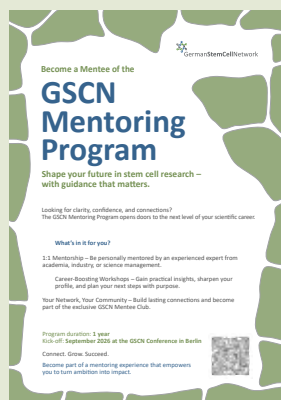
Sara Jiménez and Francisca Drummer also offered this workshop in advance of the 13th GSCN Conference in Munich, where it again met with enthusiastic response. Due to high demand, an expanded workshop - divided into beginner and advanced tracks - is planned for 2026 in Berlin ([see the GSCN website: Conferences & Events → Working Group Workshops](#)).

GSCN Mentoring Program – Apply Now!

For several years, the GSCN Mentoring Program has offered a tandem format in which five early-career researchers are paired each year with experienced mentors for a full year of guidance. Mentors provide advice and perspective to support informed

career decisions. The program also includes workshops and regular Mentee Club meetings with alumni. To date, the program has 25 alumni. The application deadline for the 2026 Mentoring Program is 31 May 2026.

More information is available on the [GSCN website under Scientific Resources → GSCN Mentoring Program](#).





Successful Non-PI Meeting in Munich

One day before the GSCN Conference 2025 in Munich, 24 early-career researchers gathered for the non-PI Meeting 2025. Participants from across Germany met to discuss their research, including experimental challenges, work environments, and career choices. Two invited guests from industry shared their perspectives on career development: Sandra Lubitz from Evotec and Katharina Debowski from StemCell Technologies discussed their professional paths and offered insights into career planning and development within the field of stem cell research. The meeting concluded with a relaxed group dinner. *The 2026 Non-PI Meeting will take place on 08 Sept. 2026 in Berlin.*



PluriCore Network Meeting 2025 – Exchange on Reprogramming, Gene Editing, and QC

On 4-5 Dec. 2025, the 8th Annual PluriCore Network Meeting took place at the Rahel Hirsch Center of the Berlin Institute of Health (BIH) at the Charité – Universitätsmedizin Berlin in Berlin. The meeting focused on cross-site and cross-institutional exchange on practice-oriented workflows related to iPSC reprogramming, documentation, differentiation and organoid models, genome editing, as well as cell characterization and genomic stability.

A total of 33 colleagues from numerous institutions participated, including Berlin Institute of Health / Charité – Universitätsmedizin Berlin and the Max Delbrück Center for Molecular Medicine (Berlin), University Medical Center Göttingen, Hannover Medical School, university hospitals in Bonn, Heidelberg, and Aachen, Helmholtz Munich, Heinrich Heine University Düsseldorf / Leibniz Research Institute for Environmental Medicine in Düsseldorf, as well as international partners from Leiden, Lund, and Vienna.

The first day began with a session on reprogramming and

digital documentation. The second day focused on neural 2D and 3D models, including aged organoid models, MEA-based approaches, neuronal differentiation, and the autonomic nervous system, as well as gene editing. Topics included strategies for the detection of large on-target events, prime editing (PE) modulators and screening approaches, virus-like particle (VLP) technologies, and immune-evasive safety concepts.

In the QC and stability session, discussions covered DNA methylation-based characterization, services for genetic integrity testing (e.g., using droplet digital PCR, ddPCR), as well as the impact of passaging methods on genomic integrity and the further development of tools for monitoring genomic stability.



GSCN Scientific Awards 2025

The **GSCN 2025 Young Investigator Award** was presented to [Aydan Bulut-Karslıoğlu](#) of the Max Planck Institute for Molecular Genetics in Berlin.

The **GSCN 2025 Hilde Mangold Award** was awarded to [Michaela Frye](#) of the German Cancer Research Center (DKFZ) in Heidelberg.

The **GSCN 2025 Publication of the Year Award** was presented to [Bryce Lim](#), [Aryan Kamal](#), [Judith Zaugg](#), [Moritz Mall](#), and colleagues for their joint publication, “Active repression of cell fate plasticity by PROX1 safeguards hepatocyte identity and prevents liver tumorigenesis,” published in *Nature Genetics* 57, 668–679 (2025).



UniStem Days 2026 in Germany

Thirteen institutions across Germany hosted UniStem Day 2026, the public outreach day for schools at research institutes and universities. Participating cities included Aachen, Berlin, Bochum, Bonn, Bonn-Rhein-Sieg University of Applied Sciences, Braunschweig, Düsseldorf, Essen, Hannover, Jena, Cologne, Munich, and Ulm. Through lectures, interactive activities, lab tours, and expert interviews, students gained insight into current stem cell research and the daily life of scientists.

In 2026, approximately 30,000 students participated across 13 countries and two continents.

Conference report 2025

The 13th GSCN Conference

15 – 17 October 2025 Helmholtz Munich, Conference Center Neuherberg



„Very good scientific program with high quality talks“



HEIKO LICKERT

Three electrifying days of discovery, dialog, and inspiration—the 13th Conference of the German Stem Cell Network (GSCN), held from 15 – 17 Oct. 2025 in Munich—proved to be an outstanding success and a true celebration of the field’s momentum. Hosted at the Helmholtz Munich research campus, almost 500 scientists from Germany and around the world gathered to exchange ideas, breakthrough data, and transformative technologies shaping the future of stem cell research. The GSCN Conference, starting on 15 Oct. 2025, set the stage for an ambitious scientific program, unfolded across several parallel sessions and sustained a vibrant, high-energy atmosphere throughout. The pre-conference setting opened with a dedicated workshop on single-cell genomics and a non-PI Meeting on 14 Oct. 2025.

Major highlights of the GSCN Conference were the of six outstanding keynote lectures delivered by internationally renowned leaders in the field: **Viviane Tabar** (New York City, USA), **Timm Schroeder** (Basel, Switzerland), **Jacob Hanna** (Rehovot, Israel), **Wolfram-Hubertus Zimmermann** (Göttingen, Germany), **Hongkui Deng** (Beijing, China), and **Maria-Elena Torres-Padilla** (Munich, Germany). Their presentations offered visionary perspectives spanning fundamental biology, technological innovation, and translational approaches, sparking intense discussion well beyond the lecture halls. The scientific depth of the meeting

was further reflected in 54 talks, three thematic symposia, and the presentation of three GSCN Awards, honoring exceptional contributions within the community. Two lively poster sessions featuring 144 posters provided ample opportunity for in-depth exchange, especially among early-career researchers, while a large industry exhibition with 39 exhibitors highlighted the latest tools, platforms, and technologies driving the field forward. Alongside fundamental research, discussions increasingly focused on disease modeling and therapeutic applications, underscoring the field’s rapid progress toward clinical impact.

Culminating in a memorable Bavarian networking evening filled with great food, music, and animated conversation, the conference captured the spirit of openness and collaboration that defines the community. With its dynamic atmosphere of curiosity, excellence, and innovation, the GSCN Conference once again highlighted the strength and vitality of the German and international stem cell community—and left participants energized and inspired for the challenges and opportunities ahead.

Conference participants were welcomed by GSCN President **Heiko Lickert** and **Martin Hrabě de Angelis**, Research Director of Helmholtz Munich. The scientific program kicked off immediately with the first scientific keynote by Viviane Tabar, marking the beginning of an engaging and productive meeting.

2
GSCN Board
meetings

2
GSCN
Mentoring
Program
Workshops

6
National
Highlight
Talks

54
Talks

18
Sessions

144
Poster

1
Non-PI
Workshop

6
International
Keynote
Lectures

3
GSCN
Awards

39
Industry
exhibition



Helmholtz
Munich,
Conference
Center
Neuherberg

The 13th GSCN Conference Facts & Figures

How do you rate...

the industry exhibition: 4,13
★★★★☆

the Presidential Symposium: 4,39
★★★★☆

the networking evening: 4,48
★★★★☆

the GSCN Get-together: 3,47
★★★★☆

the industry session: 3,88
★★★★☆

the organization of the conference: 4,42
★★★★☆

the scientific program: 4,25
★★★★☆

Scale: 5 (excellent) to 1 (unsatisfactory)

372 Regular



104 Students

the figures
include all groups
[VIPs, exhibitors,
TAs etc.]

At the Munich Press Club on 17 October 2025

GSCN Public Event

Panel discussion featuring short films and scientists on
Current research, new therapies, and existing medications:
Stem cells – the all-rounders among cells

Heiko Lickert *Helmholtz Munich, expert on diabetes*

Ole Pless *ITMP Hamburg, expert on drug testing and rare diseases*

Anette-Gabriele Ziegler *Helmholtz Munich, expert on diabetes*

Hartmut Geiger *University of Ulm, expert on aging and stem cells*

Moderator: Stefanie Seltmann

476
Conference Participants

Germany: 416

Europe: 43

International: 17

The international keynotes at the GSCN Conference 2025



Viviane Tabar, a neurosurgeon scientist and chair of the department of Neurosurgery at Memorial Sloan Kettering Cancer Center, gave the opening keynote at the GSCN Conference. She discussed the Phase 1 clinical trial of human ES-cell derived dopamine neurons grafts for Parkinson's disease. The trial enrolled 12 people, 5 of whom received a "low" cell dose and 7 received a "high" cell dose of 2.7 million cells per hemisphere. She described the trajectory of the preclinical findings, starting with the description of a robust differentiation protocol of pluripotent stem cells, into ventral midbrain neuron progenitors, the demonstration of in vivo efficacy and the transition to GMP manufacture and cell production. The work was performed in the Tabar lab and in the lab of Lorenz Studer, and the trial was sponsored by BlueRock Therapeutics, a subsidiary of Bayer. The group has reported on the 18 months data (Tabar et al. (2025) Nature 641, 978-983). She highlighted these results and provided an update on the 3-year unpublished data.

In brief the clinical trial met its stated primary endpoints of safety and feasibility at one year. All 12 patients received bilateral grafts as planned, completed one year of immunosuppression and remain enrolled in the follow-up phase of the trial. There were no deaths, no bleeding in the brain and no graft-induced dyskinesia. At three years, the safety data continued to be excellent. The secondary endpoints included

an array of typical clinical assessments, including Unified Parkinson's Disease Rating Scale (UPDRS) part III off and Hauser diaries in on and off time, as well as UPDRS part II and other scales. Overall patients in the high dose group demonstrated greater improvement on the UPDRS scale and in the patient-reported Hauser diaries. 18-Fluoro DOPA PET studies were performed longitudinally and demonstrated increased uptake in the putamen of grafted patients compared to baseline and some decrease in the ungrafted caudate. Both the clinical findings and the PET data continue to show stability at 2 years following discontinuation of the immunosuppression regimen. A multicenter randomized placebo-controlled phase 3 trial, that includes sham surgery, was already launched in 2025.

The second keynote on Wednesday afternoon was given by **Timm Schroeder** from the Department of Biosystems Science and Engineering of the ETH Zürich in Basel, Switzerland. He explained the importance of analyzing cells not only at the single cell level, but also continuously over long periods of time. Only this quantification of the dynamics of cells and molecular machineries will allow a complete understanding of what cells actually do in health and disease, and how their behavior is controlled by molecular regulators. Schroeder introduced some of the open-access tools his group develops for the quantification of single-cell dynamics. A recent deep learning-based Napari plugin software enables label-free segmentation of cellular organelles. Schroeder went on to describe approaches to combine live single-cell dynamics quantification with high-dimensional single-cell omics. This approach combines the strengths of both approaches, leading to much improved identification of poten-





Jacob Hanna is a Full Professor of Stem Cell Biology and Synthetic Embryology at the Weizmann Institute of Science in Israel. In his keynote presentation on ELSA topics at the GSCN Conference on Wednesday evening he explained how the identity of somatic and pluripotent cells can be epigenetically reprogrammed and forced to adapt a new functional cell state by different methods and distinct combinations of exogenous factors. The aspiration to utilize such in vitro reprogrammed pluripotent and somatic cells for therapeutic purposes necessitates understanding of the molecular mechanisms of reprogramming and differentiation and elucidating the extent of equivalence of the in vitro derived cells to their in vivo counterparts. In addition to the latter, in his presentation, he presented

his group's recent advances toward understanding these fundamental questions and further detailed the ongoing efforts to generate developmentally unrestricted human and mouse naïve pluripotent cells with embryonic and extra-embryonic developmental potential. He expanded on new avenues for utilizing custom made electronically controlled ex utero platforms and optimized conditions for growing natural mammalian embryos ex utero for extended periods capturing development from pre-gastrulation until advanced organogenesis, for better studying of stem cell transitions during embryogenesis and organogenesis. He further detailed how the latter platforms offered an exclusive technical platform to demonstrate and unleash the self-organizing capacity of mouse naïve PSCs to generate post-gastrulation synthetic bona fide structured and synthetic Stem-cell-based whole Embryo Models (SEMs) with both embryonic and extraembryonic compartment ex utero, as well as his lab's ability to extend these findings with naïve human PSCs and generate complete structured day 14 human developmental models and beyond. Collectively, he highlighted prospects for revolutionary platforms for advancing human disease and embryogenesis ab initio developmental modeling. Jacob also participated in an exciting group discussion moderated by Tobias Cantz (MH Hannover) on ELSA topics on Thursday morning (see below).



JACOB HANNA

tial cell fate regulators which are differentially regulated at the very time of fate decision making. He explained how these technologies were used to analyze the potential importance of signaling activity dynamics to control cell fates. Using the NF- κ B pathway as an example, his team could demonstrate that different dynamics like sustained, transient or oscillatory activity not only are regulated in a cell-type specific way in hematopoietic stem and progenitor cells. But they also correlate with different target transcriptional programs and instruct different lineage choices. Finally, Schroeder described a pipeline allowing 3D imaging of very large (e.g. whole mouse femurs) fixed tissue volumes in many colors, allowing improved quantification of the location of cell types and molecules in complex tissues. This approach was improved to enable the detection of even single protein molecules, also of secreted regulators like cytokines. The combination of all these pipelines led to the discovery of novel megakaryocyte functions in relaying systemic inflammatory inputs only to neighboring HSCs in the bone marrow.

Hongkui Deng, Director of the Stem Cell Research Center at Peking University in Beijing, China, gave a keynote lecture on Friday afternoon. He shared his lab's research in establishing a controllable reprogramming approach for generating human induced pluripotent stem cells (hPSCs) from somatic cells, taking cues from naturally occurring regeneration such as in axolotl limb regeneration. This gave rise to a new approach – chemical reprogramming – in which reprogramming to hPSCs was achieved using small molecule chemical compounds without over-



TIMM SCHROEDER



expression of transcription factors using transgenic methods, termed chemically-induced pluripotent stem cells (CiPSCs). Investigations into the mechanisms behind chemical reprogramming revealed induction of a highly plastic intermediate state with regenerative gene signatures to be key to successful conversion to pluripotency. This intermediate state functionally resembled human embryonic limb bud progenitors, suggesting a reprogramming pathway resembling tissue regeneration as

well as a reversion of typical procession of tissue development. CiPSCs have been differentiated into functional tissues and clinically translated into cellular therapies for various diseases, such as type 1 diabetes (T1D). He described their research efforts in generating PSC-derived islets spanning 20 years, culminating in a robust directed differentiation protocol that stably

and efficiently generated CiPSC-derived islets. Systematic pre-clinical evaluations in rodent and nonhuman-primate models of diabetes demonstrated safety and therapeutic efficacy of CiPSC-islets and also established a new transplantation strategy – transplantation beneath the anterior rectus sheath – that circumvents inherent limitations of the conventional intrahepatic approach to islet transplantation. Based on these preclinical findings, the first-in-human clinical study of CiPSC-islets autologously transplanted beneath the anterior rectus sheath of a patient with long-standing T1D was reported. One year follow-up showed rapid reversal of diabetes in the patient and restoration of independence from exogenous insulin after transplantation with CiPSC-islets.

Deng also described their research efforts in making better cell therapies, including the optimization of chemical repro-



HONGKUI DENG

Helmholtz Munich

The Stem Cell Center at Helmholtz Munich unites world-class research on reprogramming, cell identity, and epigenetics. Its mission is to pave the way for future medicine through cell reprogramming, manipulation of totipotent states, and the generation of functional cell types. Under the leadership of Maria-Elena Torres-Padilla and Magdalena Götz, internationally recognized researchers collaborate across disciplines. The Institute of Epigenetics and Stem Cells studies how epigenetic and transcriptional states shape cell identity and balance genome stability. The Institute of Stem Cell Research develops strategies to convert glial cells into neurons for stroke and CNS therapies. The

apoptosis group addresses stem cell resilience, while interdisciplinary work with scientists such as Heiko Lickert advances insulin-producing cell culture strategies. Other projects explore approaches in regenerative medicine to restore function of heart, liver, and salivary gland tissue.

Helmholtz Munich Stem Cell Center

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 www.helmholtz-munich.de/en/stem-cells

HELMHOLTZ MUNICH



gramming to be more efficient, generation of CiPSCs from blood cells, and the establishment of an islet differentiation system with tunable endocrine composition to facilitate improved glycemic control. Beyond CiPSCs, Hongkui's lecture also discussed harnessing cellular plasticity using chemical reprogramming in other contexts such as transdifferentiation, the capture and long-term maintenance of cell fate and function in vitro, and expansion of cell potency to extraembryonic potential. Taken together, the research establishes a new paradigm in which chemical cocktails can serve as a general approach to modulate cell plasticity, offering broad potential for application.

Maria-Elena Torres-Padilla, Director of the Institute of Epigenetics and Stem Cells at Helmholtz Munich, gave the closing keynote Friday afternoon on epigenetic reprogramming and cellular plasticity. By studying the earliest stages of embryonic de-

velopment, in the time-window covering from fertilization to blastocyst formation, their work has identified several chromatin pathways that regulate cellular plasticity and developmental progression. Inspired by the plasticity of totipotent cells in the early embryo, she presented their work also on a cell-culture model, the '2-cell-like cells', that remarkably recapitulates features of embryonic cells in the petri dish. For

example, early mouse embryos at the 2-cell stage – like 2-cell-like cells – replicate their DNA at a lower speed. Accordingly, manipulations leading to reduced DNA replication fork speed in embryonic stem cells lead to higher efficiency of reprogramming into the 2-cell-like state, but they also can increase reprogramming to totipotency upon somatic cell nuclear transfer. She also discussed the prominent roles that transposable elements play in directing developmental programs. Her group has recently expanded towards several mammalian species in addition to the mouse and showed that transposable element expression is a conserved and defining feature of pre-implantation development. By studying fundamental chromatin-related processes including DNA replication, transcription and nuclear organization, the work presented establishes chromatin plasticity as a major pillar of cellular plasticity. The manipulation of identified chromatin regulators in these processes provides a toolkit to manipulate cellular plasticity and cell fate at large.



