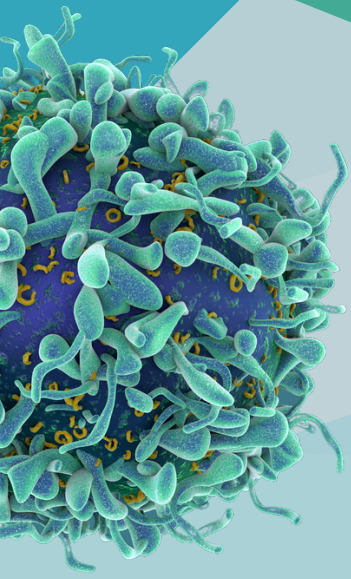
SAXOCELL®

CONFERENCE 2026

From Lab to Life: Advancing Cell and Gene Therapies Together

2 -3 June 2026 I Dresden



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With funding from the: Federal Ministry of Research, Technology and Space

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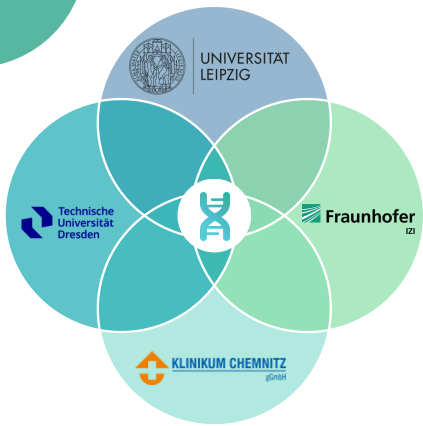
Content

The SaxoCell Cluster



Innovation for living drugs

SaxoCell is developing new ways to produce gene and cell therapies safely, efficiently and affordably. The aim is to make so-called “living drugs” available for clinical application on a large scale and thus strengthen health-care and regional value creation.

A Cluster4Future

With funding from the:
CLUSTERS 4 FUTURE Next generation innovation networks
Federal Ministry of Research, Technology and Space

SaxoCell is a winner of the Clusters4Future innovation competition organized by the Federal Ministry of Research, Technology and Space - BMFTR. Since the start of the first funding phase in 2021, SaxoCell has successfully established itself and was thus able to start the second funding period in October 2024.

The SaxoCell Speakers

Prof. Dr. Dr. Ulrike Köhl

Fraunhofer IZI & Clinical Immunology, Leipzig University

Prof. Dr. Frank Buchholz

UCC Medical Systems Biology, TU Dresden

Prof. Dr. Martin Bornhäuser

Medical Clinic I, University Hospital Dresden & NCT/UCC

Our Network

SaxoCell pursues a regional development approach with nationwide and international reach. We founded SaxoCell e.V. to ensure the cluster's long-term sustainability, to foster networking, and to promote internationalization.

Program

Tuesday, June 2nd, 2026

5.15 pm	**Registration**
6.00 – 6.30 pm	**Welcome Address**
	Welcome by the moderator • **Isabel Werdin**
	A welcome from BMFTR • **Dr. Ralf Gebel,** Head of the sub-department "Innovative Ecosystems" at the BMFTR
	A welcome from Saxony • **Alexander Dierks,** President of the Saxon State Parliament • **Prof. Dr. Heike Graßmann,** State Secretary at the SMWK
6.30 pm	**Opening of the dinner buffet**
7.00 – 8.30 pm	**Dinner Key Notes** • **Lorenz Mayr**, Future Vision and Trends in Cell and Gene Therapy • **Verena Lütschg**, Technology on the rise: Innovation requires enthusiasm
9.00 – 9.10 pm	**SaxoCell Innovation Spotlight** • **Felix Lansing**, Seamless Therapeutics
9.10 – 10 pm	**Get-together**

Program

Wednesday, June 3rd, 2026

8.15 am	**Registration & coffee**
9.00 – 9.15 am	**Welcome by the SaxoCell speakers** • **Ulrike Köhl & Frank Buchholz**
9.15 – 10.30 am	**Session 1: Cell and gene therapy in oncology** • **Marcela V. Maus**, New insights into CAR T cells • **Katrin Wetzko**, TCRs/TILs in solid tumors - state of the art • **Ulrike Weirauch**, Digital Molecular Medicine Approaches for Immunomonitoring Strategy Development and Improvement of Patient Care in Engineered Adoptive Cell Therapy • **Xiaohan Liang**, Optimizing Cell and Gene Therapy Workflows with High-Performance Proteins and Antibodies
10.30 – 10.50 am	**Coffee Break**
10.50 – 11.50 am	**Session 2: Cell and gene therapy in autoimmune diseases and degeneration** • **Dimitrios Mougiakakos**, CAR T cells in autoimmune diseases • **Fabian Müller**, CD19 CAR T cells in autoimmune disease - from deep B cell depletion to lasting remission • **Mike Karl**, Human preclinical modeling of cell therapies for vision loss
11.50 – 12.50 am	**Lunch Break & Poster session**
12.50 – 1.15 pm	**Pitch sessions for pre-seeds and start-ups** • **Christin Zündorf**, TQ Therapeutics • **Dominik Witzigmann**, NanoVation Therapeutics • **Jan Moritz Middeke**, Cancilico • **Patrick Bongartz**, BioThrust • **Katharina Günther**, Green Elephant Biotech • **Jiri Eitler**, SMART-NK Therapeutics

Program

Wednesday, June 3rd, 2026

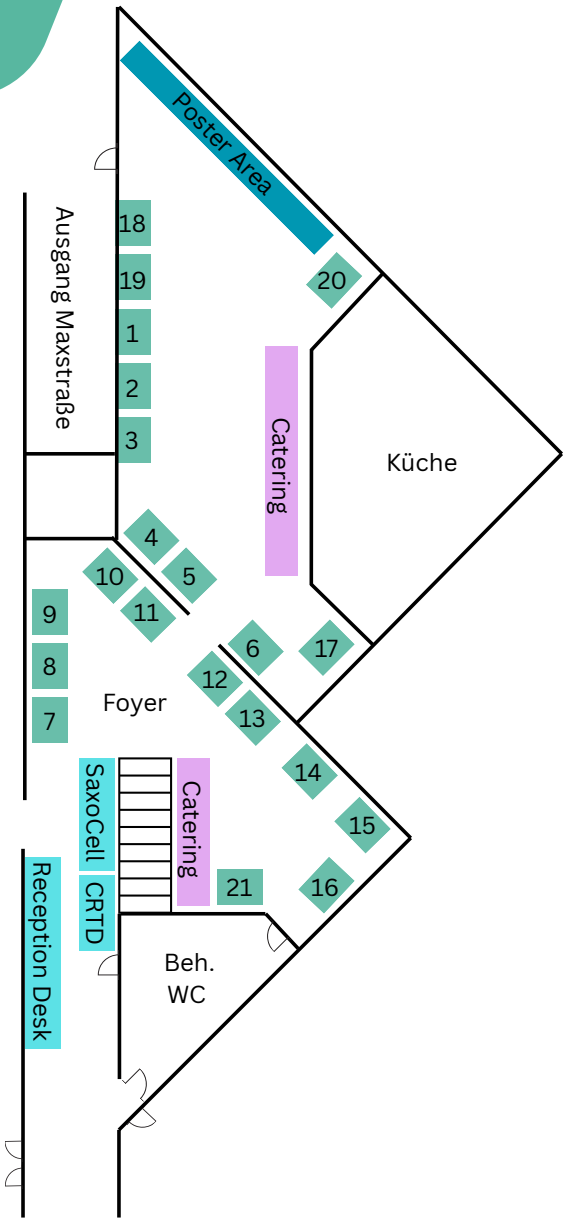
1.15 – 1.40 pm	**Coffee Break**
1.40 – 2.50 pm	**Session 3: Delivery Technologies and new trends in Genetic Engineering** • **Kathrin Schumann**, Strategies for Safer CRISPR-Engineering of Human T Cells • **Ernst Wagner**, Chamaeleon Nanocarriers for RNA Delivery and Genome Editing • **Julian Jude**, Writing The Future - From DNA to Ai • **Martin Rabel**, A next-generation ionizable lipid LNP platform enabling efficient in vivo CAR T cell generation in mice and NHP using passive and active immune cell targeting strategies
2.50 – 3.20 pm	**Coffee Break**
3.20 – 5.40 pm	**Session 4: Challenges towards clinical translation and financing** • **Marcelina Bugaj**, The Therapy Begins Before the Infusion: A Patient Perspective on Anti-CD19 CAR-T Cell Therapy in ACPA-Positive Rheumatoid Arthritis • **Christoph Conrad**, Regulation as a Compass – Learnings from Two Years of Supporting Academic Translation • **Rebekka Wehner**, Clinical relevance of multiplex IHC-based characterization of the tumor immune landscape • **Andreas Traube**, From craft to scale - Matrix Manufacturing for Cost-Efficient Cell and Gene Therapy Production • **Tomasz Baran**, Perinatal Stem Cell Banking as a Platform for ATMP Development • **Ion Tcacencu**, Regulatory Roadmaps to Translate Academic ATMP Innovations into Clinic **Panel Discussion: Regina Demlová, Martin Bornhäuser, Ralf Huss, Marion Jung**
5.40 – 6.00 pm	**Poster and Pitch Award ceremony & Closing remarks**
6.00 – 8.00 pm	**Closing Reception & Networking**

Floorplan

Penck Hotel Dresden

Exhibition

1 - Seamless Tx
2 - Scinus Cell Exp
3 - hVIVO
4 - FhIZI
5 - Sino Bio
6 - Consarctic
7 - Sartorius Cell Gen
8 - Sartorius Lab Inst
9 - QIAGEN
10 - Cytiva
11 - Miltenyi Biotec
12 - Twist Bio
13 - Famicord
14 - LeapUp
15 - WfS
16 - Novogene
17 - Vector Builder
18 - Pro Bio
19 - Cell Signaling
20 - c-LEcta
21 - BIOTYPE



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NANOVATION therapeutics

TQ therapeutics

BIOTYPE

Host & Welcome Remarks

Isabel Werdin
Host

Dr. Ralf Gebel
Head of “Innovative Ecosystems” at the BMFTR

Alexander Dierks
President of the Saxon State Parliament

Prof. Dr. Heike Graßmann
State Secretary at the SMWK

Dinner Key Notes & Spotlight

Lorenz Mayr

Managing Director BioMedTech Consulting GmbH
SaxoCell Advisory Board

Key Note

Future Vision and Trends in Cell and Gene Therapy

Dr. Verena Lütschg

Molecular Biologist, Founder & Entrepreneur

Key Note

Technology on the rise: Innovation requires enthusiasm

Felix Lansing

Co-founder and CTO of Seamless Therapeutics GmbH

SaxoCell Innovation Spotlight

Seamless Therapeutics

Speakers

Session 1

Cell and Gene therapy in oncology

June 3rd
9.15 – 10.30 am

Marcela Maus

Affiliation: Krantz Family Center for Center Research; Paula O'Keefe Endowed Chair in Cancer Research; Massachusetts General Hospital

Job position: Director Cellular Immunotherapy, Massachusetts General Hospital; Professor of Medicine, Harvard Medical School; Associate Director, Gene and Cell Therapy Institute, Mass-General-Brigham; Attending Physician, Hematopoietic Cell Transplant & Cell Therapy Program; Associate Member, Broad Institute of MIT and Harvard

CV: Dr. Marcela Maus is the Paula J. O'Keeffe Endowed Chair at Massachusetts General Hospital Cancer Center, Director of the Cellular Immunotherapy Program, and Professor at Harvard Medical School, where she leads a laboratory focused on advancing CAR T cell therapies for cancer. Trained at MIT, the University of Pennsylvania, and Memorial Sloan Kettering, she has made pioneering contributions to the development of CAR T cells, including research on treatment resistance and therapy-related toxicities. Alongside her scientific and clinical work, she mentors the next generation of researchers and enjoys family life with her husband, three children, and pets, as well as hobbies like gardening and skiing.

New insights into CAR T cells

Abstract: Information on and discussion of latest new insights and work from our group on CAR T cells.

