

Day 1: Monday 11.9.23, IZI

Time (CET)	Topic	Responsible
Day 1	With Scientific Advisory Board (SAB) und PTJ	
10:30 – 11:00	Registration	
11:00 – 11:20	Welcome of the participants and update on the status of SaxoCell	Ulrike Köhl, Ezio Bonifacio
11:20 – 11:30	Cluster4Future initiative overview and expectation	Anastasia Vogel BMBF
11:30 – 12:45	Project presentation HemRec, UltraCART, xMac	3 Projects result 15 min.+ 10 min. discussion
	Group picture	All
12:45 – 14:10	Lunch Break + Poster Session	All
14:10 – 14:50	Project presentation OPTIX, CAR-NK4.0/NK4Therapy	2 Projects result 10 min.+ 10 min. discussion
14:50 – 15:20	platforms: Systems, Omics, Clinics; Hub	
15:20 – 15:40	Break	All
15:40 – 17:00	Break-out session 1 -> each group hands in report/slides Parallel Meeting SAB Parallel Meeting Speaker	
17:00 – 17:15	Coffee Break	All
17:15 – 18:00	Key note lecture “Developing a national strategy for gene and cell therapy” Christopher Baum BIH	30 + 15 min discussion
18:00	Get together + Food and Drinks	All

SAXOCELL®



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4 FUTURE**
Next generation
innovation networks

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Federal Ministry
of Education
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LIVING DRUGS

SAXONIAN PRECISION THERAPY CLUSTER

SaxoCell Consortium Meeting and Scientific Advisory Board Meeting
11.-12. 09.2023