MARIA-ELENA TORRES-PADILLA

Photos: GSCN



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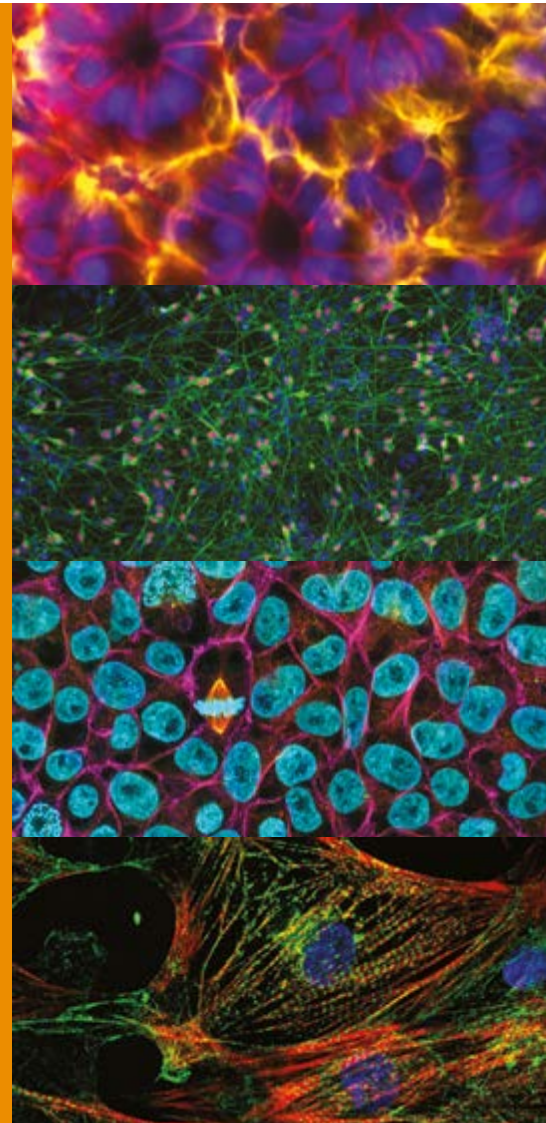
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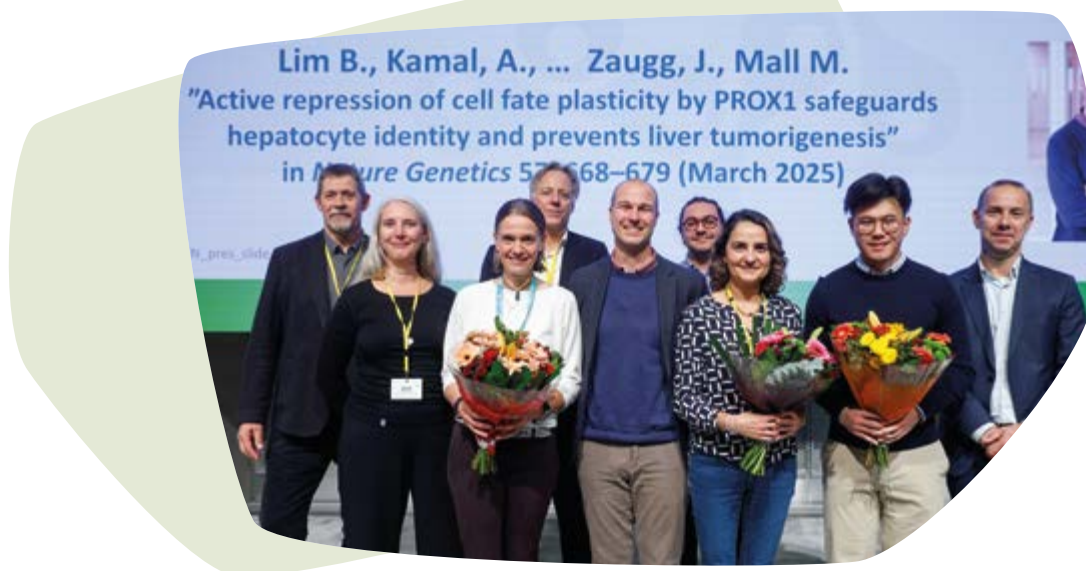
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The Presidential Symposium: Lecture at the invitation by the GSCN President and the presentations of the GSCN Awardees 2025



The Presidential Symposium 2025 offered an impressive keynote lecture by Wolfram-Hubertus Zimmermann of the University Göttingen at the invitation of GSCN President Heiko Lickert and Senior President Claudia Waskow, as well as three lectures by the GSCN Award winners.

Wolfram-Hubertus Zimmermann spoke about the translation of tissue engineered heart repair. Engineered Heart Muscle (EHM) with properties of juvenile myocardium can be constructed from pluripotent stem cell-derived cardiomyocytes and stromal cells. To facilitate EHM self-organization, cells are embedded in a collagen hydrogel and subjected to mechanical con-

ditioning. Preclinical testing in a homologous Rhesus macaque model confirmed that induced pluripotent stem cell-derived EHM allograft transplantation is feasible, safe, and efficacious under an optimized immune suppression protocol. The knowledge gained from late preclinical testing in Rhesus macaques informed the design of the



WOLFRAM-HUBERTUS ZIMMERMANN

Max Planck Institute for Molecular Genetics (MPIMG)

Research at the Max Planck Institute for Molecular Genetics (MPIMG) is focused on analysis of genomes across model organisms and humans. The essence of our interdisciplinary and collaborative approach is to combine mechanistic investigation of genome function, bioinformatics, and genomic perturbation with developmental, population, and disease biology.

Work at the MPIMG spans genomics, developmental genetics, stem cell research, transgenic mouse models, human genetics, gene regulation, epigenetics, and computational biology. In

particular, stem cell research and the analysis of cellular differentiation during embryonic development play a prominent role in exploring mechanistic relationships. Overall, we combine these approaches to lead scientific and technological breakthroughs that transform the understanding and use of genetics for the benefit of society.

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first-in-patient “Safety and Efficacy of Induced Pluripotent Stem Cell-derived Engineered Human Myocardium as Biological Ventricular Assist Tissue in Terminal Heart Failure (BioVAT-HF)” Phase I/II clinical trial (NCT04396899). First proof of remuscularization in a patient subjected to a successful heart transplantation 3 months after EHM implantation was obtained, demonstrating the feasibility of remuscularization in humans. A total of 20 patients was treated in BioVAT-HF with 16 patients treated with the in the dose finding part of BioVAT-HF identified safe maximal dose. This marks the time point for interim analysis, which was completed by the end of 2025. Collectively, our work demonstrates the first translation of tissue engineered heart repair from bench to bedside with the aiming to repair the failing human heart.

Aydan Bulut-Karslıoğlu, group leader at the Max Planck Institute for Molecular Genetics in Berlin, received the **GSCN 2025 Young Investigator Award** and presented her lecture. She presented recent findings uncovering a latent capacity for developmental pausing in human embryonic cells. Developmental pausing (diapause) is a reproductive strategy employed by various mammals to facilitate survival under unfavorable environments. Her team’s work demonstrates that inhibition of the mTOR signaling pathway induces a reversible, tissue-specific dormant state in mouse embryos as well as human embryo-like structures. Under mTOR inhibition, human blastoids maintain morphology, exhibit reduced proliferation and differentiation, and lose attachment competence to hormonally stimulated



AYDAN BULUT-KARSLIOĞLU

endometrial cells—phenotypes resembling embryonic diapause in other mammals. Upon release of inhibition, these structures resume normal development, revealing that human cells can modulate their developmental pace through conserved molecular mechanisms. Aydan highlighted the broader significance of these findings in understanding how early embryos balance growth, timing, and metabolic readiness. She connected this work to her group’s parallel studies showing that lipid metabolism and chromatin regulation stabilize cellular identity during dormancy. Together, these discoveries bridge insights from diapause biology to human reproductive timing and stem-cell engineering.

The **GSCN 2025 Hilde Mangold Award** was given to **Michaela Frye**, Head of the Division ‘Mechanisms Regulating Gene Expression’ and Deputy Scientific Director at the DKFZ in Heidelberg, Germany. She delivered her award lecture on recent advances in harnessing RNA modifications to improve cancer therapies. To ensure that the correct mRNAs are accurately transcribed, processed, efficiently transported into the cytoplasm, and then faithfully translated by ribosomes, mRNAs are decorated with about a dozen distinct nucleotide modifications during and after transcription.



MICHAELA FRYE

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Their correct deposition is essential for normal embryonic development, and aberrant modification profiles can cause human diseases such as neurological, metabolic disorders, and cancer. Over the past decade, RNA modification-based therapies have progressed from experimental concepts to clinical testing. Among these, inhibitors targeting RNA-modifying enzymes represent particularly promising therapeutic strategies. One such example is the inhibitor STC-15 targeting METTL3, the catalytic subunit responsible for forming N6-methyladenosine (m6A). Although STC-15 is already undergoing clinical testing in cancer patients, robust criteria to predict when m6A modulation will enhance or compromise therapeutic outcomes are still lacking. Without such criteria, RNA modification-based therapies will remain largely empirical. Michaela's talk focused on the cancer-specific functions of N6-methyladenosine (m6A), one of the most abundant modifications found in mRNA, in head and neck squamous cell carcinoma originating in the oral cavity. Oral squamous cell carcinoma is a common malignancy characterized by high mortality and poor prognosis. She presented novel, cancer-specific functions of vir-like m6A methyltransferase associated (VIRMA), an essential component of the multiprotein complex that mediates m6A modification formation. VIRMA is required for the efficient transcription of DNA replication and repair genes, and its depletion enhances global transcript half-lives, leading to nucleotide imbalances that rewire purine and energy metabolic pathways. In summary, Michaela demonstrated that elucidating the precise molecular mechanisms by which m6A regulates gene expression pathways is essential for effectively targeting m6A modification in cancer therapies and for using components of the methylation complex as biomarkers in human disease.

Bryce Lim, a former PhD student in the laboratory of **Moritz Mall** at the Hector Institute for Translational Brain Research at the DKFZ Heidelberg, delivered the **GSCN 2025 Publication of the Year Award** lecture at the Presidential Symposium. The prize recognized collaborative work by Bryce Lim, Aryan Kamal, Judith Zaugg, and Moritz Mall, which addresses a central question in stem cell biology: how

cells induce and maintain their identity throughout life and how failures in this process may contribute to cancer. Bryce introduced the concept of lineage-specific "safeguard repressors", transcription factors that actively preserve cell identity by repressing alternate cell fate programs and suppressing unwanted plasticity. To search for such factors, the team performed a computational screen across eighteen cell types to identify transcription factors with lifelong and cell type-specific expression. PROX1 emerged as the top hepatocyte candidate, prompting detailed functional investigation. Using cell fate reprogramming systems, he showed that PROX1 accelerates conversion of fibroblasts into hepatocytes while silencing competing lineage programs. Chromatin profiling further revealed that PROX1 restricts accessibility at target promoters, represses alternative fate regulators, and interacts with the Nucleosome Remodeling and Deacetylase (NuRD) complex to reinforce transcriptional shutdown. These mechanistic data suggest that PROX1 enforces hepatocyte identity by actively preventing diversion into other lineages. In vivo experiments highlighted the physiological importance of this repression. After liver injury, PROX1 was required for efficient hepatocyte regeneration, consistent with a role in limiting excessive plasticity during repair. In mouse liver cancer models, increasing PROX1 levels impeded tumor initiation and progression, whereas reducing PROX1 enhanced tumor burden and altered lineage states. Manipulating PROX1 shifted tumors between hepatocellular carcinoma and cholangiocarcinoma identities, demonstrating bidirectional control over cancer plasticity. Crucially, these findings were supported by patient data, which also indicated a protective role for PROX1 in maintaining hepatocyte identity and suppressing unwanted fate transitions. Together, these findings position PROX1 as a hepatocyte safeguard repressor with therapeutic potential. More broadly, the study provides a blueprint for identifying similar factors across tissues and offers new strategies to control aberrant plasticity in disease, including cancer.

BRYCE LIM



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 neuro-degenerative diseases such as Alzheimer's and Parkinson's, haematological diseases such as

leukaemia, metabolic diseases such as diabetes, and retina and bone diseases. Through Saxo-Cell, 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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The scientific GSCN sessions: Exciting ideas and data from the scientific community

Photos: GSCN

In the first session 'Stem cells in disease modeling & drug development' on Wednesday, **Annika Zink** (University Hospital Düsseldorf, HHU) presented an iPSC-based drug repurposing strategy for Leigh syndrome (LS). A compound screen in LS patient-derived neural precursor cells identified sildenafil as a candidate that normalized mitochondrial membrane potential. Sildenafil also restored neurodevelopmental signaling, improved neurite outgrowth, and corrected calcium responses in LS brain organoids. In vivo, sildenafil extended survival in mouse and pig models of LS. Individual off-label treatments in six LS patients were well tolerated and associated with clear motor improvements. The findings position sildenafil as a promising therapeutic candidate for LS.

In the session 'Stem cells in regenerative therapies', a prototypic end-to-end process for autologous Parkinson's disease (PD) cell therapy was presented by **Diana Haberhausen** (Miltenyi Biotec, Bergisch Gladbach, Germany), through which bona-fide



iPSC-derived dopaminergic progenitors were generated from both, healthy donors and PD patients. In vivo proof-of-concept was provided, demonstrating that mDA cells were functional. For ex vivo phenotyping, imaging methods were developed that



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enabled the spatial projection and quantification of transplanted cells using 3D light-sheet imaging, and the characterization of graft composition using cyclic immunofluorescent imaging in 2D. Key elements of the iPSC generation and mDA differentiation workflow were successfully transferred to semi-automated platforms, paving the way towards future clinical translation.

In the session 'Basic, translational & applied hematopoiesis', **Marius Külp** (Goethe University Frankfurt, Lab of Michael Rieger) presented a new perspective on hematopoietic differentiation:

by developing a low-input transfer RNA (tRNA)-sequencing approach applied to human blood cell populations including hematopoietic stem cells, he showed differential tRNA expression along the hematopoietic differentiation hierarchy. Subsequent integration of the tRNA supply with its corresponding demand identified codons, for which the relative abundance of tRNAs decreases upon differentiation. These tRNA supply-to-demand imbalances impose bottlenecks for mRNA translation, implying a codon-specific posttranscriptional regulation of hematopoietic differentiation. In conclusion, the presented single-codon perspective suggested a contribution of tRNA abundance to the development and instruction of cellular identities within the hematopoietic system.

Angeliki Spathopoulou (Institute of Molecular Biology, University of Innsbruck, Austria) presented a multimodal single-cell approach to dissect transcriptional and epigenetic trajectories



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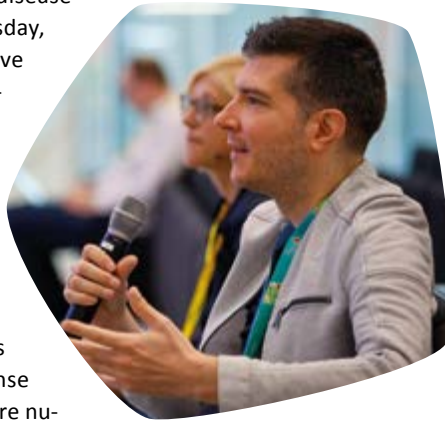
during induced pluripotent stem cell (iPSC) reprogramming in the session 'Pluripotency, differentiation & PSC-derived models'. By integrating single-nucleus RNA and ATAC sequencing with cellular barcoding, lineage trajectories were identified across critical timepoints of reprogramming. The analysis revealed that only a minority of cells achieved full pluripotency, while most diverged toward alternative identities, exposing key decision points that limit successful reprogramming. Intermediate populations displayed a gradual loss of somatic features alongside stepwise acquisition of pluripotency markers. Notably, the study identified a previously uncharacterized chromatin remodeling factor that may facilitate the mesenchymal-to-epithelial transition. This integrative approach advances the molecular understanding of cellular plasticity and suggests strategies to improve iPSC generation.

In the second session 'Stem cells in disease modeling & drug development' on Thursday, **Jasmin Aicher** (Institute of Reconstructive Neurobiology, University of Bonn) presented a human iPSC-based model to dissect cell-type-specific effects of CNTNAP2 deficiency, a condition linked to autism and epilepsy. Using neuronal cultures enriched for glutamatergic and GABAergic cells, CNTNAP2^{-/-} phenotypes emerged primarily in mixed E/I networks, where knockout networks showed fewer but longer and more intense bursts, while network bursts became more nu-

merous yet shorter and less intense. Mechanistic analyses suggest disrupted AMPA, NMDA and GABA-A receptor function, underscoring CNTNAP2's essential role in synaptic receptor localization or stabilization.

In the session 'Computational stem cell biology', **Andy Shing-Fung Chan** (Würzburg Institute of Systems Immunology, Max Planck Research Group at the Julius-Maximilians-Universität Würzburg) presented a spatio-temporal atlas that integrates single-cell and spatial transcriptomic information of the repairing adult mouse hearts after myocardial infarction. This atlas revealed dynamic ligand-receptor interactions that define multiple communication niches during wound healing. Notably, a rare population of dedifferentiating cardiomyocytes, emerged as early as 1-day post-injury, was identified in the wounded but not healthy hearts. These dedifferentiating cells are driven by

combined endothelial and immune signals in their local niches. Particularly, one of the key niche cell types is innate lymphoid cell type 2 (ILC2), which promotes cardiomyocyte plasticity while suppressing hypertrophic responses through BMP-7 signaling. Functional assays in mouse and human tissue demonstrated conserved reactivation of progenitor-like programs via the same ligand-receptor interactions, highlighting an underrepresented but promising mechanism with therapeutic potential to promote adult cardiac regeneration.



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The strategic GSCN sessions: topics for all scientific fields



The strategic session ‘Technologies in stem cell research’ was organized by Ole Pless, Sebastian Knöbel, and Sebastian Diecke and focused on ‘Assay development and high-throughput screening with hiPSC-derived 2D/3D models’. It addressed emerging technological strategies for the use of hiPSC-derived neural systems in disease modeling and drug discovery. In particular, the session highlighted advanced phenotypic profiling and cell painting–based approaches as key enablers for scalable and functionally informative screening platforms.

Johannes Wilbertz presented a high-content phenotypic profiling approach to resolve functional heterogeneity in human iPSC-derived microglia under inflammasome-activating conditions. By combining deep learning–based image analysis with single-cell feature extraction, distinct microglial subpopulations

were identified that respond differentially to NLRP3 activation and can be selectively modulated by targeted compounds. Importantly, phenotypic readouts captured rapid and functionally relevant cellular changes earlier and more sensitively than bulk transcriptomic or proteomic analyses. **Jakob Metzger** introduced a micropatterned brain organoid platform designed to overcome limitations in reproducibility and scalability of conventional organoid mod-



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Fraunhofer is the largest application-oriented research organization in Europe with over 32,000 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 transdisciplinary health research in order to improve patient treatment qualitatively and economical-

ly. 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 miniaturization, high-throughput and high-content screening, and on chemi- and bioinformatics. The indication focus is on immune-mediated diseases.

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els. The system enables statistically robust phenotyping of early human cortical development and reveals subtle disease-associated alterations in isogenic iPSC models of DYRK1A syndrome and IRF2BPL-related disorder. This approach establishes reproducible brain organoids as a reliable technology for high-throughput disease modeling and therapeutic screening. **Catarina Brito** presented a bioreactor-based, human innate immunocompetent 3D neural model addressing immune-related safety challenges in advanced therapy development. By generating hiPSC-derived neurospheroids containing neurons, astrocytes, oligodendrocytes, and integrated microglia, the platform recapitulates key neuroinflammatory responses to gene therapy vectors. The transfer to miniaturized stirred-tank bioreactors enables parallelization and higher throughput, providing a scalable and human-relevant pre-clinical assay for ATMP evaluation. **Peter Reinhardt** presented a rapid, dSMAD-independent neural induction strategy enabling robust and regionally programmable neuronal differentiation from hiPSCs. The combined inhibition of BMP, MEK, and WNT signaling generates homogeneous rostral neuroectoderm within 4–6 days and improves cortical identity prior to NGN2-driven neuronal maturation. This paradigm supports efficient regional patterning and yields disease-relevant neuronal subtypes suitable for translational in vitro assays, including Alzheimer's disease-related models.

Overall, the session highlighted a strategic shift toward integrated stem cell technologies that combine reproducibility, scalability, functional readouts, and human relevance. The presented approaches underscore the growing importance of advanced hiPSC-derived 2D and 3D model systems and phenotypic screening frameworks as enabling technologies for disease mod-



eling, drug discovery, and the development of advanced cell and gene therapies.

The session on 'Clinical trials and regulatory affairs', chaired by Zoltan Ivics and Andreas Kurtz, was dedicated to ways for making existing resources available for efficient cell therapy applications beyond their originally intended use. Presentations by **Joel Glover** (Oslo, Norway), **Joannis Mytilineos** (German National Bone Marrow Donor Registry/ ZKRD, Ulm) and

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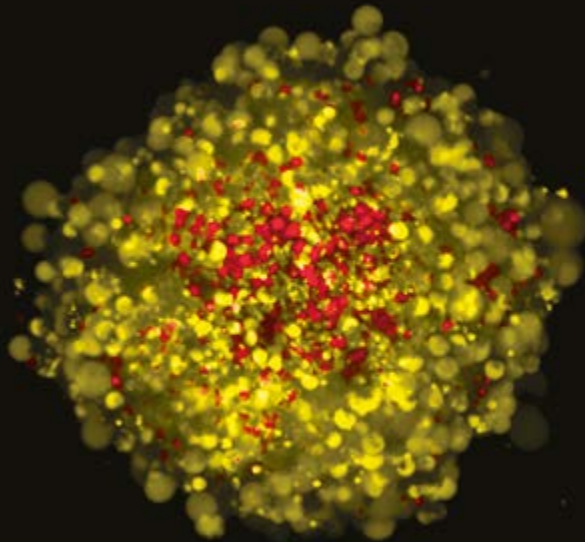
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Gerald Schumann (Paul Ehrlich Institute, Langen) covered different approaches for the suitability of bone marrow registries for the generation of human induced pluripotent stem cells (hiPSC), haplotype-selected cells for improving the immune resilience of therapeutic grafts, and the improvement of safety profiles for these cells. Haplo-selected hiPSC lines are generated to cover frequent HLA-haplotypes in specific populations, allowing a broad range of patients to receive an “off-the-shelf” product that is already HLA-compatible or requires minimal immune suppression. Regulatory and ethical issues related to these topics were discussed. A focus of the session was also the potential role haplotype-selected cells may play as a universal resource for cell therapy products in comparison to allogenic or hypoinmunogenic cells.

