SAXOCELL®

Precision Therapy Cluster for Saxony

Annual Report 2021

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Federal Ministry
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CLUSTERS
4 FUTURE
Next generation
innovation networks

2021 in brief

We are SaxoCell® - the Saxon innovation cluster for **Cell and Gene Therapy (CGT)** funded by the BMBF Clusters4Future initiative. SaxoCell brings together many academic and corporate partners to develop and improve CGT-based therapies for serious diseases. In this annual report, we would like to highlight SaxoCell's launch into the implementation phase as a cluster for future in October, 2021. All partners came together virtually for the kick-off event on November 16 and all projects have commenced activities in their ambitious endeavours. We have had the privilege to host a pioneer in gene therapy, Alain Fischer from the Imagine Institute of the College de France in Paris in October, and the honour to have Matthias Hebrok from the Diabetes Center of the University of California in San Francisco as a guest professor for four months. Our public relations team has been busy delivering our website, press releases and SaxoCell Newsletters.

In things to come in 2022, SaxoCell will be on display at the ARM Med, the German Biotechnology Days and the ISCT meetings and will feature prominently at the BIO-Europe held in Leipzig from October 24-26. Our first consortium meeting is taking place in June and we look forward to presenting our achievements to our External Advisory Board later this year.

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Researching together

Prof. Dr. Dr. Ulrike Köhl
University of Leipzig
Fraunhofer IZI

Prof. Dr. Ezio Bonifacio
Technical University Dresden

Dear Friends, SaxoCell Members, Scientific Community and further Readers,

Annual reports are a time to reflect on last year's achievements. The first year is particularly challenging for any new venture as it lays the foundation for what is to come. SaxoCell's strength lies in its complementary partners, and its success will be the ability of these partners to cooperate. After several months, it feels like much of what has happened so far has been building the team and the structures that will support the exciting SaxoCell projects, getting to know the many new enthusiastic faces (unfortunately, mostly on video conferences), and talking to university, city and state representatives about the importance of what SaxoCell can achieve. There has indeed been a lot of that, but there has also been time to enjoy the science that feeds the SaxoCell projects. Scientifically, we are in exciting times. However, we should not put aside that these are also onerous times. We believe that science (and a lot of tolerance and cooperation) will provide the solutions. Science starts from the discoveries and is complete when it delivers to society.

Achieving more together

We have had a glimpse of how science can come together and excel in a pandemic. There is a lot more to do. As speakers of this Cluster4Future, we are fortunate to see so much innovative science and discoveries and foresee what it might achieve for improving health, and particularly incurable diseases. We have labelled SaxoCell's content 'Living Medicine' with a vision to change therapy from chronic, expensive treatment to safe affordable cure. This is a bold vision, but one that is shared by SaxoCell investigators and many colleagues across the world.

With a special thanks to all the members of the SaxoCell Cluster for their dedicated work and for their constructive, solution-oriented cooperation, we leave you to share our vision in the report. We hope you enjoy it. We would also like to invite you to join us via Twitter, Instagram or LinkedIn.

The SaxoCell Speakers Ezio Bonifacio and Ulrike Köhl as well as SaxoCell Co-Speakers Martin Bornhäuser and Uwe Platzbecker.

Prof. Dr. Martin Bornhäuser
University Hospital Dresden

Prof. Dr. Uwe Platzbecker
University Hospital Leipzig

Words of welcome

The SaxoCell cluster for future is a lighthouse project in Saxony that aims to develop and optimize innovative drugs in the field of cell and gene therapy by bundling the expertise of various research institutions, hospitals and industrial partners in order to significantly improve the therapy of difficult-to-treat diseases. Here, the University of Leipzig will make an important contribution through its modern research environment in the biomedical field as well as through the affiliated, high-performance University Hospital.

Prof. Dr. Beate A. Schücking
Former Rector University of Leipzig

SaxoCell is a wonderful example of inter- and transdisciplinary cooperation. Together with our colleagues in Leipzig and Chemnitz we are forging a new critical mass in medicine for Dresden and whole Saxony. SaxoCell not only brings together the strengths of basic science and medical practice but also manufacturing, and business development. With its excellent research and modern and innovative university medicine facilities, TU Dresden is contributing to develop this socially, economically and scientifically highly relevant venture. We are looking forward to the next achievements.

Prof. Dr. Ursula Staudinger
Rector Technical University Dresden
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from our Core Institutions

With the SaxoCell future cluster, we are creating an internationally visible beacon for cell and gene therapy in Saxony. Together with our partners, we are strengthening the innovative cell and gene therapy industry, closing gaps in the value chains and leveraging synergy potential - for pioneering medicine made in Germany. This not only strengthens the region of Saxony, but will also create new therapeutic options for patients, for example in tumor diseases or autoimmune diseases.

Prof. Dr.-Ing. habil. Reimund Neugebauer
President of the Fraunhofer-Gesellschaft
Photo copyright © Fraunhofer / T. Dashuber

SaxoCell is a milestone in medical care in Saxony. With its participation, Chemnitz Hospital will make a decisive contribution to the development of novel drugs in the promising field of cell and gene therapy. Together with our partners, we are transferring modern research findings into clinical application in order to be able to treat diseases that are incurable today in the future.

Dipl.-Oec. Dirk Balster
Managing Director Klinikum Chemnitz gGmbH

Welcome from Stakeholders

Congratulations to SaxoCell. This is an excellent example of how Saxony's technology policies and investments over the last 20 years has driven local scientific innovation to create opportunities for new industry and ventures for our state. We are proud to see Saxony become a world player in global efforts to create the medicines of the future. I wish the SaxoCell team every success.

Martin Dulig

Saxon State Ministry for Economy, Labor and Transport

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From Wirtschaftsförderung Sachsen (WFS)' point of view, SaxoCell underlines the innovative strength of Saxony as a business location, which results from cross-technology cooperation. We work closely with SaxoCell and support the network in the further development of cell and gene therapies. Together, we focus on strengthening local companies through technology transfer, company spin-offs from SaxoCell and advise companies from the life sciences sector on settling in Saxony.

Thomas Horn

Managing Director of Wirtschaftsförderung Sachsen GmbH

Saxony has a long tradition of driving innovation. With its aim to develop new areas of application and production methods for personalized gene and cell therapeutics, the new Cluster4Future SaxoCell clearly follows this tradition. As central point of contact for the Saxon start-up and innovation ecosystem, the innovation platform futureSAX is excited about the implementation of SaxoCell. We share its vision to enable a sustainable economic model with high value-added potential for the entire region by taking scientific findings and turning them into business opportunities. We are very happy to support SaxoCell in its innovative and advanced ambitions with our broad network to connect innovators from industry and science, set growth impulses for sustainable innovations and increase the effectiveness of innovation processes.

We believe SaxoCell will strongly boost our Saxon environment for research institutions and companies in the field of gene and cell therapy. We wish all participants much success and all readers, many impulses!

Marina Heimann
Managing Director of futureSAX

SaxoCell
Core Institutions

Technical University Dresden

Technical University Dresden (TUD) has its roots in the Royal Saxon Technical School that was founded in 1828. Today, it is a university that unites the natural and engineering sciences with the humanities and social sciences, as well as medicine. This wide range of disciplines brings with it the obligation for the university to promote interdisciplinarity and to contribute to the integration of science and society. The TUD is one of the largest "Technical Universities" in Germany and one of the leading and most dynamic universities in Germany. As a full-curriculum university with 17 faculties in five schools, it offers a broad variety of 124 disciplines. It focuses on Health Sciences, Biomedicine & Bioengineering, Information Technology & Microelectronics, Smart Materials & Structures, Energy, Mobility & Environment as well as Culture & Societal Change and these are considered exemplary in Germany and throughout Europe. Around 32,000 students are enrolled at TUD, one in eight coming from abroad. TUD is among the 20 most innovative universities in Europe (Reuters Top 100: Europe's Most Innovative Universities) starting around 20 spin-off companies per year. It has a total budget of approx. EUR 578 million thereof approx. 46% third-party funded.

Since 2012, TUD has been one of Germany's Universities of Excellence. The Center for Regenerative Therapies Dresden (CRTD) was funded by the DFG as Research Centre and Cluster of Excellence, which among other things develops cell therapy for immune modulation and tissue replacement. The CRTD faculty currently includes two Alexander von Humboldt professors. Dresden university hospital, has many years of expertise in the field of 'investigator-initiated' and third-party clinical trials and is specialised in the application of ATMPs. This includes comprehensive immune monitoring and biomarker screening as well as biobanking of all types of tissue and liquid samples. It has extensive experience and scientific expertise in the field of haematopoietic stem cell transplantation and CAR-T cell application and production.

TECHNISCHE UNIVERSITÄT DRESDEN

University of Leipzig

Founded in 1409, Leipzig University is one of the oldest universities in Europe. It is a cosmopolitan, modern comprehensive university with 14 faculties, 465 professorships and over 31,000 students. Today, as a member of the German U15 association, the University of Leipzig is one of Germany's major universities with strong research and medical leadership. The research strength of the University of Leipzig is reflected in a DFG Research Center, five DFG Collaborative Research Centers, two Humboldt Professorships and six ERC Grants. At the same time, it is one of the universities in Germany with the highest number of start-ups (Top five in the category "Start-ups with knowledge transfer from the university"). The university is a member of the Leipzig Science Network, which deepens cooperation with universities and non-university research institutions and increases the national and international visibility of Leipzig as a science location. The university's research fields form the interface for intensive cooperation with other scientific institutions in Leipzig, including three Max Planck Institutes, two Fraunhofer Institutes, four Leibniz Institutes, two Helmholtz Centers, a federally funded integrated research and treatment center, and a high-performance University Hospital.

At the University Hospital, the Department of Cell Therapy is well established, providing promising and innovative treatment strategies (stem cells, CAR-T cells) for patients with diseases of the hematopoietic system in collaboration with the Institute of Clinical Immunology and the Fraunhofer IZI. Furthermore, the Early Clinical Trials Unit Leipzig (ECTUL) for innovative tumor therapy and therapies of other disciplines – a Phase-I-Unit, serves to catalyze translational research and the development of new drugs and treatment approaches under optimized conditions.

UNIVERSITÄT
LEIPZIG

Fraunhofer IZI Leipzig

The Fraunhofer Institute for Cell Therapy and Immunology IZI develops solutions to specific problems at the interfaces of medicine, life sciences and engineering. One of our main tasks is to conduct contract research for companies, hospitals, diagnostic laboratories and research institutes operating in the field of biotechnology, pharmaceuticals and medical engineering. The institute develops, optimizes and validates methods, materials and products within its business units cell and gene therapy, drugs & vaccines, molecular diagnostics and immunodiagnostics, as well as extracorporeal therapies. Its areas of competence lie in cell biology, immunology, drug biochemistry, bioanalytics and bioproduction as well as process development and automation. Research in these areas is centered around developments in immuno-oncology and infectious disease pathology. Besides its main location in Leipzig in the Free State of Saxony, the institute has subsidiaries in Halle, Potsdam, Rostock, Hannover and Erfurt.