Katrin Wetzko

Affiliation: Early Clinical Trial Unit, Faculty of Medicine Carl Gustav Carus affiliated to the National Center for Tumor Diseases – NCT/UCC

Job position: Deputy director of the NCT/UCC Early Clinical Trial Unit

CV: Katrin Wetzko is a hematologist/oncologist by training and deputy director of the NCT/UCC Early Clinical Trial Unit. She has over 10 years of experience in running well over 100 phase I trials in hematologic malignancies and solid tumors. She and the team of the NCT/UCC ECTU were among the first to apply chimeric antigen receptor T-cells in Germany and pioneered the use of TCR-engineered T-cells in solid tumors. Dr Wetzko led the establishment of the tumor-infiltrating lymphocyte (TIL) program at the NCT/UCC ECTU and treated more than 50 patients with this modality. She is an expert on early drug development and safety management in next generation immunotherapeutics.

Title of the Talk

TCRs/TILs in solid tumors - state of the art

Ulrike Weirauch

Affiliation: Department of Medical Bioinformatics, Fraunhofer IZI

Job Position: Researcher and science manager

CV: Ulrike Weirauch studied molecular life sciences at the University of Lübeck and earned her Ph.D. in cancer research in Prof. Achim Aigner's research group at the Biochemical-Pharmacological Center of Philipps University of Marburg. She was a postdoctoral researcher at the Independent Department of Clinical Pharmacology at the Rudolf Boehm Institute for Pharmacology and Toxicology at the University of Leipzig. Since 2021, she has been working as a researcher and science manager under Dr. Kristin Reiche in the Department of Medical Bioinformatics at the Fraunhofer Institute for Cell Therapy and Immunology IZI on projects at the intersection of molecular precision medicine and bioinformatics.

Digital Molecular Medicine Approaches for Immunomonitoring Strategy Development and Improvement of Patient Care in Engineered Adoptive Cell Therapy

Cell therapies such as CAR T-cells function as living drugs that engage in complex, dynamic interactions with the patient over time. These interactions crucially determine treatment outcome. Advanced immunomonitoring strategies provide comprehensive insights into the status of patient and therapeutic product.

We have established a digital molecular medicine pipeline combining multi-modal single-cell next-generation sequencing (NGS) with advanced bioinformatics analysis. This enables characterization of molecular and cellular signatures, as well as kinetics of therapeutic responses and toxicities. Using this approach, we identified time-dependent cellular and molecular patterns in patients with relapsed/refractory multiple myeloma treated with BCMA-directed CAR T-cells (cilta-cel or ide-cel). We demonstrated product-dependent effects driving distinct mechanisms, resulting in differences in efficacy and toxicities (PMID: 41349540). We also elucidated a case of secondary CAR+ T-cell lymphoma after BCMA-directed therapy by analyzing longitudinal T-cell evolution and clonal dynamics (PMID: 39984633). Further analyses using spatial transcriptomics and integrative epigenomic and single-cell profiling revealed pathogenic mechanisms and therapeutic vulnerabilities (manuscript under review). A dedicated pipeline for single-cell multiomics data, including CAR-engineered products, ensures harmonized and reproducible bioinformatic workflows (PMID: 41741362).

This digital molecular medicine approach integrates single-cell immunomonitoring with regulatory-compliant software engineering to advance clinical biomarker discovery. It enables patient stratification, optimization of donors for allogeneic therapies, and supports preclinical and first-in-human studies of novel cell therapy products.

Xiaohan Liang

Affiliation: Sino Biological Europe GmbH

Job position: Technical Specialist

CV: PhD Scientist with 2 years of intensive industry experience in the full lifecycle of biopharmaceutical development. Technical lead for high-value projects encompassing stable cell line development (CLD), antibody discovery, and recombinant protein expression. Proven track record in designing integrated Upstream-to Downstream strategies, conducting advanced protein characterization and providing expert technical consultation to international clients to ensure project success

Optimizing Cell and Gene Therapy Workflows with High-Performance Proteins and Antibodies

CAR-T therapy is transforming cancer treatment by engineering immune cells to specifically recognize and eliminate tumor cells. In preclinical research, the development of CAR-T antibodies and the optimization of T cell culture conditions are critical for evaluating efficacy, specificity, and safety.

High-quality antibodies from Sino Biological play a key role in target validation, CAR construct optimization, and functional assessment of engineered T cells. Well-characterized antibodies enable precise detection and activation, supporting reliable and reproducible preclinical data.

Cytokines are essential for preclinical T cell culture, promoting proliferation, survival, and maintenance of functional phenotypes. Optimized cytokine combinations enhance cell viability, support consistent experimental outcomes, and allow accurate evaluation of CAR-T cell potency and activity.

The integration of Sino Biological's antibody antibody development platforms with cytokine-driven culture systems strengthens preclinical workflows by improving reproducibility, reducing cell stress, and generating meaningful biological readouts. These tools help refine target selection, assess CAR-T functionality, and anticipate potential safety concerns before in vivo studies.

Leveraging high-quality reagents from Sino Biological enables researchers to accelerate the discovery and validation of effective CAR-T therapies, providing a strong foundation for translational and future clinical studies.

Speakers

Session 2

Cell and Gene therapy in autoimmune diseases and degeneration

June 3rd
10.50 – 11.50 am

Dimitrios Mougiakakos

Affiliation: Department of Hematology, Oncology, and Cell Therapy, Otto von Guericke University Magdeburg

Job position: Chair and Clinic Director

CV: Prof. Dr. Dimitrios Mougiakakos is Director of the Department of Hematology, Oncology, and Cell Therapy at Otto von Guericke University Magdeburg. He studied medicine in Hanover and completed his training in hematology and oncology in Freiburg, Regensburg, and Erlangen, including a research fellowship at the Karolinska Institute. He played a key role in the first clinical applications of CAR-T cell therapy for autoimmune diseases.

CAR T cells in autoimmune diseases

Chimeric antigen receptor (CAR) T-cell therapy has recently been extended from hematologic malignancies to the treatment of severe, refractory autoimmune disorders, representing a fundamental shift from chronic immunosuppression toward immune reprogramming. Early clinical applications have demonstrated that targeted elimination of autoreactive immune compartments can induce profound and durable disease control in patients with otherwise therapy-resistant autoimmune diseases. The mechanistic rationale of CAR T-cell therapy in autoimmunity is closely linked to the pleiotropic role of B cells in immune dysregulation. Beyond autoantibody production, B cells contribute to antigen presentation, cytokine secretion, and the modulation of pathogenic T-cell responses. B-cell–directed cellular therapy therefore addresses multiple immunopathogenic pathways simultaneously and provides a biological basis for sustained disease remission.

Clinical experience initially obtained in rheumatologic autoimmune diseases has expanded to neurological disorders and selected benign hematologic conditions. Accumulating evidence indicates that CAR T-cell therapy can induce long-lasting, therapy-free remissions, accompanied by a reconstitution of the immune system that differs fundamentally from conventional immunosuppressive strategies. These observations have given rise to the concept of an immunological “reset,” characterized by the restoration of immune tolerance rather than transient disease suppression.
Key aspects of clinical implementation include careful patient selection, standardized lymphodepleting conditioning, close monitoring, and structured management of treatment-related toxicities. Available data suggest a distinct safety profile in autoimmune indications, with generally lower incidence and severity of cytokine release syndrome and neurotoxicity compared with hematologic malignancies. Ongoing developments focus on improving accessibility, scalability, and efficacy of cellular immunotherapy in autoimmunity. Emerging approaches such as antigen-specific repolarization of polyclonal T cells without genetic modification, as well as next-generation platforms including allogeneic and in vivo CAR strategies, are expected to further expand the therapeutic landscape.

Fabian Müller

Affiliation: University Hospital of Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Dept. Of Internal Medicine 5 - Hematology & Oncology

Job position: Prof. for Experimental and Clinical CAR T Cell Therapy, Head of CAR T Cell Program

CV: Prof. Müller obtained his MD in Freiburg, Germany and started his clinical education in Hamburg. With a focus on targeting malignant B cells from his early research career he did a postdoctoral fellowship with Dr. Ira Pastan, at the NCI on resistance to CD22-targeted therapy in ALL and aggressive lymphoma. After his post-doc he continued the work on B cell targeting in Erlangen, Germany using first antibody directed therapies and then CAR T cells with a focus on translational concepts including tumor microenvironment and functional aspects of a patient's immune system. As head of the CAR T cell unit, he pioneers CAR T cell therapies in novel indications including solid tumors and autoimmune diseases.

CD19 CAR T cells in autoimmune disease - from deep B cell depletion to lasting remission

Loss of self-tolerance is a critical event in auto-immune diseases. How are B cells involved? Which autoimmune diseases are B cell dependent? How can a B cell depletion reset the immune system? Which format and which target is the best? Are autologous, allogenic or non-T CARs the way to go? There are many questions, several are adressed in this talk.

Mike Karl

Affiliation: TUD Dresden University of Technology, CRTD – Center for Regenerative Therapies Dresden und Deutsches Zentrum für Neurodegenerative Erkrankungen e.V. (DZNE) Dresden

Position: Professor, Retinal Stem Cell Research and Neurogenesis

CV: MD in Hamburg; Research career in Philadelphia, Seattle.
Prof. Dr. med. Mike O. Karl is a group leader at the German Center for Neurodegenerative Diseases (DZNE) and professor at the Center for Regenerative Therapies Dresden (CRTD), TU Dresden. His research focuses on human retina degeneration and therapy, with a particular emphasis on photoreceptor neurodegeneration, glia biology, and human stem cell–derived cell and organoid technologies as disease and therapy-validation models. He has made key contributions to understanding cellular mechanisms of retinal degeneration and to the development of human-based translational model systems for age-related macular degeneration and inherited retinal diseases. His work has been recognized by multiple awards in ophthalmology and regenerative medicine, and he actively bridges fundamental discovery with translational and therapeutic innovation.

Title of the talk

Human preclinical modeling of cell therapies for vision loss

Speakers

Session 3

Delivery Technologies and new trends in Genetic Engineering

June 3rd
1.40 – 2.50 pm

Kathrin Schumann

Affiliation: University of Konstanz

Job position: Professor for Immunology

CV: Kathrin Schumann studied biochemistry at the University of Tübingen and obtained her PhD at the Max Planck Institute of Biochemistry in Martinsried. During her postdoc at the University of California, San Francisco, she developed CRISPR technologies for the engineering of primary human T cells. In 2018, she was appointed as Rudolf Mößbauer Tenure Track Assistant Professor of “Engineering Immune Cells for Therapy” at TUM School of Medicine. In 2025, she took up the position of Chair of Immunology at the University of Konstanz.

Strategies for Safer CRISPR-Engineering of Human T Cells

CRISPR-engineered chimeric antigen receptor (CAR) T cells represent a leading edge in innovative cancer therapies. However, multiple studies have reported the emergence of chromosomal abnormalities caused by CRISPR editing. To date, efforts to enhance the genomic safety of T cell products have largely focused on refining CRISPR-Cas9 components, with less attention given to intrinsic T cell properties, such as their rapid expansion following T cell receptor (TCR) activation.

We identified key factors influencing indel formation in primary human T cells. We find that heightened T cell activation and faster proliferation are associated with an increased frequency of large deletions. Editing T cells in a non-activated state lowers the risk of such deletions, though it also reduces knockout efficiency. As an alternative approach, treatment with the small molecule pifithrin-α decreases the occurrence of large deletions, chromosomal translocations, and aneuploidy in a manner independent of p53, while preserving the functional capacity of CRISPR-engineered T cells, including CAR T cells. Overall, modulating T cell activation and applying pifithrin-α treatment emerge as practical strategies to enhance the genomic stability of CRISPR-engineered T cells.

Ernst Wagner

Affiliation: Ludwig-Maximilians-Universität (LMU) München

Job position: Professor, Chair of Pharmaceutical Biotechnology

CV: Ernst Wagner is Chair of Pharmaceutical Biotechnology, Department Pharmacy, LMU Munich (since 2001) and member of Munich Center of Nanoscience (CeNS). He was Director Cancer Vaccines, Boehringer Ingelheim 1992-2001 (world-wide first polymer-based gene therapy in 1994), Group Leader at IMP Vienna and the Vienna University Biocenter (1987-1995), postdoc at ETH Zurich (1985-1987), PhD in chemistry (1985, TU Vienna). He is Academician of the European Academy of Sciences, member of College of Fellows of Controlled Release Society (CRS), Honorary Professor at Sichuan U and at Jinan U. He authored ≥ 529 publications, with > 56 000 citations, h-index 119 (GS).