UNIVERSITÄT
LEIPZIG



Speakers & cluster profile

Speakers



Ulrike Köhl
Fraunhofer IZI
University of Leipzig



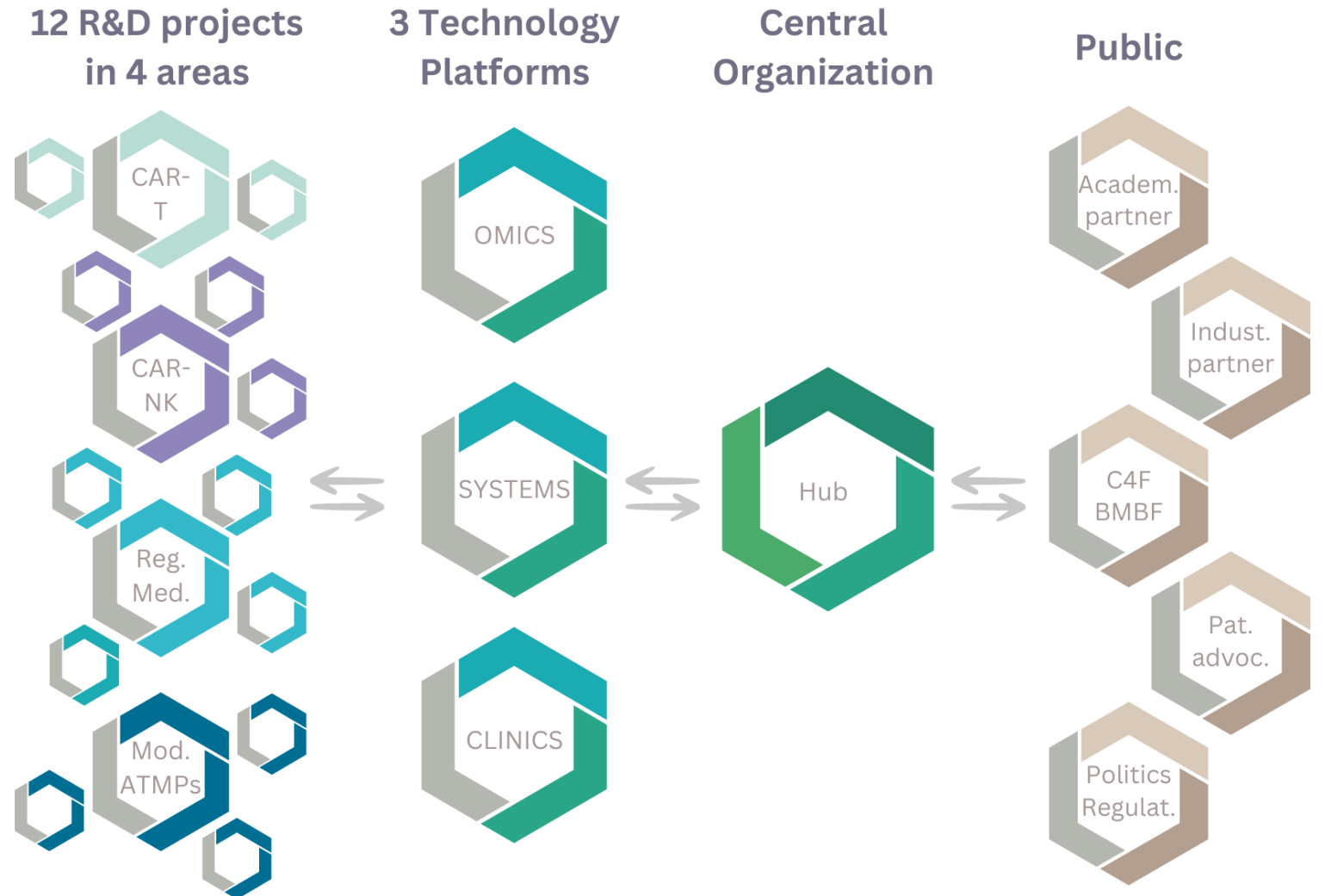
Ezio Bonifacio
CRTD
TU Dresden



Martin Bornhäuser
University Hospital
Dresden

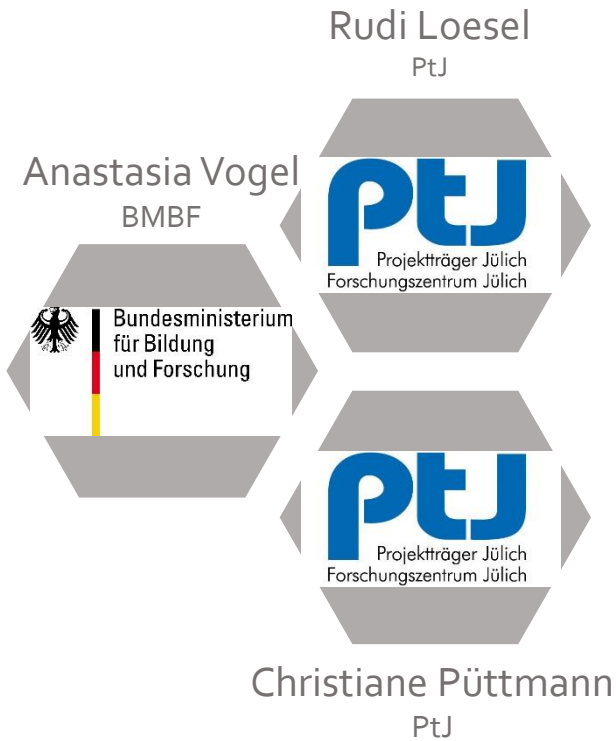


Uwe Platzbecker
University Hospital
Leipzig



Introduction of the attendees

Representatives of BMBF & PtJ



Anastasia Vogel
BMBF

Bundesministerium
für Bildung
und Forschung

Rudi Loesel
PtJ

PtJ
Projekträger Jülich
Forschungszentrum Jülich

Christiane Püttmann
PtJ

PtJ
Projekträger Jülich
Forschungszentrum Jülich

Keynote Speaker



Christopher Baum
BIH / Charité

Scientific Advisory Board

Lorenz Mayr
Mayr BioMedTech Consulting



Ute Modlich
Zurich University



Axel Schambach
Hanover Medical School



Gereon Mänzel
Patient advocacy



Soenke Brunswieck
7AlpsBio

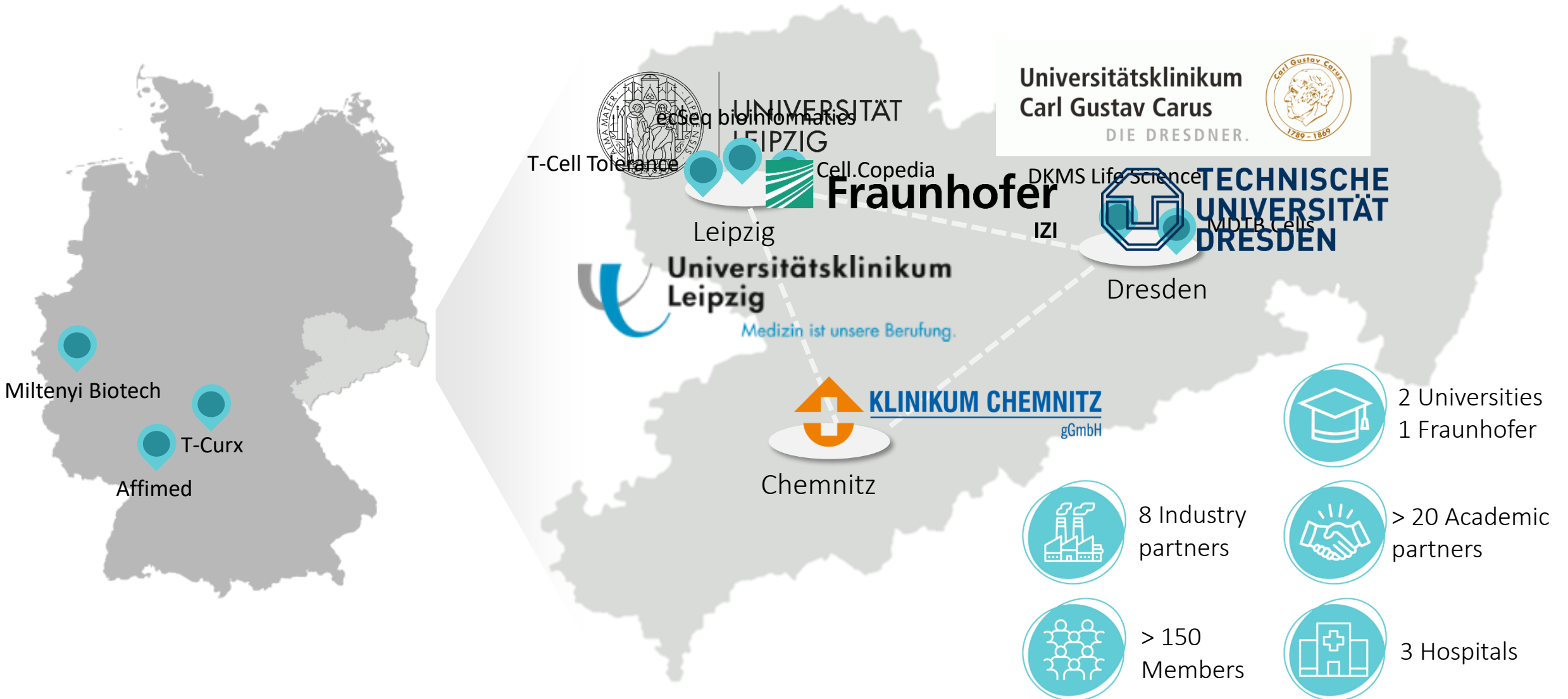


Nadine Winter
Patient advocacy

Achieving more together



Achieving more together

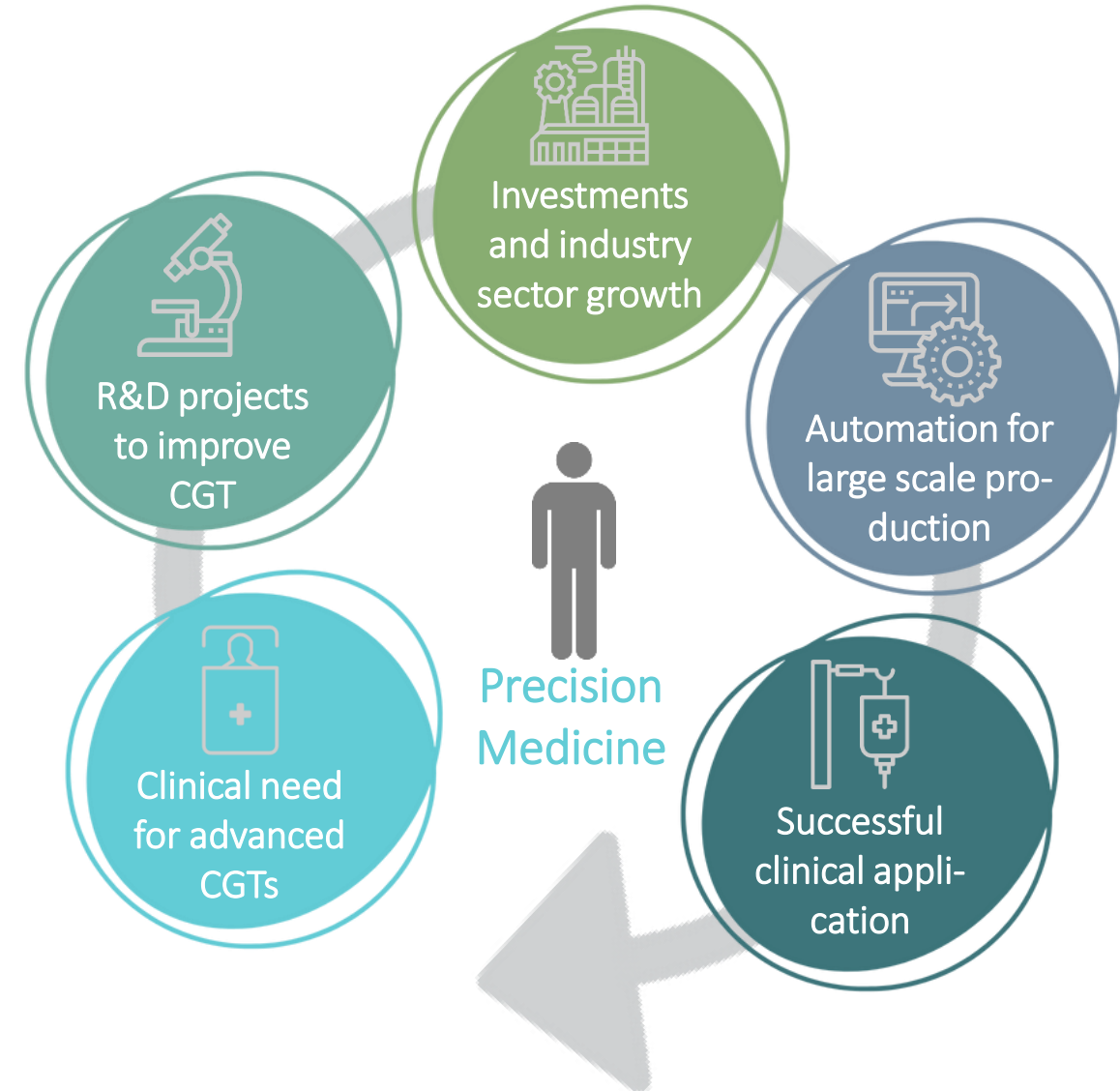


The vision of SaxoCell

Novel gene and cell therapeutics i.e. "living drugs"

- Cluster technologies developed with local company partners and represent incentive for investors and industrial partners

Saxonian **science** and **industry** for effective, affordable, safe **cell therapy to cure** and **prevent disease** globally



Long-term vision

5 year

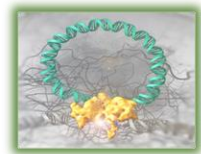
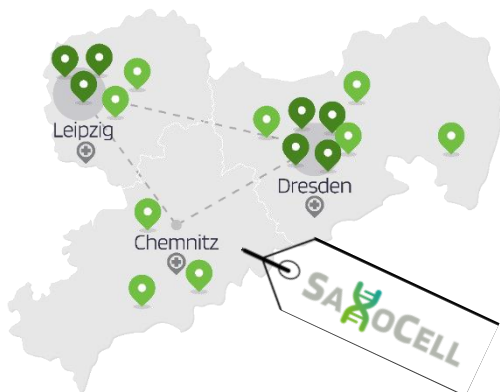
- Establishment of the brand name SaxoCell
- New jobs & a GMP training center
- Advanced processes for production and design of ATMPs and vectors

10 years

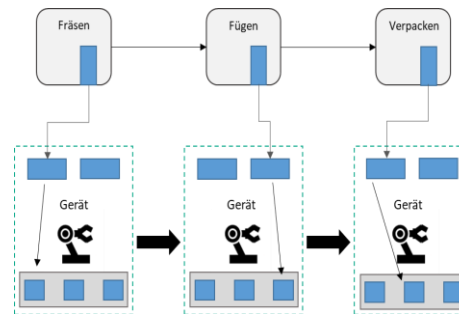
- Healing of various diseases
- Automated processes for in vivo & ex vivo therapies
- New spin-offs and settlements as well as worldwide visibility

20 years

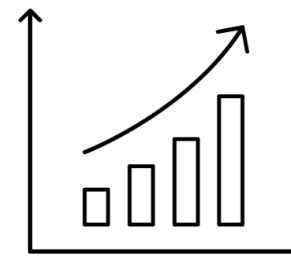
- Cost-effective healing of many diseases
- Universally applicable genome surgery & „off the shelf“ therapies
- SaxoCell as new leading industry in Saxony & EU – large investments