In our business unit “Cell and Gene Therapy” are our technologies covering the entire early value chain in cell and gene therapy R&D. We develop a pipeline of proprietary ATMPs (Advanced Therapy Medicinal Products) as well as innovative platformtechnologies. In parallel, we support development efforts of our industry partners with these technologies. Further along the development value chain are we also offering GLP toxicology and safety studies for ATMPs and develop reliable safety assessment strategies for ATMPs. In the ATMP manufacturing area are we supporting our partners and internal programs with comprehensive GMP process development, optimization and automation capabilities as well as with large scale contract manufacturing services. We collaborate closely with the Leipzig University Hospital and thus can also support the conduct of clinical trials.

Fraunhofer IZI

Chemnitz Hospital

With 1,785 beds, Chemnitz Hospital is one of the largest hospitals in Germany and offers a wide range of diagnostic and therapeutic services. Approximately 62,000 full and partial inpatients and around 80,000 outpatients are treated here annually at the highest medical level.

In order to continuously improve medical care in southwestern Saxony, the maximum-care hospital is increasingly promoting science and research. Thus, since the winter semester 2020/2021, the model course of study in human medicine, MEDiC for short, has been offered at the Medical Campus of Chemnitz Hospital, which interlinks scientific principles with clinical practice.

In addition, the Clinical Studies Center at the Chemnitz Oncology Center organizes the participation of numerous oncology departments in around 120 clinical studies annually. In this way, the latest scientific findings from clinical research are quickly integrated into existing therapy concepts and innovative treatment options are introduced. The focus is also on interdisciplinary cooperation with physicians in private practice, surrounding hospitals and other partners in health care management, science and industry.

The Clinic for Hematology, Oncology and Stem Cell Transplantation headed by PD Dr. Mathias Hänel specializes in the optimization and application of immune and cell therapies for various hematological neoplasms. The clinic has various targeted, individualized treatment concepts and is one of the largest hematological-oncological therapy centers in Germany.

KLINIKUM CHEMNITZ gGmbH

SaxoCell Structure

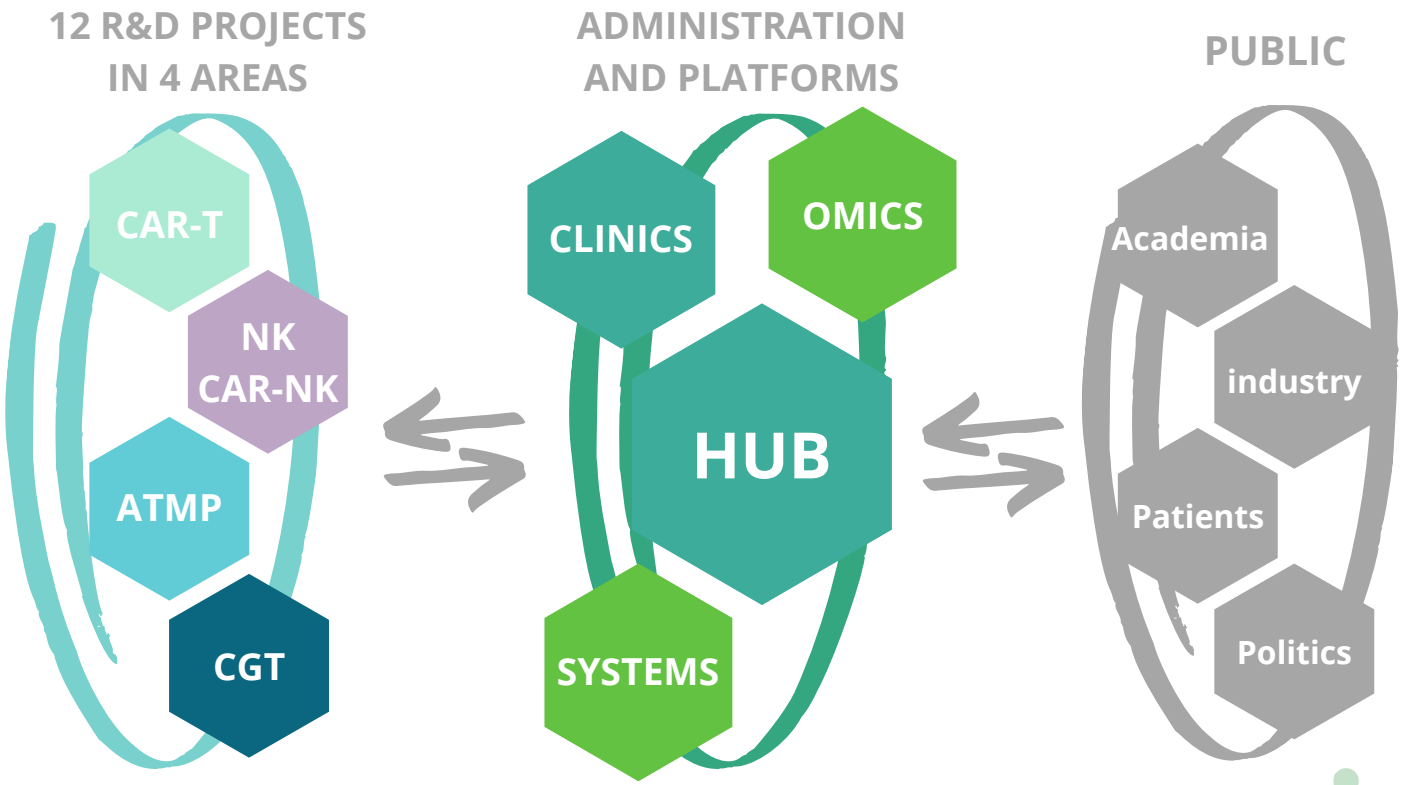
SaxoCell Portrait

SaxoCell stands for the development of new application areas and production methods for **gene and cell therapeutics**, so-called "living drugs". SaxoCell channels local discoveries toward the design and production of cells with precise targets and function for safer, more effective clinical therapy. SaxoCell's path from discovery to clinic and its competence in modular industrial scale cell production will secure a sustainable economic model for the Saxony region.

SaxoCell will significantly improve **regional networking in Saxony** in the field of cell and gene therapy, integrate further partners and initiatives nationwide and close corresponding gaps in the value chains. In this way, synergy potentials will be raised and realized, which in turn will greatly increase the visibility of Saxon and nationwide partners in the field of cell and gene therapy, facilitate access to funding and, through clinical and regulatory cooperation, accelerate clinical implementation. Through these and other activities, SaxoCell will thus significantly increase the attractiveness for investments of national and international companies in this industrial sector and contribute substantially to the development and further strengthening of an innovative cell and gene therapy industry in Saxony, Germany.

The Structure of SaxoCell

An Overview



SaxoCell Hub

SaxoCell Hub

Innovation support measure

The SaxoCell Hub is the central interaction and control interface within the cluster serving as an innovation-promoting network. It is composed of **PAP** (Pipeline Acceleration Programme), the **CMP** (Cluster Matching Programme) and **ICP** (Innovation Culture Programme). The Hub benefits from the scientific excellence and the industry transfer experience of our core institutions. The named programmes and their actors are in close exchange and interaction with each other.

PAP

- Project management
- Identification of new projects
- Reporting

CMP

- Cluster Strategy
- Cluster sustainability
- Joint Research Infrastructure

ICP

- PR, marketing & transfer
- Contracts & patents
- Trainings & Innovation culture

The SaxoCell Hub interacts closely with cluster partners, project partners, external partners and stakeholders, as well as the Steering Board. The Hub thus plays a central role in realising the cluster goals. The Hub's areas of activity and interaction include project management, training and qualification measures, access to expertise and infrastructure to cluster and project marketing and transfer of results, as well as other measures to support our partners and create an efficient transfer culture.

In October 2021, the Hub successfully organised a SaxoCell mini symposium, attended by over 180 participants, both on-site and virtually. The keynote speech was given by Alan Fischer, accompanied by presentations by SaxoCell PIs, Anja Feldmann, Frank Buchholz and Michael Sieweke. Additional activities included public discussions with Matthias Hebrok from the UCSF and Frank Buchholz on start up cultures in the USA and Germany.

The SaxoCell kick-off meeting in November 2021 provided the opportunity to network and become familiar with the possibilities within the cluster. Furthermore, the Hub members had the chance to present SaxoCell at various events, e.g. at the Saxon Transfer Forum 2021 organised by futureSax, BIOEurope Digital 2021 and further bilateral meetings with regional decision makers. In addition to the SaxoCell website, the hub has also started activites on Twitter, LinkedIn and Instagram.

Sophia Kolbe
Fraunhofer IZI

Andrea Zimmermann
Uni Leipzig

Dorit Teichmann
TU Dresden

Maren Henneken
TU Dresden

Thomas Tradler
Fraunhofer IZI

Anette Bartsch
Fraunhofer IZI

Paul Starz
Fraunhofer IZI

Luisa Brückner
TU Dresden

Stefanie Binder
Uni Leipzig

Ilka Henze
Fraunhofer IZI

Beatrice Berneck
Uni Leipzig

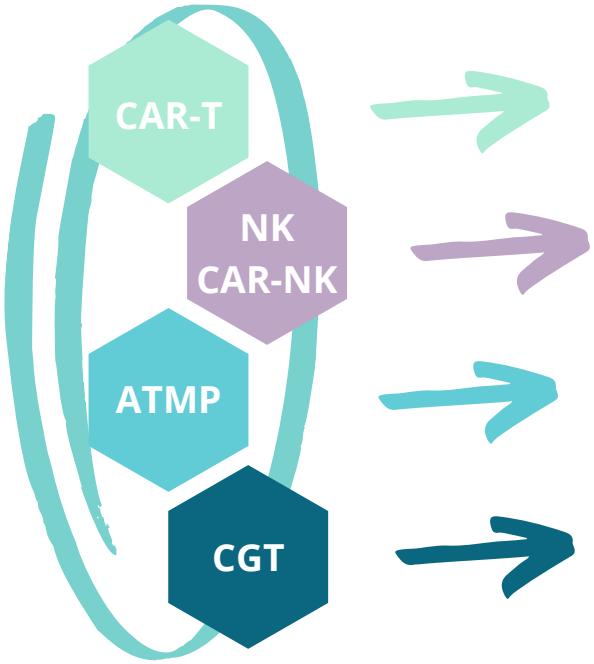
Nicole Schütz
Uni Leipzig

The SaxoCell projects are individually supervised by the PAP team. The needs for further training or required support are shared with the ICP team to plan and implement suitable measures. Area meetings and other exciting events and exchange formats such as "spark" meets are planned throughout the following year.

To increase international visibility for the cluster and allow an efficient transfer of project R&D results, the ICP team will present the cluster at a number of cell and gene therapy sector as well as life science partnering conferences.