Chamaeleon Nanocarriers for RNA Delivery and Genome Editing

Improved, targeted delivery of RNA drugs is an important goal. A bio-inspired chemical evolution strategy of identified small sequence-defined lipopeptides with outstanding RNA transfer efficacy, easy available by simple (4-5 step) synthesis using natural or artificial amino acids, and lipo amino fatty acids (LAFs). LAF-peptides are dynamic in their response to endosomal pH ("molecular chameleons"), resulting superior endosomal escape. Refinement of carriers in sequence and topologies generated U-shape topologies with polar domain between LAF lipids, and Bundle topologies with the polar domain at the end. Bundle carriers transfect in full serum at very low mRNA dose (only ~2 nanoparticles/cell). Upon systemic administration of mRNA complexes, expression is found in the majority of organs of mice, with the highest levels in the spleen. Formulation of siRNA into LAF-LNPs results in in vivo gene silencing in liver endothelial cells or, upon coating of LNPs with PEG-cRGDfk, gene silencing targeted into tumor endothelial cells. Carriers for CRISPER Cas9/sgRNA trigger genome editing in cell culture at ultra-low dose and upon i.v. application in skeletal muscle, heart muscle or brain of mice.

Molecular mechanisms of carriers are enlightened by biophysical (LogD), ultrastructural (TEM, SAXS) characterization and MD calculations. The LAF domains trigger strongly pH-dependent distribution from lipid phase at physiological pH to lipid/water interface at endosomal pH, demonstrated by a 2 log unit change in logD and supported by MD. Carrier topologies drastically differ in their interaction with lipid membranes, as analyzed by SAXS in cholesterol bulk phases. The flexible U-shapes form standard lamellar phases and the more rigid dendritic Bundles fusogenic form inverted phases, with immediate impact on transfection mechanism and kinetics.

Julian Jude

Affiliation: Twist Bioscience

Job position: Director Emerging Applications SynBio

CV: Julian Jude is the Global Director of Emerging Applications at Twist Bioscience. His career spans functional genomics, genome engineering, and technological development in academia and industry. He developed shRNA and CRISPR screening platforms, conducted over 70 genome-wide FGX screens, co-created the Vienna Bioactivity gRNA algorithm, and established a CROP-Seq platform at a startup. Before joining Twist in 2019, he advised scientists worldwide on custom workflows and built strategic partnerships. After a brief role in AI-metagenomics as Genome Engineering Lead at Basecamp Research, where he built novel nucleases, he returned to Twist in 2024, combining his deep expertise in functional genomics with a passion for emerging technologies and Twist's synthetic DNA capabilities to help accelerate discoveries across the life sciences.

Writing The Future - From DNA to Ai

Twist Bioscience's Julian Jude will present how the company's cutting-edge silicon-based DNA synthesis platform is revolutionizing scientific research across sectors including industrial biotechnology, agriculture, and biopharma.

Artificial intelligence is reshaping how we design, understand, and engineer biological systems, but the true impact of AI depends on how seamlessly digital predictions can be transformed into real biological molecules. In this talk, we explore how Twist's synthetic DNA platform enables exactly that: bridging the digital and physical worlds to bring AI-generated biological designs to life.

At the core of this transformation are Twist's high-fidelity and scalable pooled DNA modalities — up to 1800 base pairs in length — which allow researchers to rapidly and cost-effectively build complex libraries of proteins, mRNA UTRs, promoters, and more, directly from in silico models. We'll explore how scientists are using Twist's synthetic DNA solutions to translate machine learning predictions into functional biological components, enabling a new generation of discoveries in areas such as antibody engineering, enzyme optimisation, and novel nuclease development.

The talk will include case studies showcasing how Twist's synthetic DNA is used to close the loop between AI and wet-lab biology.

Martin Rabel

Affiliation: Cytiva

Position: BPS Business Development & Licensing Manager

CV: Martin Rabel, Ph.D., leads Cytiva's BioPharma Services in EMEA, with a focus on RNA-LNP technologies and CDMO solutions. He supports nucleic acid therapy development through Cytiva's lipid nanoparticle platform and integrated development, analytical, and manufacturing services. With a background in Pharmacy and Nanomedicine, he drives innovation across the biopharma landscape while delivering scientific and commercial excellence.

Next-Gen Ionizable Lipid LNPs Enable In Vivo CAR T-Cell Generation via Passive and Active Targeting

Ex vivo CAR T cell manufacturing is constrained by complex logistics, long vein-to-vein timelines, and high cost, motivating in vivo approaches that enable repeatable, on-demand dosing. Here we describe an ionizable RNA–lipid nanoparticle (LNP) platform with intrinsic spleen and lymph node tropism, coupled to a scalable analytical and conjugation framework for T cell targeting. Reporter RNA-loaded and Cre-recombinase mRNA LNPs were characterized for size, polydispersity, and encapsulation efficiency, administered intravenously in mice, and evaluated by IVIS imaging, flow cytometry, and tdTomato recombination. A lead LNP formulation was scaled using controlled mixing, tangential flow filtration, sterile filtration, UHPLC-CAD, high-resolution mass spectrometry, and SEC-MALS, then tested in cynomolgus monkeys for biodistribution and tolerability. Untargeted LNPs showed strong immune-organ accumulation, with spleen-to-liver ratios >3:1 in mice and >4:1 in non-human primates, and lymph node-to-liver ratios near 1:1. Cell analyses indicated preferential transfection of dendritic cells and macrophages, with ~10% T and NK cell transfection and minimal B cell delivery.

To improve T cell selectivity, an anti-CD8 antibody/nanobody was conjugated to the lead LNP. Increasing ligand density boosted CD8+ T cell transfection to 60%, and further optimization achieved up to 80% transfection in blood and spleen, with strong preference for CD8+ over CD4+ T cells. When loaded with CD19 CAR mRNA, targeted LNPs suppressed Nalm6 proliferation and induced tumor regression in humanized mice at 0.25 mg/kg. Preliminary cynomolgus data show >40% CAR expression in CD8+ T cells at 0.1 mg/kg with acceptable safety. These results establish a scalable immune-tropic LNP platform for in vivo CAR T generation and support clinical translation of repeat-dosing RNA delivery systems for precise in vivo cell engineering.

Speakers

Session 4

Challenges towards clinical translation and financing

June 3rd
3.20 – 5.40 pm

Marcelina Bugaj

Position: Patient Advocacy

The Therapy Begins Before the Infusion: A Patient Perspective on Anti-CD19 CAR-T Cell Therapy in ACPA-Positive Rheumatoid Arthritis

For a subset of patients with ACPA-positive rheumatoid arthritis, current therapeutic strategies remain insufficient, with incomplete disease control and limited durability of response. Novel approaches such as anti-CD19 CAR-T cell therapy aim to address autoimmune disease at a mechanistic level by targeting autoreactive B-cell populations.

Christoph Conrad

Affiliation: Berlin Institute of Health @ Charité (BIH@Charité), Regulatory Support Unit

Position: Head of Staff Office Regulatory Affairs and Regulatory Support Unit

CV: Dr. Christoph Conrad worked for many years on vaccine evaluation at the Paul Ehrlich Institute (PEI) and later headed the Office for Scientific and Regulatory Advice (OSRA), an infrastructure of the German Center for Infection Research (DZIF). He also gained international and governmental experience at the WHO in Geneva, the BMBF (now BMFTR), and the Federal Chancellery. Since July 2022, he has been Head of Staff Office Regulatory Affairs at the BIH and, since June 2024, also leads the newly established Regulatory Support Unit.

Regulation as a Compass – Learnings from Two Years of Supporting Academic Translation

Translating innovative therapies from academic research into clinical application remains a fundamental challenge, particularly in the context of highly complex modalities such as cell and gene therapies. While scientific excellence is rarely the limiting factor, many projects encounter structural and procedural hurdles along the development pathway.

Drawing on over two years of experience from a national Regulatory Support Unit (RSU) for academic developers, this talk reflects on the role early regulatory guidance can play in navigating these challenges. Rather than framing regulation as a barrier, it will explore how regulatory orientation can function as a strategic tool to structure development, align disciplines, and reduce uncertainty.

Rebekka Wehner

Affiliation: Institute of Immunology, Faculty of Medicine Carl Gustav Carus, TUD Dresden; National Center for Tumor Diseases (NCT), NCT/UCC Dresden, Helmholtz-Zentrum Dresden-Rossendorf (HZDR); German Cancer Consortium (DKTK), German Cancer Research Center (DKFZ), Heidelberg, Germany

Job position: Postdoc at Institute of Immunology, TU Dresden
Coordinator, NCT Immune Monitoring Unit Dresden

CV: Rebekka Wehner graduated in biology, did her Ph.D. and habilitation on dendritic cells. In the Institute of Immunology, medical faculty, TU Dresden, her research focuses on human immune cells like dendritic cells, monocytes/macrophages, natural killer cells, and T cells in the context of anti-tumor immune responses and therapies. Since 2016, she coordinates the NCT/UCC Immune Monitoring Unit Dresden, which offers an accompanying immune monitoring program during clinical studies. She supports the characterization of immune cells in blood, bone marrow, and tissues of tumor patients using multiplex flow cytometry and fluorescence-based immunohistochemistry.

Clinical relevance of multiplex IHC-based characterization of the tumor immune landscape

In various tumor entities the immune architecture plays an essential role for the clinical outcome of cancer patients and their response to therapy. The significant impact of tumor-associated dendritic cells, monocytes/macrophages, B cells, and T lymphocytes has been published by us and others in recent years. In this context, not only the frequency, but also the functional properties and spatial organization of tumor-infiltrating immune cells are crucial. Fluorescence-based multiplex immunohistochemistry (mIHC) is an excellent tool for high-dimensional characterization of the tumor immune microenvironment, providing detailed insights into the phenotype and localization of immune cells.

In the current presentation, I will describe our journey from basic research to clinical application of mIHC. First, we analyzed the immune-cell composition in different cancer types and their association with prognosis and therapy response. This enabled us to identify components of the tumor immune architecture such as dendritic cells, proliferating B cells, and tertiary lymphoid structures as independent prognostic or predictive biomarkers. In addition, we measured the anti-tumor capacity of therapeutically relevant CAR T cells confronted with patient-derived organoids. As a next step, we apply the gained knowledge and expertise to various translational projects, clinical trials, and molecular tumor boards recommending treatment options. Based on these findings, we want to use mIHC as a clinically actionable tool for improved patient stratification and the identification of more effective individualized therapeutic strategies.

Andreas Traube

Affiliation: Fraunhofer IPA

Position: Geschäftsbereichsleiter Gesundheitsindustrie und Life Sciences

CV: Degree in mechanical engineering with a focus on production engineering. Passionate about the intersection of bio-workflows and automation; established and led the laboratory automation and bioproduction divisions at Fraunhofer IPA. Serial entrepreneur (Dispendix, Nanolockin, Liquimetrix)

From craft to scale - Matrix Manufacturing for Cost-Efficient Cell and Gene Therapy Production

Current manufacturing approaches for cell and gene therapies are still largely manual and inherently difficult to scale efficiently. Even existing automated devices and machinery fail to fully address this challenge, as throughput increases are typically achieved through linear scaling—resulting in disproportionately rising operational costs. To enable broad patient access, future production systems must be flexible, modular, and inherently scalable.

In this presentation, we introduce a novel manufacturing paradigm based on matrix production, enabling the cost and quality characteristics of mass production while maintaining the flexibility required for highly individualized therapies. A key enabler of this approach is the configurability of the system via standardized interfaces, allowing dynamic orchestration of production workflows.

Central to the concept is a closed cassette-based process format, ensuring safe, reproducible, and contamination-free operation. These cassettes can be manufactured at high volumes and low cost, forming the basis of a scalable “farming matrix” that grows with demand and autonomously monitors its own performance.

Through comprehensive process monitoring, advanced AI-driven methods can be leveraged for rapid process development, optimization, and quality assurance. This approach paves the way for a future in which cell and gene therapies can be produced efficiently, reliably, and at scale—ultimately making these transformative treatments accessible to a much broader patient population.