Designer-recombinases



Full automation



ATMP studies phase III/IV



Increased quality of life

What we did in the past year

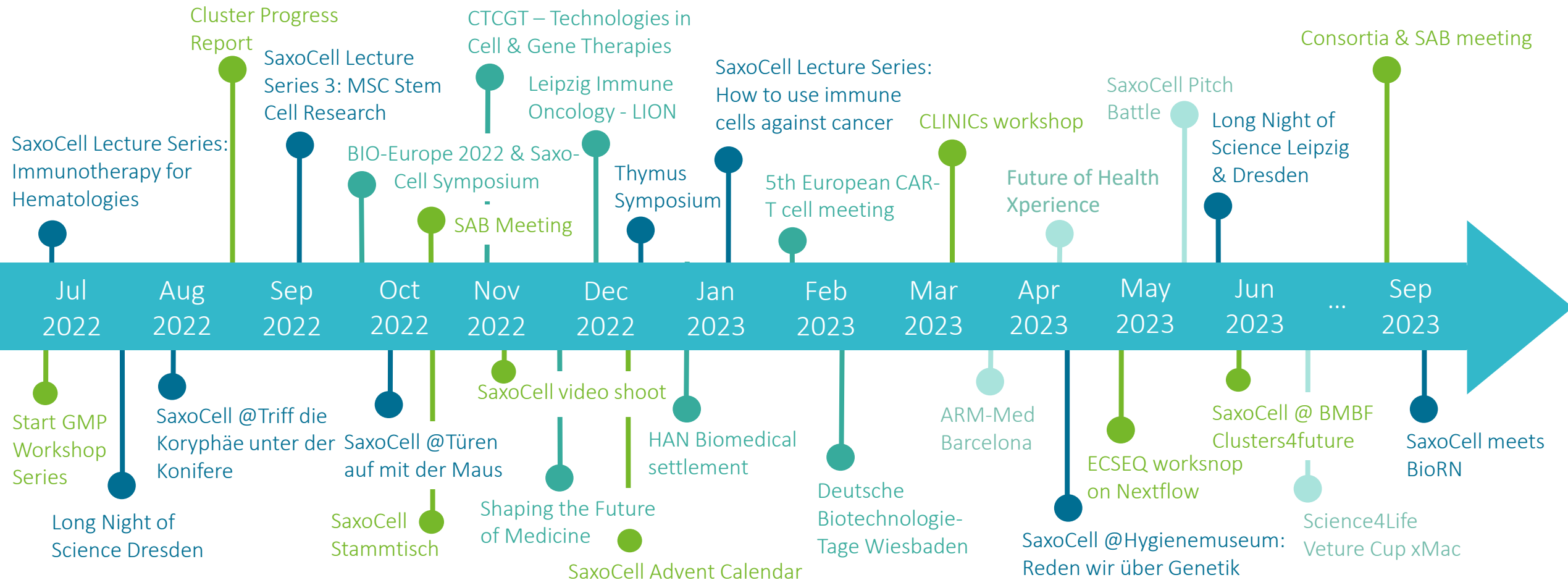


Transfer

Conferences

Public event

Cluster-internal



Some highlights from the past year



Transfer

Conferences / Meetings

Cluster-internal

Public event

Cluster
Progress Report

Immune
Oncology - LION

BIO-Europe 2022
& Saxo-Cell
Symposium

SAB
Meeting

HAN Biomedical
settlement

CLINICs workshop

SaxoCell Pitch
Battle

SaxoCell @ BMBF
Clusters4future

Science4Life
Venture Cup xMac

Consortia &
SAB meeting

Sep
2022

Oct
2022

Nov
2022

Dec
2022

Jan
2023

Feb
2023

Mar
2023

Apr
2023

May
2023

Jun
2023

Jul
2023

Aug
2023

Sep
2023

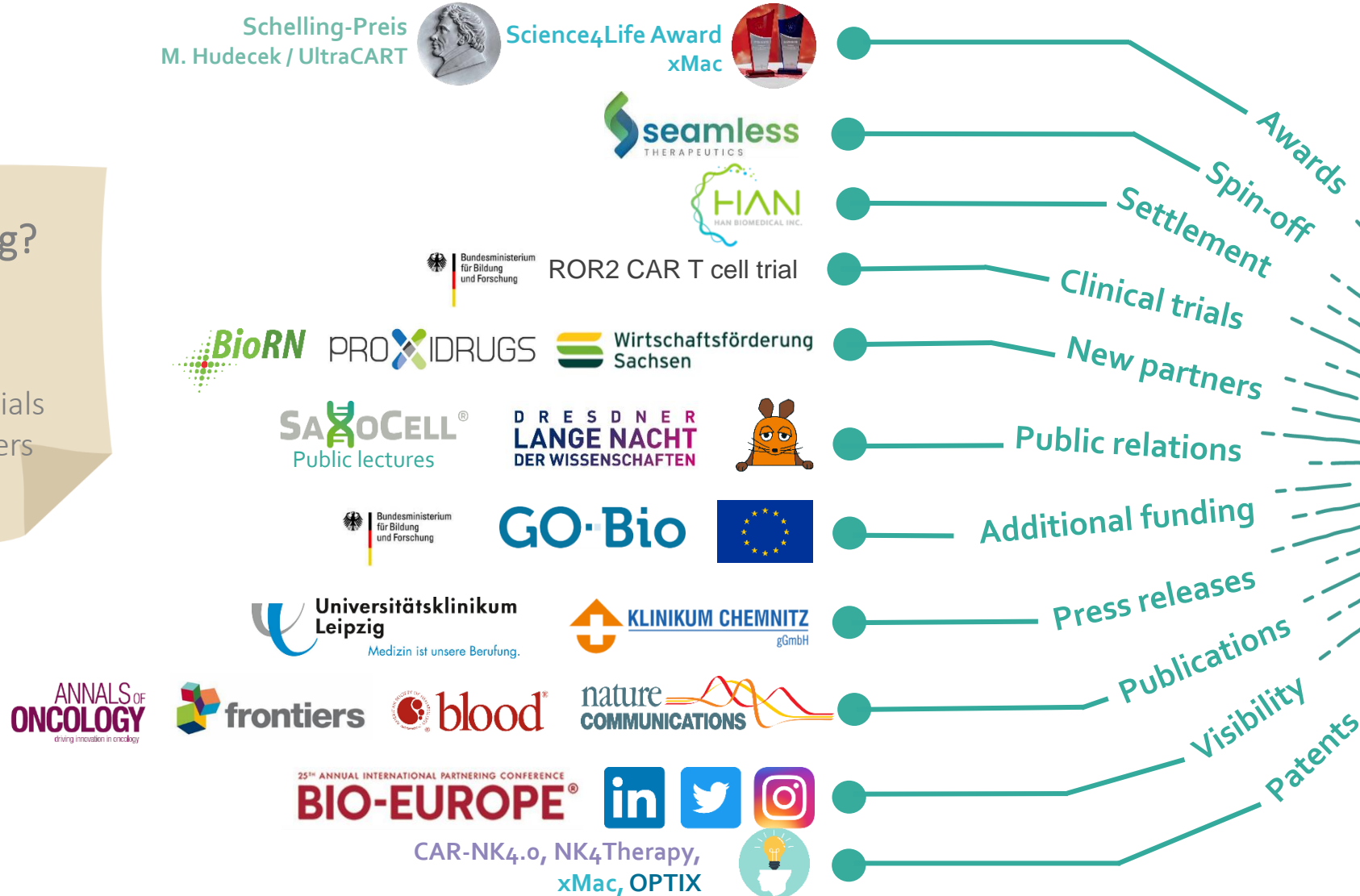
SaxoCell @Türen auf
mit der Maus

SaxoCell @Hygienemuseum:
Reden wir über Genetik

Measures of success in the 1st phase

What is missing?

- More funding
- More spin-offs
- More clinical trials
- Growing partners



Strength & challenges

CHALLENGES

Additional regulatory requirements

Funding & time of clinical trials

Spin-offs & settlement of industry

Patenting by
Scientists

STRENGTH

CGT expertise

Basic and applied research

Infrastructure

Established network: research, industry, service partners

Governmental Commitment

Saxony as nationwide beacon for CGT



Project pitches #1: 15 min + 10 min



Day 1: Monday 11.9.23

11:30-12:45

HemRec & spin-off Seamless Therapeutics GmbH

Frank Buchholz (TUD) & Anne-Kristin Heninger (Seamless Therapeutics GmbH)