SaxoCell Projects

12 SaxoCell Projects in 4 Areas



AlloCART & UltraCART

CAR-NK 4.0, CAReNK-AID & NK4Therapy

HemRec, ZellTWund, xMac & MSC-PreStiGe

OPTIX, ECP-CAR & TheraSTAR

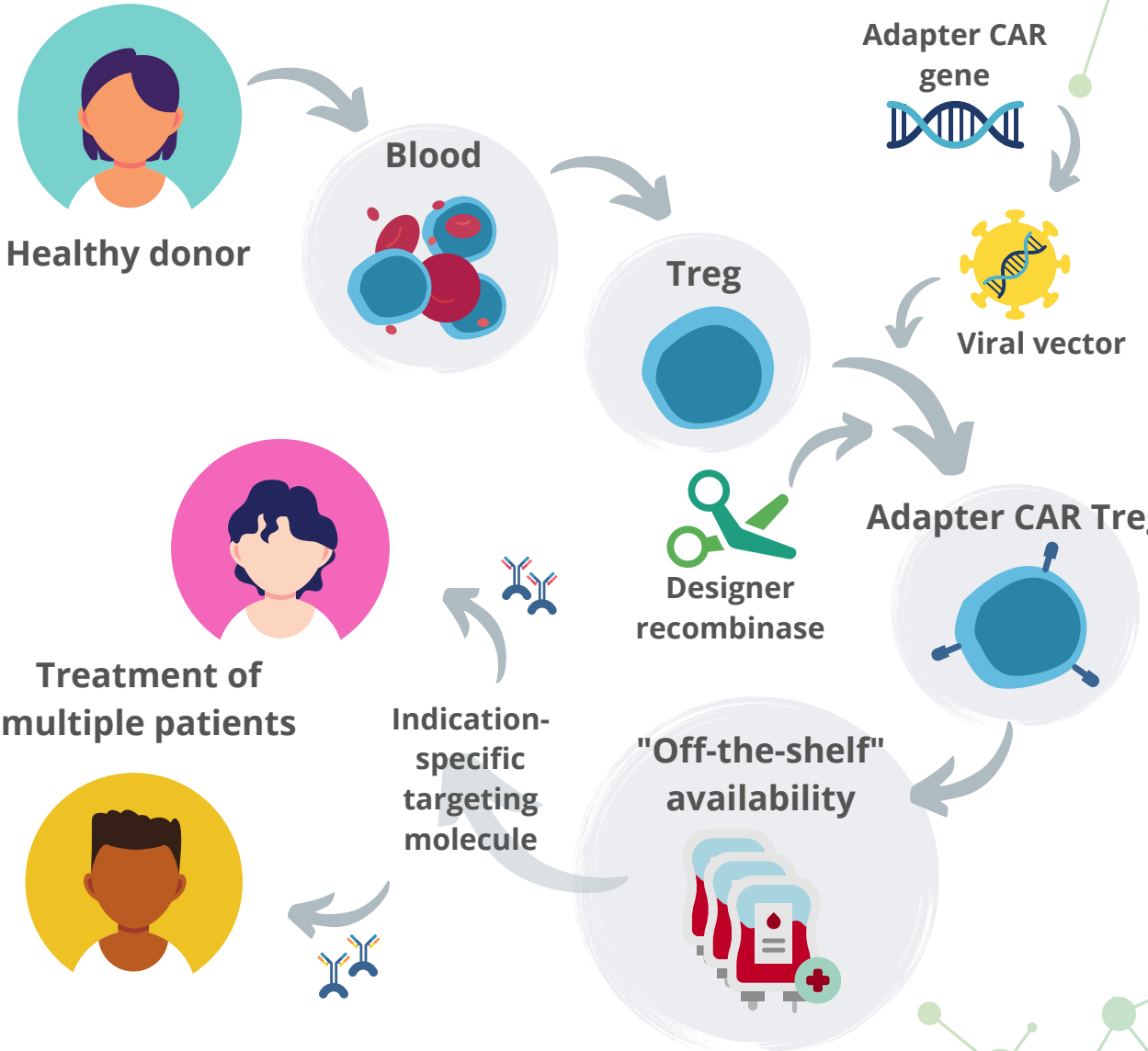
AlloCART

AlloCART, the project for the "Preclinical Development of Switchable UniCAR-T as well as UniCAR-Treg" focuses on the development of a serial production of a cell type that suppresses excessive immune responses in healthy humans. These so-called regulatory T cells (Treg) are to be isolated and propagated from healthy donors. The Treg will be equipped with novel 2-component adaptors (UniCAR technology) that promote docking to the target tissue to locally suppress inflammatory responses.

In particular, novel cell isolation and genetic modification techniques are used to generate UniCAR Treg.

Project Manager: Prof. Dr. Martin Bornhäuser and Dr. Anke Fuchs

Project Partners: Helmholtz Center Dresden Rossendorf, University Hospital Dresden, Technical University Dresden


Healthy donor
Blood
Treg
Adapter CAR gene
Viral vector
Designer recombinase
Adapter CAR Treg
"Off-the-shelf" availability
Indication-specific targeting molecule
Treatment of multiple patients

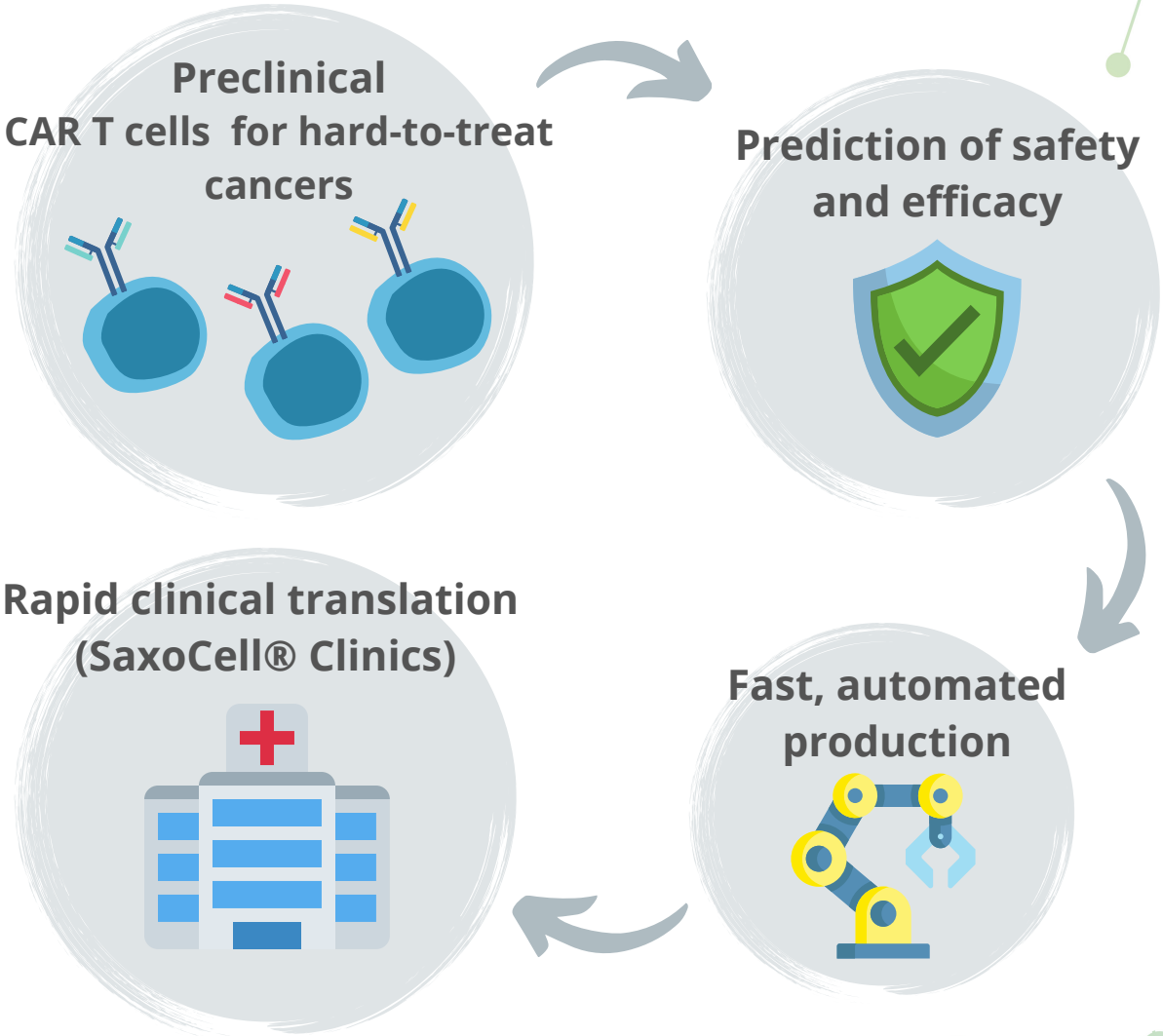
UltraCART

The UltraCAR-T project is dedicated to the core topic of cellular immunotherapy with genetically modified CAR-T cells using virus-free gene-transfer technology based on proof-of-concept work performed in preclinical and clinical studies at the University of Würzburg. The project is pursuing technologically advanced CAR-T products with therapeutic potential in hematology and oncology through the CAR-T biotech start-up T-CURX GmbH and advanced clinical-grade manufacturing through Fraunhofer IZI.

In the context of the SaxoCell future cluster, the value chain for such advanced CAR-T products will be developed and exploited.

Project Manager: Prof. Dr. Michael Hudecek

Project Partners: Fraunhofer IZI, University Hospital Würzburg, University of Leipzig, T-CURX GmbH


Preclinical
CAR T cells for hard-to-treat cancers
Prediction of safety and efficacy
Fast, automated production
Rapid clinical translation (SaxoCell® Clinics)

CAR-NK 4.0

This collaboration project is focusing on the development of a platform technology for the automated manufacturing of allogeneic chimeric antigen receptor natural killer (CAR NK) cells for the treatment of specific cancerous diseases. Besides the promising results obtained in the therapy of B cell malignancies using CAR T cells, conclusive concepts for treatment of myeloid neoplasms and malignant tumors are still missing. One of the biggest hurdles in the development of autologous (CAR T) cell therapies is the impaired quality and functionality of the patient's own immune cells. To conquer some of these obstacles expertise from academic (Fraunhofer IZI) and industry partners (Affimed GmbH; Miltenyi Biotec B.V. & Co. KG) as well as from two hospitals (Universitätsklinikum Leipzig; Klinikum Chemnitz gGmbH) is bundled within this CAR-NK 4.0 project. In this context, NK cells of healthy donors will be used as promising starting material for the manufacturing process allowing for allogeneic cell therapies.

The project scope is covering the whole value chain of an advanced therapy medical product comprising pre-clinical development, process optimization and the translation to a GMP-compliant CAR-NK manufacturing process. In detail, three aims are addressed: (i) development of an automated AI-assisted CAR-NK cell manufacturing platform (ii) pre-clinical investigation and preparation of a phase I study with an allogeneic CD123-addressing CAR-NK approach treating myeloid neoplasms (iii) increase of the therapeutic efficiency of CAR-NK cell therapy and its manufacturing by implementing novel technologies, such as a bi-specific target approach, optimized AAV gene transfer method, and a new cell activation approach.