Tomasz Baran

Affiliation: FamiCord AG

Job position: Chief Medical Officer of FamiCord

CV: Tomasz Baran, MD, MBA, is Chief Medical Officer of FamiCord - the largest cord blood bank in Europe and 3rd largest worldwide. He joined cord blood banking activity in 2010, prior to that he has been holding various position in pharmaceutical industry. In his current role Tomasz is responsible for medical communication on stem cell banking and use in therapies. He presented this topic on several international events – including Cord Blood Connect (USA), Perinatal Stem Cell Conference (USA) and Advanced Therapies (UK). Tomasz is also involved in development of cell&gene therapies manufacturing activity of FamiCord. Tomasz Baran serves ad Board of Directors member at Cord Blood Association (currently incorporated into AABB).

CMO of FamiCord AG, Perinatal Stem Cell Banking as a Platform for ATMP Development

This talk will focus on perinatal stem cell banking as an enabling platform for the development of advanced therapy medicinal products (ATMPs). Perinatal sources such as cord blood, cord tissue, and placental tissues offer ethically accessible, biologically potent starting materials with growing relevance for both established and emerging cell-based therapies.

The presentation will briefly outline key considerations that link early-life tissue sourcing with clinical and manufacturing requirements for ATMP development, including quality, traceability, scalability, and regulatory compliance. Selected examples will illustrate how banking strategies influence downstream feasibility of clinical translation.

In this context, the role of integrated platforms combining perinatal tissue sourcing with GMP-aligned manufacturing will be discussed, drawing on FamiCord's experience as a large European perinatal cell bank and CDMO supporting cell-based product development.
The talk will highlight how perinatal stem cell banking can move beyond storage to become a strategic component of sustainable ATMP pipelines.

Ion Tcacencu

Affiliation: Consulting unit of hVIVO

Job position: Consultant CMC

CV: Ion Tcacencu, MD, PhD holds a doctorate from Karolinska Institutet in regenerative medicine and brings over 17 years of academic expertise in cell and tissue engineering. After transitioning into industry to lead quality and manufacturing at a cell therapy startup, he joined hVIVO as a CMC consultant. He supports academic ATMP developers with regulatory strategy, CMC development, market landscape analysis, and GMP-ready programmes — as well as technical due diligence for investors.

Regulatory Roadmaps to Translate Academic ATMP Innovations into Clinic

Academic innovators developing ATMPs often encounter significant challenges when translating early-stage discoveries into first-in-human studies. Academic teams typically have limited regulatory experience, which can lead to gaps in understanding the requirements governing ATMP classification, manufacturing, safety, and clinical development.

A structured regulatory roadmap helps bridge these gaps by providing a strategic framework that aligns scientific innovation with regulatory expectations, reduces development risks, and prevents costly re-work. Integrating CMC, non-clinical, and clinical planning early in development ensures coherent project progression and enables proactive identification of challenges such as scalability, product characterization, and compliance with GMP standards.

That alignment together with the early interactions with regulators (e.g., Innovation Task Force meeting, Scientific Advice procedures) would supports the creation of a robust Target Product Profile and the realistic resource planning.

Ultimately, a well-designed regulatory roadmap strengthens the evidence package needed for clinical trial applications and enhances opportunities for funding and strategic partnerships. By integrating scientific, regulatory, and CMC considerations from the beginning, academic teams increase the chance of a successful transition into clinic.

Panelists

Panel Discussion

How to Overcome the Valley of Death in CGT Development

Regina Demlová

Affiliation: Centre of Excellence CREATIC (Central European Advanced Therapy and Immunotherapy Centre), Masaryk University, Brno, Czech Republic

Job position: Director of CREATIC CoE

CV: Dr. Regina Demlová (MD, PhD) is a clinical pharmacologist specializing in oncology and personalized therapies including ATMPs. She is an Associate Professor of Clinical Pharmacology at the Faculty of Medicine, Masaryk University in Brno, Czech Republic, where she also serves as Head of the Department of Pharmacology. For over a decade, she has been a leading figure in the development of academic clinical research in the Czech Republic, having established and currently leading the national clinical research infrastructure CZECRIN and the Centre of Excellence CREATIC, dedicated to the research, development, GMP production, clinical trials, and regulatory aspects of advanced cell and gene therapies.

Martin Bornhäuser

Affiliation: Medical Clinic I, University Hospital Dresden & NCT/UCC

Job position: Director Medical Clinic I, University Hospital Dresden

CV: Prof. Martin Bornhäuser is Director of the Department of Medicine and Medical Clinic I at the University Hospital Carl Gustav Carus at TU Dresden. He is also one of the Managing Directors of the National Center for Tumor Diseases Dresden (NCT/UCC). Prof. Bornhäuser completed his medical training at the University of Kiel, where he also obtained his doctorate at the Institute of Sports Medicine. From 1993 to 1994, he worked in the Department of Hematology and Medical Oncology at the University Hospital Tübingen. He is a board-certified specialist in internal medicine, hematology, and oncology. Prof. Bornhäuser is an internationally recognized expert in the treatment of leukemias, stem cell transplantation, and cellular immunotherapy.

Ralf Huss

Affiliation: BioM Biotech Development GmbH, Bavarian Biotechnology Cluster

Job position: Managing Director of BioM Biotech Development GmbH and Spokesperson for the Bavarian Biotechnology Cluster

CV: Prof. Dr. Ralf Huss is managing director of BioM in Martinsried/Munich. Until the end of 2022, he was founding Director of the Institute of Digital Medicine (IDM) and Prof. of Pathology and Molecular Diagnostics at University Hospital Augsburg, Germany. Previously he spent many years in pharmaceutical and diagnostic industry, founded some biotech enterprises and authored more than 180 papers on cancer and stem cell research as well as the use on AI in digital medicine.

Marion Jung

Affiliation: T-CURX

Job position: COO at T-CURX

CV: Dr. Marion Jung is a molecular biologist who earned her Ph.D. at LMU Munich under Nobel laureate Svante Pääbo and has more than 20 years of experience in building and scaling biotechnology companies. As co-founder and CEO of ChromoTek, she led the company through its successful sale to the Proteintech Group in 2020 and subsequently took on leadership roles at Proteintech and, starting in 2024, as COO of T-CURX, a CAR-T immunotherapy startup. In addition, she brings extensive expertise in venture capital (including Earlybird), innovation policy, and government consulting through her involvement in committees such as the High-Tech Forum and the German High-Tech Start-up Fund.

Abstracts
Pitches

Pitch session for pre-seeds and start-ups

June 3rd
12.50 – 1.15 pm

Christin Zündorf

TQ Therapeutics GmbH

Christin Zündorf is Chief Business Officer at TQ Therapeutics responsible for commercial, organizational & strategic topics. With previously over eight years of experience in strategic consulting across the pharmaceutical and life science industry, her expertise lies in commercial strategy and organization design with deep knowledge in commercial strategy, launch excellence, pricing and market access.

Dominik Witzigmann

NanoVation Therapeutics

Dominik Witzigmann is an entrepreneurial scientist and 2024 Highly Cited Researcher, recognized among the world's leading experts in nucleic acid delivery. He held research positions at leading institutions in safety/toxicology, RNAi and cancer, targeted DNA delivery, and RNA-based genome editing, before joining Pieter Cullis to focus on extrahepatic RNA delivery. He has served in leadership roles within NanoMedicines Innovation Network and the CRS Gene Delivery and Genome Editing Focus Group. Dominik also co-founded NanoVation Therapeutics to advance next-generation LNP technologies for genetic medicines.

Jan Moritz Middeke

Cancilico

Jan Moritz Middeke is a hematologist and oncologist at the Department of Internal Medicine I, University Hospital Dresden, serving as Managing Senior Physician since 2025. Since 2019, he has led the "Artificial Intelligence in Hematology" research group at the university hospital, the Else Kröner Fresenius Center for Digital Health, and TU Dresden, focusing on AI in cancer and hematology research. He studied medicine at Ludwig Maximilian University of Munich, earned his doctorate in 2013, and completed his habilitation (PD) in 2026. He also co-founded the DGHO working group "Artificial Intelligence in Hematology and Oncology" and the German ITP Register.

BioThrust ComfyCell – The World's First Bionic Bioreactor for Scalable Cell Therapy Manufacturing

Patrick Bongartz

BioThrust GmbH | Pauwelsstr. 17, 52074 Aachen, Germany | www.biothrust.com

BioThrust has developed the ComfyCell, the world's first bionic bioreactor enabling scalable, high-quality manufacturing of sensitive cell types for advanced therapies. At its core, the proprietary Membrane Stirrer functions as an artificial lung integrated into the bioreactor, enabling fully bubble-free aeration and dramatically reducing shear stress by up to 99% while achieving significantly enhanced gas transfer. This unique design allows efficient cultivation of stem cells, including iPSCs and MSCs, as well as immune cells such as NK, CAR-NK, and T cells at scales that cannot be reached with conventional systems.

Current biomanufacturing technologies face a fundamental bottleneck: while small-scale systems are suitable for research, and stirred-tank bioreactors are standard in biologics production, neither is compatible with the sensitivity of advanced therapeutic cells. Conventional systems rely on sparging, generating shear forces and turbulence that damage fragile cells and limit scalable production. As a result, cell and gene therapy manufacturing remains inefficient and costly, restricting patient access to potentially curative treatments.

The ComfyCell overcomes these limitations through membrane-based, bubble-free gas transfer that maintains optimal culture conditions even at large volumes. This enables scalable and cost-efficient production of cell therapies and establishes a new standard for bioprocessing in advanced therapy manufacturing.

BioThrust's platform is at TRL 7–8 and includes validated single-use and reusable systems ranging from 300 mL to 10 L, with larger-scale systems under development. The technology has demonstrated exceptional performance, including record iPSC expansion, strong NK and T cell proliferation, and significant cost reductions compared to conventional systems. With strong patent protection across key components, BioThrust addresses a rapidly growing global market for cell and gene therapy manufacturing, positioning its platform as a foundational enabling technology for future blockbuster therapies.

Green Elephant Biotech – Archimedes® One: Dynamic Adherent Bioreactor for Scalable Cell Manufacturing

Katharina Günther

Green Elephant Biotech GmbH
Green Elephant Biotech is developing the Archimedes® One, a dynamic adherent bioreactor designed to simplify and scale the manufacturing of adherent cell therapies. The system is based on the patented CellScrew® geometry, which combines concentric growth surfaces with gentle rotational mixing inspired by the Archimedes screw principle. This enables controlled medium distribution, low shear conditions, and high-density cell expansion in a compact and scalable format.

Current adherent cell manufacturing systems are limited by high process complexity, intensive manual handling, and inefficient use of cleanroom capacity. These constraints lead to poor reproducibility, high production costs, and limited scalability. Existing technologies are not designed to reflect native adherent cell biology at commercial scale, resulting in significant barriers to clinical and industrial adoption.

Archimedes® One addresses these challenges by integrating controlled perfusion culture, automated harvesting, and full process monitoring into a single-use, pre-assembled system. The platform behaves like a perfusion bioreactor adapted for adherent cells, offering full control of key parameters such as pH, dissolved oxygen, and temperature via standard biocontroller interfaces. By eliminating conditioning vessels and reducing system complexity, it significantly lowers operational burden while improving reproducibility and scalability.

The technology enables large growth surfaces of up to 10,000 cm² and supports GMP-compatible workflows with minimal manual intervention. Archimedes® One is currently at TRL 6, protected by granted and filed intellectual property, and addresses a growing global market for adherent cell manufacturing technologies. With its combination of biological alignment, automation, and cost efficiency, it provides a robust solution for scalable production of adherent cell-based therapies.

SMART-NK – A Selective CAR-NK Platform for Scalable Immune Reset in Autoimmune Diseases

Jiri Eitler

DRK Blutspendedienst Nord-Ost gGmbH

SMART-NK is a modular CAR-NK cell therapy platform designed to enable selective immune reset in autoimmune diseases by precisely targeting disease-driving autoreactive B-cell clones. Using BCR-specific CAR constructs, the platform selectively eliminates pathogenic B cells while preserving protective immune function. Proprietary NK cell engineering further enhances cellular activity, safety, and persistence, enabling the development of scalable, off-the-shelf allogeneic therapies.