frank.buchholz@tu-dresden.de; anne.heningerseamlesstx.com

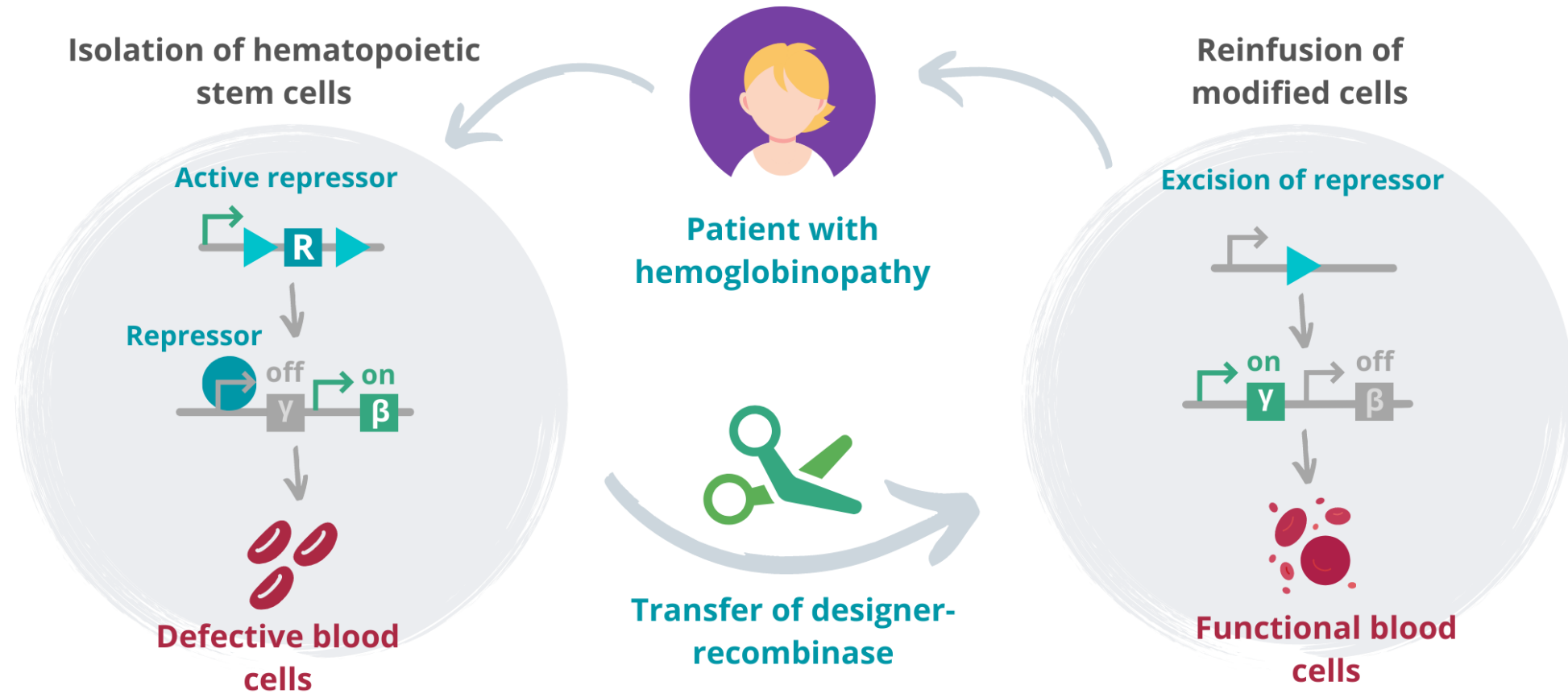
UltraCART

Michael Hudecek (IZI & UKW), Hudecek_M@ukw.de

xMac

Michael Sieweke (CRTD), Michael.Sieweke@tu-dresden.de

HemRec – Project Overview

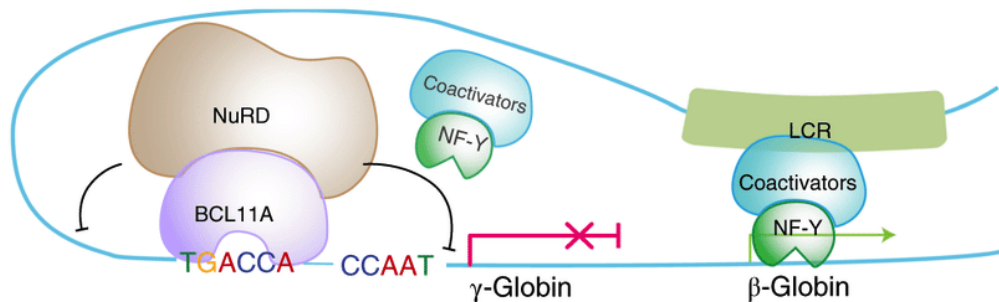


HemRec – Objectives

BCL11A (B cell lymphoma factor 11a)

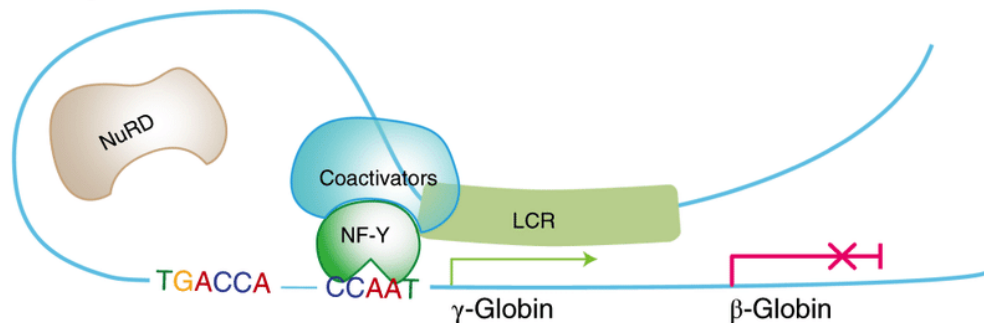
- Plays a major role in hemoglobin switching by repressing γ -globin expression

Adult stage erythroid cells

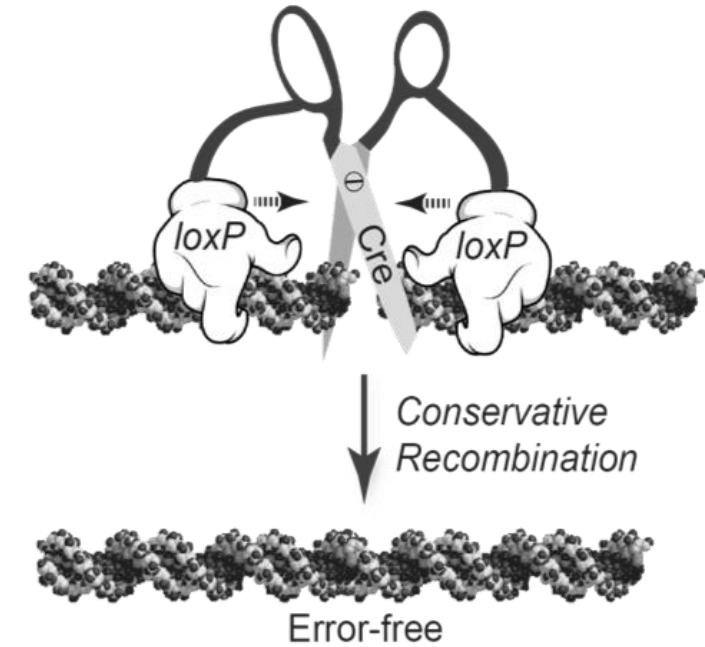


Erythroid cells:

Fetal stage, HPFH mutations or BCL11A LoF



Recombinase

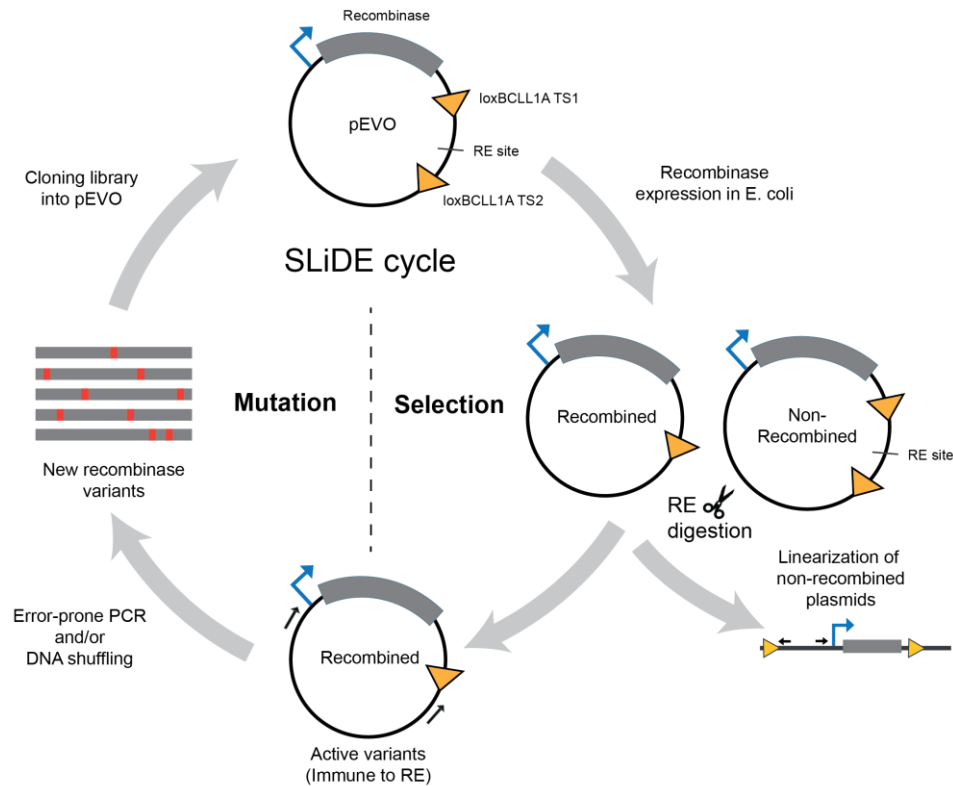
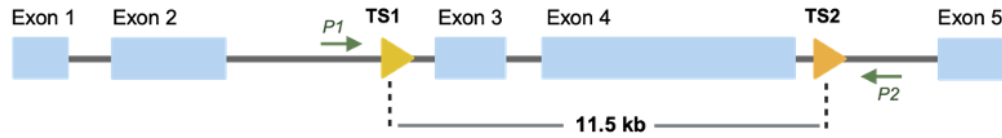


- 20+ years *in vivo* applications
- Precise
- Cut is directly repaired by the enzyme itself!
- Small in size

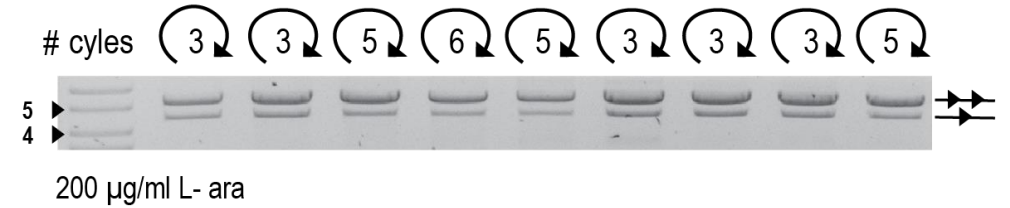
HemRec – Generation of a BCL11A recombinase