Project Manager: Prof. Dr. Dr. Ulrike Köhl

Project Partners: Fraunhofer IZI, University Hospital Leipzig, University of Leipzig, Chemnitz Hospital, Affimed, Miltenyi Biotec

Research to enhance cytotoxicity of effector cells

Development of bispecific CAR constructs

Optimization of CAR constructs & automated CAR NK cell manufacturing

SaxoCell SYSTEMS

Combination CAR NK & multispecific ICEs

Patents/ Publications

Study plan design CAR NK cells in MDS

SaxoCell CLINICS

AAV vector mediated delivery system into NK cells

CAReNK-AID

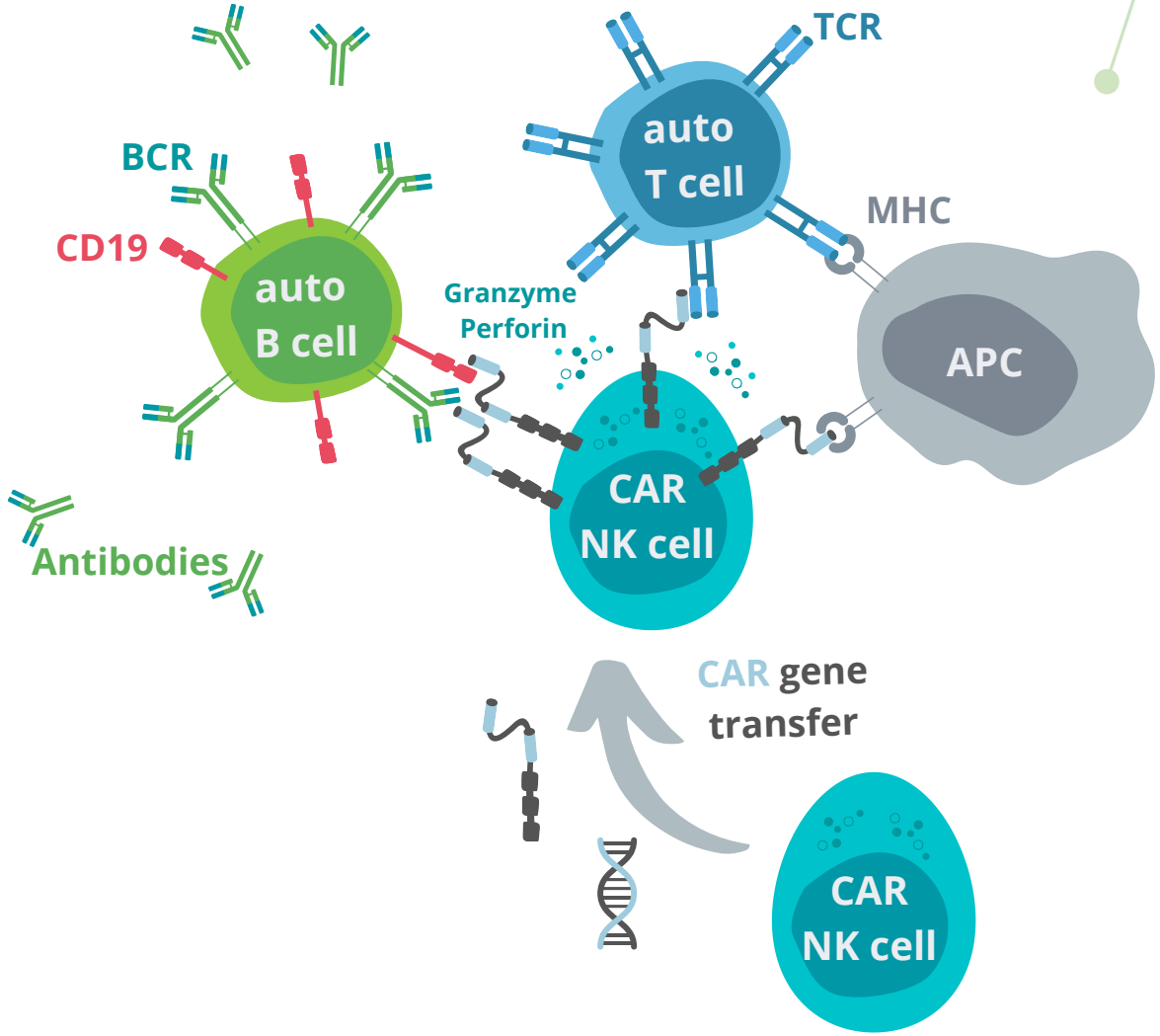
Chimeric Antigen Receptor engineered Natural Killer cells for the treatment of Autoimmune disease.

While CAR-T cells have revolutionized the treatment of some leukemias and lymphomas by eliminating malignant B lymphocytes, this approach has so far not been used for autoimmune diseases, where elimination of autoimmune reactive B-lymphocytes would also promise a therapeutic benefit. The CAReNK-AID project aims to expand chimeric antigen technology into severe cases of autoimmune diseases. The patient´s own immune effectors, such as natural killer (NK) cells, will be retargeted to eliminate B- and T-lymphocytes that drive the autoimmune disease. CAR´s will be developed that recognize disease specific targets for the redirection of disease driving immune cells and will also develop clinical grade processes for non-viral genetic engineering and expansion of Natural Killer cells.

In the first funding phase, the project aims to complete preclinical proof of concept in a representative autoimmune disease. The project is based on IP and comprehensive expertise of the project partners regarding an experienced consortium contributing expertise in the biology and clinical treatment of autoimmune diseases but also in process development and translation of cell based medicines into the clinic.

Project Manager: Prof. Dr. Torsten Tonn

Project Partners: Technical University Dresden, University Hospital Dresden, University of Leipzig


TCR
auto
T cell
BCR
CD19
auto
B cell
MHC
Granzyme
Perforin
APC
CAR
NK cell
Antibodies
CAR gene
transfer
CAR
NK cell

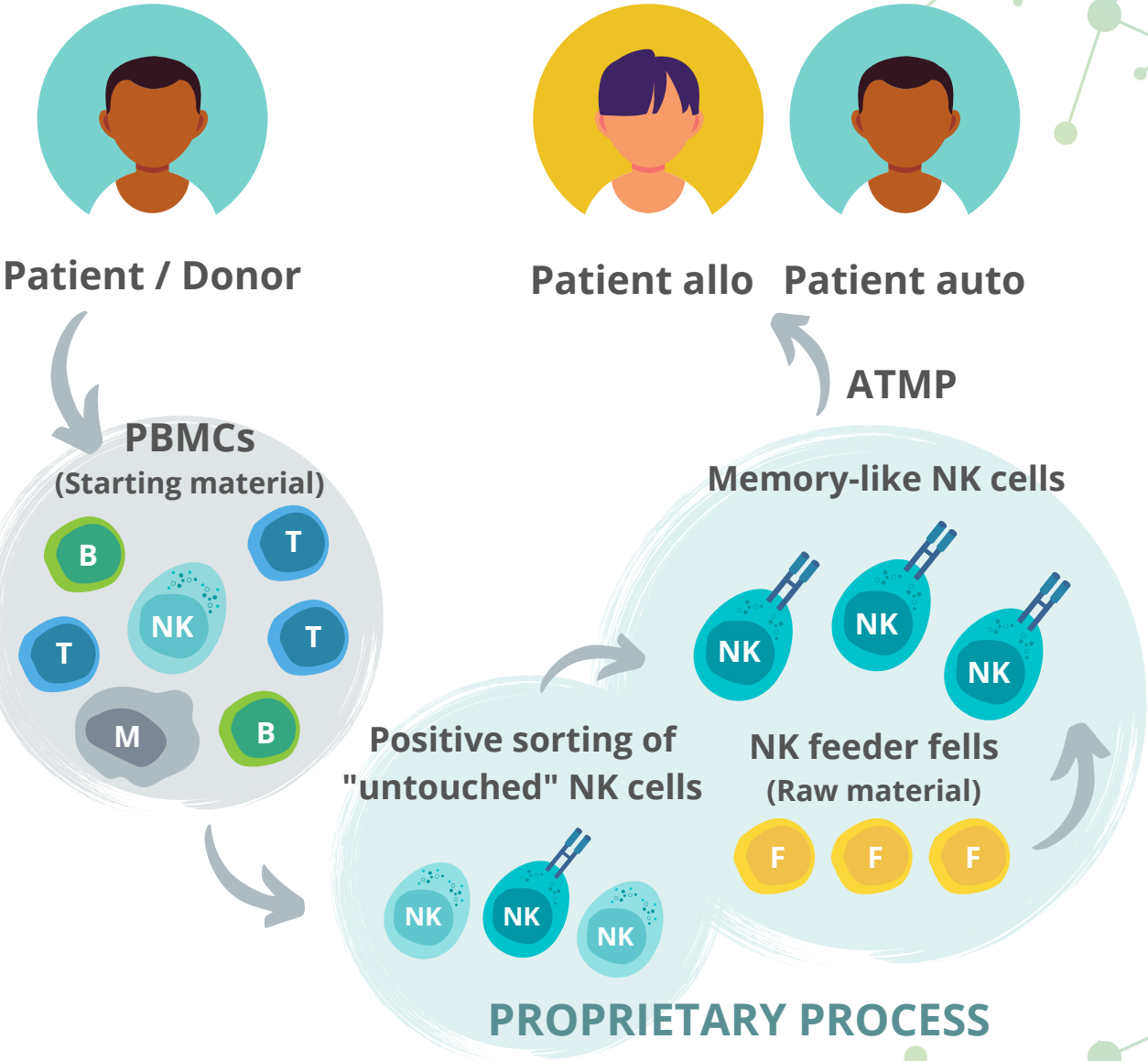
NK4Therapy

Natural killer (NK) cells are innate lymphoid cells that mediate immune responses against virus-infected cells and cancer. The NK4Therapy project exploits the potential of terminally differentiated NK cells expressing the activating receptor CD94/NKG2C and associated with acquisition of the maturation marker CD57. Both markers are hallmarking a shift toward greater effector function, including improved antibody-dependent cellular cytotoxicity (ADCC) and potent natural cytotoxicity after engagement with target cells.

It is planned to exploit the intrinsic natural cytotoxicity of the NKG2C+/CD57+ NK cells towards solid cancers with expression of ligands for CD94/NKG2C. In addition, such NK cells can be used in an autologous or allogeneic setting for therapy of viral infections and in particular as consolidation therapy in immunocompromised patients. A novel method for isolation of NK cells from a Saxon SME and a proprietary technology for large-scale expansion of NK cells from the TU Dresden will be merged into a GMP-compliant NK cell production process for accelerating market maturity.