Current treatments for autoimmune diseases rely primarily on chronic immunosuppression, which is non-curative and associated with significant long-term side effects. While CAR-T therapies have shown potential for immune reset, their broad B-cell depletion, complex autologous manufacturing, and safety concerns limit widespread application. There is a clear need for safer, more scalable, and more selective therapeutic approaches.

SMART-NK addresses these limitations by combining precision targeting with NK-cell-based safety and scalability. The platform enables selective depletion of autoreactive B cells while maintaining overall immune competence, offering a potential pathway toward durable disease remission. Its allogeneic design supports simplified manufacturing and broader clinical accessibility.

The lead candidate SMART-101 is initially developed for bullous pemphigoid as a proof-of-concept indication, with expansion potential across multiple autoimmune diseases. The platform is currently at TRL 3, with demonstrated proof-of-concept data and ongoing preclinical development. With strong intellectual property positioning and access to a large and growing autoimmune therapeutics market, SMART-NK represents a scalable and differentiated approach toward next-generation immune therapies.

Abstracts
Posters

Poster session

June 3rd
During Lunch Break

Designer recombinase-mediated reactivation of fetal hemoglobin for the treatment of beta-hemoglobinopathies

Manavi Jain[1], Sara Orugo Medina[1], Georg Girke[1], Nadja Schubert[2], Lukas Theo Schmitt[1], Maciej Paszkowski-Rogacz[1,3], Duran Sürün[1], Frank Buchholz[1]

1 Medical Faculty and University Hospital Carl Gustav Carus, UCC Section Medical Systems Biology, Dresden, TU Dresden 01307, Germany
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3 Present Address: Seamless Therapeutics GmbH, Tatzberg 47/49, 01307 Dresden, Germany

Hemoglobinopathies, including sickle cell disease (SCD) and β-thalassemia (β-thal), are among the most prevalent monogenic disorders worldwide and represent a major global health burden. These diseases arise from mutations in the β-globin gene that impair β-globin production or function. Although allogeneic hematopoietic stem cell transplantation (HSCT) can provide a cure, its clinical application remains limited by donor availability and the risk of immunological complications. Consequently, genome-edited autologous HSCT has emerged as a promising therapeutic alternative. One particularly attractive strategy is the reactivation of fetal hemoglobin (HbF), as individuals with hereditary persistence of fetal hemoglobin (HPFH) maintain elevated HbF levels and exhibit markedly reduced disease severity. This natural protective effect has therefore motivated the development of genome engineering approaches aimed at restoring endogenous HbF expression.

Tyrosine site-specific recombinases (Y-SSRs) enable highly precise and predictable DNA excision between defined target sites, making them attractive tools for therapeutic genome engineering. In this study, we engineered designer Y-SSRs to target BCL11A, a key transcriptional repressor of the γ-globin genes (HBG). Using substrate-linked directed evolution, recombinase libraries were generated and screened by high-throughput deep sequencing to identify variants with activity toward therapeutic loxBCL11A target sites. Ongoing optimization includes fusion with zinc-finger DNA-binding domains and the development of mammalian evolution and screening platforms to identify highly specific and efficient variants. Functional validation is performed in HUDEP-2 erythroid progenitor cells and primary CD34⁺ hematopoietic stem and progenitor cells, aiming to establish designer recombinases as a best-in-class genome editing platform for therapeutic HbF reactivation in β-hemoglobinopathies.

Keywords: Designer recombinases, β-Hemoglobinopathies, Fetal hemoglobin (HbF), precision genome editing, BCL11A, Directed evolution

Identification of integration sites in cell-based gene therapies

Dennis Löffler, Nhu-Nguyen Pham, Alexander Scholz, Markus Kreuz, Kristin Reiche, Conny Blumert

Several approved and numerous experimental cell-based gene therapies utilize integrating viral vectors. They are being tested and used to treat genetic disorders, hematological cancers, and autoimmune diseases. The stable integration of CAR constructs into the genome of a host cell can offer significant therapeutic benefits. On the other hand, it has the potential to disrupt genes and/or their regulatory elements in the genome that could drive malignant transformation of CAR T cells. In recent years, several cases of secondary CAR+ T cell lymphomas have been described in the literature, linking their development with a mutation at the insertion site by the CAR construct. *1, 2, 3*

To assess integration sites of the various vectors, we use a pipeline we developed for integration site analysis. Our approach is based on the targeted enrichment of integration sites using custom polymerase chain reaction (PCR) primers tailored to each vector system. This process generates an enriched DNA library for next generation sequencing (NGS) on the Illumina NextSeq2000.

The NGS data are then demultiplexed and used as input for a multi-step, computer-assisted analysis of insertion sites. First, the data are preprocessed and filtered using cutadapt v3.5 and bowtie2 to reduce false positive results and obtain sequences that exclusively map to the host genome, thus excluding potential contamination. Several quality control points in the pipeline ensure the reliability of the integration site candidates, e.g., defined minimum number of reads mapping quality (MAPQ) or exclusion of the insertion site with lesser reads, if two potential sites are in close proximity. Filtered sequences are reported and classified (Kraken2) to enable transparent result presentation visual inspection (IGV). The integration site candidates are subjected to further analyses (R packages: Biostrings, seqLogo), to identify preferred integration patterns of the CAR constructs. Accumulated genomic sequences were found on various chromosomes and on both strands. Further, safe harbour analyses (R packages: genomation, GenomicRanges) with genome annotation and oncogene annotation were used to generate statistics on integration into genes, their exons, introns, transcription start sites (TSS), promoter regions or flanking gene regions. A more detailed list of affected (onco-)genes was generated by comparing the list of integration sites with host genome annotation (BEDTools).

Development status / TRL

TLR 5-6 (Technology Development and Demonstration on patient samples successful)

References

1. Braun, T., Rade, M., Merz, M. et al. Nat Med 31, 1145–1153 (2025).
2. Braun, T., Kuschel, F., Reiche, K. et al. Leukemia 39, 1337–1341 (2025).
3. Berg, P., Bakker, C., Sander, M. et al. Gene Ther (2025).

Enhanced therapeutic potential of cord blood–derived Tregs over adult blood and thymus-derived Tregs for allogeneic cell therapy.

Samikshya Santosh Nirmala

Background & Aim: FOXP3⁺ regulatory T cells (Tregs) represent 4–7% of circulating CD4⁺ T cells and are central to immune tolerance and homeostasis, making them attractive candidates for preventing transplant rejection and treating autoimmune and inflammatory diseases, including graft-versus-host disease (GvHD) (1–3). However, clinical trials have reported highly variable in vivo persistence and efficacy, likely reflecting differences in Treg source, ex vivo expansion strategies, and final product phenotype. This study aims to systematically compare Tregs derived from three clinically relevant sources—adult peripheral blood (AB), umbilical cord blood (CB), and pediatric thymus (Thy) (4)-across functional, phenotypic, and manufacturing-relevant parameters to define their relative therapeutic potential for future allogeneic applications.

Methods: Highly pure Tregs were isolated using a combination of published magnetic and flow-based sorting strategies, including the MACSQuant Tyto cell sorter (5). Cells were expanded ex vivo for 14 days using polymer-based anti-CD3/CD28 stimulation in the presence of high-dose IL-2. Post-expansion products were phenotyped by flow cytometry. Bona fide Treg identity was confirmed by TSDR demethylation analysis and absence of IL-2 production upon activation. Suppressive function was assessed using a proliferation-based in vitro suppression assay, and lineage stability was evaluated under Th1- and Th17-polarizing inflammatory cytokine conditions.

Results: Isolation of highly pure FOXP3⁺ Tregs from CB was the most cost-effective among all sources, requiring only a FACS isolation step using the MACSQuant Tyto due to low starting cell numbers. CB-derived Tregs showed robust ex vivo expansion (median 2678-fold; range 1035–5989-fold; n=4) while maintaining a stable Treg identity, with 99.9% TSDR demethylation across all donors. Consistently, IL-2 expression remained minimal within CB-Tregs after expansion (median 1.13%; range 1.03–2.74%; n=4). Functionally, CB-Tregs exhibited the strongest suppressive capacity against both CD4⁺ and CD8⁺ allogeneic effector T cells and retained phenotypic stability after repeated restimulation and exposure to pro-inflammatory cytokines compared to AB- and Thy-Tregs.

Conclusion: Among the three clinically relevant sources evaluated, CB emerged as the most promising for future allogeneic Treg therapies.

Development status / TRL: TRL3

References:

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2. Zou C, Li P, Li B et al. Cell. 2026 Jan 8;189(1):6–22.
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5. Lakshmi K, Jutrzenka-Trzebiatowski A von, Loureiro L et al. J Transl Med. 2025 Dec 17;23(1):1399

The Olympics of RNA-based CAR-T cell generation Establishing a high-performance RNA platform for CAR-T cell therapy

Gebhardt, C.1; Serfling, R.1; Bär, C.2,3; Tretbar, S.1

1 Department of Cell and Gene Therapy Development, Fraunhofer IZI, Leipzig
2 Institute of Molecular and Translational Therapeutic Strategies, Hannover Medical School MHH, Hannover
3 Department of Preclinical Pharmacology and Toxicology, Fraunhofer Institute for Toxicology and Experimental Medicine ITEM, Hannover

Chimeric antigen receptor (CAR)-T cell therapy has emerged as a transformative approach in cancer immunotherapy. However, all currently approved CAR-T products (as of March 2026) rely on viral vectors for random genomic integration, which raises safety concerns such as insertional mutagenesis and prolonged on-target, off-tumor toxicity. In addition, their manufacturing remains complex, time-consuming, and costly.

To overcome these limitations, we explore a non-integrating, RNA-based strategy for generating transient CAR-T cells. While conventional CAR-mRNA offers a safer and more flexible alternative to viral vectors, its rapid degradation and dilution in proliferating T cells significantly limit therapeutic efficacy.

This project addresses this key bottleneck by developing and systematically comparing next-generation RNA architectures with enhanced stability or self-amplifying capacity - namely circular RNA (circRNA), self-amplifying RNA (saRNA), and trans-amplifying RNA (taRNA). These formats enable sustained, but still transient protein expression without genomic integration.

We performed functional optimization of all RNA candidates in primary human T cells using both an eGFP reporter and a CD123-targeting CAR construct. Key parameters assessed included expression kinetics, T cell viability, and T cell phenotyping following electroporation. Optimization was performed considering RNA sequence, RNA production, and RNA modifications. The most promising candidates are currently evaluated in direct comparison for CAR-T cell generation by electroporation, including in vitro cytotoxicity. Lead candidates will be further validated using lipid nanoparticle (LNP)-mediated delivery and in vivo killing activity.

By establishing a high-performance RNA platform for primary T cells, this work aims to enable safer, rapidly manufacturable, and cost-effective CAR-T therapies, thereby broadening patient access and simplifying manufacturing.

Development status / TLR: TLR3

Scalable GMP-Compatible Production of Universal Adapter CAR Tregs for Organ-Targeted Suppression

Kavitha Lakshmi ǂ [1,2], Alexandra von Jutrzenka-Trzebiatowski ǂ [3], Liliana Loureiro[3], Karla Elizabeth González Soto[3], Katja Peter[3], José Manuel Marín Morales[1,2], Samikshya Santosh Nirmala[1,2], Nicole Berndt[3], Claudia Arndt[2,3], Yueyuan Hu[1,4], Claudia Peitzsch[1], Anna Taubenberger[2,5], Martin Bornhäuser[6,7,8], Michael Bachmann*[3,6,7], Anja Feldmann*[3,6,7], Anke Fuchs*[1,2,7]

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4 DKMS Stem Cell Bank, Deutsche Knochenmarkspenderdatei (DKMS), Dresden
5 Biotechnology Center, CMCB, TU Dresden
6 National Center for Tumor Diseases (NCT), NCT/UCC Dresden, Faculty of Medicine TU Dresden & HZDR
7 German Cancer Consortium (DKTK), Partner Site Dresden and DKFZ, Heidelberg
8 Department of Hematology, Cell Therapy and Medical Oncology, University Hospital Carl Gustav Carus, Dresden

Adoptive transfer of regulatory T cells (Tregs) is a strategy to promote immune tolerance in conditions such as graft-versus-host disease (GvHD). To improve their localization and antigen-specific activity, Tregs can be engineered with chimeric antigen receptors (CARs), however, conventional CAR-Tregs are limited by complex, costly manufacturing and fixed single-antigen specificity. To overcome these challenges, we utilized a novel universal adapter RevCAR system, which incorporates a non-specific peptide and enables flexible targeting via antigen-specific adapter molecules (RevTMs). To support clinical translation, we established an automated, GMP-compatible, clinical-scale manufacturing workflow: Tregs were magnetically enriched from leukapheresis using the CliniMACS® Plus, sorted on the MACSQuant® Tyto®, virally transduced and expanded on the CliniMACS Prodigy® to achieve therapeutically relevant numbers. Across five manufacturing runs, $CD4^+CD25^{high}CD127^{low}FOXP3^+$ Tregs with a median starting purity of 94% could be expanded to a median of 602×10^6 cells, maintaining high final purity (median: 91.9%) and RevCAR expression (median: 60%). Expanded cells retained FOXP3 and Helios expression under inflammatory conditions, produced minimal pro-inflammatory cytokines, and demonstrated dose-dependent suppression. Importantly, they showed antigen-specific activation upon engagement with a proof-of-concept target, carcinoembryonic antigen (CEA), which has previously been shown to be highly expressed in the inflamed gastrointestinal tract. These results establish a scalable, GMP-compatible platform for generating RevCAR Tregs and highlight their potential as an off-the-shelf therapy for spatially targeted immunomodulation in immune-mediated diseases.