BCL11A gene
Chr. 2



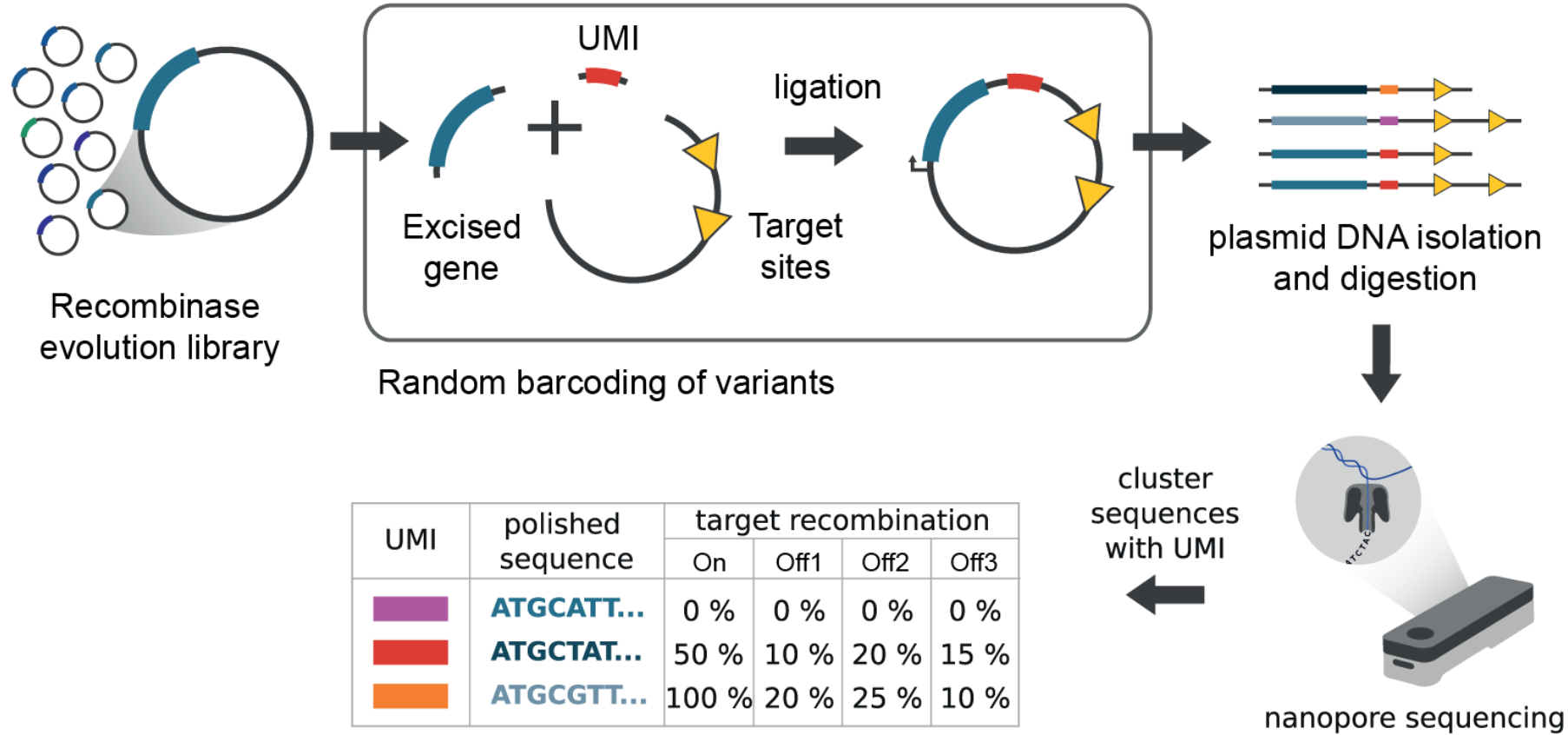
Subsites for evolution on TS1



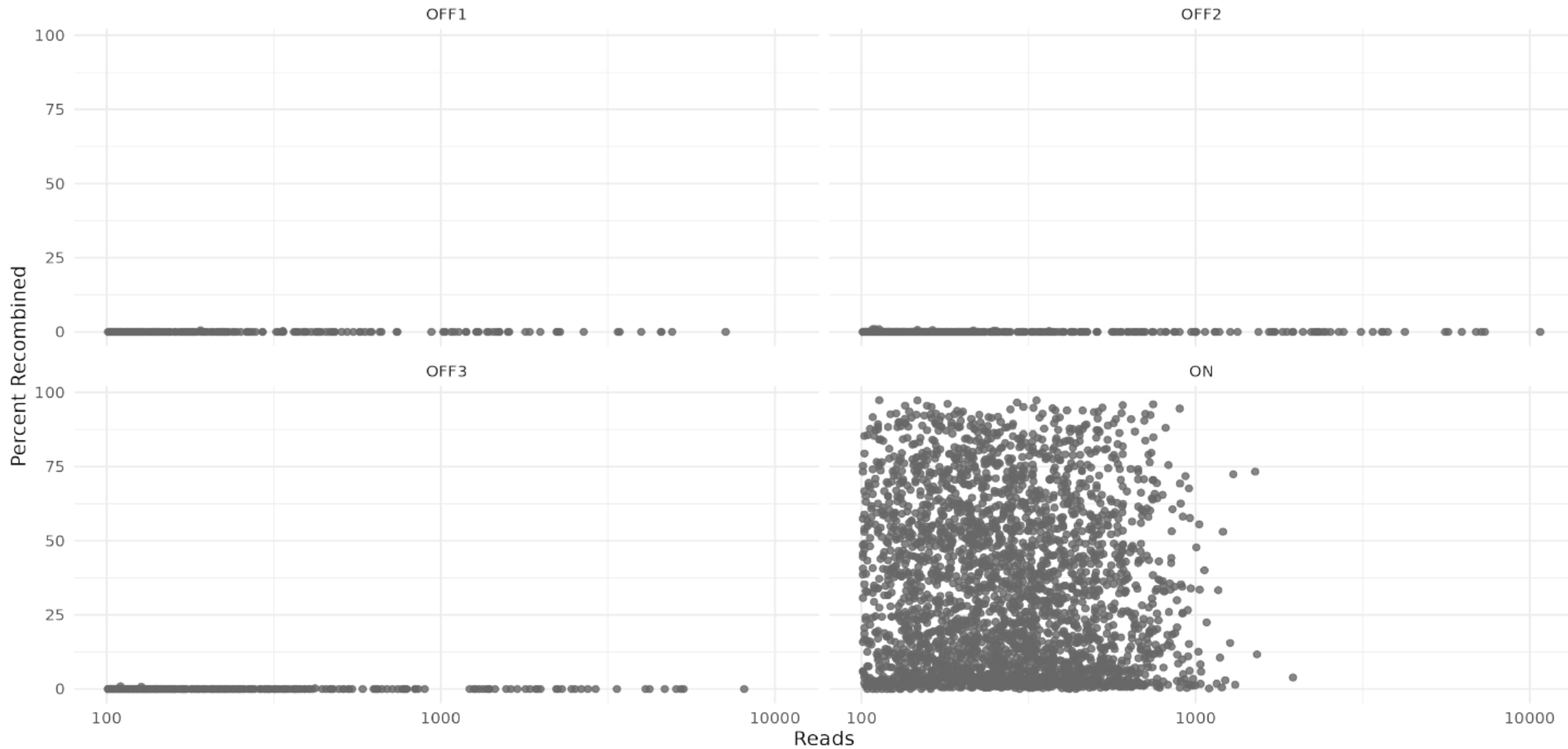
Subsites for evolution on TS2



HemRec – DEQSeq to identify favorable clones

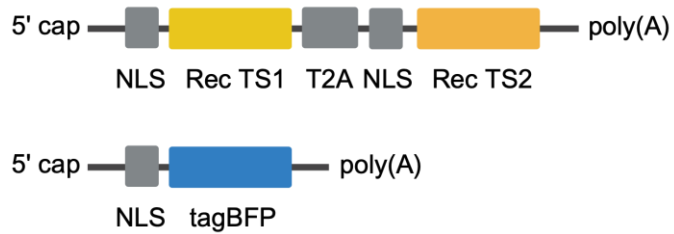


HemRec – DEQSeq to identify favorable clones

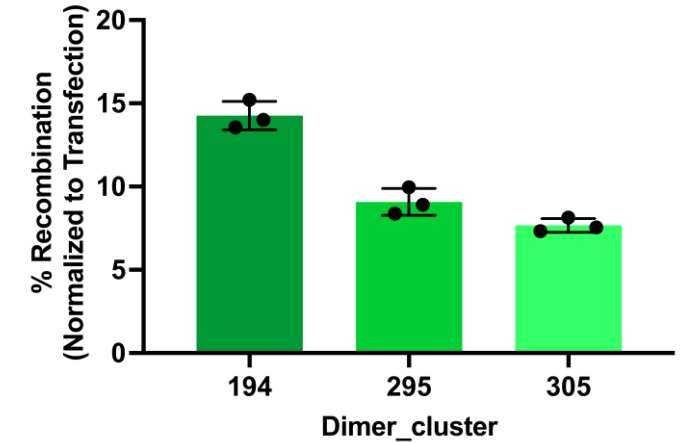
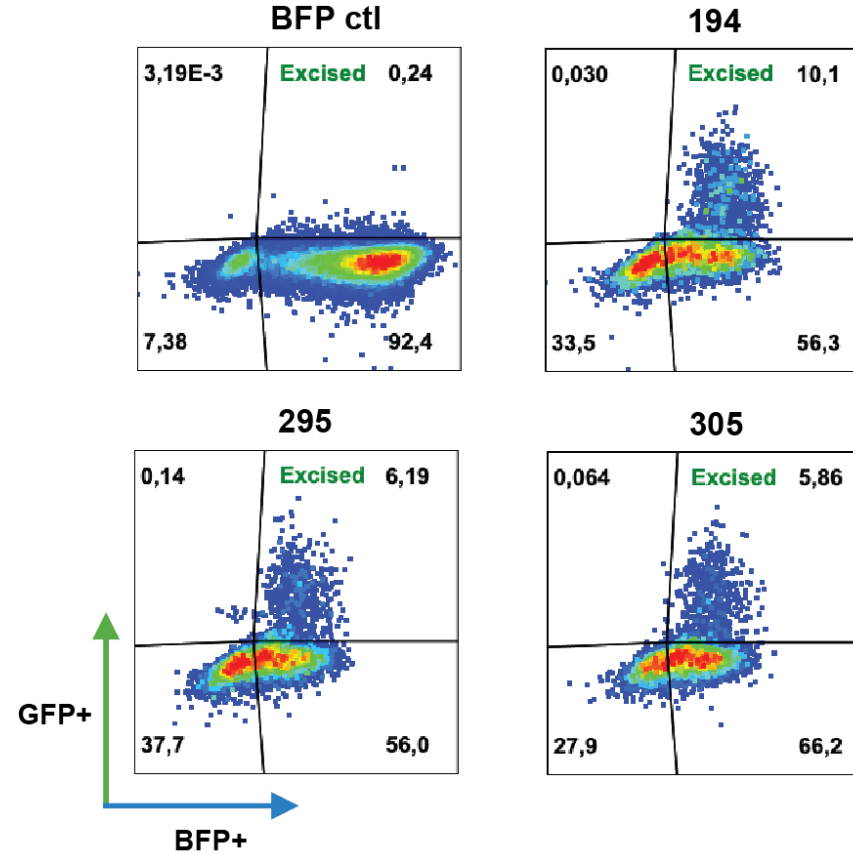
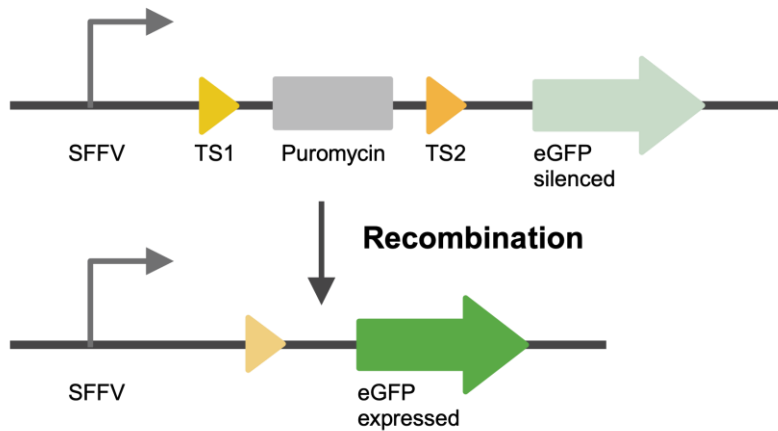