Project Manager: Prof. Dr. Achim Temme

Project Partners: University Hospital Dresden, Transfusion Medicine Technical University Dresden, Cell.Copedia GmbH Leipzig


Patient / Donor
Patient allo
Patient auto
ATMP
PBMCs
(Starting material)
B
T
NK
T
T
M
B
Memory-like NK cells
NK
NK
NK
Positive sorting of
"untouched" NK cells
NK feeder fells
(Raw material)
F
F
F
NK
NK
NK
PROPRIETARY PROCESS

HemRec

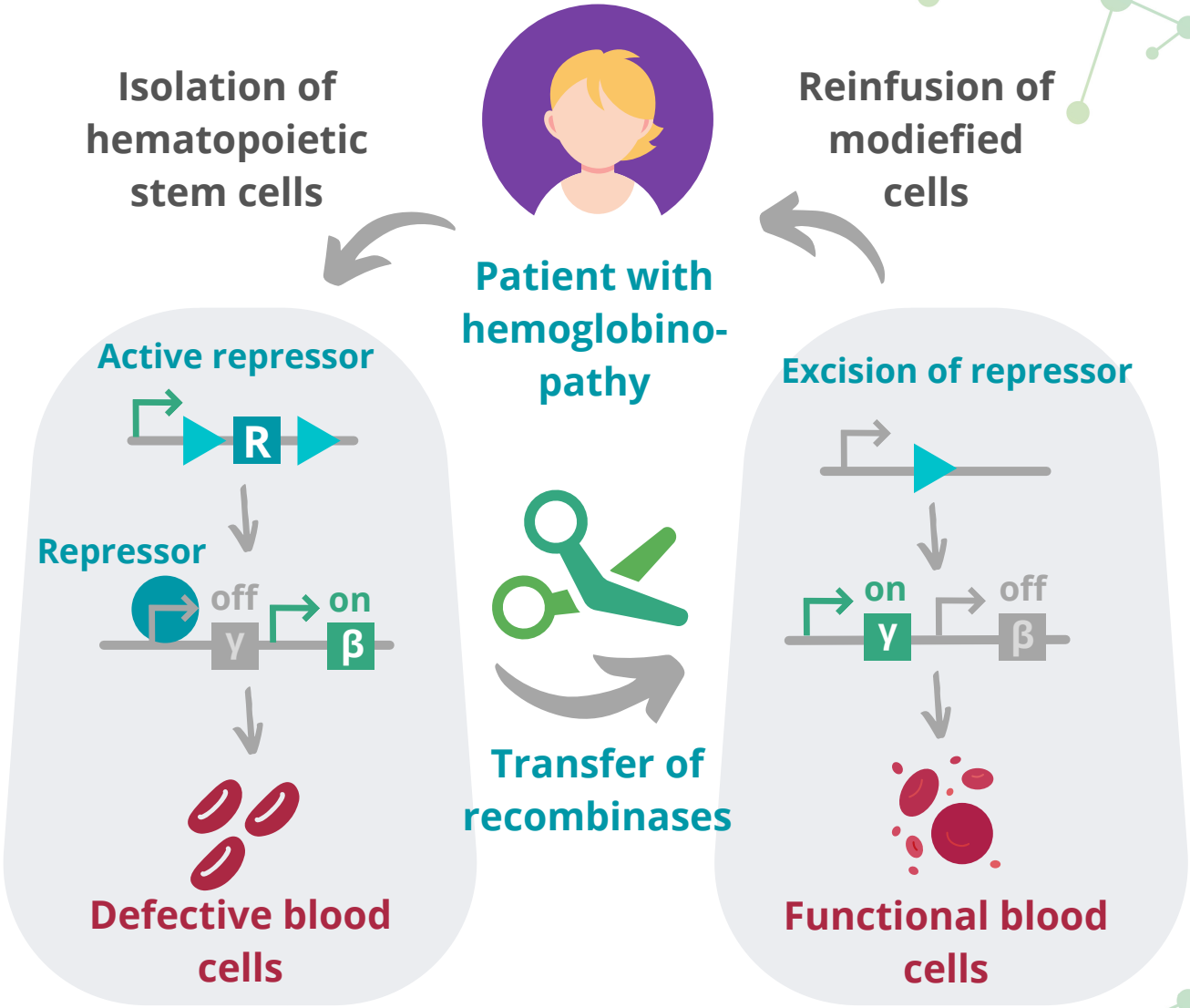
The HemRec project is based on the development of proprietary designer recombinases by the group of Frank Buchholz (TUD). The platform technology has already been incorporated into a spin-off company (RecTech GmbH) founded during the first funding period.

Within the SaxoCell project "HemRec", the team plans to develop a generally applicable designer-recombinase based healing strategy for ß-chain hemoglobinopathies. This designer-recombinase is intended to excise a small DNA fragment from hematopoietic stem cells of diseased patients, ultimately leading to the reactivation of gamma-globin and thus to the long-term production of healthy red blood cells.

To achieve this goal and to clinically translate the project, the research group started working closely with the DKMS Life Science Lab. Its strength lies in the safe and flexible genome editing.

Project Manager: Prof. Dr. Frank Buchholz

Project Partners: Technical University Dresden, DKMS Life Science Lab gGmbH


Isolation of hematopoietic stem cells
Reinfusion of modiefied cells
Patient with hemoglobino-pathy
Active repressor
R
Repressor
off
γ
on
β
Defective blood cells
Transfer of recombinases
Excision of repressor
on
γ
off
β
Functional blood cells

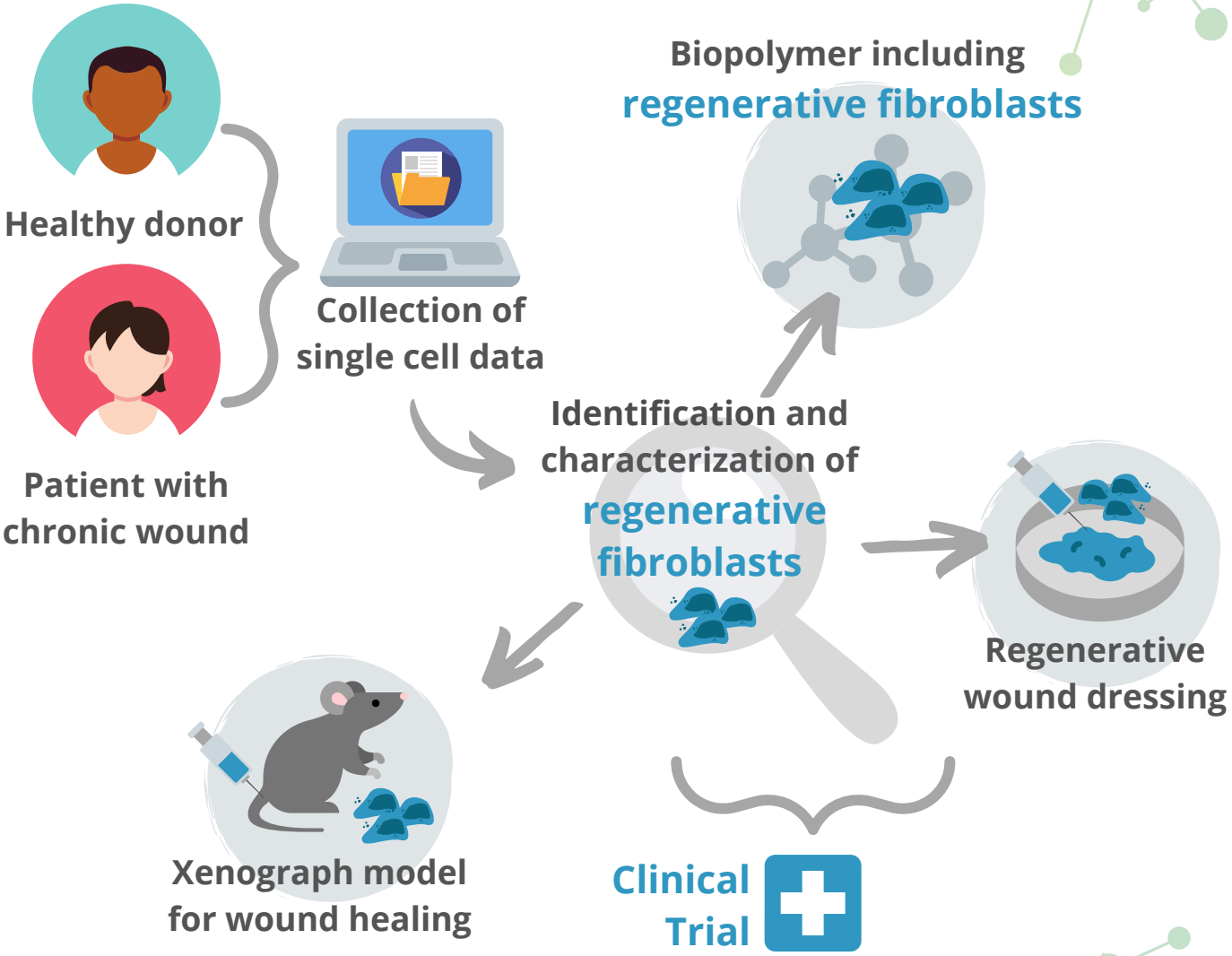
ZellTWund

The ZellTWund project is based on the derivation and clinical use of purified pro-regenerative cells (in particular fibroblast subpopulations) from human skin as an approach to skin regeneration in chronic, non-healing wounds.

The therapeutic approach uses degradable biopolymers that integrate pro-regenerative autologous stromal cells. The project has already generated interest from an undisclosed swedish company and the partners intend to jointly develop the approach within the SaxoCell cluster.

Project Manager: Prof. Dr. Jan Christoph Simon

Project Partners: University Hospital Leipzig, University of Leipzig, Helmholtz Center Munich


Healthy donor
Patient with chronic wound
Collection of single cell data
Biopolymer including regenerative fibroblasts
Identification and characterization of regenerative fibroblasts
Regenerative wound dressing
Xenograph model for wound healing
Clinical Trial

xMac

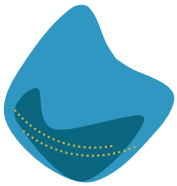
The xMac project is based on the scientific discoveries of Prof. Sieweke's group about the expansion potential of adult macrophages, as well as the differentiation and expansion of macrophages from human induced pluripotent stem cells. Macrophages have great potential as a broadly applicable cell therapeutic of the future.

The focus in the first project phase is on the development of a manufacturing process under GMP conditions to provide investigational products for clinical trials in the field of infectious and pulmonary diseases, but also oncology, as well as the development of universally applicable preparations for allogeneic transplantation.

Project Manager: Prof. Dr. Michael H. Sieweke

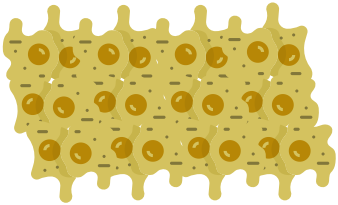
Project Partners: Technical University Dresden

Why Macrophages?
Macrophages are ideal Tumor Killers!