Published Paper

Lakshmi, K., Jutrzenka-Trzebiatowski, A. V., Loureiro, L., et al. Journal of Translational Medicine, 2025, 23(1), 1399.

Modulation of CAR T Cell Immunoreactivity Using MAX.16H5 Antibody Incubation for the Generation of Immunotolerant allogeneic CAR T cells

Alexander Renner, Nadja Hilger, Lily Stahl, Stephan Fricke, Mathias Hänel, Ulrich Blache, Ulrike Köhl, Paul Warncke, André-René Blaudszun

Despite the success of cell therapy in treating hematological malignancies, side effects like cytokine release syndrome (CRS) pose severe threats to patients. Clinical experience with autologous CD19 chimeric antigen receptor (CAR) T cell therapy revealed that CRS occurs in up to 90% of patients (1). Previous studies suggest that CD4 CAR T cells contribute to the development of side effects more than CD8+ CAR T cells (2, 3), which might be overcome by blockage of interactions between CD4 on CAR T cells and host cells. Moreover, allogeneic CAR T cell approaches carry a risk of graft-versus-host disease (GvHD) and are constrained by the need for complex genetic modifications.

To counteract the high CRS rate and to expand the range of CAR T cell products for allogeneic use, we employed MAX.16H5, a non-depleting antibody with high affinity for CD4. Pan CD19 and CD123 directed CAR T cells were generated via gamma-retroviral transduction and treated with MAX.16H5 antibody prior to assessing functional parameters. In in vitro cocultures of CAR T cells and diffuse large B cell lymphoma (DLBCL) cell lines antigen-specific cytotoxicity was observed and not negatively impacted by the antibody. Additionally, CD19 CAR T cells showed increased expression of activation markers like CD137 and CD25 in coculture with target cells bearing CD19. Here, CD8+ CAR T cells showed elevated levels of both markers compared to CD4+ CAR T cells, which was not dependent on MAX.16H5 treatment. Furthermore, proliferation of CD19 CAR T cells increased independently of MAX.16H5 incubation when cocultured with DLBCL cell lines compared to CD123 CAR T cells. Subsequently, analysis of cytokines in cocultures of CAR T cells and cell lines as well as peripheral blood mononuclear cells (PBMCs) from autologous and allogeneic donors will be carried out to study further implications of MAX.16H5 for CRS and GvHD, respectively. This study emphasizes the potential of MAX.16H5 antibody pre-incubation of CAR T cell products to reduce side effects caused by CD4+ T cells while maintaining product function.

Development status / TLR: TRL 3

References:

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Development of CAR-macrophages using novel non-viral genome engineering approaches for immunotherapy

Zsófia Szabó[1], Lacramioara Botezatu[2], Heike Pfäffle[2], Maik Friedrich[1,2], Alexander Ewe[3], Achim Aigner[3] and Zoltán Ivics[1,2]

1 Institute for Clinical Immunology, Leipzig University
2 Department of Clinical Gene Transfer, Fraunhofer Institute for Cell Therapy and Immunology, Leipzig
3 Rudolf-Boehm-Institute for Pharmacology and Toxicology, Clinical Pharmacology, Leipzig University

B cell-mediated autoimmune disorders like systemic lupus erythematosus (SLE) and systemic sclerosis (SSc) involve dysregulated immune responses that lead to chronic inflammation and organ damage. CAR-T cells genetically engineered with lentiviral vectors in an autologous setting represent the state-of-the-art adoptive immunotherapies with proven efficacy in leukemia and some autoimmune disorders.

To overcome some of the limitations of CAR-T cell therapy, CAR-macrophages (CAR-Ms) emerge as a promising approach by synergizing the innate tumor-resilience and "engulfing nature" of macrophages with CAR technology. Furthermore, genetic engineering technologies that bypass the use of viral vectors are on the rise due to their simplicity, scalability and economically more affordable manufacturing. Our project focuses on developing innovative non-viral strategies for genetically engineering human monocytes/macrophages to target and clear autoreactive B cells in SLE and SSc. We will generate CD19-CAR-expressing macrophages (CD19-CAR-M) using mRNA, circular RNA (circRNA), or self-amplifying RNA (saRNA) delivered via lipid nanoparticles (LNPs), cationic polymers, or electroporation. Minicircles or nanoplasmids encoding CD19-CAR will also be delivered using hyperactive SB100X transposase mRNA for stable expression in macrophages through the Sleeping Beauty (SB) transposon platform. We have optimized protocols for monocyte isolation and macrophage culture to improve viability and differentiation. We are assessing transfection efficiency of various constructs with fluorescent reporters and CAR genes. Comprehensive in vitro testing will evaluate functionality, focusing on phagocytosis and cytokine response, while prioritizing safety. The successful development of non-virally engineered CD19-CAR macrophages could provide a scalable, low-toxicity cell therapy platform for autoimmune diseases, potentially bridging current autologous CAR approaches with future allogeneic immunotherapies.

Development status/TRL:
TRL 2: Technology Concept Formulated
TRL 3: Analytical and Experimental Proof of Concept

Tumor-targeted TLR3 agonist immunoconjugates reprogram the glioma microenvironment and induce antitumor immunity in vivo

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Glioblastoma remains a highly aggressive brain tumor characterized by recurrence, therapeutic resistance, and a profoundly immunosuppressive tumor microenvironment. To enable local innate immune activation while limiting systemic exposure to free dsRNA, we evaluated a modular immunoconjugate platform termed Rapid Inducer of Cellular Inflammation and Apoptosis (RICIA) for EGFRvIII-directed delivery of the dsRNA-based TLR3 agonist RIBOXXOL to glioma cells. Anti-EGFRvIII RICIA consists of mono-biotinylated EGFRvIII-specific single-chain antibody fragments, NeutrAvidin, and mono-biotinylated RIBOXXOL. In vitro, anti-EGFRvIII RICIA was selectively internalized by EGFRvIII-positive human and murine glioma cells via receptor-mediated endocytosis and induced a strictly TLR3-dependent type I interferon response. In immunocompetent VM/Dk mice bearing syngeneic SMAvIIIFfLuc gliomas, systemic anti-EGFRvIII RICIA significantly inhibited subcutaneous tumor growth, promoted inflammatory remodeling of the tumor microenvironment, increased the frequency of functional $GrzB^{+}/PD\text{-}1^{-}$ cytotoxic T lymphocytes, induced EGFRvIII neo-epitope-specific antibodies, and generated protective immune memory upon tumor rechallenge. In an orthotopic model, a single stereotactic intratumoral administration prolonged survival and induced complete tumor clearance in a subset of animals. Additional biodistribution studies showed preferential retention of anti-EGFRvIII RICIA in tumor tissue compared with non-targeted control conjugates, while serum cytokine analyses indicated minimal systemic immune activation at therapeutic doses. Together, these data support tumor-targeted TLR3 agonist delivery as a promising preclinical platform for in situ immunomodulation of glioma and as a modular strategy that may be adaptable to other target antigens and RNA payloads.

Development status / TRL:
Preclinical proof-of-concept; estimated TRL 3
The platform has been validated in vitro and in immunocompetent syngeneic mouse models, with evidence for target-dependent uptake, TLR3-dependent mechanism of action, in vivo efficacy, biodistribution, and initial tolerability. Current development priorities include optimization of dosing regimens, evaluation in models with heterogeneous target expression, further mechanistic dissection of tumor-cell versus myeloid-cell contributions, manufacturability of the modular conjugate format, and expansion of safety studies required for translational development.

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The MaculaPatch: A Customizable Cell Therapy for Retinal Repair and Vision Restoration developed in a Preclinical Human Organoid Platform

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Over 200 million patients worldwide are affected by vision loss due to retinal degeneration. Once light-sensitive photoreceptor neurons are lost, they cannot be replaced yet. Effective cell therapies remain a major unmet need. Current experimental strategies are limited by cell product instability, low purity, and cannot be customized to the patient's needs. Further, whether transplanted photoreceptors can integrate into a human retina and which disease stage is most promising remains still unknown. Here, we developed the first preclinical human research platform to study and develop cell therapies based on hiPSC-derived retina organoids: Human photoreceptors were enriched from organoids and transplanted as single cells onto human retina organoid recipients, mimicking current in vivo approaches. Donor cells spontaneously and progressively integrated into the host retina over six weeks and survived longer-term. Contrary to current belief, transplants integrated even in advanced pathology stages with glial scarring, resembling conditions in patients most in need of cell replacement. However, neither of the two main replacement strategies currently under investigation (single cells or retina sheet transplants) spontaneously restores the structure of the native photoreceptor layer, recapitulating previous animal in vivo studies. To address this, we here developed the MaculaPatch, a stable 3D photoreceptor cell complex (assembloid) that can be customized in size, shape, and cellular composition. The MaculaPatch allows precise transplant positioning and supports structural restoration of a photoreceptor-like layer. These findings establish a human preclinical platform for retina cell therapy research, and introduce a customizable photoreceptor cell therapy product with potential to therapeutically either repair retinal defects or restore retinal structure after vision loss.

Development status / TRL:
TRL3 – Experimental proof-of-concept in human organoids. In planning: proof-of-concept in animals in vivo.

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Restoration of TP53 Function by Adenine Base Editing in Patient-Derived Lung Cancer Organoids

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Lung cancer remains the leading cause of cancer-related mortality in Europe, accounting for approximately 376,000 deaths annually1. More than half of patients present with metastatic disease, requiring systemic treatment. Although therapeutic options have expanded in recent years, including targeted approaches for tumours with specific mutations, treatment efficacy is often limited by the development of resistance, underlining the urgent need for novel therapeutic strategies.

TP53 mutations are among the most common genetic alterations in lung cancer, occurring in roughly 50% of non-small cell lung cancer (NSCLC) and 75–90% of small cell lung cancer (SCLC)2,3. These mutations drive tumour progression, metastasis, and therapeutic resistance, and are associated with poor clinical outcomes. Precise correction of mutant TP53 in its endogenous context therefore represents a compelling strategy to restore tumour suppressor function. Base editing enables targeted correction of genetic alterations that are not amenable to conventional pharmacological approaches, offering potential for precision medicine in TP53- mutant cancers.

Here, we aimed to restore TP53 function in patient-derived lung tumour organoids harbouring clinically relevant mutations—NSCLC (C275Y) and SCLC (R273H)—using viral delivery of ABE8e and sgRNA. TP53 restoration reduced tumour cell viability in NSCLC organoids in vitro, and preliminary findings indicate that TP53 editing is also feasible in SCLC organoids. Overall, these results support ABE-mediated TP53 correction as a promising therapeutic strategy for TP53-mutant lung cancer. Future studies are required to evaluate the efficacy of lipid nanoparticle (LNP)-mediated in vivo delivery, as well as its short- and long-term safety.