HemRec – RecBCL11A tests in human cells

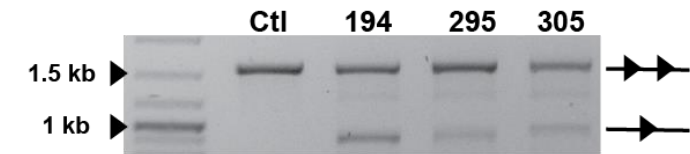
mRNA expression construct



Integrated reporter construct

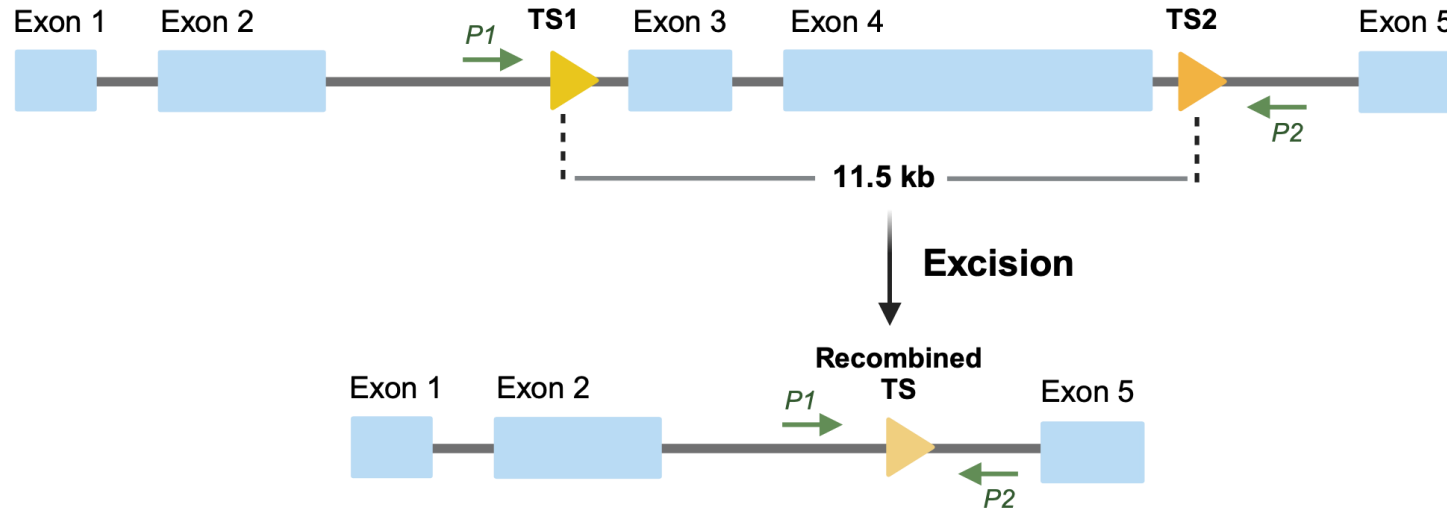


PCR on integrated reporter

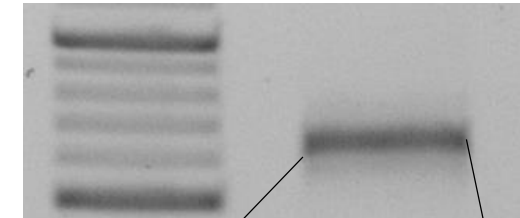


HemRec – RecBCL11A tests in human cells

BCL11A gene
Chr. 2



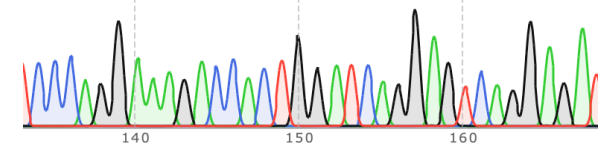
PCR on genomic DNA of mRNA transfected cells with primer pair P1+P2