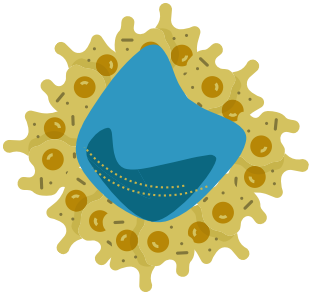


Macrophage

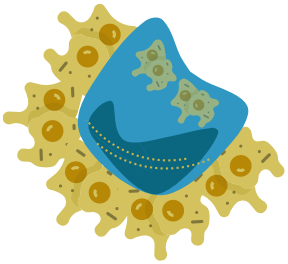
Search and identify



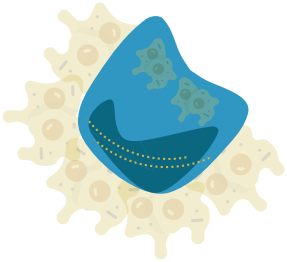
Solid tumor



Infiltrate



Phagocytise



Kill

MSC-PreStiGe

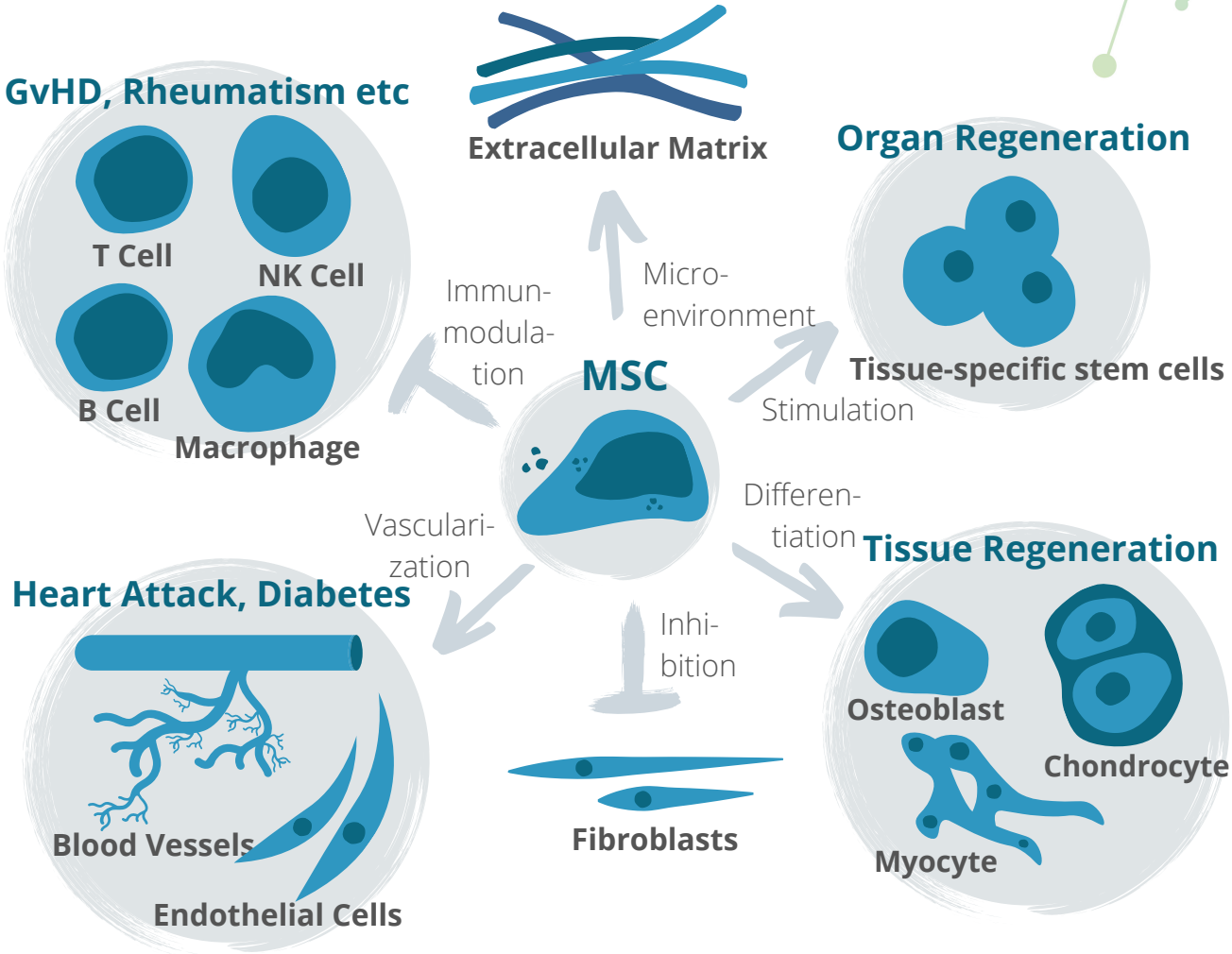
The MSC-PreStiGe project exploits the immunomodulatory potential of mesenchymal stromal cells (MSC) extracted from umbilical cord tissue. This juvenile MSC population is particularly characterized by an immense expansion potential, which allows the treatment of up to 25 patients with only one cell product. A first indication to be tested for the use of this preparation will be severe acute graft-versus-host disease (GvHD) after allogeneic stem cell transplantation. MSCs are considered to be highly potent drug candidates for many inflammation-associated diseases for which there are currently no satisfactory therapies and which are associated with high mortality or high long-term morbidity.

The MSC application opportunities are based on the results of 20 years of worldwide research with over 80,000 publications. Until now, this drug substance cannot be produced industrially in large quantities with a clearly defined quality under pharmaceutical conditions at low cost.

In the project, an industrial value chain for the MSC drug substance Desacell® is being developed and established in Saxony. As a result, MSCs will be available in the SaxoCell cluster in large quantities in GMP quality under pharmaceutical conditions. Therefore, allogeneic MSCs with high therapeutic potential will be available off-the shelf at reasonable costs that can be applied easily and quickly.

Project Manager: Prof. Dr. Mario Rüdiger

Project Partners: Technical University Dresden, University Hospital Dresden, DKMS Stem Cell Bank gGmbH, MDTB Cells GmbH


GvHD, Rheumatism etc
T Cell
NK Cell
B Cell
Macrophage
Extracellular Matrix
Organ Regeneration
Tissue-specific stem cells
Immun-
modula-
tion
Micro-
environment
MSC
Stimulation
Differen-
tiation
Vasculari-
zation
Inhi-
bition
Tissue Regeneration
Osteoblast
Chondrocyte
Myocyte
Heart Attack, Diabetes
Blood Vessels
Endothelial Cells
Fibroblasts

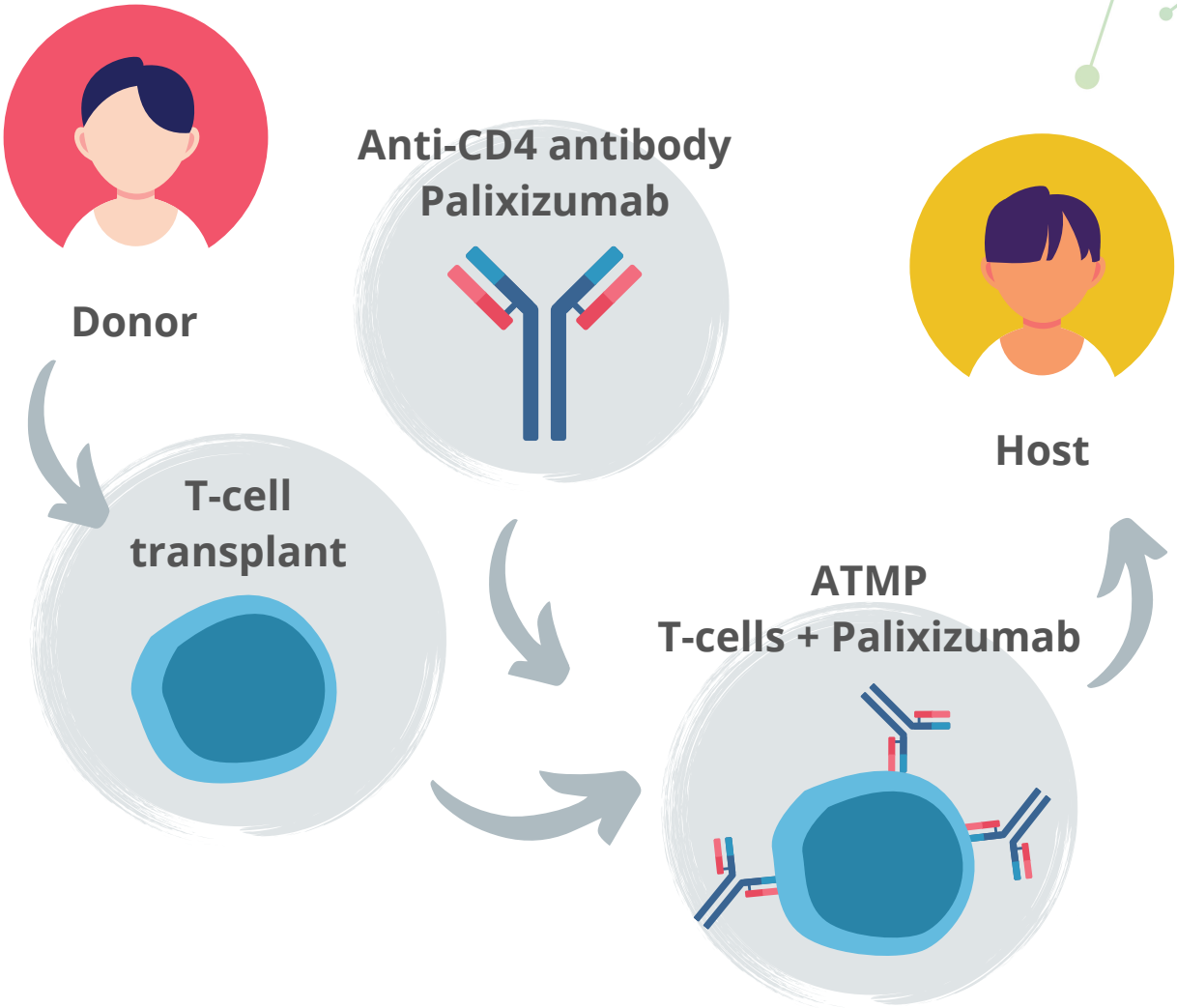
OPTIX

The OPTIX project addresses the optimization and clinical translation of a manufacturing process for an antibody-modified stem cell transplant (Palintra®) followed by a prospective, multicenter, single-arm first-in-man phase I/II trial under coordination and leadership of the Saxon company Tcell Tolerance GmbH, as well as translational research to further elucidate the mechanism of action.

The project involves the modification of an allogeneic hematopoietic stem cell transplant for the treatment of hematological neoplasms, whereby the modification is intended to reduce graft-versus-host disease while preserving the graft-versus-leukemia effect.

Project Manager: Lilly Stahl

Project Partners: Fraunhofer IZI, University Hospital Leipzig, University Hospital Dresden, Hospital Chemnitz, Tcell Tolerance GmbH


Donor
Anti-CD4 antibody
Palixizumab
Host
T-cell
transplant
ATMP
T-cells + Palixizumab