Joel Glover described the pathway taken in Norway to make available the national bone marrow registry for the generation of hiPSC – lines for clinical use, which required close interaction

with ethical and regulatory bodies in Norway and resulted in a new model informed consent procedure. This work is integrated in a European Network (Haplo-iPS) towards the generation of hiPSC from haplo-selected cord blood samples. The number of haplo-selected samples to cover the Norwegian and European populations, respectively, was determined. **Joannis Mytilineos** described the situation in Germany with respect to the use of bone marrow registry material and outlined the relevant pathways to be taken. Importantly, the number and distribution of haplo-selected samples and their population coverage were detailed, together with insights into the necessary efforts and resources needed to make these accessible for the German and European patients. Clinical advantages of using haplo-selected cell therapeutics were emphasized. **Gerald Schumann** expanded the discussion towards the potential risks of haplo-selected cell therapeutics and described means to make these cells safer by the introduction of safety switches.

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From Regenerative Biology to Reconstructive Therapy

The center was funded as the REBIRTH Cluster of Excellence from 2006 to 2019 as part of the German federal and state governments' Excellence Initiative and now continues as a virtual 'Research Center for Translational Regenerative Medicine'.

The network addresses some of the major questions in health research and the associated challenges for medicine. The vision is to develop new therapeutic concepts based on biological principles that go beyond existing approaches. These new regenerative therapies

are intended to contribute to the cure of serious diseases of the heart, lungs, liver, and blood (including diseases of the immune system).

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Career Development: Navigating difficult situations

Photos: GSCN

The career development workshop during the GSCN Conference in Munich focused on communication in challenging situations. Participants met with coach Nele Haasen to learn how to remain calm and clear in difficult workplace situations. Haasen made participants aware that the reality we perceive is always shaped by our own perspectives and worldviews, and that we can never fully grasp the complete picture. Prejudices and biases influence how communication partners perceive a situation and can lead to misunderstandings. In most cases, these misunderstandings are not based on bad intentions, but we need to be aware of them in order to address them.

Nele Haasen introduced techniques and methods to help participants better understand their counterparts and identify what lies behind what is being said. Active listening and clear "I" statements can help shape communication and enable more constructive conversations. In particular, the workshop addressed how to deal with one's own emotions, as these often stem from past experiences and can be triggered by specific stimuli. In the final part of the workshop, Nele Haasen offered advice on how to prepare for difficult conversations. She highlighted four key points: being clear about the goals one wants to achieve, being aware



of whom one is speaking to and how to approach that person, having a clear strategy for presenting the most important points, and being mindful of the context of the conversation, since not everything can be discussed in every context.

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ELSA: Embryo Models and Genome Engineering



JACOB HANNA



This year's ELSA symposium 'Embryo models meet genome engineering: A dialog on ethics and innovation' explored the interface between advanced biomedical research and its ethical implications. Recent advances in three-dimensional tissue culture and matrix interactions have enabled the generation of highly authentic models of human physiology. These developments are evident not only in somatic organoids, such as neuro-organoids, but also in increasingly sophisticated embryo models that are now reaching more advanced stages of development.

On Wednesday evening, **Jacob Hanna** from the Weizmann Institute of Science delivered the keynote lecture on synthetic ex-utero embryogenesis. During the ELSA symposium on Thursday, he further elaborated on the rapid progress in embryo modeling, which is reaching increasingly advanced developmental stages and could potentially lead to entities that exhibit features such as early but functional human gametes or hematopoietic stem cells. Together with **Stefan Stricker**, a neuroscientist and researcher working on cerebral organoids at Helmholtz Munich, various aspects of personhood and the moral status of stem cell-derived entities were discussed. Although no final conclusions were reached, the discussions stimulated reflection on how innovation in biomedical research intersects with moral responsibility. They also highlighted the importance of transparent, interdisciplinary debate for shaping future practices and for fostering broader societal engagement.

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Poster prizes and travel grants

Active Bioscience and PeptiGrowth donated poster prizes of € 500 each for the GSCN Conference. The winners in 2025 are:

Nina Henning

Leibniz Institute on Aging (FLI), Jena

“Organ identity imprints non-linear aging of the hematopoietic system”

Session: Stem cells in aging & disease (cancer stem cells)

Angeliki Koufali

Institute for Pharmacology and Toxicology, Medical University Göttingen

“Human otic Bioengineered Neuronal Organoids (oBENOs) mimic early inner ear development and physiology”

Session: Tissue-derived stem cells & organoids

Zeynep Aydin

DKFZ, Heidelberg

“Retrospective gene expression analysis in neural stem cells”

Session: Stem cells in regenerative therapies

Angelika Dannert

University Hospital LMU Munich, Munich

“A human iPSC model of tauopathies engineered for 4R Tau isoform expression endogenously develops late-stage neuronal Tau pathology”

Session: Stem cells in disease modeling & drug development



Winners of the GSCN travel grants for the GSCN Conference

The winners of the GSCN travel grants 2025, each worth 400 €, are:

Annasara Artoli (Mannheim)

Mari Ozaki (Ireland)

Meiying Xue (Berlin)

Sohana Islam Khan (Halle)

Susanna Quach (Berlin)

Photos: GSCN

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Highlights of social events at GSCN Conference 2025

The conference offered a welcoming get-together at the cafeteria of the Helmholtz Campus on the first conference day, setting the stage for a collegial evening in the spirit of the stem cell community.

The second evening at the Gasthof Neuwirt in Garching offered a more festive and at the same time very Bavarian atmosphere, featuring gourmet cuisine and an intensely celebrated dancing after the dinner. The high-energy setting attracted researchers and industry representatives to the dance floor, where many impressed with enthusiasm well into the night.



Public panel discussion

On the last evening of the conference, selected stem cell researchers offered their insights to the citizens of Munich in the heart of the city: At the panel discussion at the Presseclub Munich at the Marienplatz, **Heiko Lickert** (Helmholtz Munich), **Anette-Gabriele Ziegler** (Helmholtz Munich), **Hartmut Geiger** (University Ulm) and **Ole Pless** (Fraunhofer IMP, Hamburg) discussed the latest findings in their research areas with moderator **Stefanie Seltmann** (Heidelberg). Organoids, diabetes, rare diseases, repurposed drugs, stem cell aging and political support for research were shown as short videos and discussed on the podium and later with the very interested audience and at the get-together.



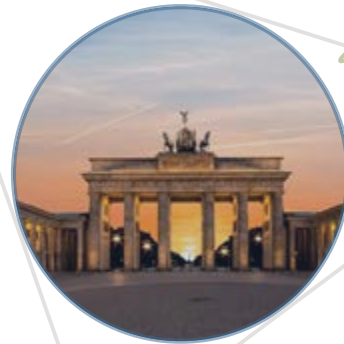
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- *Janet Rossant* (Toronto, Canada)
- *Jason Spence* (Ann Arbor, USA)
- *Takanori Takebe* (Cincinnati, USA & Tokyo, Japan)
- *Paresh Vyas* (Oxford, UK)

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GSCN Awardees: Young Investigator, Hilde Mangold Award, Publication of the Year

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Abstract submission deadline for oral presentations: 1 June 2026
(Oral presentations chosen from the best abstracts)
Abstract submission deadline for poster presentations: 27 July 2026

Scientific sessions

- Pluripotency, differentiation & PSC-derived models
- Tissue-derived stem cells & organoids
- Hematopoietic stem cells
- Stem cells in aging & diseases
- Stem cells in regenerative therapies
- Stem cells in disease modeling & drug development
- Computational stem cell biology

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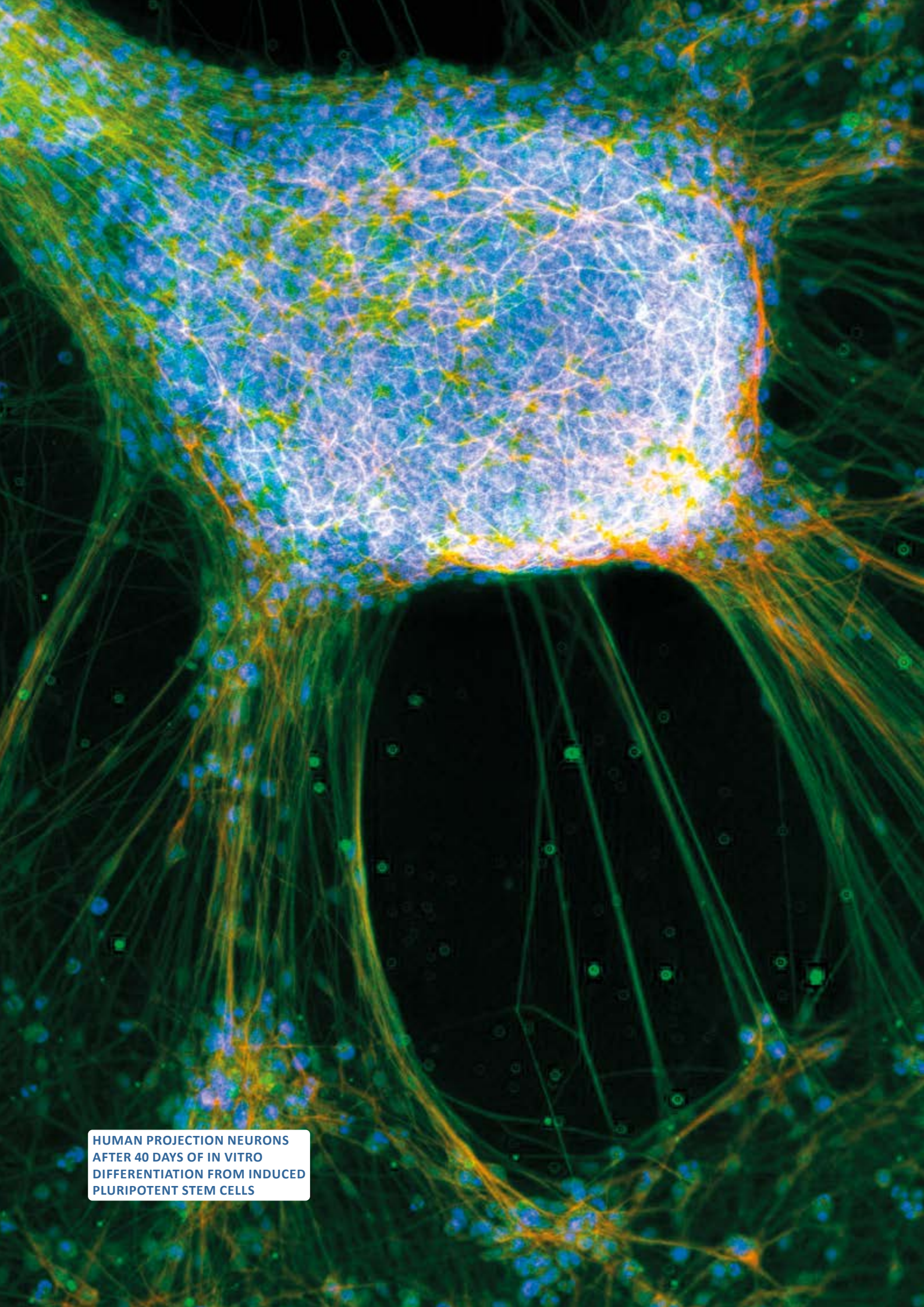
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Hypoimmune stem cells

Transplants with an invisibility cloak

Genetically modified stem cells that are not rejected by the immune system are considered a forward-looking innovation in cell therapy. The technology could make immunosuppression in transplantation unnecessary – and thus make such treatments suitable for far more patients. First clinical trials are already underway.

The human immune system is a master of discrimination. It identifies what belongs to the body – and what does not – based on the subtlest molecular structures, protecting us daily from pathogens.

In transplantation, however, this very strength becomes a dilemma: because foreign organs or cells are quickly recognized and rejected, physicians must weaken the defense system with immunosuppressive agents – with sometimes considerable side effects, such as an increased risk of infections and cancer.

But now, new research shows that the immunological boundary between “foreign” and “self” is by no means as immovable as long assumed. Cells with genetically modified surface structures – molecular “cloaks,” so to speak – can apparently escape detection by immune cells and antibodies, entirely without immunosuppression. For cell therapy, experts believe, such “hypoimmune” transplants would be a revolution.

“Our approach truly overcomes the transplantation barrier,” says Sonja Schrepfer, immunobiologist at Cedars-Sinai Medical Center in Los Angeles and co-founder of the US company Sana Biotechnology. Schrepfer is regarded as one of the pioneers of the new technology, which fascinates researchers worldwide. Just last year she showed, together with an international team

and in a 42-year-old patient with type 1 diabetes, that her strategy might indeed work.¹ In parts, the widely noted case report reads almost like the script of a scientific crime novel:

For five hours and eleven minutes, the pancreas of a deceased donor lay under controlled cooling at the University Hospital in Uppsala, Sweden. The team then isolated the hormone-active islets of Langerhans from the tissue – tiny cell clusters containing insulin-producing β -cells and other important cell types such as glucagon-producing alpha cells. The cell aggregates were transported to a specialized laboratory in Oslo, where their surface proteins were specifically modified via CRISPR/Cas and viral gene transfer, and then flown back to Uppsala. Finally, the physicians injected the modified “islets” into the patient’s left forearm using 17 small syringes.

The remarkable result: the foreign cells engrafted in the muscle tissue of the man, who had had diabetes since childhood – although he took no immunosuppressive medication at all. He is the first patient with diabetes in whom a transplantation of foreign islet cells succeeded without immune protection. The journal *Nature Medicine* even named the pilot experiment one of its twelve “remarkable advances” of 2025.² According to the latest information, the transplanted cells continue to produce insulin.³



SONJA SCHREPFER

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

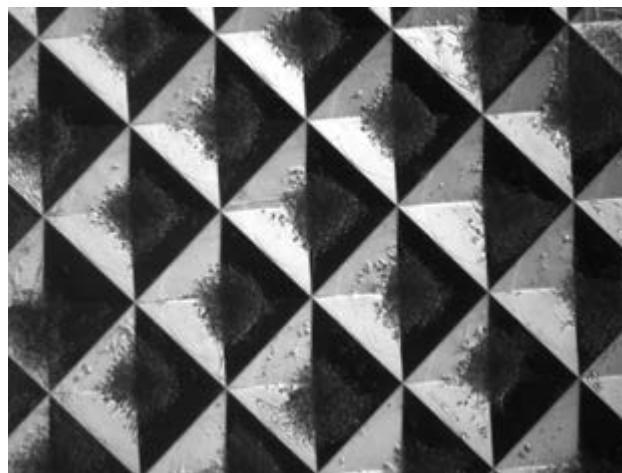
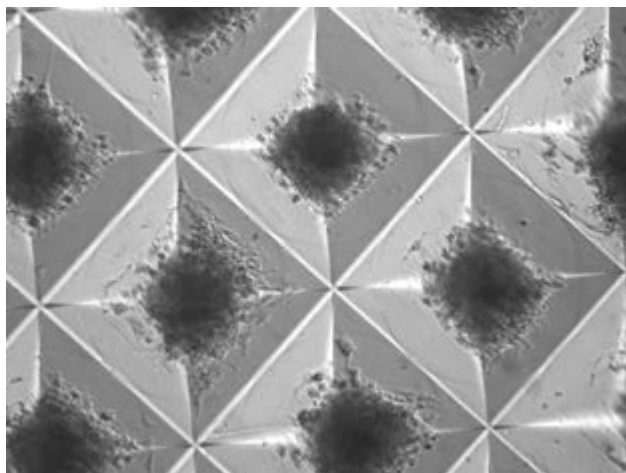
enriched by the wealth of knowledge and experience older people possess.

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.

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EMBRYOID BODIES – 3D CLUSTERS OF PLURIPOTENT STEM CELLS IN SONJA SCHREPFER'S LABORATORY AFTER 24 HOURS

"We already knew four weeks after the cell transplantation that there would be no rejection," says Schrepfer. Normally, the immune system attacks foreign tissue within two to three weeks with a strong defensive reaction. But with the genetically edited islet cells, this reaction did not occur at all.

Pilot trials in patients

Of course, Schrepfer knows that the case study merely provides an initial indication that the idea of hypoimmune cell therapy works – its clinical benefit still has to be proven. The researchers transplanted only 80 million new islet cells into the patient, while a person with type 1 diabetes would need at least ten times as many to become fully independent of injected insulin. And the transplant came from a deceased donor, which rules out broad application from the outset.

However, Sana Biotechnology is already working on a further developed strategy. Using the same molecular methods, the company first generates hypoimmune pluripotent stem cells from which unlimited numbers of immune-compatible islet cells can be grown. As early as 2024, Schrepfer's team showed in dia-

betic mice that such stem-cell-derived hypoimmune transplants can regulate glucose metabolism.⁴ Sana now plans to test the approach in a Phase I clinical trial in patients, possibly even this year, as CEO Steve Harr told Nature.⁵ The competing US company Vertex Pharmaceuticals in Boston is reportedly pursuing a similar approach but has so far released no details.

"Many groups are now working intensively on hypoimmune stem cells," confirms Heiko Lickert, director of the Institute for Diabetes and Regeneration Research at Helmholtz Munich and currently president of the German Stem Cell Network (GSCN). "The method represents nothing less than a paradigm shift in cell therapy."

Until now, treatments with so-called autologous cells were conceptually regarded as the gold standard for avoiding immune rejection. Patient-derived cells are reprogrammed into a stem cell state and then expanded to produce mature functional cells. Surprisingly, however, the immune system sometimes attacks even such autologous transplants. Molecular signatures on the surface can change during laboratory manipulation.⁶ In addition, autologous cell products must be manufactured individually – at costs that can reach several hundred thousand euros per patient.⁷

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There are also approaches to protect stem cell products with special polymer encapsulation or to establish biobanks with stem cell lines from particular donors whose immunological features match a larger share of the population.⁸ But the prospects for success remain uncertain. Indeed, many of today's most promising clinical studies in stem cell therapy rely on foreign cells shielded by immunosuppressive drugs (see page 47).

The potential advantages of hypoimmune stem cells, Lickert emphasizes, are clear. "Up to now, we have usually talked about cell therapies as a last resort for only a few severely ill patients." Hypoimmune transplants that make side-effect-prone immunosuppression unnecessary could be used in far more patients – and could therefore also be produced more efficiently and economically. Only a few immunologically compatible stem cell lines might be needed, Lickert speculates. He and many colleagues are already envisioning a "one-cell-fits-all" strategy that would abolish the molecular distinction between "self" and "foreign."

Cells without a molecular "self"

That such a scenario appears realistic at all is mainly due to the greatly expanded understanding of molecular immune mechanisms. Dozens of surface molecules and receptors that regulate the interplay between immune and tissue cells have now been identified. Particularly important is the major histocompatibility complex (MHC). This gene complex encodes highly variable surface proteins that function as molecular name-tags determining the compatibility of tissues from different individuals. In humans, they are known as human leukocyte antigens (HLA),

since the molecules were first discovered on white blood cells.⁹

Their fascinating mode of action has gradually been deciphered: HLA molecules are assembled inside the cell, loaded with tiny protein fragments from cellular metabolism, and then displayed on the cell surface. They show the immune system the internal state and identity of a cell.

T cells constantly scan these molecular "displays." They recognize both unfamiliar HLA antigens – such as those on transplanted tissue – and abnormal fragments embedded in the complexes, for example viral proteins during infection. HLA-I molecules activate cytotoxic T cells, which destroy suspicious cells, whereas HLA-II complexes stimulate helper T cells and trigger coordinated immune responses.

Remarkably, some viruses and cancer cells manage to downregulate HLA production to escape T-cell recognition. Something similar occurs in pregnancy: cells in the fetal part of the placenta (the trophoblast) express hardly any classical HLA complexes and instead display inhibitory molecules, preventing rejection by the maternal immune system.¹⁰

These mechanisms resemble a molecular cat-and-mouse game – and Schrepfer's team made deliberate use of them. In a first step, the researchers disabled the entire HLA system of the transplanted islet cells using CRISPR/Cas. As a result, the cells remained "under the radar" of T-cell surveillance, a form of immune evasion. But this alone would not have sufficed: cells completely lacking HLA antigens – a state immunologists call "missing self" – are attacked by natural killer cells and macrophages of the innate immune system.