Recombined TS

CCCAGGAAAGACCACTGGATCAGGAGTCAGGAGAT

CCCAGGAAAGACCACTGGATCAGGAGTCAGGAGAT



Confirmed deletion of endogenous BCL11A gene ←

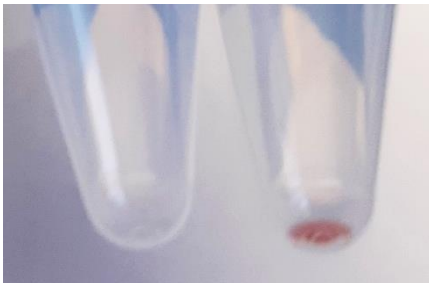
HemRec – Established in vitro assays



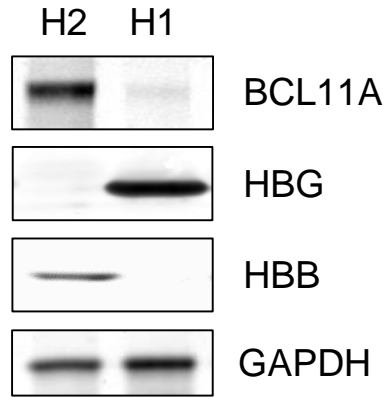
HUDEP cells

undifferentiated

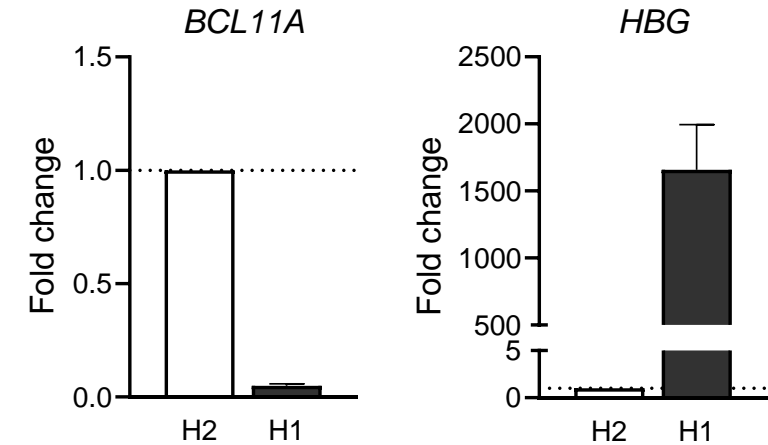
differentiated



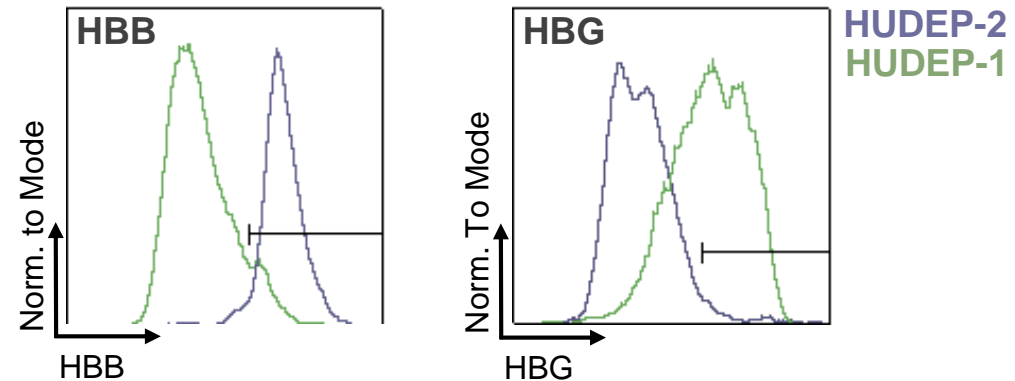
Western Blot



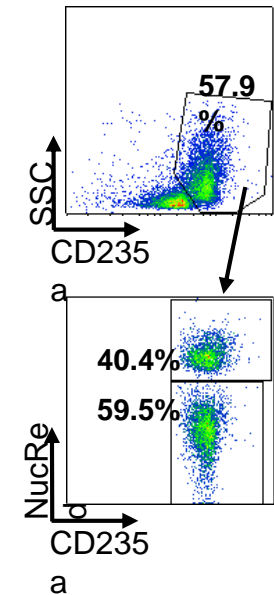
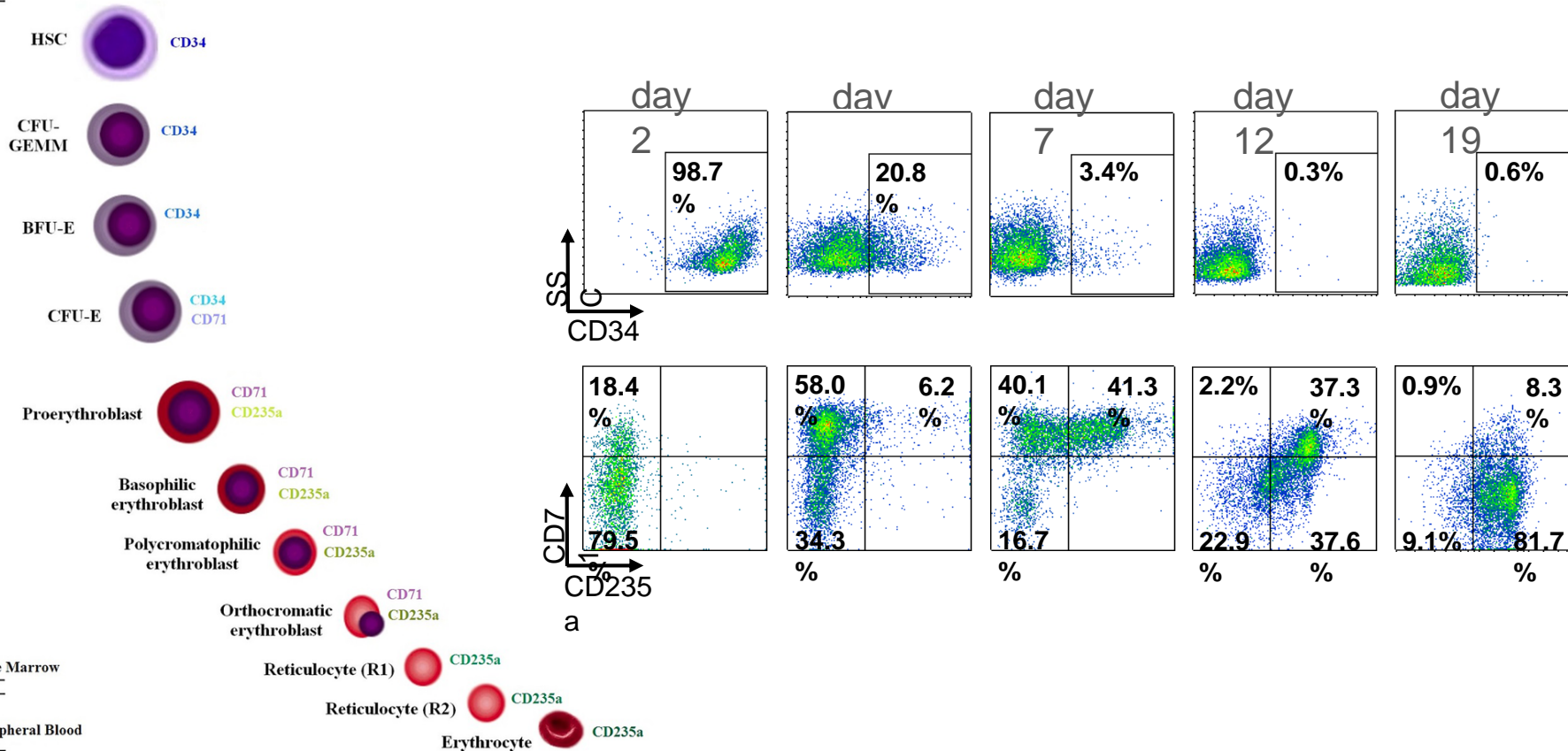
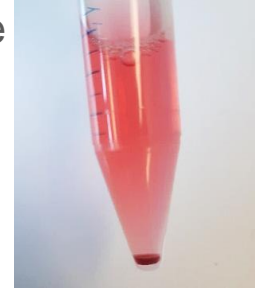
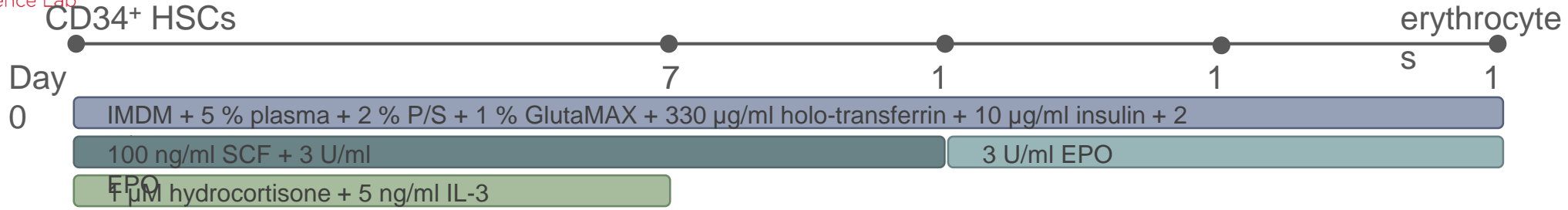
qPCR



Intracellular Hb staining



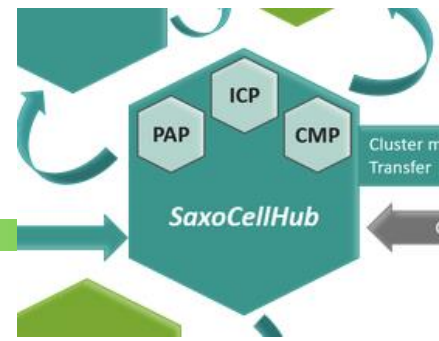
HemRec – Established in vitro assays



AREA 3 – ATMPS

- Optimizing final RecBCL11A recombinase
- In depth analysis of final RecBCL11A recombinase
- Application of RecBCL11A to established assays in human cells incl. HSCs
- Analysis of the BCL11A deletion in patient cells with support of DKMS
- Transplantation experiments in humanized mouse model with support of DKMS
- Preparation for first in human studies with support of DKMS

HemRec – Synergies



SAXOCELL®



DKMSx
Life Science Lab



DKMSx
Life Science Lab



DKMSx
Life Science Lab



seamless



AREA 3 – ATMIPS



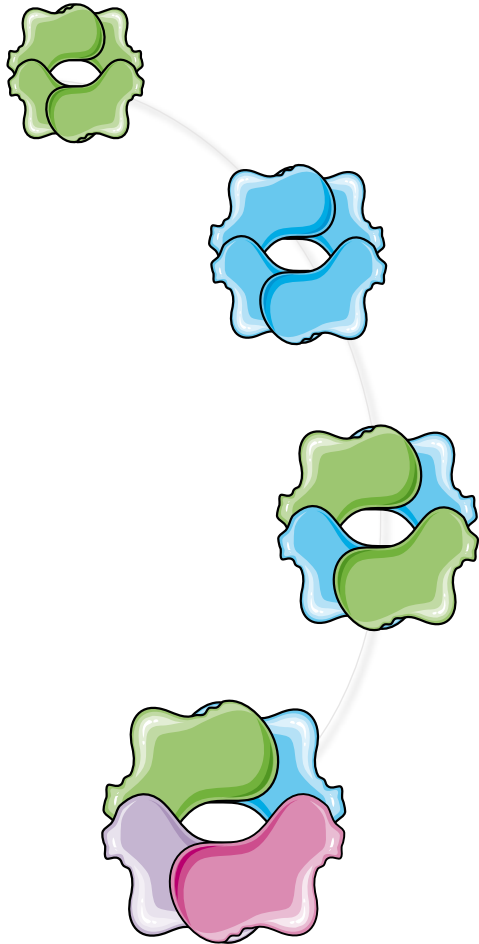
seamless

THERAPEUTICS

**Introducing
True Genome Tailoring**



Novel precision genetic medicines based on true genome tailoring



Pioneers in genome tailoring

Building on **recombinases**, a class of enzymes **widely used for decades** to precisely modify the genome of mice and other animal models

Four proprietary genome tailoring platforms covering excision, inversion, exchange and insertion of DNA fragments

Strong and broad IP portfolio

Raised \$24m Seed led by top-tier VCs

Founded in 2022 in Dresden and grown to 18 FTE Q3/2023

Forbion.

wellingtonpartners



Open to collaboration opportunities



We know the underlying genetic cause for many diseases, but we did not have the right tools to correct them