Development status / TRL: TRL 4

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Development of Innovative Bioreactor Platforms for Scalable Production of Allogeneic NK Cell Therapeutics

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NK cells represent a promising alternative to T-cell–based therapies due to their innate ability to recognize and eliminate malignant or infected cells without prior antigen sensitization. Unlike T cells, NK cells carry a reduced risk of graft-versus-host disease and can be applied in allogeneic, off-the-shelf cell therapy settings. However, the broader clinical translation of NK cell therapies remains limited by challenges in cell availability, donor variability, and restricted expansion capacity in vitro. To overcome these bottlenecks, scalable and efficient bioprocesses are essential.

This project is a collaborative effort between the Fraunhofer IZI and BioThrust to develop innovative bioreactor systems for the large-scale production of allogeneic NK cell therapeutics. Within the SaxoCell Cluster, we focus on optimizing expansion protocols for primary NK cells and advancing the differentiation of NK cells from induced pluripotent stem cells toward scalable bioreactor conditions. To further advance this effort, BioThrust is committed to developing and optimizing an in-situ flow-optimized single-cell retention filtration system for integration into its single-use bioreactor platform. Key performance readouts include online data analytics as pH and dissolved oxygen and off-line process analytics such as viability, metabolic profiles, expansion kinetics, culture purity, and subsequent cell quality using comprehensive flow cytometric profiling of NK-specific receptors, activation markers, and exhaustion signatures. Functional characterization involves cytotoxicity assessment via calcein-release and degranulation analysis.

Comparative evaluation of primary, expanded, and iPSC-derived NK cells will guide the establishment of a robust and cost-efficient biomanufacturing platform, supporting the sustainable supply of NK cells for next-generation immunotherapies. Development status: Lab-scale optimization of NK cell expansion and iPSC differentiation in an established bioreactor platform (≤300 mL), with ongoing integration of a prototype flow-optimized single-cell retention system. Phenotypic and functional characterization pipelines are established.

Development status / TRL: TRL6-7

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A macrocyclic molecular glue allosterically enhances Cas9 specificity and supports translational RNP delivery for safer gene and cell therapy

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CRISPR/Cas9 has become a foundational platform for gene and cell therapy because it enables programmable, sequence-specific genome editing across a wide range of therapeutic settings, including ex vivo cell engineering and in vivo correction of disease-causing mutations. Its versatility also makes CRISPR/(d)Cas9 highly attractive for epigenetic modulation and next-generation precision medicines. However, broad clinical implementation remains limited by a central challenge: imperfect discrimination between fully matched and mismatched guide RNA–DNA hybrids, which can cause unwanted off-target editing and compromise safety. Current strategies to address this problem largely rely on re-engineering the Cas9 protein or redesigning the sgRNA, approaches that can be labor-intensive and difficult to generalize across applications.[1]

We hypothesized that small molecules could provide an orthogonal and translationally attractive solution by enabling reversible, dose-dependent, and non-genetic control over CRISPR effector function. In this context, our laboratory has been developing small-molecule approaches to modulate (epi)genetic editing outcomes.[2-4] Here, we report the identification of a naturally occurring, FDA-approved macrocyclic compound that acts as a potent Cas9 stabilizer. The compound was discovered through a high-throughput fluorophore-based screen and binds Cas9 with sub-nanomolar affinity. Single-particle cryo-EM reveals that this molecular glue occupies a previously uncharacterized allosteric pocket at the REC-NUC junction. Binding at this site stabilizes an open ribonucleoprotein architecture and guides Cas9 through critical conformational transitions associated with target recognition. Functionally, the compound significantly improves on-target fidelity while reducing off-target activity in vitro and in cellular knockout reporter assays.

Importantly, we also demonstrate translational potential using lipid nanoparticles for RNP delivery. Cryo-TEM analysis indicates that the enhancer promotes more organized RNP assembly within LNPs, resulting in smaller particle size, improved cellular uptake, and reduced toxicity relative to RNP-only formulations. Together, these findings identify a chemically addressable regulatory junction in Cas9 and establish macrocyclic small molecules as a new modality for improving the safety, controllability, and therapeutic utility of CRISPR-based gene and cell therapy.

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Development of transposon-modified TCR-T cells for the personalized therapy of solid tumors

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The overarching aim of the SB-TRACT project is to develop innovative T cell products that have been modified using non-viral gene transfer methods. The objective of one part of the project is to identify the optimal transfection method and starting material for transposon-based TCR-T cells to generate mKRAS-specific TCR-T candidates for in vitro and in vivo testing. Endogenous TCR-knock out and recombinant TCR knock-in are performed in parallel. Therefore, T cells from healthy donors are initially transfected using electroporation (Lonza) and the protocol transferred to lipid nanoparticles (Cytiva). SB100X transposase mRNA is co-delivered with different innovative transposon DNA formats (dbDNA, cclDNA, cccDNA) and challenged against minicircle or nanoplasmid DNA. TCR surface expression is assessed by flow cytometry. We anticipate robust transfection efficiency and TCR expression for both methods, electroporation and LNP delivery. The best combination of transposon format, transfection method, and starting material will be identified, and mKRAS-specific TCR-T cells will be produced for further preclinical testing. The project aims to establish a scalable, transposon-based TCR-T production platform yielding high-quality, tumor-reactive TCR-T cells suitable for in vitro and in vivo evaluation.

Targeted Nucleic Acid Delivery to T Cells Using Immuno-Polymeric Nanoparticles (i-PNPs)

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Non-viral delivery approaches hold significant potential for improving CAR T cell manufacturing processes. Currently approved CAR T cell products predominantly rely on viral transduction; however, viral vectors involve complex production workflows, high costs, and potential safety concerns such as insertional mutagenesis. Alternative non-viral strategies, including electroporation and lipid nanoparticles (LNPs), have shown promising results. Polymeric nanoparticles (PNPs) represent an attractive alternative platform technology due to their comparatively simple preparation and potential applicability in both, ex vivo and in vivo settings, partly owing to their lower tendency for liver tropism.

In this study, we investigated polymeric nanoparticle (PNP) systems for the delivery of DNA (plasmid DNA and minicircle DNA) or mRNA. For nucleic acid complexation, tyrosine-modified polyethylenimines (PEIs) and polypropylenimine dendrimers (PPIs) were employed [1-3]. The nanoparticle surface was functionalized with targeting ligands (CD3 antibody or CD3 single-chain fragment) for enhancing cellular uptake. The design we employed enables the straightforward preparation of immuno-polymeric nanoparticles (i-PNPs).

Various i-PNP formulations carrying EGFP-encoding DNA or mRNA were evaluated in Jurkat cells as a model T cell line. Transgene expression was analyzed by flow cytometry and live-cell imaging. Based on these results, formulations were further optimized by varying nucleic acid concentration, polymer type, polymer/nucleic acid ratio and ligand density. This initial optimization enabled the identification of i- PNP candidates capable of delivering both, DNA vectors (plasmid and minicircle DNA) and mRNA, with the long-term objective of co-delivering both nucleic acid types within a single nanoparticle formulation.

Selected i-PNPs were subsequently evaluated for transfection of primary T cells. Preliminary results indicate that additional optimization is required, including further refinement of nanoparticle formulations as well as optimization of T cell culture and transfection conditions.

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Systematic Comparison of Media and Equipment to Define a Standardized Freezing Process for Leukopaks – SB-TRACT

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The freezing procedure of leukopaks strongly influences post-thaw quality and functionality of cells. The growing number of commercially available cryomedia, including protein-supplemented and dextran-based formulations, as well as new technical devices, highlights the need for systematic comparison. The objective of this study was to define cryopreservation conditions that preserve leukocyte quality for generating optimized starting material for cell and gene therapies.

A broad comparison of cryopreservation media was performed in vial format, evaluating formulations with varying DMSO concentrations, protein supplementation, plasma-derived media, CryoStor® CS5 and CS10, and the reduced-DMSO dextran-based medium PentaHibe®. Cell counts and viability of up to five donors were determined using the automated NucleoCounter® NC-200™. Media containing 5–10% DMSO consistently provided the highest viability (mean 93%) and recovery (mean 103%), while reduced DMSO concentrations, including PentaHibe®, resulted in markedly lower post-thaw quality. Protein supplementation improved cell protection, particularly in media with lower DMSO content. Selected 5% DMSO CryoStor®-based media were subsequently tested in process-relevant bag format. Their consistent performance under manufacturing-like conditions (96% mean viability, 96% mean recovery) demonstrated robustness for scaled cryopreservation processes and the benefit of enhanced protein concentration. Paired vial and bag samples showed variability within acceptable limits (maximal 5% lower viability and 10% lower recovery in bags), confirming vials as suitable surrogates for quality control.

In parallel, the controlled-rate freezers ViaFreezeTM Quad from Cytiva (nitrogen-free) and CryoMed™ 7455 from Thermo Scientific (nitrogen-based) were compared. The ViaFreezeTM Quad offered easier handling and setup but was limited by cassette geometry and processing capacity. The CryoMed™ achieved cooling rates closer to the target and resulted in slightly higher post-thaw viability (mean 92% vs 91%) and recovery (mean 96% vs 93%). Despite these differences, the ViaFreezeTM Quad represents a feasible option where liquid nitrogen is unavailable.

In conclusion, cryomedia containing 5–10% DMSO were identified as the most reliable option for preserving cell quality in frozen leukopak material. Nitrogen-based controlled-rate freezing remains the preferred method when nitrogen supply is available, but the ViaFreezeTM Quad is a suitable alternative.

Development status: TRL 9

NK Cell-Based Therapies Against Fibrosis

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Background
Fibrosis drives morbidity and mortality in chronic inflammatory diseases, yet targeted therapies remain limited. Fibroblast activation protein (FAP) has emerged as a promising antifibrotic target. We evaluated FcR-engineered NK-92 (FcR-NK-92) cells in combination with the anti-FAP antibody sibrotuzumab, as well as FAP-specific CAR-NK-92 cells, in in vitro and human ex vivo fibrosis models.

Methods
NK cell activity was assessed by CD107a expression and europium release assays, with cytokine and effector molecule secretion (IFN-γ, perforin, granzyme) measured by Luminex. Antifibrotic effects were determined via collagen, α-SMA, and related markers, alongside histological and OCT-based tissue analysis.

Results
FAP expression was confirmed across systemic sclerosis, cutaneous GvHD, and hypertrophic scars. Both FcR-NK-92 plus sibrotuzumab and FAP-CAR-NK-92 cells induced selective fibroblast killing and reduced collagen expression in vitro, accompanied by increased IFN-γ, perforin, and granzyme release. In ex vivo fibrotic skin, FAP-CAR-NK-92 treatment led to marked lymphocyte infiltration and fibroblast depletion, supported by histological and transcriptional analyses.

Conclusion
FcR- and CAR-engineered NK-92 cells effectively target FAP^+ fibroblasts, reduce collagen deposition, and promote tissue remodeling. These findings support NK cell–based immunotherapy as a promising antifibrotic strategy with strong translational potential.

Developmental Status
This work represents a preclinical proof-of-concept study demonstrating efficacy in in vitro and human ex vivo models. Further in vivo validation and safety assessments are underway.

RevCAR system for targeting and modulating the immunosuppressive tumor microenvironment of solid tumors

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Conventional CAR-T therapy has shown immense success in the field of cancer immunotherapy. However, once infused in the patients, they cannot be controlled when there are adverse side-effects2. The modular Reverse Universal CAR (RevCAR) system, developed by the Feldmann group, requires a bispecific, adapter molecule named Reverse target module (RevTM) to kill the tumor cells. This modular technology enables effective and rapid “switching off” of the RevCAR system by stopping the infusion of the short-lived RevTM when side effects occur.

Moreover, despite the huge success of CAR-T cell therapy against hematological malignancies, solid tumors remain challenging to treat. The solid tumor microenvironment (TME) serves as a physical and immunological barrier that limits the effectiveness of CAR T cell therapy. One way in which the TME downregulates T-cell activity is by overexpressing immune checkpoints such as PD-L1. Targeting such molecules with the RevCAR system, transforms an immunosuppressive protein into a T-cell activating one. Therefore, a PD-L1 RevTM capable of redirecting RevCAR T-cells to specifically target and kill PD-L1-expressing tumor cells was designed. The system was functionally validated in regard of target-specific RevCAR-T-cell activation and tumor cell killing in vitro and in vivo1.