In a second step, the researchers therefore introduced the

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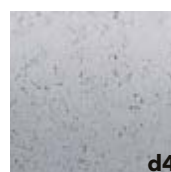
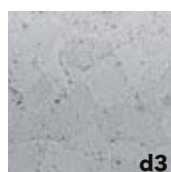


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DNA for a special membrane protein into the islet cells using a viral vector. The molecule, CD47, inhibits both NK cells and macrophages. Many tumors use it as a “don’t-eat-me signal” to evade phagocytes.¹¹ With this modification, the islet transplants were protected not only from T cells but also from innate immune cells. Schrepfer’s team has named these doubly protected hypoimmune cell lines “HIP” cells.

Camouflaged against immune cells – and antibodies

Nonetheless: as sophisticated as HIP technology appears, it is evidently not the final word. “The technological development is by no means finished,” Schrepfer emphasizes. Although the genetically modified transplants no longer offer any direct target for cellular immune attack – T cells do not recognize them at all because of the missing HLA antigens, and the CD47 protection nips the counterattack of innate immune cells in the bud.

But things are more complex when it comes to immune reactions triggered by antibodies, says Schrepfer. “Such rejection reactions are a notorious problem in transplantation medicine,” the immunobiologist notes. Y-shaped antibodies bind with their “arms” to surface antigens on the foreign cells. With their free “tail,” they then trigger immune cascades in the so-called complement system and also put natural killer cells on high alert.

The crucial point, Schrepfer explains, is that antibodies can recognize both foreign HLA molecules and various other antigens that appear independently on the cell surface. This means that even in HIP cells, an Achilles’ heel remains.

It is still unclear what this means for transplants in type 1 diabetes. It is known that in this autoimmune disease, immune cells and autoantibodies target the body’s own insulin-producing β -cells in the pancreas. This is the very reason the disease develops. Cell transplants therefore come under double scrutiny from the immune system: because they are foreign – and because they are β -cells.¹²

Although T cells play the decisive role in the autoimmune reaction in diabetes – and are unable to attack hypoimmune HIP transplants.¹³ Sophisticated animal experiments from Schrepfer’s lab show that modified islets can escape autoimmune attacks.¹⁴ At the same time, however, it is clear that at least some of the disease-specific autoantigens are not tied to the HLA system and

could therefore, in principle, be detected by existing autoantibodies, Schrepfer cautions.

For this reason, when the team was selecting a suitable subject for its pilot study in Uppsala, it defined one autoantibody common in type 1 diabetes (against the transporter protein “ZnT8”) as an exclusion criterion, because it might have endangered the transplant. Of course, this precaution simultaneously undermines the idea of a universal cell line that would truly be suitable for all patients.

Schrepfer – who has since left Sana Biotechnology to continue her research independently – is already thinking of the next step for precisely these reasons: together with her team, she has now equipped pluripotent stem cells with an additional membrane protein to neutralize antibody attacks on top of the camouflage against immune cells. The molecule, known by the abbreviation CD64, captures the free “tail” of antibodies and thereby prevents the cytotoxic chain reaction. Even highly potent immune factors, such as the Rhesus blood group antibody, could not harm cells modified in this way. The special trick is that CD64 protection against antibodies can be combined with the HIP strategy against immune cells in one and the same stem-cell line.¹⁵

Suicide genes as safety switches

Meanwhile, other teams have long been pursuing additional approaches – and a veritable competition has emerged for the most promising hypoimmune cell technologies.¹⁶ “There may well not be a single clear winner in the end,” notes the well-known stem cell biologist Andras Nagy of the Lunenfeld-Tanenbaum Research Institute in Toronto. Yet he firmly believes that stem cell lines can be modified, one way or another, so that practically no human immune system in the world would reject them.

Nagy and his colleagues rely on a completely different strategy from Schrepfer and her team. Instead of eliminating the HLA antigens on the cell surface, his group coats the transplanted cells with a kind of molecular protective layer. It consists of various immunomodulatory proteins. Nagy calls the method “cloaking.” “The protective coat not only reduces the recognition of foreign therapeutic cells, but can also shield them when immune cells try to kill them,” explains the cell biologist.

At present, the researchers are working with genetically mo-

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Communication Along the Gut–Brain Axis

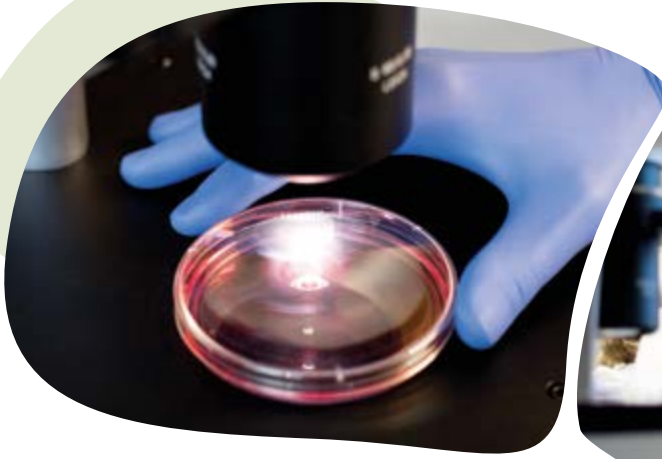
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and therapeutic strategies targeting disorders of the nervous system.

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IN THE LAB: SONJA SCHREPFER WITH TOBIAS DEUSE - A KEY CONTRIBUTOR TO THE DEVELOPMENT OF HYPOIMMUNE CELLS.

dified stem cell lines that carry a set of eight special proteins on their surface. These include molecules that bind to cytotoxic T cells and can trigger their death, as well as the “don’t-eat-me signal” CD47 against phagocytes. The team also uses a so-called non-classical HLA antigen known as HLA-G, borrowed from the placenta’s molecular toolkit: there, it ensures that fetal tissue is tolerated by the maternal immune system.¹⁷

Only recently, Nagy and Australian colleagues showed that

neurons derived from such stem cell lines can produce the neurotransmitter dopamine. When the researchers transplanted these nerve cells into the brains of laboratory animals with Parkinson-like symptoms, the animals’ motor deficits promptly improved. The effect is already well known from earlier transplantation studies with dopamine neurons. However, the molecularly cloaked nerve cells from Nagy’s team provoked no immune reaction at all in the laboratory animals. Transplants lacking

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the molecular cloak, by contrast, activated various immune cell populations, and certain inflammatory molecules increased in the blood and cerebrospinal fluid of the animals.¹⁸

There has been much debate about the role of immune responses in neuronal cell transplants – and whether long-term immune protection is even necessary. In current stem cell trials for Parkinson's disease, for example, patients typically receive immunosuppressive medication only during the first year after transplantation; thereafter the drugs are discontinued (see page 47). The immune response in the brain is considerably weaker than in most other organs – experts speak of an “immune privilege.”



ANDRAS NAGY

“However, this does not mean that the central nervous system is free of immune reactions,” comments Heiko Lickert. It is now known that the brain has its own immune cells, the so-called microglia. In addition, T cells can cross the physiological blood-brain barrier during infections and migrate into the tissue. “Hypoimmune cell transplants that trigger no immune reaction would therefore be advantageous not only for diabetes or for cardiac cell therapies, but in all application areas, including in the brain,”

Lickert is convinced.

Despite all these advantages, Nagy does not wish to conceal the downside of hypoimmune transplants: they deprive the organism of its ability to control them. “If we hide cells from the immune system, that entails serious risks,” Nagy warns. Such cells would not trigger a rejection even if they were infected by viruses or if they mutated into tumor cells and began to proliferate uncontrollably. Experts see this as a potential hazard.

Nagy likes to add a quotation from Henry van Dyke, a 20th-century professor of English literature at Princeton University, to his email signature: “Man is the only creature that dares to light a fire and live with it. Because he alone has learned to put it out.” The message is clear: hypoimmune cell therapies may be a revolutionary technology – but they require a safety anchor in case something goes wrong.

For this reason, Nagy and his team developed a molecular mechanism years ago by which renegade cells in the body can be selectively switched off. The researchers refer to it as a “kill switch.”

The principle: at a site in the genome essential for cell division, an additional so-called suicide gene is inserted, such as the gene for a specific enzyme from the herpesvirus. Whenever the cells proliferate uncontrollably like a tumor, the viral enzyme is automatically produced as well. The clever part is that this enzyme converts an antiviral drug (ganciclovir) into a cell poison. The overgrowing cells can thus be eliminated simply by administering the antiviral drug.¹⁹

In their Parkinson study, Nagy and colleagues were able to show that the kill switch even works in the central nervous system of a living organism. When the researchers treated their laboratory animals with ganciclovir after transplantation, the



ANALYSIS OF THE IMMUNE RESPONSE IN THE LAB OF SONJA SCHREPPEL

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 several locations throughout Germany with the aim of transferring the results from cancer and stem cell research to the clinic.

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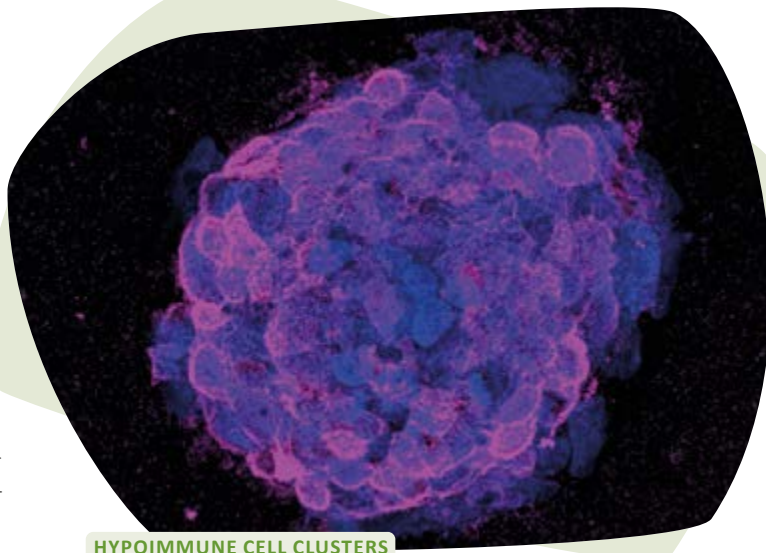
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HYPOIMMUNE CELL CLUSTERS
BY SONJA SCHREPFER

undifferentiated and proliferating cells in the animals' brains disappeared, increasing the safety of the experimental therapy

New cell therapies for autoimmune diseases and cancer

Meanwhile, clinical trials of hypoimmune technologies are already underway in a very different field: cellular immunotherapy. Some experts even consider this to be a particularly obvious area of application.

The treatment principle itself is well established: in patients with leukemias or lymphomas, for example, the body's own immune cells can be taken from the blood and equipped in the laboratory with a genetically engineered receptor, known as a "chimeric antigen receptor," or CAR for short. The cultured CAR cells are then reinfused and, thanks to the artificial receptor molecule, selectively attack the cancer cells in the body.

However, the individualized manufacturing process for each patient is complex and costly. Hypoimmune CAR cells, by contrast, could in principle be transferred to virtually any recipient and might even be better tolerated. And because they can be pre-produced from stem cells on a large scale, experts argue, they could be made available as an off-the-shelf product at significantly lower cost when needed.

For example, the US company Century Therapeutics produces natural killer cells from a multiply modified stem cell line. These cells carry a specific CAR on their surface and can thus attack B cells in the body – while at the same time exhibiting hypoimmune properties. In this way, the cells combine two molecular strategies in one and the same product.²⁰

Century is already testing its cell technology in a pilot study in severe autoimmune diseases such as so-called lupus erythematosus.²¹ It is known that in this condition hyperactive B cells form harmful autoantibodies. The therapeutic killer cells are intended to eliminate precisely these B cells.

The competing company Fate Therapeutics is also pursuing this sophisticated approach. In addition to hypoimmune natural

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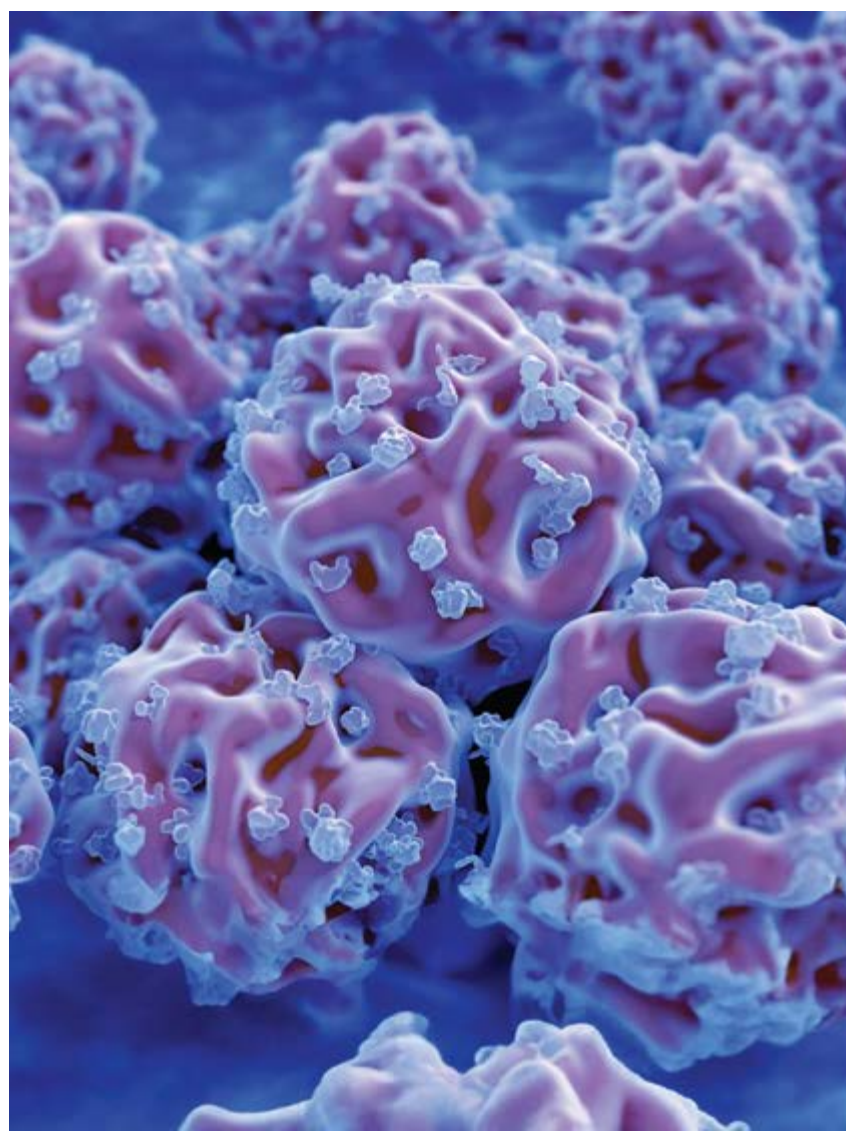
ANDRAS NAGY WITH TEAM
MEMBER IN HIS LAB

killer cells with a CAR receptor²², the San Diego-based team has an even more advanced product in its portfolio: T cells equipped with two different CARs. According to Fate, the cells grown from an immune-compatible stem cell line recognize several pathological cell types in the body – and moreover exhibit increased tissue fitness and greater therapeutic potency. The researchers now hope to have a new weapon at hand, for example against lupus or aggressive B-cell tumors.²³

Do hypimmune cell technologies belong to the future? “In any case, it is impressive how dynamically they are developing,” comments Sonja Schrepfer, who with her team is also working on hypimmune CAR-T cells. It is clear, however, that for each

medical application – whether diabetes, Parkinson’s disease, or cancer – specific cell products would have to be developed and concretely tested in clinical studies.

Paradoxically, the abundance of molecular strategies by which cells can evade the immune system could initially turn out to be an obstacle to practical implementation. For it runs counter to the idea of creating standardized, immune-compatible stem-cell lines. In the coming years, Schrepfer believes, there will probably be a selection of the best methods. At the same time, however, the competing approaches are unquestionably advantageous, she adds. “They demonstrate the potential of this research – and move the entire field forward more quickly.” *Author: Martin Lindner*



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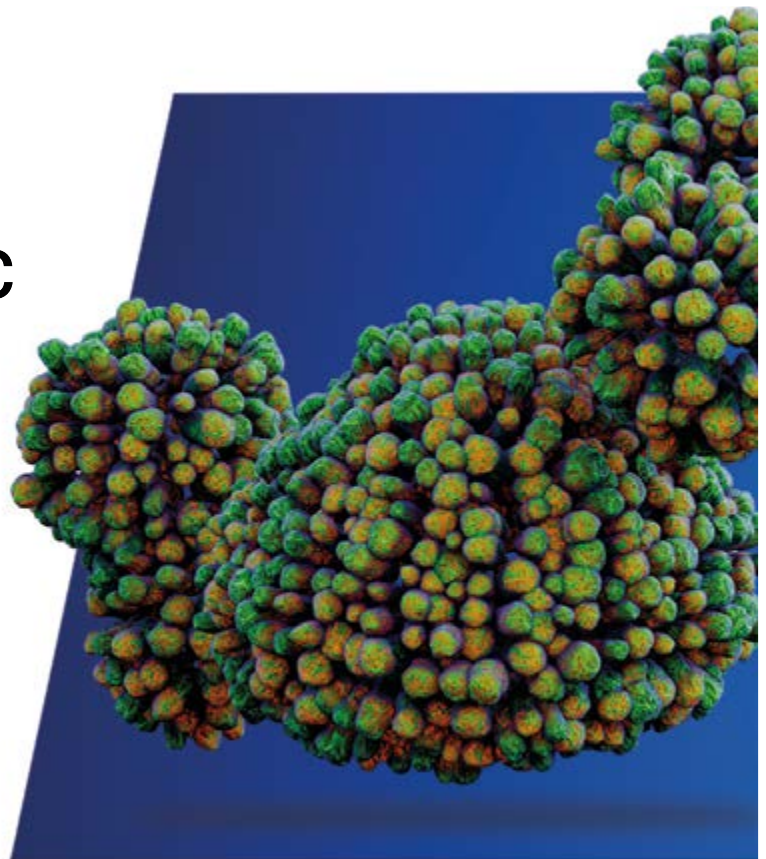
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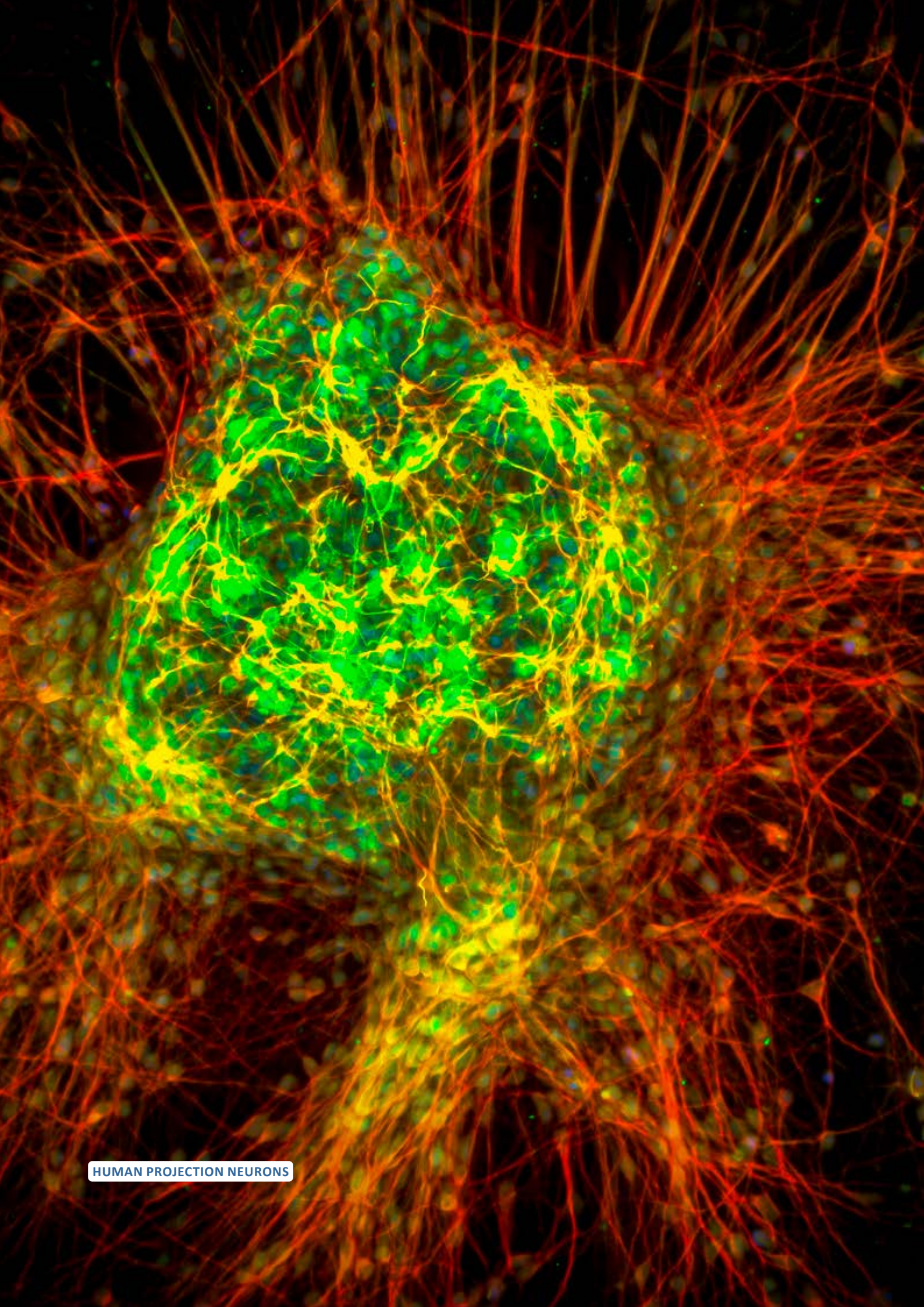
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Stem Cell Trials

Milestones on the path to clinical application

International teams are testing the efficacy of stem cell therapies for the first time in several pivotal trials. Regenerative approaches are particularly advanced in type 1 diabetes, epilepsy, Parkinson's disease, and heart failure—and could soon find their way into clinical practice.