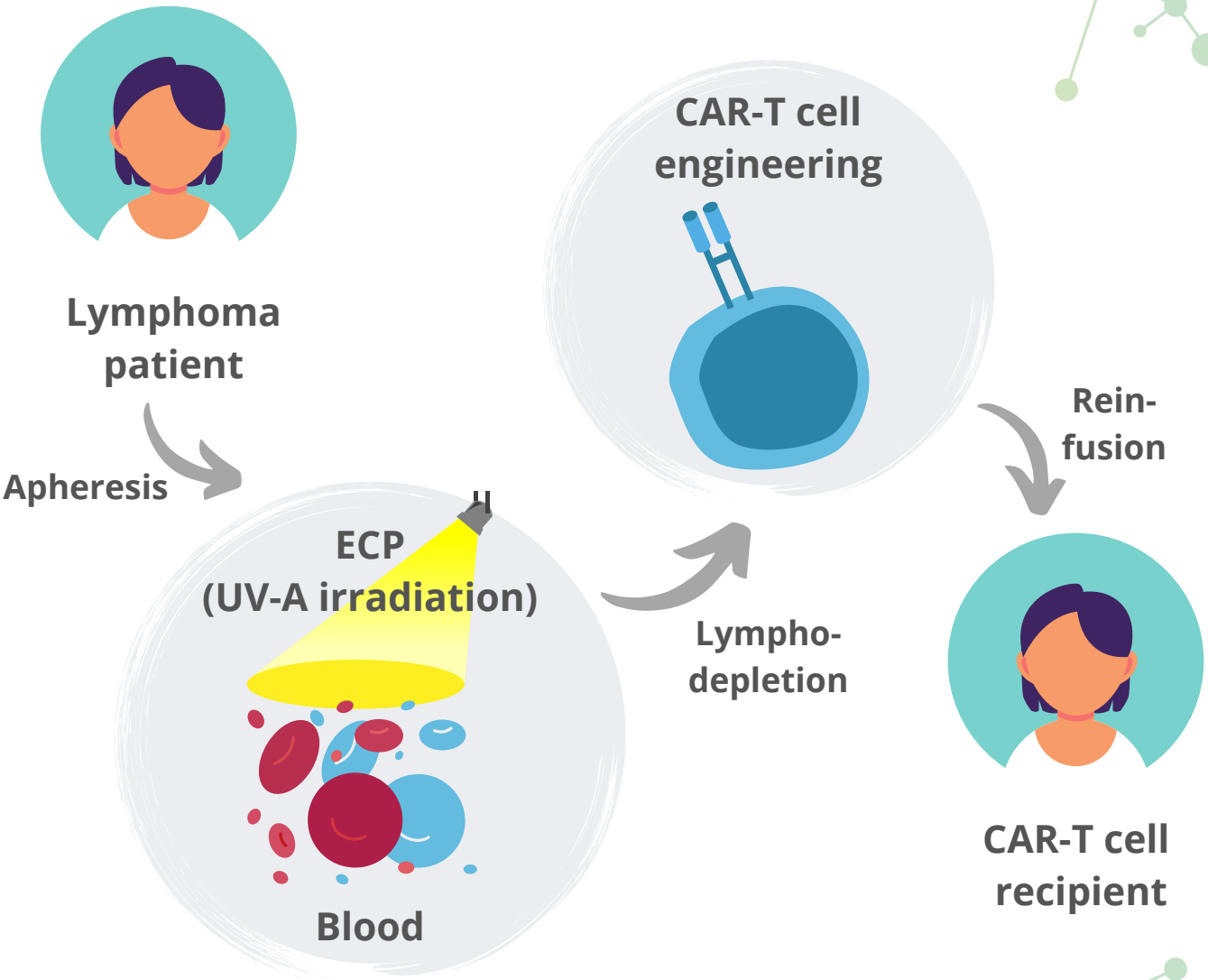
ECP-CAR

One of the most relevant steps in the successful CAR-T cell therapy is the preparation of the patient for the application of the CAR-T cells. The patient's "normal" immune cells would hinder the growth and function of CAR-T cells, thus it is necessary to temporarily reduce or eliminate the patient's immune cells by using chemotherapy. Moreover, in some cases, severe side effects caused by a global cytokine release may occur due to the immune reaction upon CAR-T cell therapy. To address this issue, a clinical trial will be conducted to determine if the immunomodulation with extracorporeal photophoresis (ECP) prior to lymphodepletion can impact the safety and efficacy of conventional CAR-T treatment. In ECP, the patient's blood cells are treated *ex vivo* with 8-methoxy psoralen, then irradiated with ultraviolet light (UV-A) and reapplied to the patient, which is expected to eliminate immune cells and optimize the growth and function of CAR-T cells.

The patients treated in this study will undergo complex analyses of their immune system before and after ECP, helping us to understand (1) the complex immunological mechanisms on tumor microenvironment induced by ECP but also (2) the individual characteristics and functionality of the applied CAR-T cells. Taken together, the SaxoCell® project ECP-CAR will investigate the additive effect of immune modulation by ECP in a randomized phase II study with regard to its safety and efficacy.

Project Manager: Dr. Vladan Vucinic

Project Partners: University Hospital Leipzig, University of Leipzig, University Hospital Dresden


Lymphoma patient
Apheresis
ECP (UV-A irradiation)
Blood
Lympho-depletion
CAR-T cell engineering
Rein-fusion
CAR-T cell recipient

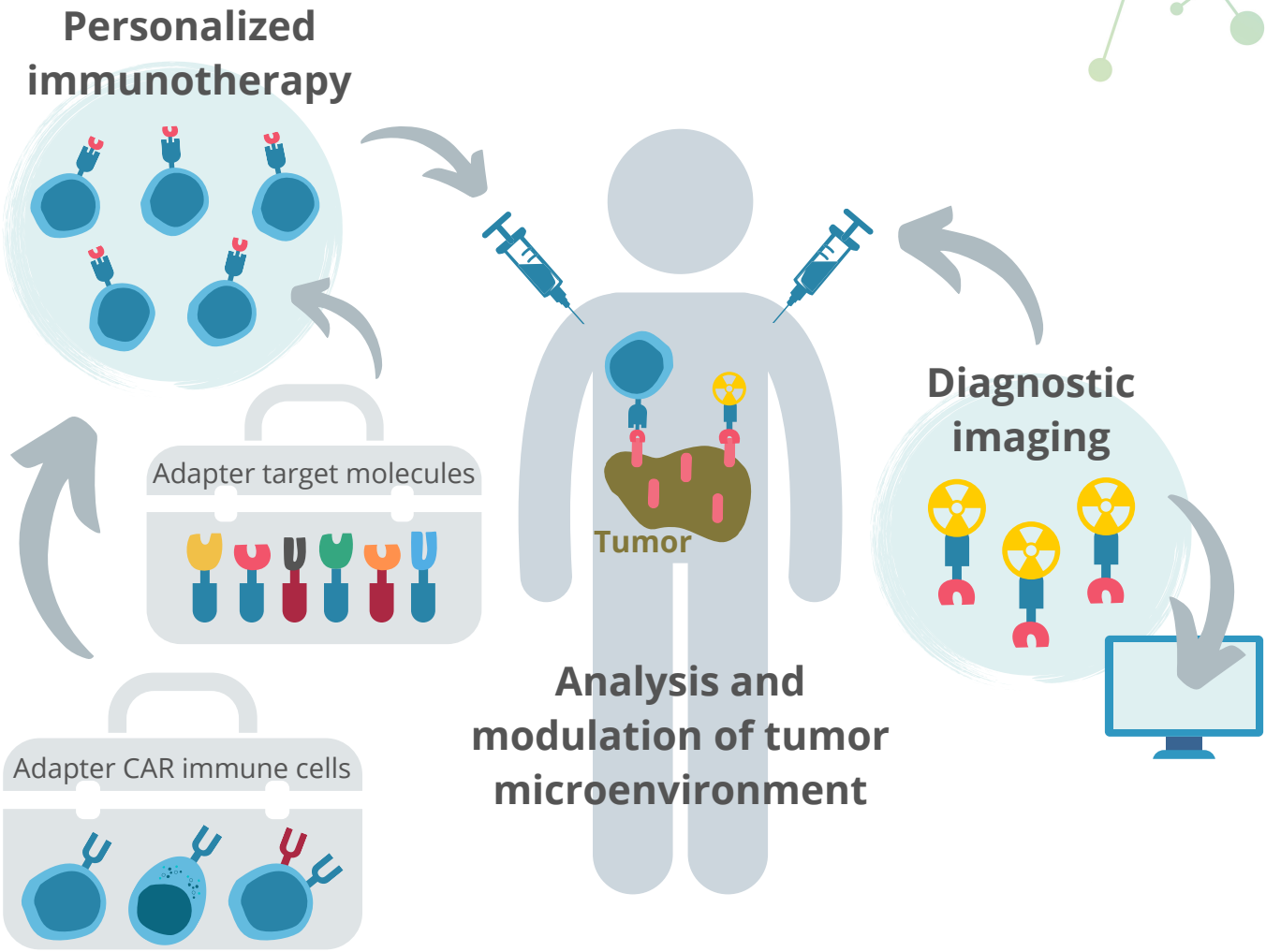
TheraSTAR

The TheraSTAR project aims to develop theranostic target molecules (for therapy and diagnostics) and adapter CAR platforms that significantly support both conventional CAR and universal adapter CAR (e.g. UniCAR, RevCAR) technologies in the SaxoCell® cluster, broaden their application and improve their safety and efficacy. In this context, target molecules will be developed that redirect adapter CAR-armed immune cells to kill tumor cells and further enable a modulation of the tumor microenvironment which is thought to have a beneficial impact on the therapeutic efficacy. To improve safety and specificity of CAR-based cellular therapies, in the TheraSTAR project adapter CAR platform technologies will be developed that are switchable and can be programmed for combinatorial tumor targeting. Besides immunotherapy, the theranostic approach can be used for radionuclide therapy and additionally allows monitoring of the tumors and course of immunotherapy in patients using imaging techniques (PET/SPECT). Due to their modular character, the platform technologies are broadly applicable for targeting of different tumor entities as well as infectious, autoimmune or graft-versus-host diseases.

These theranostic platform technologies enable unique and versatile combinations of therapy and diagnosis paving the way for an improved, effective, safe and personalized immunotherapy.

Project Manager: Dr. Anja Feldmann

Project Partners: Technical University Dresden, Helmholtz Center Dresden Rossendorf


Personalized immunotherapy
Adapter target molecules
Adapter CAR immune cells
Tumor
Analysis and modulation of tumor microenvironment
Diagnostic imaging

SaxoCell Platforms

SaxoCell OMICS

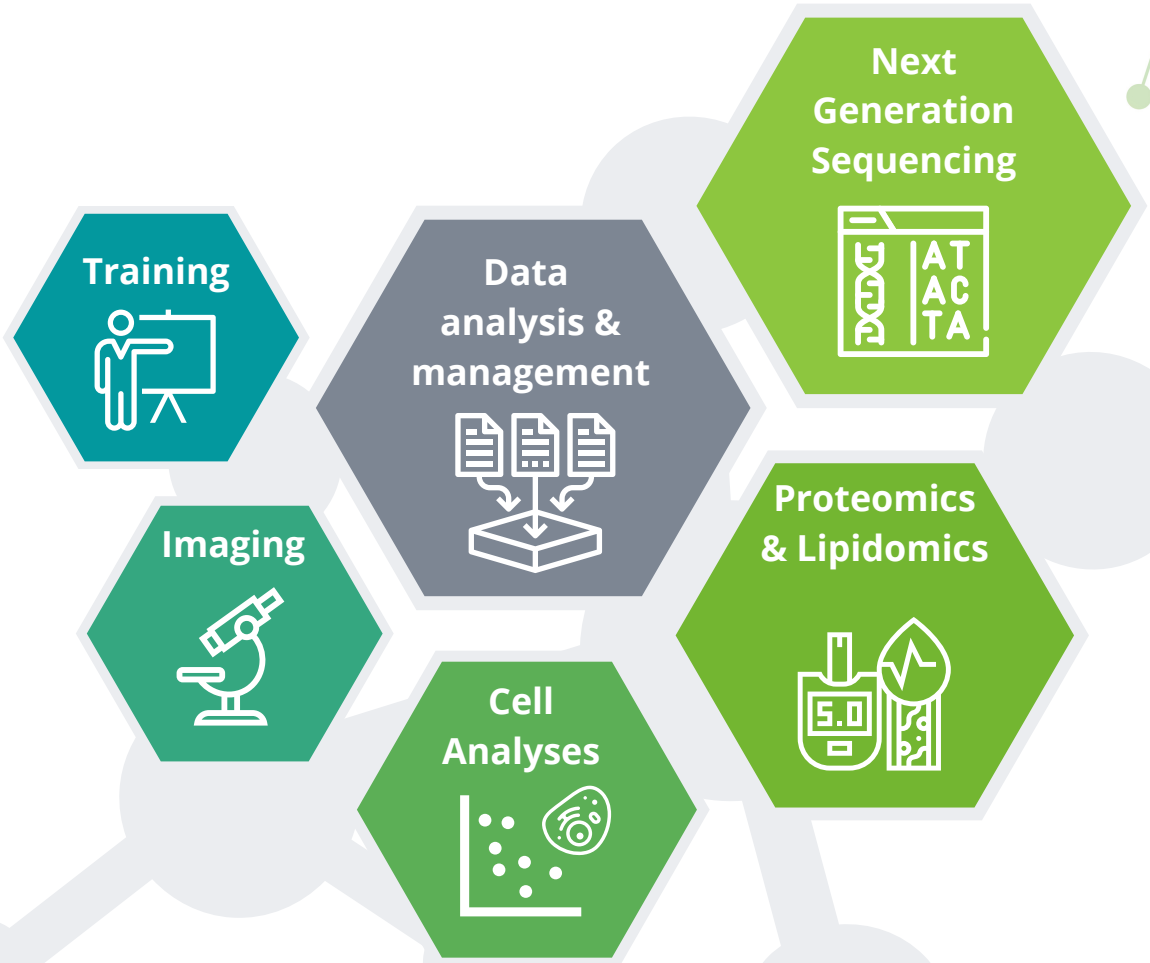
The SaxoCell OMICS platform ensures optimal and early support for the development and production of gene and cell therapeutics within the Cluster. Therefore, SaxoCell OMICS pursues four strategic goals for the cluster:

1. The provision of efficient and harmonized processes for monitoring the delivery and tolerability of novel therapies
2. The identification of mechanisms of action, novel targets and resistance
3. The development of improved quality criteria for the manufacturing process
4. The development of predictive biomarkers

SaxoCell OMICS' collaboration with SaxoCell projects and platforms enhances the competitiveness of biotechnology and bioanalytical companies in the SaxoCell region.

Prof. Dr. Ezio Bonifacio
CRTD, TU Dresden

Dr. Kristin Reiche
Fraunhofer IZI


Next Generation Sequencing
AT
AC
TA
Training
Data analysis & management
Proteomics & Lipidomics
5.0
Imaging
Cell Analyses

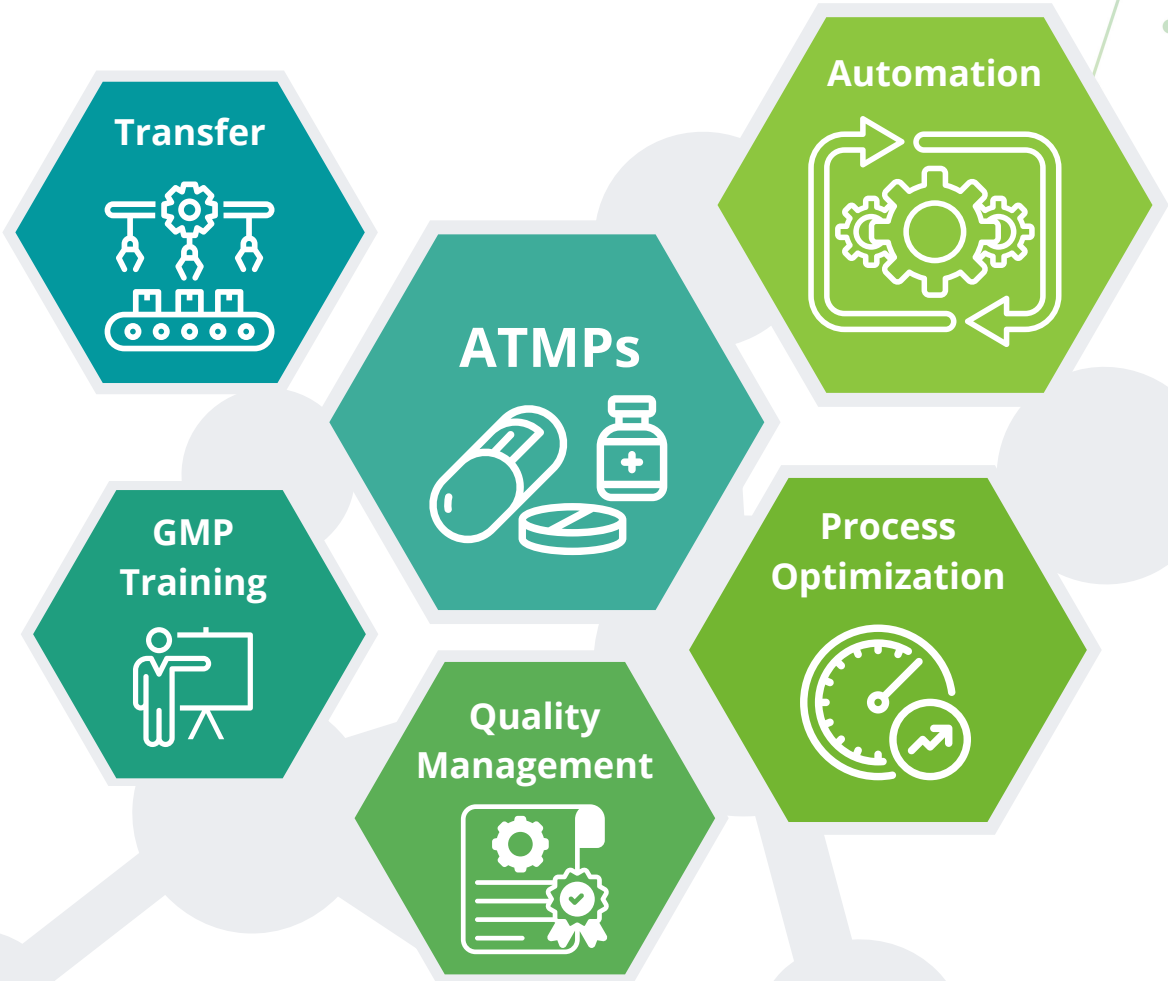
SaxoCell SYSTEMS

PD Dr. Stephan Fricke
Fraunhofer IZI

The production of ATMPs by means of widely applicable, standardized processes on an industrial scale requires automation solutions. Initial concepts for the high-throughput manufacture of ATMPs have already been outlined in SaxoCell. Specifically, protocols and concepts for automated ATMP production are to be developed and the link to new types of quality control will be addressed. The aim is to map this standardization strategy in the project as far as possible using generic process modules.

Dr. Ulrich Blache
Fraunhofer IZI

In addition, ATMP manufacturing processes may benefit from **machine learning** algorithms, in order to automate the safe and efficient production of cell therapeutics. This will enable stakeholders to move towards robust scaling of cell production for clinical purposes. All aspects will be developed with Good Manufacturing Practice (GMP) compatibility in mind and GMP training methods will be developed.


Transfer
Automation
ATMPs
GMP
Training
Process
Optimization
Quality
Management

SaxoCell CLINICS

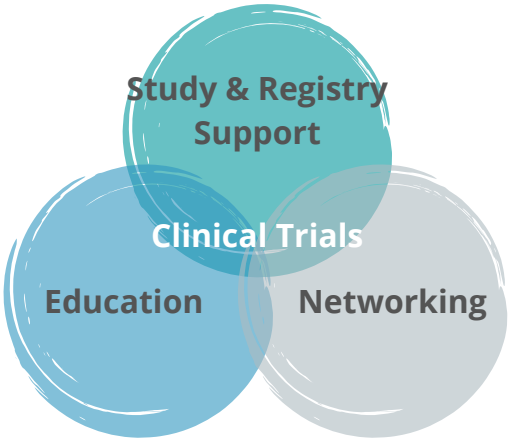
SaxoCell CLINICS is responsible for the clinical support of all innovative research projects of SaxoCell as well as for the **bundling of the clinical expertise** of the three locations Leipzig, Dresden and Chemnitz.

SaxoCell CLINICS acts as a contact, interface and communicator in the field of ATMPs between research institutes, authorities (PEI, ethics committees), industrial partners, patient advocacy groups, study groups and other SaxoCell platforms.

SaxoCell CLINICS is structured to provide **various services at different levels** and, besides practical **advice** on the conduct of studies, the platform offers **educational initiatives** in order to train the SaxoCell network partners in clinical trial management.

Prof. Dr. Uwe Platzbecker
University Hospital Leipzig

Silke Gloaguen
University Hospital Leipzig



Summary of SaxoCell CLINICS tasks and services

Clinical trial support

- **Feasibility:** Discussion of planned study projects involving relevant stakeholders, such as the project team, advisory board and possibly regulatory authorities.
- **Assessment of regulatory framework:** SaxoCell CLINICS supports with regulatory classification of a planned study and with study Sponsor identification (according to AMG).
- **Start-up support for clinical studies:** The SaxoCell CLINICS platform supports the project network with advice on study management set-up, the development of essential trial documents and the choice of an appropriate study management organization/CRO. SaxoCell CLINICS accompanies clinical study projects during this transition.

Education and training

SaxoCell CLINICS organizes educational meetings on clinical trial management for the project partners. The platform works with internal and external partners in order to offer comprehensive training according to the project partners' needs.

Consulting and network formation

Networking within the SaxoCell cluster and with regional and national authorities, patient representatives and health insurance companies.

SaxoCell Bio

SaxoCell CLINICS supports the development and coordination of an ATMP-based patient registry and its associated biobank, which derives samples from ATMP studies carried out in the cluster framework.

SaxoCell Advisory Board

Scientific Advisory Board

The external advisory board is composed of recognized experts who are able to provide profound insight and advice regarding SaxoCell's manifold activities.

Prof. Ute Modlich
PEI, Langen

Prof. Axel Schambach
MHH, Hanover

Dr. Jessica Morison
CRISPR Therapeutics, Boston

Dr. Lorenz Mayr
Vector BioPharma AG

Jan Geissler
Patient advocacy, Munich

Nadine Winter
Patient advocacy, Dresden

SaxoCell Funding

SaxoCell - selected by the BMBF's Clusters4Future programme

SaxoCell is one of seven clusters within of the innovation programme "Clusters4Future" of the Federal Ministry of Education and Research (BMBF). Our concept for a Saxon future cluster SaxoCell in the promising field of cell and gene therapy was selected by an expert jury together with six other projects from a total of 137 applicants in the first phase of the competition.

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Federal Ministry of Education and Research

CLUSTERS 4 FUTURE
Next generation innovation networks

The seven future clusters
of the first competitive round

The seven winners are Germany's next generation innovation networks of the future. Their claim is to find suitable solutions for the major challenges of our time. The topics are as diverse as the winners' concepts: neuromorphic hardware for autonomous systems, **personalized cell and gene therapy methods**, sustainable marine research, quantum technology, new approaches to drug development and hydrogen. To achieve this, universities, research institutions, companies, social and other relevant players in the regions have joined forces, sharing exclusive knowledge with each other and pooling their expertise.

Impressum

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SaxoCell®

Precision Therapy Cluster for Saxony

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CLUSTERS 4 FUTURE
Next generation innovation networks