Moreover, there is a strong need for in vitro models that recapitulate the complexity of solid tumors. Therefore, we used tumor cell line- and patient-derived spheroids/organoids to show proof of concept that our adapter RevCAR T cells can efficiently kill tumor cells in such complex clinic-relevant 3D models. Moreover, we have further characterized such 3D tumor test models and explored the infiltrated RevCAR-T-cells using multiplex immunohistochemistry. Taken together, these models and studies would help us develop a promising therapeutic approach for targeting and modulating the tumor microenvironment to improve solid tumor treatment.

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D4-peptide nanofibrils as efficient transduction enhancers for ex vivo gene transfer in CAR-T and NK cell generation

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Chimeric antigen receptor (CAR)-T and natural killer (NK) cell therapies are promising treatments for hematologic malignancies and are increasingly explored for solid tumors and autoimmune diseases (Balkhi et al., 2025; Patel et al., 2025). However, their manufacturing remains labor-intensive and costly. A key limitation is inefficient viral transduction due to electrostatic repulsion between negatively charged viral and cellular membranes. Transduction enhancers such as peptide nanofibrils (PNFs) can overcome this limitation, reducing costs and improving yields, but established enhancers like Vectofusin-1 show variable performance depending on the viral vector system (Rauch-Wirth et al., 2023).

We identified a novel PNF, D4, through in silico screening and optimization. Its transduction efficiency was evaluated across viral vectors and cell types and compared to Vectofusin-1. Mechanistic studies included imaging of virus–PNF–cell interactions and simulation of a CAR-T production process to assess stability and degradation.

D4 PNFs showed comparable or superior transduction efficiency relative to Vectofusin-1. Notably, D4 enhanced transduction independently of viral vector type (lentiviral or retroviral) and pseudotyping glycoprotein, including VSV-G–pseudotyped lentiviral vectors, which are poorly enhanced by Vectofusin-1. In NK cells, D4 increased transduction without spinfection, improving infection rates from 0.4% to ~23% for RD114-LV and from 15% to 65% for BaEV-LV (Rauch-Wirth et al., 2023).

Mechanistically, D4 PNFs showed high viral binding site density, facilitating virus–PNF complex formation that is actively captured by filopodia and transported to the cell body, promoting membrane fusion or endocytic uptake. After internalization, PNFs were degraded in lysosomes, with ~98% of D4 aggregates cleared within three days in a CAR-T production simulation. Importantly, D4 did not impair cell viability or proliferation. In cell-free conditions, aggregates gradually disassembled, suggesting a favorable safety profile with reduced persistence and lower risk of immune activation or vascular occlusion (Rauch-Wirth and La Roche et al., 2026).

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Genome-wide CRISPR screening identifies tumor-intrinsic resistance mechanisms to NK cell cytotoxicity

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Natural killer (NK) cells can rapidly identify and destroy malignant cells, making them a promising tool for cancer immunotherapy. Enhancing NK cell efficacy through chimeric antigen receptors (CARs) or Fc receptors (CD16) combined with monoclonal antibodies to induce antibody-dependent cellular cytotoxicity (ADCC) has shown significant therapeutic potential. However, resistance to NK cell-mediated cytotoxicity, particularly in solid tumors, remains a major challenge.

To dissect mechanisms of cancer cell resistance, we performed six genome-wide CRISPR-Cas9 knockout screens in leukemia, breast, and pancreatic cancer cell lines co-cultured with the clinically relevant NK cell line NK-92 or its derivatives engineered to express an ErbB2-specific CAR or high-affinity Fc receptors in combination with therapeutic antibodies. Genomic DNA from surviving cancer cells was sequenced and analyzed using Model-based Analysis of Genome-wide CRISPR/Cas9 Knockout (MAGeCK).

Pathway analysis revealed diverse mechanisms by which cancer cells evade NK cell cytotoxicity. Each screen identified multiple high-ranking genes associated with resistance or susceptibility to NK cell killing. Functional validation using high-throughput live-cell imaging cytotoxicity assays confirmed key regulators of resistance. Among these, ICAM-1 was identified as a critical checkpoint required for natural and trastuzumab-mediated NK cell cytotoxicity, whereas ErbB2-targeted CAR-NK cells overcame this resistance. In addition, we identified a transcriptional regulator involved in tumor cell stress-response pathways whose inhibition sensitized cancer cells to NK cell-induced apoptosis.

Together, these findings highlight clinically relevant resistance mechanisms and provide insights to improve NK cell-based therapies for resistant cancers.

Development status / TRL: Basic research, TRL 1

From Concept to Practice: Enabling Matrix Production with a Cube-based Manufacturing Platform

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The manufacturing of Advanced Therapy Medicinal Products (ATMPs) faces critical challenges: high costs, manual handling, lock-in effect, and limited scalability, which restrict broad patient access. As the number of approved cell and gene therapies increases and more products reach broader clinical use, many manufacturing processes remain fragmented, manual, and only transferable to a limited extent.

To address these challenges, we introduce the evaluation of an innovative cube-based manufacturing approach implemented in a modular platform concept. The system consists of dockable, closed functional units (“cubes”), each performing defined process steps in aseptic conditions. A proof-of-concept prototype was developed to evaluate feasibility, demonstrating that the cube principle enables safe and standardized cell processing. In addition to technical proof-of-concept testing, process analyses and cost considerations were conducted on a conceptual basis using mesenchymal stromal cell (MSC) workflows. The next steps include expanding cube variants not only for cell andgene therapies but also for subprocesses that require high safety levels and safe containment (e.g., ADCs).

The concept offers an easy, pragmatic entry into modular manufacturing by integrating cubes into existing isolator systems. This allows application-specific adaptations and individual solutions within established GMP infrastructures, while enabling gradual automation, factoring in the rising potential of isolators.

Beyond linear production, the modular cube approach aligns with matrix manufacturing principles, enabling concurrent processes under harmonized environmental conditions. By combining modular cubes, transfer port technology, and isolator-based automation, this concept represents a concrete step toward turning matrix production for ATMPs into reality and supporting scalable, compliant manufacturing to improve patient access to advanced therapies.

Development status / TRL
The first cube prototypes have been developed to enable initial experimental studies, such as cell culture incubations. In a proof-of-concept study, we demonstrated the cube-based platform's ability to maintain aseptic integrity and support automated cell culture workflows. Tests confirmed aseptic handling, process stability, and biological functionality on a miniature scale.

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AI-Guided Discovery of Cancer-Selective Protein Degraders

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Mithryon™

Mithryon™ develops an advanced AI-guided discovery platform that identifies opportunities for highly selective protein degradation in cancer. Instead of relying on a narrow set of conventional degradation pathways, the platform explores a broader and largely underutilized space of biological mechanisms to enable next-generation targeted therapeutics. It integrates diverse biological inputs and proprietary analytical models to highlight promising degradation strategies with the potential for improved selectivity, reduced systemic burden, and applicability to targets historically considered challenging.

Despite the promise of targeted protein degradation, the field faces two persistent barriers: a strong dependence on a limited number of known pathways, which restricts differentiation and selectivity, and the difficulty of addressing oncogenic drivers that are poorly tractable with small molecules or biologics. At the same time, many biologically relevant mechanisms remain insufficiently explored in oncology, representing a significant untapped opportunity for therapeutic innovation.

Mithryon identifies and ranks new degradation strategies by combining integrated biological analytics based on multi-source datasets, predictive AI models for target and mechanism suitability, structural and contextual feasibility assessments, and selectivity and therapeutic-window profiling supported by decision tools that enable rapid interpretation by discovery teams. All outputs are designed to support early-stage strategy development without requiring or disclosing proprietary internal mechanisms.

Unlike conventional computational discovery tools focused on target identification or ligand prediction, Mithryon is specifically designed to broaden the degradation landscape itself, enabling more selective and cancer-aligned therapeutic strategies while maintaining strict confidentiality around methodology and data. The platform is currently advancing exploratory oncology pilots, with IP development centered on proprietary analytical frameworks, prioritization strategies, and confidential experimental workflows.

Mithryon's vision is to enable a new generation of precision degraders by systematically uncovering opportunities aligned with tumor biology, delivering therapeutic concepts that are highly selective, clinically meaningful, and designed with patient safety in mind.

AI-Designed Catalytic Extracellular Degraders (CEDs): A New Era of Protein Degradation

Schwarze, B.

Event-based pharmacology represents an emerging therapeutic approach that leverages the induction of specific biological events to trigger downstream, often irreversible cascades such as protein degradation [1,2]. This contrasts with traditional occupancy-based pharmacology, where drug efficacy depends on continuous target binding, a principle relevant to both small molecules and antibodies. A prominent example of event-based strategies is proteolysis-targeting chimaeras (PROTACs), which exploit the cell's own degradation machinery to eliminate otherwise "undruggable" intracellular targets [3]. However, PROTACs are largely limited to intracellular proteins due to their reliance on cytosolic ligand engagement, leaving the extracellular space comparatively underexplored.

To extend targeted protein degradation beyond the cell interior, lysosome-targeting chimaeras (LYTACs) have been developed to direct extracellular and membrane-bound proteins to lysosomal degradation via recruitment of lysosomal transport receptors (LTRs) [4,5]. While this approach holds promise for diseases such as cancer, cardiovascular disorders, and neurodegeneration, current LYTAC systems are limited by competition with natural ligands, stoichiometric constraints, poor tissue specificity, and dependence on complex antibody engineering.

To overcome these challenges, we introduce AI-designed Catalytic Extracellular Degraders (CEDs), which use de novo minibinders to induce bio-orthogonal endocytosis, avoid endogenous receptor competition, and enable pH-dependent catalytic turnover with improved tissue targeting. Building on the validated LangTAC technology [6], which targets the C-type lectin receptor CD207 (langerin), we integrate AI-based protein design to enhance recruitment and lysosomal trafficking of pathogenic proteins while broadening the range of targetable receptors.

The CED platform provides three key advantages: scalability through rapid de novo binder generation, modularity for applications ranging from tumour microenvironment modulation to cell therapy enhancement, and catalytic efficiency enabling sustained protein removal at lower doses compared to stoichiometric or first-generation systems. By targeting the extracellular proteome, CEDs establish a new frontier for high-precision catalytic therapeutics. The underlying LangTAC technology is currently at TRL 4–5, while the AI-driven design layer is at TRL 2–3, representing a key step toward unlocking the platform's full therapeutic potential.

References

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GreenPharming: Sustainable Plant-Based Biomanufac-turing of Immunomodulatory Biologics for Translational Medicine

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The clinical success of CAR-T and emerging CAR-NK cell therapies has created a rapidly growing demand for high-quality cytokines and antibody-based components required for cell expansion, activation, and functional modulation. However, current manufacturing systems for these biologics remain costly, resource-intensive, and vulnerable to supply chain constraints – limiting scalability and broader clinical accessibility.

To address this bottleneck, we are developing GreenPharming, a sustainable plant-based biomanufacturing platform designed to support next-generation cell therapies. The platform is based on a Plant Factory with Artificial Lighting (PFAL) integrated into a circular energy system, combining vertical farming, hydroponics, and renewable energy sources. Using transient expression in Nicotiana benthamiana, GreenPharming enables the production of key immunomodulatory factors for CAR-T and CAR-NK workflows, including IL-2, IL-7, IL-15, IL-18, and IL-21, as well as antibody-derived formats for cell targeting and modulation. By integrating upstream expression, downstream purification, and functional bioassays, the platform enables rapid production of high-quality proteins with defined functional activity for CAR-T and CAR-NK cell applications.

A central feature of GreenPharming is its role as a regional, decentralized manufacturing unit. The pilot facility is currently being established in the industrial park Schwarze Pumpe (Lusatia, Germany), contributing to structural transformation in a former coal region and aligning with the vision of a Net Zero Valley. By coupling biomanufacturing with renewable energy infrastructure, GreenPharming aims to provide a resilient and sustainable supply of critical biologics for academic and industrial cell therapy pipelines, including partners within the SaxoCell ecosystem.

Together, this approach positions GreenPharming as an enabling technology at the interface of sustainable bioproduction and advanced cell therapy, with the potential to reduce costs, increase accessibility, and strengthen regional innovation networks.

Development status / TRL
TRL 4-5 (technology validated in lab to early pilot stage)