The idea has always been bold—but now it is becoming tangible: regenerative therapy using pluripotent stem cells. According to the latest findings, these all-rounders among human cells can actually replace worn-out tissues or lost bodily functions. Several advanced clinical trials are currently testing the approach in diabetes, heart failure, Parkinson's disease, and epilepsy. It appears that cell replacement therapy has moved beyond its infancy.

"Phase III trials relevant for approval are currently underway for three different stem cell products—we've never seen that before," says Agnete Kirkeby, associate professor at the Novo Nordisk Foundation Center for Stem Cell Medicine in Copenhagen and a recognized expert in the field. "The technologies have matured significantly in recent years; we've learned a great deal." Many experts share Kirkeby's view: the field is at a turning point.

In the late 1990s, US researchers first succeeded in isolating stem cells from human embryos in the laboratory and testing their virtually unlimited developmental potential—a groundbreaking moment for medicine.¹ Nearly a decade later, a Japanese team led by future Nobel Prize laureate Shinya Yamanaka presented a molecular genetic method that can be used to reprogram even fully differentiated body cells back into a stem cell state.²

However, neither embryonic nor reprogrammed ("induced") pluripotent stem cells initially led to a change in therapy. Innovative culture methods were needed to generate specific tissue cells from these undifferentiated all-rounders at scale. Sophisticated animal models for disease-specific analyses and cell transplantation protocols for clinical testing were also required.

Only recently, Kirkeby and colleagues compiled all clinical trials involving pluripotent stem cells—from the first pilot study in 2010 through the end of 2024.³ According to their analysis, more than 1,200 patients worldwide have so far been treated experimentally in 115 studies using over 80 different stem cell products. Some approaches came to nothing, others fell short of expectations—not an unusual picture for medical innovation.

By now, however, it seems clear that this research is bearing fruit. Will stem cell therapy soon move from a medical vision to clinical reality?



AGNETE KIRKEBY

Diabetes: Hormone-producing islets in the liver

Take type 1 diabetes as an example: this autoimmune disease, which usually begins in childhood or adolescence, destroys the insulin-producing β cells in the pancreas. The result is a lifelong dependence on injected insulin.

But stem cell-based therapy may reverse this process. Just last year, an international study team reported interim results in patients with long-standing type 1 diabetes: the researchers had transplanted freshly generated, hormonally active "islets" into them.⁴

In addition to insulin-producing β cells, these microscopic cell clusters also include α cells for the counteracting hormone glucagon and occur naturally in the pancreas. For the ongoing study by the US company Vertex Pharmaceuticals, however, they were grown from an embryonic stem cell line.

The findings so far: ten out of twelve patients no longer needed insulin injections one year after the cell transplant—with blood sugar levels close to normal. The lab-grown "islets" had fully taken over control of glucose metabolism.

"The results exceed even our own expectations," says diabetes specialist Barbara Ludwig of the University Hospital Dresden, whose team is part of the research consortium. The hope now is that a one-time islet transplantation will restore a non-diabetic metabolic state in the long term—making patients significantly more independent in their daily lives.

With a total of around 50 patients enrolled, Vertex has now moved its study into the decisive Phase III testing stage.⁵ If the results are positive, the company is likely to apply for regulatory approval of its cell product fairly quickly in the United States and Europe, but also in countries increasingly affected by type 1 diabetes, such as Saudi Arabia.⁶

The basic idea is not even new: physicians have long been employing islet transplants in very speci-



BARBARA LUDWIG



fic cases—though traditionally using islet cells from deceased donors.⁷ The cell clusters are delivered via a catheter into the blood vessels of the liver, where they engraft as independent endocrine mini-organs. The same procedure is used in the Vertex study. The key advantage, of course, is that the stem cell-derived product, unlike scarce donor tissue, could theoretically be produced in unlimited quantities.

“Nevertheless, our message is not that we will soon treat the majority of type 1 diabetics with a cell transplant,” Ludwig emphasizes. “We must carefully consider for whom this treatment is justified.”

On the one hand, the potential benefits are obvious. According to the diabetes expert, especially for patients who repeatedly slip into dangerous hypoglycemic states without realizing it— and are therefore involved in traffic accidents, for example— islet transplantation is a promising option.

On the other hand, most people with type 1 diabetes can already be treated effectively with modern insulin pumps—a far less expensive technology. In addition, to prevent rejection of the transplanted foreign islet cells, patient’s immune systems must be suppressed with medication.

“This inevitably increases the risk of infection, even though serious side effects are fortunately rare,” says Ludwig. One

study participant, for example, died of meningitis after undergoing a complicated Ear, Nose, and Throat surgery. Although the procedure was unrelated to the cell therapy, the necessary immunosuppression may well have contributed to the course of the infection.

Like Ludwig, many experts assume that island transplantation will initially remain a specialized therapy given the complex considerations involved. Vertex itself has estimated that of the nearly four million people with type 1 diabetes in Europe and North America, only about 60,000 would initially be eligible for the treatment.⁸

In the future, however, so-called hypoimmune cell transplants could prove to be a true game changer. Various teams—including researchers at Vertex—are currently working to generate transplants from genetically modified stem cells that are not rejected by the immune system (see page 37).

Immunosuppression with medication could then be reduced or even eliminated, and the risk-benefit ratio would be much better, Ludwig speculates. Accordingly, the number of diabetics undergoing islet transplantation could quickly increase five- or tenfold.

Parkinson’s disease and epilepsy: New neurons for the brain

Agnete Kirkeby shares this view. “Long-term immunosuppression is, of course, a stumbling block for cell therapy,” says the researcher. This is precisely why the idea of hypoimmune transplants is so appealing.

Kirkeby herself and her colleagues are currently involved in a stem cell trial that appears no less remarkable than the Vertex study. In this study, a total of eight Parkinson’s patients underwent stereotactic surgery to have special neural precursor cells transplanted into their brains.⁹

Animal studies have shown that these precursors can mature in the brain tissue over many months and then produce the neurotransmitter dopamine—the very neurotransmitter that is lacking in Parkinson’s disease due to the gradual death of specialized nerve cells. Kirkeby says that safety data will be released this year, and that efficacy results are expected during next year to show whether the cell transplant reduces the typical motor and cognitive deficits in patients.

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”.

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Three further—even more advanced—studies prove that this hope is not unfounded. Recently, American-Canadian¹⁰, Japanese¹¹, and Korean¹² teams independently reported on nearly identical neuronal cell transplants in a total of around 30 patients with Parkinson's disease. The journal Nature Medicine even included this trio of studies in its selection of "notable advances 2025."¹³

While the Japanese researchers derived their dopamine precursor cells from induced pluripotent stem cells, the other two groups used embryonic stem cells. The teams transplanted between roughly two and ten million lab-grown cells into their patients' putamen, a brain region crucial for the fine control of movement.

A general conclusion was that such transplants are not only feasible without major side effects but also appear to improve dopamine metabolism and alleviate disease symptoms—particularly at higher cell doses. According to current knowledge, only a few of the transplanted precursor neurons permanently survive in the brain. However, the idea is that these can integrate into motor circuits, thereby making movements more fluid again.

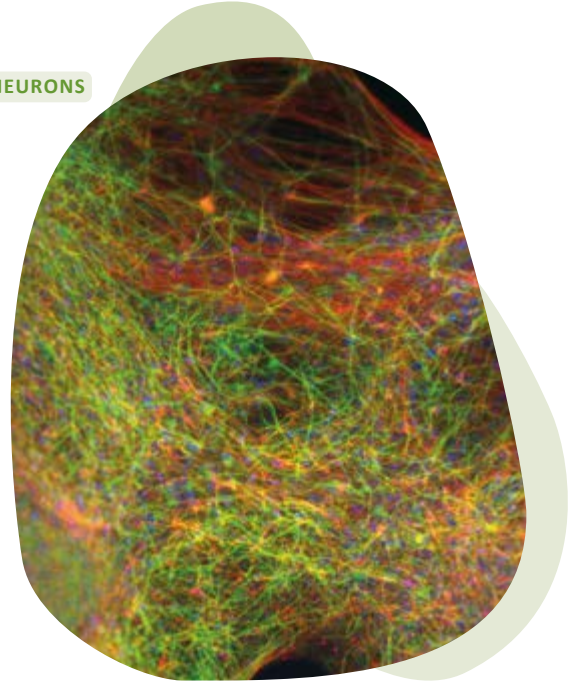
The researchers involved still caution against premature promises. It is well known that symptoms in Parkinson's disease often fluctuate—and that brain dopamine metabolism can even be influenced by a placebo pill.¹⁴ Thus, the positive effects observed with cell therapy could, in principle, reflect psychological artifacts.

However, the initiator of the American-Canadian project, the US company BlueRock Therapeutics, has already launched a large Phase III trial precisely to address these doubts: around one hundred patients with Parkinson's disease will either receive

a neuronal cell transplant—or undergo sham surgery. Comparison with such a sham procedure is considered a rigorous test of therapeutic efficacy. Final clinical data are expected by 2032.¹⁵

Stem cell researchers are pursuing the same strategy in another condition: epilepsy. The characteristic seizures arise from uncontrolled neuronal hyperactivity, often triggered by a speci-

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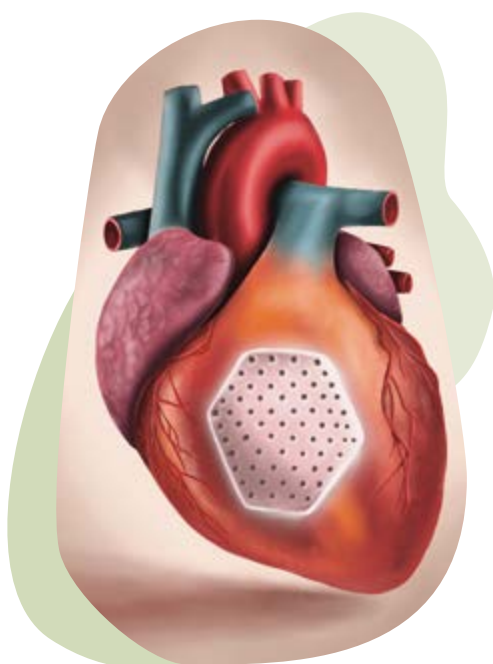
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fic focus in the brain—for example due to degenerative processes or post-infectious scarring.

However, researchers at the California-based company NeuroTherapeutics have shown experimentally that the seizure mechanism can be significantly dampened with cell transplantation. The team generated inhibitory interneurons from an embryonic stem cell line and transplanted them into the brains of epileptic mice. There, the cells integrated into neural networks through new synapses and regulated their uncontrolled activity.¹⁶

Early clinical results suggest that the strategy also works in patients with a common and sometimes difficult-to-treat form of the disease known as mesial temporal lobe epilepsy. According to NeuroTherapeutics, seizures in affected individuals are reduced by up to 90 percent when inhibitory interneurons are specifically transplanted into the epileptic focus.¹⁷ The company is now testing the effects in a large Phase III trial—again with sham-operated patients as a control group.¹⁸



HEART MUSCLE PATCH

If the results are positive, this would be a significant conceptual milestone for stem cell therapy. Vertex's diabetes study has shown that stem cell-derived products can independently take over specific physiological functions. However, the current tests on the central nervous system also suggest that transplanted cells can even integrate into complex tissue structures—demonstrating genuine regenerative potential.

Heart failure: Tissue patches on the muscle wall

What applies to the brain also applies to the heart: here too, it may be possible to repair worn tissue. “We want to repair the heart by rebuilding muscle,” says Wolfram-Hubertus Zimmermann, a tissue engineering expert at the University Medical Center Göttingen and co-founder of the Göttingen-based company Repairon.

Using induced pluripotent stem cells, Zimmermann's team—together with the biotech company—cultivates human cardiac muscle and connective tissue cells and embeds them in a supportive collagen gel. This process produces bioartificial heart muscle patches in the laboratory, about four by four centimeters in size and one millimeter thick. They are intended to restore strength to the heart's ventricles—for example in severe heart failure following a heart attack.

Around two dozen patients have already been treated in an ongoing study¹⁹ at heart centers in Göttingen and Lübeck, Zimmermann reports. During a minimally invasive procedure known as a minithoracotomy, surgeons sew up to 20 tissue patches onto the weakened ventricular wall. Extensive experiments in rhesus monkeys had shown that the transplanted muscle cells mature within the heart and increase its contractile strength²⁰—findings that now appear to be confirmed in patients, as Zimmermann describes. “The ventricular wall becomes thicker, pumping capacity improves, and quality of life increases.”

A key point, he adds, is that the engineered muscle integrates functionally into the heart. Heart contraction is known to be controlled by electrical signals that propagate in a coordinated manner through the atria and ventricles. Mechanical cues during each heartbeat also contribute to synchronized muscle cell activity and are even essential during embryonic heart development.²¹

“Such mechano-electrical integration could explain how the transplants become incorporated into the heart tissue,”

Translation Center for Regenerative Therapies (TLZ-RT)

The rapid transformation of the latest biomedical findings into preclinical applications accelerates product development in the pharmaceutical, medical, and cosmetic sectors and opens up new therapeutic possibilities. The Translational Center for Regenerative Therapies (TLZ-RT) at the Fraunhofer Institute for Silicate Research ISC in Würzburg develops innovative solutions at the intersection of materials research, biotechnology, and medicine, working closely with industry and research partners.

TLZ-RT is structured into three departments. The in vitro test systems department develops functional tissue and disease models of human barrier organs based on primary cells and induced pluripotent stem cells (hiPSCs), supporting animal-free drug development. The laboratory automation department designs flexible automation platforms, specialized bioreactors, and incubators for standardized cell culture processes. The bio-materials department develops biofunctional, biodegradable materials and nanoparticles for applications in regenerative medicine, diagnostics, and drug delivery.



Fraunhofer Institute for Silicate Research ISC
Translation Center for Regenerative
Therapies (TLZ-RT)

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Zimmermann speculates. It would also explain why no cardiac arrhythmias caused by the implanted muscle patches have been observed in treated patients so far.

Whether therapeutic success can be sustained long term remains unclear. As early as next year, Zimmermann and colleagues, together with additional teams, plan to launch an international Phase III trial sponsored by Repairon. The researchers hope it will lead to regulatory approval of the bio-artificial heart muscle. Alongside cell products for diabetes, Parkinson's disease, and epilepsy, it would be the fourth product derived from pluripotent stem cells that could potentially enter clinical practice.

Nevertheless, hurdles remain—particularly due to practical and logistical challenges. "Even for a large Phase III trial, production of the transplants must be scaled up," Zimmermann emphasizes, referring to what is known as "upscaling."

About 40 million cardiac muscle and connective tissue cells are required for a single heart patch. With typically around 20 patches transplanted per patient, this amounts to nearly one billion cells that must be produced using quality-assured processes. A similar scale applies to islet cell transplants for type 1 diabetes.

In addition, while the neurons transplanted for Parkinson's disease and epilepsy can be pre-produced, frozen, and thawed as needed, the more complex islet and heart muscle grafts, which consist of different cell types, are freshly produced. The entire process, from cell culture to transplant, takes many weeks, and the final, cleared product must then be implanted within 72 hours, Zimmermann says.

"You can reach many places in the world by plane within this

time frame," the researcher notes. Nevertheless, additional manufacturing partners, for example in the United States, may be needed for the planned trial. Repairon also aims to pre-produce and freeze the heart muscle and connective tissue cells, so that only the final transplants need to be assembled fresh in local laboratories.

Quite apart from the tricky logistical issues, experts are discussing another difficulty: even if market approval were granted, it would by no means be guaranteed that the new stem cell treatments would be widely adopted. Industry observers refer to this phenomenon as the "second valley of death."²² Advanced cell and gene therapies can sometimes prove too costly and complex in practice, or large pharmaceutical companies—capable of advancing and commercializing the technology—may withdraw from development.

Just last fall, the Danish pharmaceutical company Novo Nordisk, previously a major player in the field, discontinued its cell therapy research in diabetes, Parkinson's disease, and heart failure. According to observers, one reason may simply be the more tangible profits available in other areas.²³ However, if the ongoing Phase III trials deliver convincing clinical data, "industry interest could quickly return," Zimmermann predicts.



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AGNETE KIRKEBY'S WORKING
GROUP IN COPENHAGEN

Cancer, autoimmune diseases, blindness: Perspectives for therapy

Meanwhile, additional clinical prospects for the use of pluripotent stem cells are emerging. One particularly promising area of application is cellular immunotherapy.

A simple reason is that the core therapeutic principle has already been established. For example, in leukemias or lymphomas, a patient's own immune cells can be collected from the blood and equipped in the laboratory with a genetically engineered receptor known as a "chimeric antigen receptor," or CAR. When these CAR cells are reinfused, they can specifically attack cancer cells in the body thanks to the artificial receptor molecule.

The approach is also being explored in autoimmune diseases such as lupus erythematosus. Hyperactive B cells, which produce autoantibodies in an uncontrolled manner, play a major role in the disease process—but could be eliminated by CAR-T cell therapy.²⁴

Many teams are now working to derive therapeutic CAR cells not from individual patients' blood cells but from genetically modified stem cell lines. In this way, they could be produced cost-effectively at scale and used as standardized off-the-shelf products—while also being equipped with immunocompatible surface properties (see page 37). Initial clinical pilot studies with such stem cell-based CAR cell products are already underway.²⁵

Stem cell researchers are also hoping for progress in yet another field: degenerative retinal diseases. In particular, numerous stem cell trials have been conducted in recent years for age-related macular degeneration, in which the retinal region responsible for sharp vision gradually deteriorates. The principle is to transplant newly generated retinal pigment epithelium into the retina. These cells regulate nutrient transport for the light-sensitive rods and cones and support their function.

It is not yet clear how effective these cell transplants are. "The studies conducted to date have provided variable results," comments Agnete Kirkeby. In general, the approach appears to be more promising in earlier stages of the disease than in later phases, she adds. Accordingly, trials are increasingly enrolling patients with milder disease.

Meanwhile, BlueRock—alongside its widely noted Phase III trial in Parkinson's disease—has launched another noteworthy clinical study. For the first time on a large scale, instead of retinal pigment epithelium, the light-sensitive photoreceptor cells themselves are being transplanted. More than 50 patients with hereditary eye diseases such as retinitis pigmentosa will receive fresh precursor cells for rods and cones grown from a stem cell line to counteract progressive vision loss.²⁶ Blindness has always been symbolic of the loss of bodily functions—and the promise of stem cell therapy. The new study may now bring that promise closer to reality.

Author: Martin Lindner

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. Through the coordination of the imi project EBISC2 – The European Bank for iPS Cells – and the global stem cell registry hPSCreg, the Fraunhofer IBMT has 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 in-

telligent sensors, bioinformatic data applications and cryobiotechnology are being developed. The most important criterion here is the generation and cryopreservation of large quantities of stem cells with consistently high quality.

**The Fraunhofer Institute for
Biomedical Engineering IBMT**
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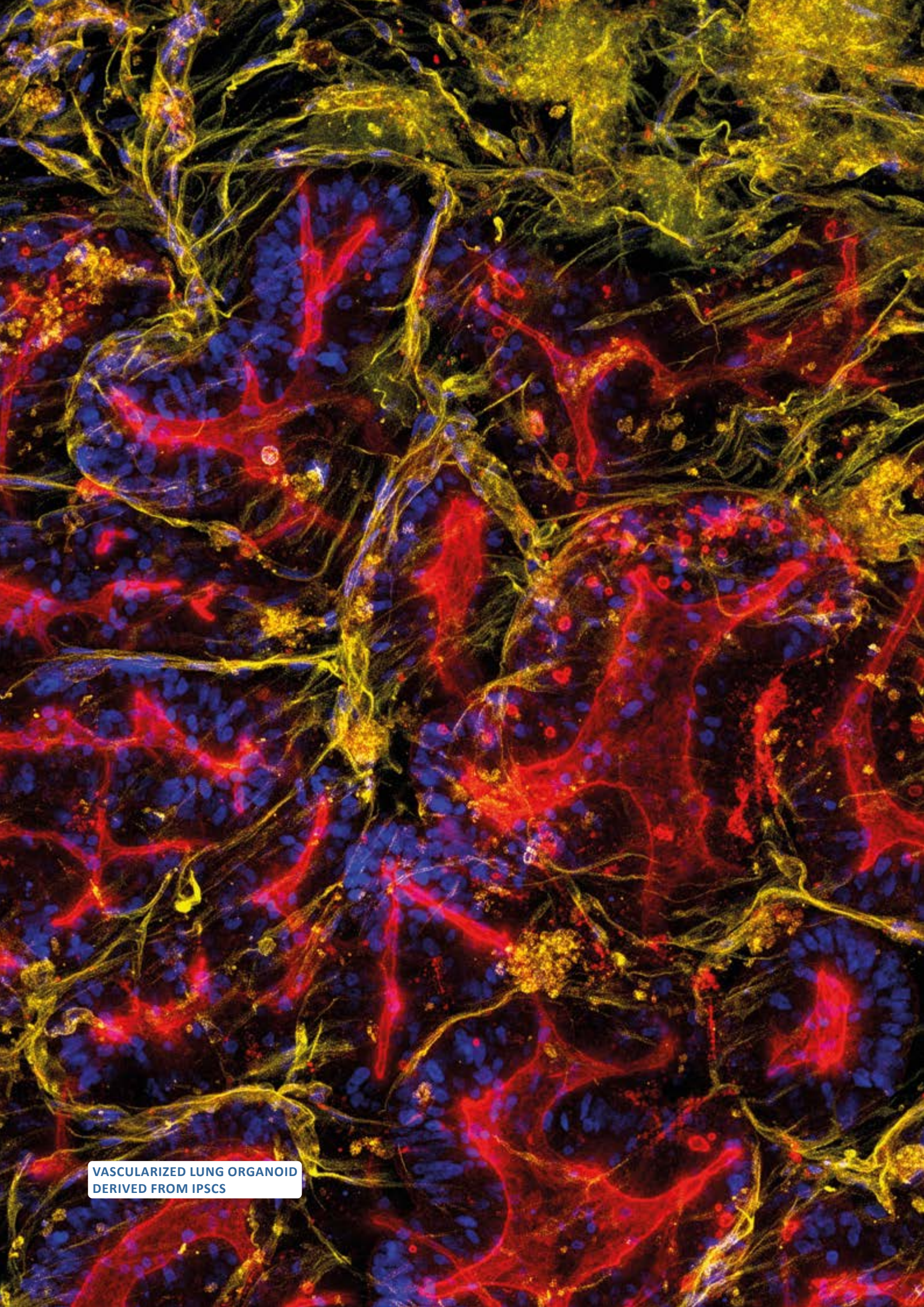


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Background image: Human Airway Organoids frozen in CELLBANKER 1® and imaged post-thaw. IF for DAPI, KRT5 (basal cell marker), Phalloidin (blue/red/green). Images courtesy of the Clevers Lab, Hubrecht Institute.



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“It takes a whole village to bring a medical product to patients”

The GeneNovate® entrepreneurship program aims to inspire scientists and physicians to explore entrepreneurship, equip them with the necessary knowledge, and accelerate the transfer of innovative medical solutions to patients by building a strong network of experts.

After completing her biology degree, earning a PhD in immunology, and working as a postdoctoral researcher in London, Sandra Ammann was ready for a new challenge. “I didn’t want to remain in academia forever,” she recalls, thinking back to three years ago.

At that moment she met Toni Cathomen, Professor of Gene and Cell Therapy at the University of Freiburg. Cathomen had a promising idea for testing the safety of gene therapies and was planning to launch a startup – but he needed someone to lead the project.

“I think this would be a great position for you,” he suggested to Ammann. “Yes, let’s do it!” she replied without hesitation. But soon doubts crept in. “I thought: okay, I know science – but what about everything else?” By coincidence, Cathomen and Ammann met Elke Luger, head of the National Network Office for Gene and Cell Therapies, at the ESGCT conference in Rome. During dinner, the conversation turned to the planned startup, and Luger mentioned the brand-new GeneNovate® program. “That was a perfect fit,” Ammann recalls. “I signed up, commuted from Freiburg to Heidelberg for the workshops, and learned an incredible amount.”

Building an entrepreneurship culture in gene and cell therapy and expert network

“With the GeneNovate® entrepreneurship program in the field of gene- and cell-based therapies, we want to support researchers and physicians in translating their ideas from the laboratory into real products,” says Elke Luger. “This kind of knowledge is still missing from most academic curricula.”

A second major goal is to create a nationwide network of experts that participants can rely on when new challenges arise. I see GeneNovate® as a structure that – like the proverb ‘It takes a whole village to raise a child’ – helps nurture product ideas that emerge in the laboratory,” Luger explains. “Without the expertise of the entire GCT ‘village’, many of these ideas would either never reach patients or would do so only very slowly.”

Together with the experienced consultant Ingo Schroeter, the GeneNovate® team developed a workshop series that provides comprehensive insight into entrepreneurship and startup creation. “I wanted to be part of a team that truly changes something in healthcare,” says Schroeter, who previously helped transform Philips into a health technology company and contributed to building its corporate venturing activities.



“Germany and Europe produce outstanding basic research,” he says. “But when it comes to translating discoveries into real applications, we fall far behind. The value creation often ends up in the United States or China.” For Schroeter, the network aspect of GeneNovate® is key. “If we succeed in bringing together the expertise and resources that are scattered across Germany, we can build something powerful – and become far more competitive than what I’ve seen in the United States.”

Workshops that turn ideas into ventures

In six full-day in-person workshops held in English, participants learn the fundamentals of entrepreneurship. They form teams, receive guidance from experienced mentors, develop a short pitch presentation, and build valuable professional networks. Each workshop is preceded by a two-hour online session covering the theoretical background.

Workshop 1

Introduction to Entrepreneurship | Changing the Healthcare Industry | Creating & Presenting Pitch Decks

Workshop 2

Value Proposition & Business Model Canvas | IP Protection & Management

Workshop 3

Analyze your Market | Create your Business Model | Build your Business Case

Workshop 4

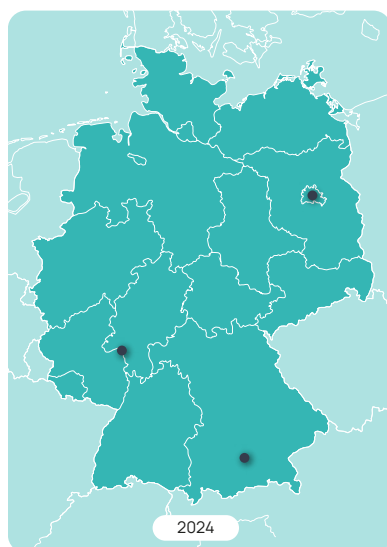
Regulation | Develop your Product/Solution | Go-to-Market: Understand and win customers

Workshop 5

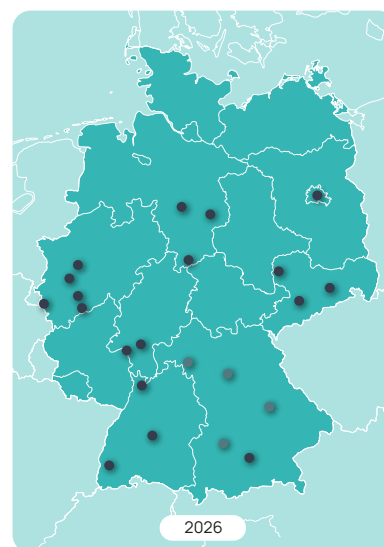
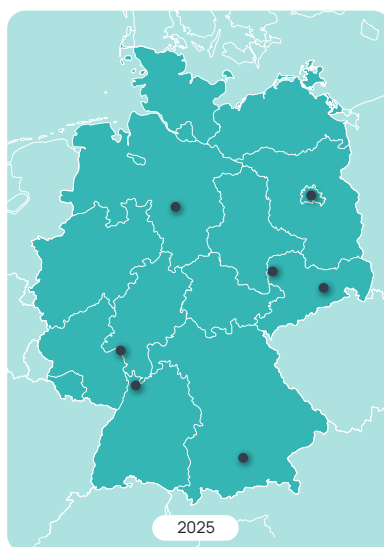
Legal Foundations for Startups | Team management | Project Management | Establish and manage Partnerships

Workshop 6

Financing and Funding | Investor discussions & Negotiations | Exit options & Strategic value



● GeneNovate® regions
● Future GeneNovate® regions



IN ITS THIRD YEAR, THE GENENOVATE® PROGRAM IS ALREADY OFFERED IN NINE REGIONS. IN 2027, FOUR MORE CITIES WILL BE ADDED: THE WERA REGION, INCLUDING THE LOCATIONS WÜRZBURG, ERFURT, REGENSBURG, AND AUGSBURG.

Young ideas – not young people

“Initially, we promoted the program by highlighting our search for early-career doctors and researchers,” Luger recalls. “But that wasn’t the right approach. What we are looking for are young ideas.” As a result, the GeneNovate® workshops now bring together a diverse group of participants – from master’s students and postdocs to professors, department heads, and even experienced founders.

“That diversity is incredibly enriching,” Elke Luger says.

Each location hosts 15 to 30 participants, who form interdisciplinary teams. Initially, Ingo Schroeter led the workshops alone, but today more local experts from industry, technology transfer, finance, and successful startups contribute their expertise. Each team is also paired with an experienced mentor, who helps refine the project idea and prepare the final pitch. At the Final Event they present their ideas to a jury consisting

of business angels, venture capital investors, experienced entrepreneurs, and representatives from politics. Winning teams receive individualized coaching and an invitation to the GeneNovate® Investors’ Day.

1,000 trainees by 2030

“In the first year, 2024, we started with 54 participants at three locations – Berlin, Munich, and Mainz,” Elke Luger explains. Interest grew quickly. In 2026, the program is already running in nine regions. With nearly 200 participants, more than 50 mentors, and over 100 experts, GeneNovate® is now close to nationwide coverage. At the beginning, mentors from many sectors had to be recruited actively. Today, many are so convinced of the program that they ask whether they can continue supporting it – pro bono.

“Our goal is to train 1,000 professionals in gene- and cell-therapy by 2030, and we are well on our way to achieving it,” says Elke

National Network Office for Gene- and Cell-Based Therapies | GCT Germany

The National Network Office GCT Germany was established as part of the National Strategy GCT. We provide a nationwide point of contact and platform for national and international actors and stakeholders from the fields of science, business, patient and self-help organizations, politics, and society, as well as government agencies and foundations. Together with patient and self-help organizations, we develop measures to actively incorporate their perspectives into projects at an early stage.

Our Mission: The Network Office GCT is building a national GCT community information and

networking. We consolidate the expertise and activities of our stakeholders and create sustainable synergies. www.GCT-Germany.de
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Luger. Project ideas are diverse – ranging from RNA inhalation sprays for pulmonary fibrosis to macrophage-based cell therapies for solid tumors.

“These don’t all have to be gene therapies,” Schroeter explains. “For such complex treatments to reach the market, we also need complementary innovations – for example bioinformatic tools for data analyses, diagnostic solutions, small molecules for combination therapies, or safety technologies like the one developed by Sandra Ammann.”



ELKE LUGER

“As a scientist, you don’t think about that”

Sandra Ammann participated in the second GeneNovate® cohort in 2025. “What I found particularly inspiring was hearing founders from different startups talk about their real experiences of launching companies,” she says. She also described the session on how to file patents extremely valuable – how to approach them, how long the process takes, and why precise wording is crucial. “And as a founder you have to report an invention and start the patent process before publishing,” she explains. “That’s something you simply don’t think about as a scientist.” Another key lesson was the importance of a strong team and network. “Through GeneNovate® we found an excellent mentor, Daniel Gau, who is now member of our supervisory board and

helped us tremendously with our pitch,” Ammann says. “Scientists tend to focus on details – but in a pitch things need to be quick and simple. When you think ‘Oh no, this doesn’t sound scientific anymore,’ then the pitch is actually perfect.”

Success in the EXIST competition

Their pitch proved convincing: Ammann and her team from BiObservR successfully secured funding in the EXIST Research Transfer competition, a program of the German Federal Ministry for Economic Affairs that supports research-based startup projects.

The team will receive funding for 24 months to prepare for the company’s launch. BiObservR has developed and patented the CAST-Seq method, which allows researchers to test the safety of gene therapies. In gene therapy, patient cells are repaired using the CRISPR-Cas gene editing system, multiplied, and then returned to the patients. However, the gene editing tool may not only modify the intended target gene but also other regions of the genome – known as off-target effects.

These potential changes must therefore be carefully analyzed before the cells are returned to the patient. “It is crucial to check whether any modifications could potentially trigger cancer,” Ammann explains. “That would obviously be catastrophic.” The method has already been accepted by regulatory authorities. Demand is high: 70 projects from Europe and even the United States have already been analyzed by Ammann’s team.



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INGO SCHRÖTER



A new professional life

Life as a startup founder is very different from life as a scientist – something Ammann actually enjoys. “You suddenly deal with many administrative tasks you never had to think about before. There are lots of meetings, and project management becomes crucial. The work is much more diverse.” BiObservR’s next goal is to offer its services commercially. To develop a solid business model, Ammann brought a business economist with startup experience onto the team. “He will make sure our pricing works and that the company is profitable.” Some former colleagues told her they would find such a step too risky. Ammann understands that perspective – but she also sees the opportunities.

“Of course you don’t know exactly what will happen. But you learn so much that even if the startup doesn’t succeed, you still gain valuable experience and excellent prospects for your next career step.”

Encouraging courage – and changing mindsets

Ingo Schroeter knows that founding a startup requires courage. “The theoretical knowledge is important – especially the parts specific to precision medicine,” he says. “But what matters even more is the personal experience shared in our workshops.” In every workshop, GeneNovate® invites a guest startup founder to talk openly about challenges, failures, and moments when perseverance was essential. These conversations help participants develop the soft skills needed to deal with setbacks.

“Everyone listens, everyone helps, and everyone shares their experience,” Schroeter says. “That’s what really distinguishes this program from other startup initiatives.”

Another goal is to change the mindset of researchers, says Elke Luger. “In the traditional academic career path, everything revolves around publications. Founding a company is still not widely recognized as a valuable achievement in German academia. That is something we want to change.”

Max Delbrück Center

In an ageing society, extending health-span will require not only treating illness, but stopping it before symptoms occur. “At the Max Delbrück Center, we are working on precision prevention – and stem cell-based technologies are an integral part of our efforts,” says Professor Maike Sander, Scientific Director of the Max Delbrück Center. To gain a detailed understanding of the cellular changes that unfold as a person’s health transitions into disease, scientists are engineering complex model systems, such

as assembloids, organs-on-a-chip or vascularized organoids. They have also pioneered high-throughput screenings that use organoids grown from individual patients’ cells.

Other teams harness single-cell and spatial multi-omics approaches to map disease progression with unprecedented resolution. Advanced AI models are helping them to uncover patterns and possible mechanisms within these complex data sets – enabling discovery for tomorrow’s medicine.

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Looking beyond Germany

The success of GeneNovate® has attracted international attention. Universities such as Oxford and Cambridge have already contacted the organizers to explore potential collaborations. “We are also in discussions with partners in Switzerland and Finland,” Luger says. Researchers from France are already participating in workshops in Cologne because it is geographically close.

The next step is clear: launching the first GeneNovate® satellite program outside Germany – in Paris next year. According to Schroeter, the program’s strength lies in its network.

“I still believe that in four or five years the biotech landscape in Germany and Europe will look different,” he says. “And that will be because a network of people with the same drive has come together.”



GENE NOVATE® FINAL EVENT 2025 IN BERLIN

Looking ahead

And what does the future hold for Sandra Ammann? “I’m confident that in five years we will have a strong business model and a successful company offering valuable services for gene therapies,” she says. “And hopefully I’ll still be the CEO.” If so, that would also be a success story for GeneNovate®.

Author: Stefanie Seltmann

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CLIC: Building the conditions for translational biotech to succeed

The BIH Clinical Incubator (CLIC) is a platform of the Berlin Institute of Health (BIH) that assists academic research teams as well as entrepreneurs with their projects on the path to founding a start-up, thereby advancing the development of Advanced and Personalized Therapies (APTs). Under the leadership of Garima Bhardwaj, CLIC aims to support teams with the necessary infrastructure, technical mentorship and regulatory advice for their projects in the field of Advanced Medical Therapy Products (ATMPs). Garima Bhardwaj describes her vision for the GSCN annual magazine.



FOUNDATION OF CLIC 2025

“Is Berlin ready to build globally competitive biotech companies?”

It is a question I have been asked in boardrooms, strategy sessions, and conference corridors since moving from Boston to Berlin two years ago. It is usually posed with optimism, occasionally with skepticism, and always with genuine curiosity.

The answer is not binary.

Berlin does not lack scientific excellence. It does not lack clinical depth. It does not lack ambition. What it has historically lacked is something less visible but more decisive: translational density — the accumulated experience, connective tissue, and

operational discipline that allow early-stage science to become durable companies.

In Boston, that density is cultural. Regulatory strategy is discussed early. Manufacturing considerations are rarely treated as afterthoughts. Investors expect development logic, not just data. Founders encounter repeat entrepreneurs and operators who have navigated the journey before.

Berlin is building that maturity now.

The BIH Clinical Incubator at Charité — CLIC — was created as one contribution to that evolution. Not to replicate another



GARIMA BHARDWAJ

Photos: BIH

ecosystem, but to strengthen the conditions under which translational biotech can succeed within Germany's institutional framework while remaining globally competitive.

CLIC is a public-private partnership embedded within the Berlin Institute of Health (BIH) at Charité and developed in collaboration with the BioLabs network. It supports early-stage biotechs across advanced and personalized medicine — from cellular and genetic therapies to engineered biologics, biomaterials, and enabling technologies that improve development and clinical execution.

The unifying principle is not modality.

It is translation.

And translation is where even strong science encounters friction.

Where friction actually occurs

In early-stage biotech, progress rarely stalls because of a single failed experiment. More often, it slows at the intersections — between science and regulation, between discovery and manufacturing, between academic culture and investor expectations.

A team may generate compelling preclinical data yet have limited clarity on its regulatory pathway. A clinician-founder may underestimate the operational realities of scaling production. A computational platform may not yet be anchored in a reim-

bursable clinical workflow. An academic spin-off may approach capital markets without fully articulating development risk.

None of these gaps reflect weakness. They reflect the inherent complexity of translational medicine.

In mature ecosystems, accumulated experience softens these edges. Knowledge circulates. Expectations are clearer. Advisors and peers compress learning curves.

In ecosystems still consolidating their translational infrastructure, that connective layer must be built deliberately.

CLIC was designed as part of that connective layer.

Beyond infrastructure: Designing structured proximity

An incubator can be many things. At minimum, it can provide high-quality laboratory space and shared resources. That foundation is essential, particularly in advanced biomedical research.

But physical infrastructure alone does not materially improve translational outcomes.

What shifts trajectories is structured proximity — proximity to clinicians who understand patient pathways, to regulatory thinking that shapes development plans, to manufacturing expertise that influences scalability, to investors who evaluate global competitiveness, and to peers navigating similar inflection points.

CLIC's position within BIH at Charité enables access to clinical and translational expertise. Collaboration with BioLabs (<https://www.biolabs.io>) introduces internationally refined standards for lab operations and community building. The intention is to create an environment where founders encounter critical development questions earlier, in a setting that supports rather than penalizes iteration.

Proximity, when structured, becomes discipline.

Clinical integration as early strategy

Being located near a hospital does not automatically translate into advantage. Advantage emerges when founders actively engage with clinical realities.

Early dialogue with physician-entrepreneurs can clarify which endpoints matter, how patients move through care systems, and where adoption barriers are likely to arise. These conversations

ISAR Bioscience GmbH

ISAR Bioscience is a translational company that develops technologies and new therapies for degenerative diseases. We work closely with research institutions and companies in the biotechnology and pharmaceutical industries. In doing so, we act as a bridge between these institutions, creating a direct link between basic research and new therapies and products.

Our focus is on the pathological loss of organ function as a result of aging, premature degeneration, or a malfunctioning immune system.

We use induced pluripotent stem cells, known as iPS cells, to create cell culture models for these diseases and test new therapies—for example, innovative antibodies for Alzheimer's disease. For some diseases, we also develop very specific cells that are used, for example, as therapeutics for autoimmune diseases. We also develop LNP/RNA-based therapies.

ISAR Bioscience GmbH receives core funding from the Free State of Bavaria and has won project from the European Innovation Council (EIC), BMWK, and BMFT, and others.



ISAR Bioscience GmbH
Semmelweisstraße 5 · 82152 Planegg
🌐 www.isarbioscience.de



can refine — and occasionally significantly reshape — development strategies before substantial resources are committed.

Within CLIC, structured clinical engagement is encouraged early. The objective is not to eliminate uncertainty, but to reduce preventable misalignment. When development plans reflect real-world clinical context from the outset, downstream adjustments are often less disruptive.

The same principle applies to regulatory planning.

Introducing regulatory and manufacturing thinking early

In hindsight analyses of delayed or stalled programs, two themes recur: regulatory strategy was introduced too late, and manufacturing complexity was underestimated.

Advanced and personalized therapies — whether cellular, genetic, biologic, or platform-based — are particularly sensitive to these dimensions. Chemistry, Manufacturing, and Controls (CMC) considerations influence scalability, reproducibility, cost structures, and investor confidence. Regulatory frameworks shape the design of preclinical and clinical studies long before formal submissions occur.

When these factors are deferred, they tend to re-emerge at higher technical and financial cost.

CLIC integrates early working discussions around Target Product Profiles, IND/CTA logic, CRO engagement, quality systems, and manufacturing awareness. These are not abstract seminars; they are practical sessions intended to align scientific progress with development feasibility.

IUF – Leibniz Research Institute for Environmental Medicine

IUF
LEIBNIZ-INSTITUT
FÜR UMWELT-
MEDIZINISCHE
FORSCHUNG

The central research mission of the IUF is the targeted and personalized prevention of environmentally induced aging and associated diseases. To this end, the IUF is investigating the role of environmental factors, the underlying mechanisms, how they interact, who is particularly affected and how we can counteract the negative effects of environmental factors in detail. The work focusses on the effects of solar radiation, air pollution, selected chemicals and the interaction with climate factors – on the lung, the skin, the central nervous system and the immune system. IUF uses human-induced pluripotent stem cells (iPSCs) to

generate 2D and 3D models which allow to look into environmentally induced aging processes and associated diseases. In addition, tools are developed to advance quality controls of iPSCs.

IUF – Leibniz Research Institute for Environmental Medicine
Auf'm Hennekamp 50 · 40225 Düsseldorf
🌐 www.iuf-duesseldorf.de/en



In ecosystems where such discipline is cultural, founders internalize it implicitly. Where that culture is still forming, it must be designed.

Operating within — and improving — institutional reality

Germany's research institutions are rigorous, and rightly so. Company creation within a university hospital context involves governance frameworks, contracts, compliance standards, and safety protocols that cannot be bypassed.

For founders, this can appear complex.

A founder-centric incubator in this environment must therefore prioritize transparency. Clear onboarding pathways, predictable expectations, and active communication across institutional interfaces reduce uncertainty without compromising standards.

CLIC operates within this balance: introducing agility where possible while preserving the integrity essential in a clinical-adjacent setting.

From an international perspective, this balance represents both a challenge and an opportunity for Berlin. The city's academic depth is a structural strength. Making company formation within that depth more systematic — less dependent on individual navigation — is part of the next phase of ecosystem maturity.

Community as operational leverage

Another lesson from more mature ecosystems is that community is not ornamental. It is operational.

When founders share experiences about CRO selection, regulatory feedback, manufacturing setbacks, or investor diligence, collective learning accelerates. When company building becomes visible within academic environments, it gains legitimacy. When investors encounter a curated and credible pipeline, engagement deepens.

The BioLabs model emphasizes this community layer intentionally. Within Berlin, it contributes to a broader cultural shift — positioning entrepreneurship as a natural extension of translational research rather than a divergence from it.

Over time, such normalization matters. It influences career

decisions of postdoctoral researchers, shapes clinician engagement, and signals seriousness to external capital.

Density builds trust. Trust attracts participation. Participation strengthens density.

Berlin in a global context

The question of whether Berlin can compete globally in advanced biotech often reflects a comparison mindset. A more productive framing considers how Berlin can leverage its own strengths.

Those strengths include deep academic research capacity, clinical excellence, increasing international talent, and growing venture participation. The area for continued development lies in operational coherence — aligning science, clinical practice, regulatory planning, manufacturing awareness, and capital into integrated pathways.

CLIC represents one structural effort toward that coherence. It is not a standalone solution, nor is it intended to be. Ecosystems mature through cumulative infrastructure and shared intent.

Translation becomes repeatable when structures support it.

From initiative to discipline

The long-term aspiration extends beyond hosting startups. It is to strengthen translation as a discipline.

When translation becomes systematic, fewer ventures rely on extraordinary individual navigation. Development plans are grounded earlier. Manufacturing logic informs research design. Clinical partnerships are structured. Investor conversations reflect realistic pathways.

Berlin is positioned to play a meaningful role in the future of advanced and personalized medicine. Realizing that role requires platforms that combine scientific depth with operational clarity.

CLIC was designed with that premise in mind.

In translational science, discovery is indispensable. But it is structure that carries discovery to patients.

Building that structure — thoughtfully, collaboratively, and with an international perspective — is the work ahead.

Author: Garima Bhardwaj

Photo: BIH

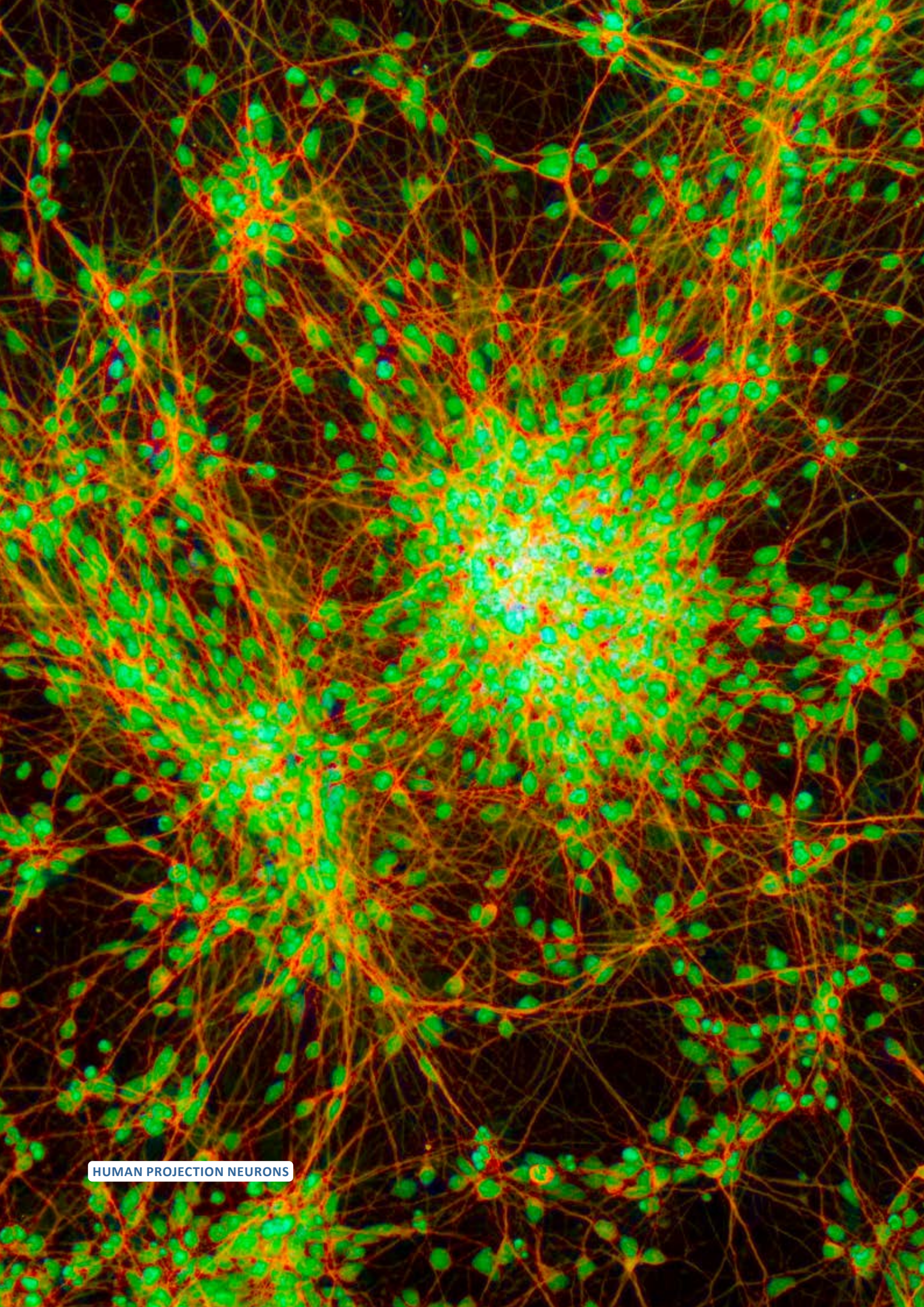
Leibniz Institute for Zoo and Wildlife Research (Leibniz-IZW) in the Forschungsverbund Berlin e.V.

The Leibniz-IZW is an internationally renowned research institute of the Leibniz Association. Pursuing the research goals of "Understanding and improving adaptability", it investigates the evolutionary adaptations of wildlife as well as the challenges they face in the context of global environmental change. The scientists furthermore develop new concepts and measures for conservation. To this end, it uses its broad interdisciplinary expertise in areas such as evolutionary ecology and genetics, wildlife diseases and reproduction management in close dialogue with interest groups and the public.

The "Reproduction Management" department, headed by Prof Dr Thomas B. Hildebrandt, develops techniques for the collection and long-term storage of living cell material from wildlife species. The collected samples and the developed technologies, for example stem cell technologies, can open up new perspectives for the conservation of highly endangered species. The Leibniz-IZW is actively building an international network, including expert meetings with leading scientists worldwide, to exchange knowledge on these technologies.



Leibniz Institute for Zoo and Wildlife Research
Alfred-Kowalke-Straße 17 · 10315 Berlin
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HUMAN PROJECTION NEURONS

HI-STEM, the Heidelberg Institute for Stem Cell Technology and Experimental Medicine

The new institute was actually supposed to be called I-STEM: Institute for Stem Cell Technology and Experimental Medicine. But that abbreviation was already taken. „So we made a virtue of necessity and added the H for Heidelberg,” explains Andreas Trumpp, founding director of HI-STEM. „And it sounds much better that way!”

HI-STEM was founded in 2008 as a public-private partnership between the publicly funded German Cancer Research Center (DKFZ) and the private Dietmar Hopp Foundation in Heidelberg. „As a non-profit limited liability company (gGmbH), it was important to be able to conduct innovative research without restrictions,” emphasizes Trumpp. A commercially oriented limited liability company, as originally planned, would hardly have been able to conduct free research, as a profit-sharing agreement would have had to be negotiated for every cooperation or material transfer, no matter how small. „In terms of research freedom, HI-STEM as a gGmbH is comparable to a public research institute and has its own employment contracts as well as its own structures and obligations to the authorities. This gives us certain freedoms, enabling us to respond directly to rapidly advancing research worldwide and keep pace with it, even taking the lead in some areas,” explains Trumpp.



mant tumor cells, they must first be awakened and stimulated to divide.

At the beginning, five working groups started at HI-STEM and devoted themselves mainly to basic research, such as the characterization of healthy blood stem cells and the role of inflammation in the regeneration of the blood system or the formation of leukemia stem cells. The scientists also gained new insights into „dormancy,” the deep sleep of stem cells, including what triggers it, how it can be ended, and why it exists in the first

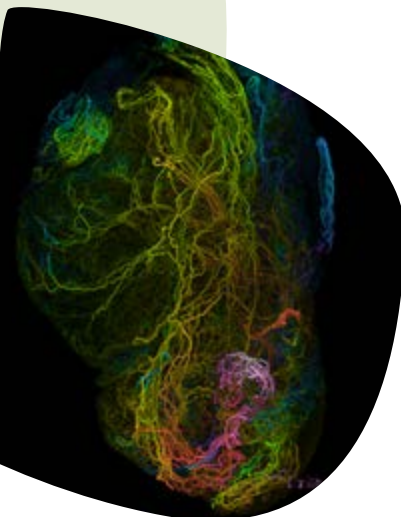
place. Today, nine groups work at HI-STEM, and the institute has grown from an initial 40 to over 90 employees. This has also led to an increase in funding: whereas between 2008 and 2013 the institute received 1.5 million euros per year, HI-STEM now receives twice that amount from the Dietmar Hopp Foundation. The DKFZ has incorporated Andreas Trumpp's „Stem Cells and Cancer” department into the gGmbH and makes the DKFZ's modern infrastructure available to all HI-STEM employees. HI-STEM is still located on the fourth floor of the DKFZ, „but we are bursting at the seams,” admits Trumpp. Some groups have therefore been „outsourced” to other floors of the main building or to adjacent buildings.

Defeating cancer with stem cell research

HI-STEM's ambitious goal is to defeat cancer through stem cell research. „As cancer researchers, we were rather outsiders in stem cell research because we didn't want to use stem cells to regenerate lost cells in degenerative diseases, as most research approaches do, but rather to destroy malignant cancer stem cells,” reports the molecular biologist, who was appointed to the DKFZ in 2008 from the Swiss Cancer Research Institute at EPFL in Lausanne. Cancer stem cells are responsible for the development, spread, and frequently observed resistance to therapy of tumors. The dreaded metastases are also initiated by metastasis stem cells, which spread throughout the body via the bloodstream. Trumpp's research group had just discovered that cancer stem cells fall into a kind of deep sleep during chemotherapy and thus often survive cancer therapy unscathed. They have acquired the ability to sleep reversibly from healthy stem cells. In order to completely kill such dor-

Arrival at the clinic

„Over the years, we have expanded our range of topics and have actually arrived at the clinic,” says Trumpp. „The close proximity to Heidelberg University Hospital and the National Center for Tumor Diseases (NCT) has proven to be a great advantage.” One of the groups at HI-STEM is working on the emerging field of cancer neuroscience and is planning a clinical trial with patients suffering from pancreatic cancer. The aim is to selectively kill peripheral nerve cells that innervate the tumor, thereby depriving the tumor of certain growth signals and at the same time making it sensitive to immunotherapy. Trumpp himself is leading a project with the goal of providing patients with acute myeloid leukemia (AML) with precise, targeted treatment. Until now,



almost all newly diagnosed patients have received aggressive chemotherapy—even though only slightly more than half actually benefit from it. „With our MAC score, we can predict with almost 100% certainty who will respond to a newer drug called venetoclax, a BCL-2 inhibitor, and then offer these AML patients a more effective and better tolerated therapy.“ The goal is to optimally prepare younger and physically fit patients in particular for stem cell transplantation. The MAC score is already being used by clinics in the US, Mexico, and Germany. Together with colleagues from Becton Dickinson, HI-STEM plans to develop a standardized antibody test kit so that even clinics without special expertise can use the new diagnostic tool and obtain results within a few hours for selecting patients

for Venetoclax therapy. A second clinical trial on colon cancer is being planned in collaboration with the California-based company Gilead Sciences Inc., in which colon cancer stem cells will be targeted with an antibody-drug conjugate. And one of the HI-STEM groups is actually working on regenerative stem cell therapies. These are intended to help Parkinson's patients, as well as children and adults suffering from radiation-induced neurodegeneration, a side effect of cancer treatment. To this end, the scientists extract blood cells from patients and reprogram them into neural stem cells. From these, they can generate various types of neural cells, which they intend to transplant into patients to replace the lost cells with the aim of treating the clinical symptoms at their root cause.

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. Prof. Dr. Andreas Trumpp and ten Research Group Leaders direct an international research team of more than fifty employees.

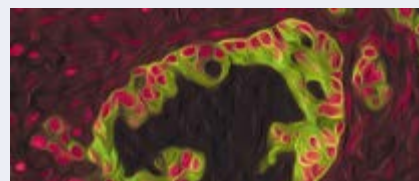
The HI-STEM Research Groups:

- Hematopoietic and Leukemic Stem Cells (Andreas Trumpp)
- Pattern Recognition and Digital Medicine (Daniel Hübschmann)
- Experimental Hematology (Michael Milsom)
- Stress induced activation of HSCs (Marieke Essers)
- Cancer Stem Cells and Metastasis (Martin Sprick & Andreas Trumpp)
- Neural Reprogramming and Clinical Translation (Marc Thier)
- Cancer Progression and Metastasis (Rene Jackstadt)
- Mechanisms of Cell Death and Drug Resistance (Hamed Alborzinia)
- Hematology and Immune Engineering (Mirco Friedrich)
- Global Precision Medicine (Shubhankar Sood)



HI-STEM

HEIDELBERG INSTITUTE
FOR STEM CELL TECHNOLOGY
AND EXPERIMENTAL MEDICINE



**HI-STEM gGmbH within the
German Cancer Research Center (DKFZ)**

Im Neuenheimer Feld 280 · 69120

Heidelberg

🌐 www.hi-stem.de

The secret to success

HI-STEM scientists have published over 200 papers in the past 17 years, many of them in top-tier journals such as Nature, Cell, Science, and Cancer Discovery. In addition, they have secured nearly a dozen patents, raised substantial amounts of additional third-party funding, and won prestigious research awards. Former HI-STEM colleagues now lead research groups at universities, research institutions, or in the pharmaceutical industry. Nina Cabezas-Wallscheid, for example, is a professor of stem cell biology and aging at ETH Zurich. She fondly remembers her time at HI-STEM: „Here, I acquired essential scientific skills and tools and increased my visibility and networking within the scientific community. Both were valuable and a springboard for my professional career.“ Simon Haas holds a Heisenberg Professorship for Systems Medicine in Hematology at the Berlin Institute of Health at Charité. He says: „HI-STEM offers an exceptional scientific environment. Here, scientific creativity is combined with innovative technologies with the aim of advancing biomedical translation. My time at HI-STEM continues to influence the way I conduct research to this day.“ The institute has long been known among cancer and stem cell researchers in Germany and abroad, with applications for doctoral, postdoctoral, and group leader positions coming in from all over the world.

And what is the secret of its success? First and foremost, of course, the generous funding provided by the Dietmar Hopp Foundation and the DKFZ. But also: „My motto has always been to attract particularly intelligent, creative, and team-oriented



employees to HI-STEM and then give them as much freedom as possible. This motivates the young scientists and they often come up with completely new insights that answer questions that no one could have asked before. That's what's really exciting about research, what inspires and motivates," reveals Andreas Trumpp. „This strategy has paid off.“

Author: Stefanie Seltmann



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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 current President (Chairperson), the Senior President (1st Vice Chairperson), the President-elect (2nd Vice Chairperson), the Treasurer and the Assessor. In the current period from **Sept. 2025**, the Executive Board is made up of the following persons:

Acting President (Chairman)	Prof. Dr. Heiko Lickert (Institute of Diabetes and Regeneration Research, Helmholtz Munich) ✉ heiko.lickert@helmholtz-muenchen.de
Senior President (1 st vice chair)	Prof. Dr. Claudia Waskow (Leibniz Institute on Aging FLI, Jena) ✉ claudia.waskow@uni-jena.de
Designated President (2 nd vice chair)	Prof. Dr. Sina Bartfeld (TU Berlin) ✉ s.bartfeld@tu-berlin.de
Treasurer	Dr. Michael Cross (University of Leipzig) ✉ michael.cross@medizin.uni-leipzig.de
Assessor	Prof. Dr. Andreas Trumpp (DKFZ Heidelberg) a.trumpp@dkfz.de



MEMBERS OF THE GSCN BOARDS

Extended Board

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

Mareike Albert (TU Dresden) ✉ mareike.albert@tu-dresden.de	Oliver Brüstle (University hospital Bonn, Life & Brain) ✉ r.neuro@uni-bonn.de
Ingmar Glauche (TU Dresden) ✉ ingmar.glauche@tu-dresden.de	Mina Gouti (MDC Berlin) ✉ mina.gouti@mdc-berlin.de
Nina Graffmann (University Düsseldorf) ✉ nina.graffmann@med.uni-duesseldorf.de	Anne Grapin-Botton (MPI of Molecular Cell Biology and Genetics, Dresden) ✉ botton@mpi-cbg.de
Nico Lachmann (MH Hannover) ✉ lachmann.nico@mh-hannover.de	Stefan Liebau (University Tübingen) ✉ stefan.liebau@uni-tuebingen.de
Ana Martin-Villalba (DKFZ Heidelberg) ✉ a.martin-villalba@dkfz.de	Elvira Mass (Limes Institute Bonn) ✉ emass@uni-bonn.de
Ole Pleß (Fraunhofer ITMP, Hamburg) ✉ ole.pless@itmp.fraunhofer.de	Laura Steenpass (DSMZ – Leibniz Institute, Braunschweig) ✉ laura.steenpass@dsmz.de
Anja Trillhaase (Breitenfelde) ✉ anja-trillhaase@gmx.de	Wolfgang Wagner (University hospital RWTH Aachen) ✉ wwagner@ukaachen.de
Robert Zweigerdt (MH Hannover) ✉ zweigerdt.robert@mh-hannover.de	

Nina Graffmann and Stefan Liebau were elected to the Extended Board in 2025. Oliver Brüstle was re-elected to the Extended Board after one year of absence. Anne Grapin-Botton was also re-elected to the Extended Board. Long-standing board members Nina Cabezas-Wallscheid, Hartmut Geiger, and Meritxell Huch stepped down from the Extended Board in 2025. The GSCN thanks them for their commitment and hopes that, as regular members and coordinators of GSCN working groups, they will continue to advocate for the network's interests and remain available to support its activities.

Working group initiators

Scientific working groups

Pluripotency, differentiation & PSC-derived models

Micha Drukker (University of Leiden, NL)
✉ m.drukker@lacdr.leidenuniv.nl

Mina Gouti

Ralf Jauch (University Hongkong)

✉ ralf@hku.hk

Hans Schöler (emeritiert)

✉ h.schoeler@mpi-muenster.mpg.de

Tissue stem cells & organoids**Sina Bartfeld****Thomas Braun** (MPI for Heart and Lung Research, Bad Nauheim)✉ thomas.braun@mpi-bn.mpg.de**Ana Martin-Villalba****Elly Tanaka** (IMBA Institute Vienna)✉ elly.tanaka@imba.oeaw.ac.at**Basic, translational & applied hematopoiesis****Nina Cabezas-Wallscheid** (ETH Zürich)✉ nina.cabezas@hest.ethz.ch**Simon Haas** (BIMSB/MDC & BIH Berlin)✉ simon.haas@bih-charite.de**Mick Milsom** (HI-STEM Heidelberg)✉ m.milsom@hi-stem.de**Timm Schroeder** (ETH Zürich, Basel)✉ tim.schroeder@bsse.ethz.ch**Claudia Waskow****Stem cells in aging & diseases (cancer stem cells)****Hartmut Geiger** (University of Ulm)✉ hartmut-geiger@uni-ulm.de**Michael Rieger** (Goethe University Frankfurt)✉ m.rieger@em.uni-frankfurt.de**Andreas Trumpp****Stem cells in regenerative therapies****Michael Cross****Ulrich Martin** (MHH Hannover, LBAO)✉ martin.ulrich@mh-hannover.de**Wolfgang Wagner****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.l., TU München)✉ klaugwitz@med1.med.tum.de**Harald Stachelscheid** (Berlin Institute of Health (BIH) at Charité)✉ harald.stachelscheid@bih-charite.de**Computational stem cell biology & systems biology****Georg Füllen** (IBIMA Rostock)✉ fuellen@uni-rostock.de**Ingmar Glauche** (TU Dresden)**Carsten Marr** (Helmholtz Munich)✉ carsten.marr@helmholtz-muenchen.de**Ingo Roeder** (TU Dresden)✉ ingo.roeder@tu-dresden.de

Strategic working groups

Funding programs & policies

Ulrich Martin
N.N.

Career development

Marieke Essers (DKFZ & HI-STEM Heidelberg)
✉ marieke.essers@hi-stem.de
Karin Höhne (Berlin Institute of Health (BIH) @ Charité)
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Pascal Röderer (University hospital RWTH Aachen)
✉ proederer@ukaachen.de
Insa Schröder (GSI Darmstadt)
✉ i.schroeder@gsi.de

Clinical trials & regulatory affairs

Andreas Kurtz (Berlin Institute of Health (BIH) @ Charité)
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Torsten Tonn (DRK-Blutspendedienst Baden-Württemberg – Hessen)
✉ t.tonn@blutspende.de
Zoltán Ivics (Fraunhofer IZI, Leipzig)
✉ zoltan.ivics@izi.fraunhofer.de

Public engagement & outreach activities

Tobias Cantz (MHH Hannover)
✉ cantz.tobias@mh-hannover.de
Ira Herrmann (Life & Brain, Bonn)
✉ iherrmann@lifeandbrain.com

Ethical, legal and social aspects - ELSA

Tobias Cantz
tbd

Patient information (e.g. stem cell therapies)

Ira Herrmann
Richard Schäfer (University hospital Freiburg, Institute for Transfusion Medicine and Gene Therapy)
✉ richard.schaefer@uniklinik-freiburg.de

Technologies in stem cell research

Sebastian Diecke (Max Delbrück Center, Berlin)
✉ sebastian.diecke@mdc-berlin.de
Sebastian Knöbel (Miltenyi GmbH, Bergisch Gladbach)
✉ sebastiank@miltenyi.com
Ole Pleß (Fraunhofer ITMP, Hamburg)
✉ ole.pless@itmp.fraunhofer.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 office. In 2025, the following meetings of the Executive Board took place:

- 06 Aug. 2025
- 14 Oct. 2025

Meeting of the Extended Board

- 14 Oct. 2025

General meeting

- 15 Oct. 2025 in Munich

Overview of members 2025

Total members		524
Natural persons	Full members	295
	Junior members	186
Legal entities	Research institutes	20
	Company > 20 full-time employees	8
	Company < 20 employees full-time	14
	Partner companies	1
Terminations of members in 2025		50

Members of the working groups

Scientific working groups	Pluripotency, differentiation & PSC-derived models	270
	Tissue stem cells & organoids	229
	Basic, translational & applied hematopoiesis	114
	Stem cells in aging & disease (cancer stem cells)	224
	Stem cells in disease modeling & drug development	264
	Stem cells in regenerative therapies	268
	Computational stem cell biology & systems biology	92
Strategic working groups	Funding program & policies	201
	Career development	217
	Clinical trials & regulatory affairs	164
	Public engagement & outreach activities	101
	Patient information (e.g. stem cell therapies)	51
	Ethical, legal and social aspects - ELSA	52
	Technologies in stem cell research	307

Status 31 Dec. 2025

Member institutes

- 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 Regenerative Therapies (TLC-RT) (TERM, Würzburg)

- GCT Network Office Berlin
- Helmholtz Munich, German Research Center for Environmental Health
- Institute for Reconstructive Neurobiology, University Hospital Bonn
- ISAR Bioscience, Munich
- IUF - Leibniz Research Institute for Environmental Medicine GmbH, Düsseldorf
- Clinical Research Unit 5024 (CRU 5024), Erlangen
- Leibniz Institute on Aging - Fritz Lipmann Institute (FLI) e.V., Jena
- Leibniz Institute for Zoo and Wildlife Research on the Forschungsverbund Berlin e.V.
- 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, Mainz

Member companies

- Active Bioscience GmbH
- AMSBIO
- Biolamina
- bio-techne GmbH
- BioMérieux Germany GmbH
- bit.bio
- BlueRock Therapeutics
- Catalent Düsseldorf GmbH
- Eppendorf SE
- Green Elephant Biotech GmbH
- HI-STEM gGmbH
- iota Sciences
- Miltenyi Biotec B.V. & Co. KG
- OLS – OMNI Life Science GmbH & Co. KG
- PELOBiotech GmbH
- PeptiGrowth Inc.
- Proteintech Germany
- Sartorius Lab Instruments GmbH & Co. KG
- STEMCELL Technologies GmbH
- Takara Bio Europe SAS
- Thermo Fisher Scientific – LSG
- TreeFrog Therapeutics

Partner companies

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

General Meeting of the GSCN

On 15 Oct. 2025, the GSCN General Assembly 2025 took place as part of the 13th GSCN Conference with 101 participants. The minutes and the presentation of the General Assembly are available on the GSCN Intranet HumHub in the Membership Documents folder.



Activities 2025/2026

The Network

GSCN Conference 2025

The 13th GSCN Conference took place in Munich with 500 participants and was characterized by intensive scientific exchange. From **15 to 17 Oct. 2025**, the GSCN met at the Neuherberg Conference Center with around 500 scientists, an industry exhibition with 39 exhibitors, 144 posters, 54 talks, and six international keynotes.

Non-PI Meeting 2025

The non-PI Meeting brought together 24 early-career researchers on **14 Oct. 2025** at the Neuherberg Conference Center near Munich. In addition to discussing their own scientific work and everyday professional challenges, participants explored career paths with invited PIs. The organizers Pascal Röderer (Aachen) and Gülce Percin (Cologne) independently and excellently organized the meeting; overnight accommodation and a joint evening dinner were funded by the GSCN.

Scientific Awards – GSCN Awards 2025

The **GSCN 2025 Young Investigator Award** goes to **Aydan Bulut-Karslıoğlu** from the Max Planck Institute for Molecular Genetics in Berlin.

The **GSCN 2025 Hilde Mangold Award** goes to **Michaela Frye** from the German Cancer Research Center (DKFZ) in Heidelberg.

The **GSCN 2025 Publication of the Year Award** goes to **Bryce Lim, Aryan Kamal, ... , Judith Zaugg** and **Moritz Mall**. They receive the “GSCN 2025 Publication of the Year Award” for their joint publication “Active repression of cell fate plasticity by PROX1 safeguards hepatocyte identity and prevents liver tumorigenesis” in the journal *Nature Genetics* 57, 668–679 (2025).

The hybrid GSCN Stem Cell Club

The GSCN Stem Cell Club (GSCC) is a format of the BIH Dialog Platform Stem Cell Research. It is an on-site lecture with one external and one Berlin-based speaker from stem cell research, which is also offered as a hybrid lecture. In Berlin, the two talks are followed by a social gathering with drinks and finger food to encourage on-site networking. The event has also become established globally: participants worldwide are interested in the monthly meeting and join online. The line-up of speakers is remarkable (see details on the GSCN website: [Conferences & Events → GSCN Stem Cell Club \(GSCC\)](#)), and the discussions work excellently in hybrid format.

4x GSCN-on-Tour in 2025

GSCN Managing Director Daniel Besser and communicator Stefanie Mahler traveled four times across Germany in 2025 for the realisation of a local stem cell symposium:

31 March 2025: Leipzig (Michael Cross)

2 April 2025: Hanover (Uli Martin)

24 Nov. 2025: Cologne & Bonn (Kurt Pfannkuche & Oliver Brüstle)

26 Nov. 2025: Aachen (Wolfgang Wagner)

The idea: GSCN presents itself as a network, organizes a stem cell symposium on site with local speakers, and brings together many researchers from the various institutes of a city. All four GSCN on Tour events were very successful, featuring exciting lecture days with many opportunities for get-togethers and networking.

The GSCN participated in 2025 with sessions, public events, and financial support in many successful online and on-site events:

GSCN at the ISSCR Annual Meeting 2025

The GSCN had a strong presence at the ISSCR Meeting from **11 to 14 June 2025** in Hong Kong, China.

The GSCN once again very successfully organized the GSCN Meeting Hub on 13 June 2025 in the exhibition hall of the conference as a meeting point for German scientists and other interested colleagues.

As a ‘WunderBar’ event, the GSCN invited German stem cell scientists, many friends, and the German consuls in Hong Kong on the evening of 11 June 2025 to a club for drinks and finger food to continue networking at the ISSCR – a WunderBar evening full of successful encounters.

IGDL Conference 2025

Interdisciplinary Group for Laboratory and Flow Cytometry (IGDL) took place from March 5 to 8, 2025, and from March 4 to 7, 2026, in Frankfurt am Main. The GSCN participated with several joint sessions in both years, including a presentation by Heiko Lickert in 2025 and Nina Cabezas-Wallscheid in 2026. Andreas Trumpp also gave a keynote in 2026.

DGTI Annual Congress 2025

The GSCN provided financial support for the annual conference of the German Society for Blood, Cells & Tissues (DGTI) held in Mannheim from 17 to 19 Sept. 2025. The joint GSCN-DGTI session took place on Friday 19 Sept. from 10:30 to 12:00 h. The speakers were Robert Zweigerdt (MH Hannover), Gülce Percin (CECAD Cologne), Mengdi Yin (LMU Munich), and Rabea Dettmer (MH Hannover), who also received a “Best Abstract Award” from the DGTI.

EuroGCT Workshop 2025 in Berlin

The EuroGCT workshop for science communication on 17 and 18 Nov. 2025 took place in Berlin at the Rahel Hirsch Center (BIH/Charité). Stefanie Mahler and Daniel Besser jointly shaped the program together with the EuroGCT office in Edinburgh. Together with other European partners, they exchanged ideas on formats of public outreach, AI in research and communication, and patient involvement in clinical trials.

Public GSCN Scientific Events 2025

Computational GSCN Workshop in Berlin and Munich

Within the GSCN working group workshop series, “Computational Stem Cell Biology,” led by Sara Jiménez (Helmholtz Munich), offered two outstanding workshops:

From **7 to 9 April 2025**, Sara Jiménez and Tim Treis from the Fabian Theis Lab / Helmholtz Munich provided beginners and advanced participants with in-depth insights into data analysis and quality control using the two languages R and Python. The workshop was offered again in a similar format from **13 to 15 Oct. 2025** with Sara Jiménez and Franziska Drummer at the Helmholtz Center Munich in Neuherberg.

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

On **20 Nov. 2025**, the GSCN, together with the partners biotechnologieverbund berlin-brandenburg (bbb) e.V., Paul Ehrlich Institute (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? Manufacturing and Translation of ATMPs and Tissue- & Cell-based products” in Potsdam. Driven by remarkable research successes, innovative therapy and product concepts for Advanced Therapy Medicinal Products (ATMPs) are increasingly becoming the focus of interest. The keynote was given by Heiko Lickert, Helmholtz Munich and President of the GSCN.

GSCN Travel Grants 2025

GSCN travel grants provide researchers in Germany as well as GSCN members abroad with financial support to participate in international stem cell research conferences and meetings. Numerous scientists have already been able to attend major events as a result.

6th European Summer School on Microfluidics

 13 Oct. 2025 – 17 Oct. 2025

Niharika Patlolla (Hannover Medical School, MHH)

Stem Cell Summer School, Spetses, Greece

 12 Sept. 2025 – 19 Sept. 2025

Theresa Nägler (Hannover Medical School, MHH)

27th European Brain Barriers Meeting, Bern, Switzerland

 8 Sept. 2025 – 10 Sept. 2025

Markus Glaser (University Hospital Würzburg)

European Hematology Association (EHA) Congress, Milan, Italy

 12 June 2025 – 15 June 2025

Alexander Seitz (Institute of Stem Cell Biology, RWTH Aachen))

ISSCR 2025, Hong Kong

 11 June 2025 – 14 June 2025

Irene Talon (Max Planck Institute for Molecular Genetics, Berlin)

Miriana Dardano (MHH Hanover)

Laim Wilson (MHH Hanover)

63rd Annual Particle Therapy Co-operating Group (PTCOG) Conference, Buenos Aires, Argentina

 2 June 2025 – 7 June 2025

Tamara Bender (GSI Helmholtz Centre for Heavy Ion Research, Darmstadt)

Gordon Research Conference (GRC) 2025 Epithelia Differentiation and Keratinization, Ventura, California, US

 31 May 2025 – 1 June 2025

Yidan Jiang (European Molecular Biology Laboratory (EMBL), Heidelberg)

Gordon Research Seminar and Conference: Functional Genomics of Human Brain Development and Disease, Ventura, California, US

 5 April 2025 – 11 April 2025

Jule Truberg (DKFZ Heidelberg)

Stem Cell Models of Neurodegeneration, Edinburgh, UK

 26 March 2025 – 28 March 2025

Julien Klimmt (Paquet lab, Institute for Stroke and Dementia Research, LMU Munich)

European School of Haematology 5th Scientific Workshop: The Haematological Tumour Microenvironment and its Therapeutic Targeting, London, UK

 16 Feb. 2025 – 18 Feb. 2025

Osman Abhimata Nugraha (Institute for Medical Informatics and Biometry (IMB), TU Dresden)

Science Communication

Public relations and public outreach present the tasks and work of an organization as target-group-oriented information for different audiences. In stem cell research, these audiences for the GSCN include political decision-makers, students, patients, and the interested public.

GSCN publishes Nature Cell Biology Comment on GSCN

Stefanie Mahler, Sina Bartfeld and Daniel Besser published as a comment in Nature Cell Biology on 6 Nov. 2025 a paper on the history, structure, tasks and plans of the GSCN and drew a vision of a possible European Stem Cell Network. Find the article in Nature Cell Biology here.

UniStem Day 2025

UniStem Day in Germany took place on 14 March 2025 in 14 cities. A special focus was on North Rhine-Westphalia with 10 cities and 17 institutes, as well as Berlin, Dresden, and Jena. The stem cell day for students serves to convey current stem cell research, enable encounters with scientists, and encourage discussion in the life sciences, ethics, and diverse research career paths.

Public Event Munich 2025

On 17 Oct. 2025, the GSCN organized a public event at the Munich Press Club at Marienplatz featuring short videos and a panel discussion on the topic “Responsible for Growth, Diseases and New Therapies: Stem Cells – the All-Rounders Among Cells.”

Panel participants **Heiko Lickert** (Helmholtz Munich), **Anette-Gabriele Ziegler** (Helmholtz Munich), **Hartmut Geiger** (University of Ulm), and **Ole Pless** (Fraunhofer IMP, Hamburg) discussed the latest findings from their research fields with moderator **Stefanie Selmann** (Heidelberg). Topics included diabetes, rare diseases, the further development of approved drugs for entirely different indications (drug repurposing), and the aging of stem cells.

Poster Exhibition “Cells for Life”

The modular and interactive poster exhibition “Cells for Life” or “Stem Cells for Life,” with its digital “information spaces,” was used in 2025 on various occasions and at different locations and institutes.

GSCN Teaching Material “Stammzellen-verstehen.de” and “Understanding-stemcell.info”

The GSCN teaching material is available to the general public in both languages. Teachers in particular, as well as continuing education programs for biology teachers, make frequent use of it. An update of the material is planned.

Outstanding Media Contacts

In 2025, the GSCN was approached by journalists throughout the entire year for interviews and background discussions. Daniel Besser was a sought-after interview partner both in and for newspaper articles – but especially for background briefings for journalists to contextualize stem cell research with regard to scientific and ethical questions.

Additional GSCN Events

- Stem cell event for medical students at the Charité on **23 May 2025** and **21 Nov. 2025** at the Rahel Hirsch Center.
- Public lecture “Speakers Corner” at the Berlin Science Week on **1. Nov. 2025**
- Lecture for students on **8 Jan. 2025** at Heinrich-Schliemann-Gymnasium about the “Call a Scientist” initiative of biotechnologieverbund berlin-brandenburg (bbb).

Social Media GSCN

The GSCN uses many channels for its communication: via the HumHub member platform, the newsletter, the social media channels LinkedIn and Bluesky, the GSCN websites, and Facebook, the GSCN reaches its members and interested followers. Patients also get in touch throughout the year seeking assessments of clinical studies and the prospects of stem cell therapies.

Finances

The GSCN is a non-profit association and financed itself in 2025 through membership fees as well as through the joint Dialog Platform Stem Cell Research of the Berlin Institute of Health (BIH) at the Charité. According to §4 of the GSCN statutes, the amount of membership fees is regulated in a contribution schedule adopted by the General Assembly. The membership fees are listed on the GSCN membership application form.

The financial year corresponds to the calendar year. Membership fees are due at the beginning of the financial year. The Executive Board is responsible for preparing the association's annual financial statement and presenting it to the General Assembly. Detailed financial reporting is provided at the General Assembly meetings.

It should be noted that termination of GSCN membership can be carried out easily and informally by email to the GSCN office (office@gscn.org). The notice must be received by 30 Nov. of the year in order to terminate membership for the next financial year (from 1 Jan.).



FIRST HONORARY MEMBER OF
THE GSCN 2025 IS HANS SCHÖLER



GSCN

GermanStemCellNetwork