Broadening the scope of genome editing to tackle severe diseases

Rare orphan genetic disorders

editas
MEDICINE

Intellia
THERAPEUTICS

CRISPR
THERAPEUTICS

Beam
THERAPEUTICS

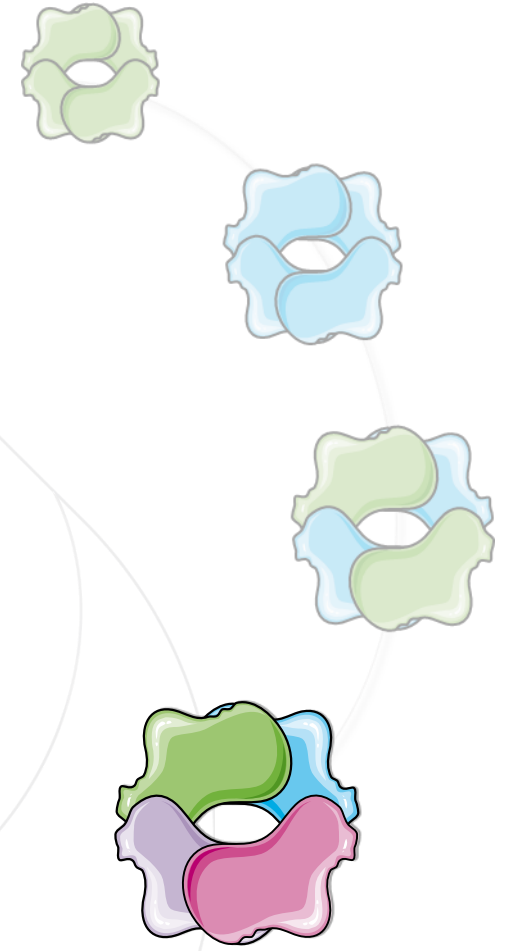
prime
medicine

seamless
THERAPEUTICS



Seamless Tx is uniquely positioned to address current limitations in gene editing

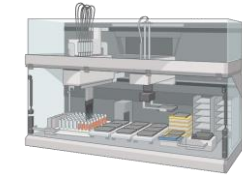
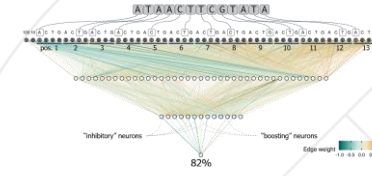
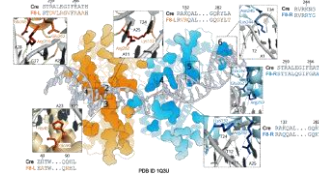
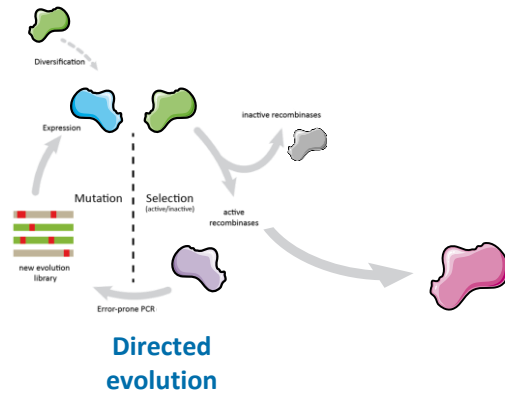
	Nuclease Competitors	Natural Recombinase	Genome Tailoring
Precision Predictable gene modification outcome	✗	✓	✓
Efficiency and breadth Independent of cellular processes	✗	✓	✓
Versatility Modification of small and large DNA fragments	✓	✓	✓
Programmability Quick adaptation to other targets	✓	✗	✓
Delivery One component, small in size	✓	✓	✓
Usability Clear IP situation	✗	✗	✓





Seed phase – platform and pipeline expansion

Platform and innovation



- Directed molecular evolution is at the core of our platform to train recombinases to novel target sequences
- Continuous improvement of technology platform to greatly accelerate the development of site-specific recombinases
- Increase throughput and speed of the discovery engine
- Identify delivery partners to develop recombinase-based therapeutics

Pipeline

- Building internal and partnered company pipeline



Seamless Tx building a high value pipeline of disease-modifying assets



Insertion

Gene Body insertions

Cystic Fibrosis

Safe harbor insertions

T-cell engineering
HSC engineering
Enzyme replacement



Exchange

Correction

Alpha1 antitrypsin deficiency
Rett syndrome
Cardiomyopathies
Cardiac arrhythmias
Early Onset Parkinson
Glycogen storage disease
Retinitis pigmentosa
Hearing loss



Inversion

Large inversions

Hemophilia A
Hunter's Syndrome



Excision

Expansion repeat disorders

Myotonic Dystrophy type 1
Spinocerebellar ataxias

Large duplications

Charcot Marie Tooth 1

Exon skipping

Duchenne's Muscular Distrophy

Viral insertions

HBV
HPV

in vivo knock outs

PCSK9
Sickle cell disease



Experienced team in gene editing backed by top tier VC

Executive Management



Dr. Anne-K. Heninger
Co-founder and acting CEO



Dr. Felix Lansing
Co-founder and CSO



Dr. Arturo Urrios
Head of Business Development



Anne Burger
CFO

Platform Development Leadership



Dr. Teresa Rojo Romanos
Co-founder and
Director of R&D



Dr. Martin Schneider
Director of Protein evolution



Dr. Maciej Paszkowski-Rogacz
Co-founder and
Director Bioinformatic

Board members & Advisors



Dr. Karl Nögler
Board Director
wellingtonpartners



Dr. Dmitrij Hristodorov
Board Director
Forbion.



Prof. Dr. Frank Buchholz
Scientific co-founder



seamless

THERAPEUTICS

Dr. Anne-Kristin Heninger, Acting CEO

anne.heninger@seamlesstx.com

Dr. Felix Lansing, CSO

felix.lansing@seamlesstx.com

Dr. Arturo Urrios, Head of BD

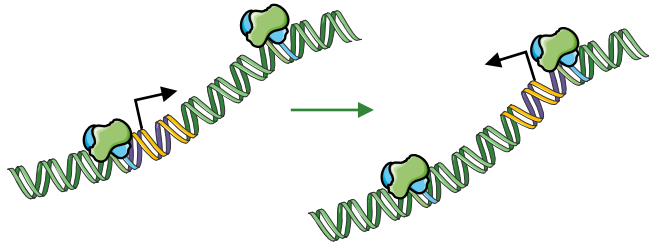
arturo.urrrios@seamlesstx.com



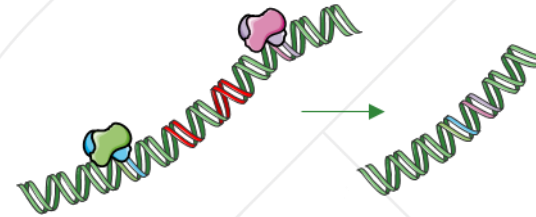
Seamless Tx's modular platform opens a new approach to target diseases



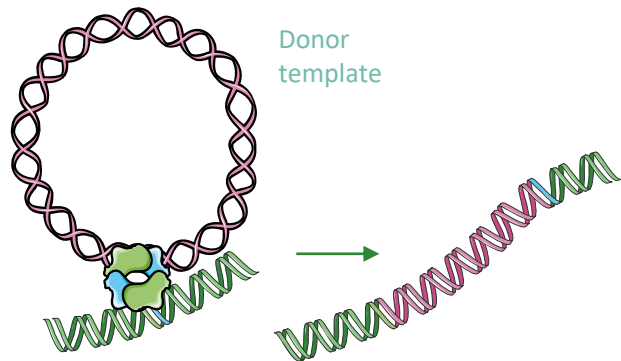
Inversion



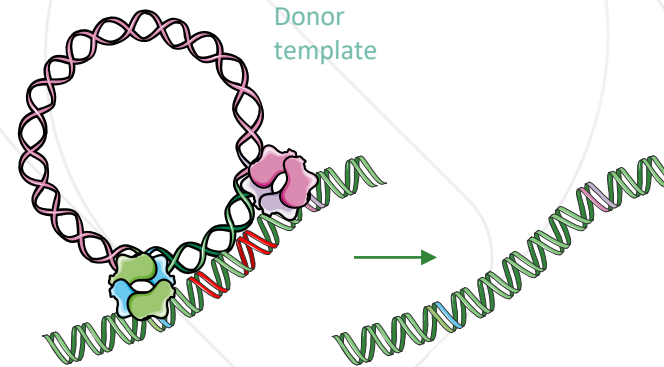
Excision



Insertion



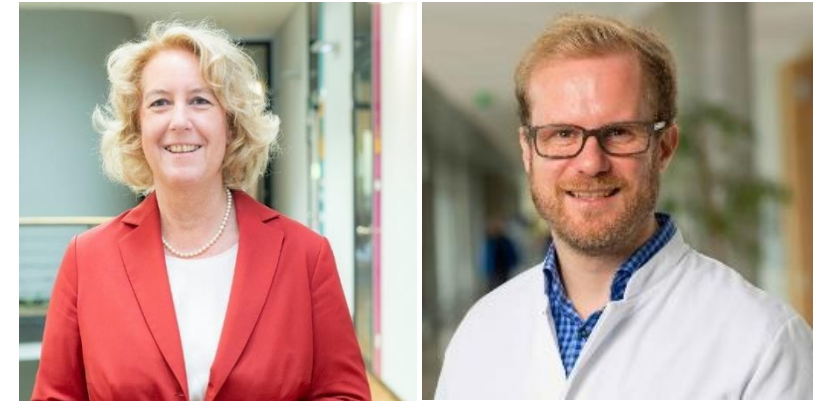
Exchange



Cancer Immunotherapy With Next-Generation CAR-T Cells

PIs

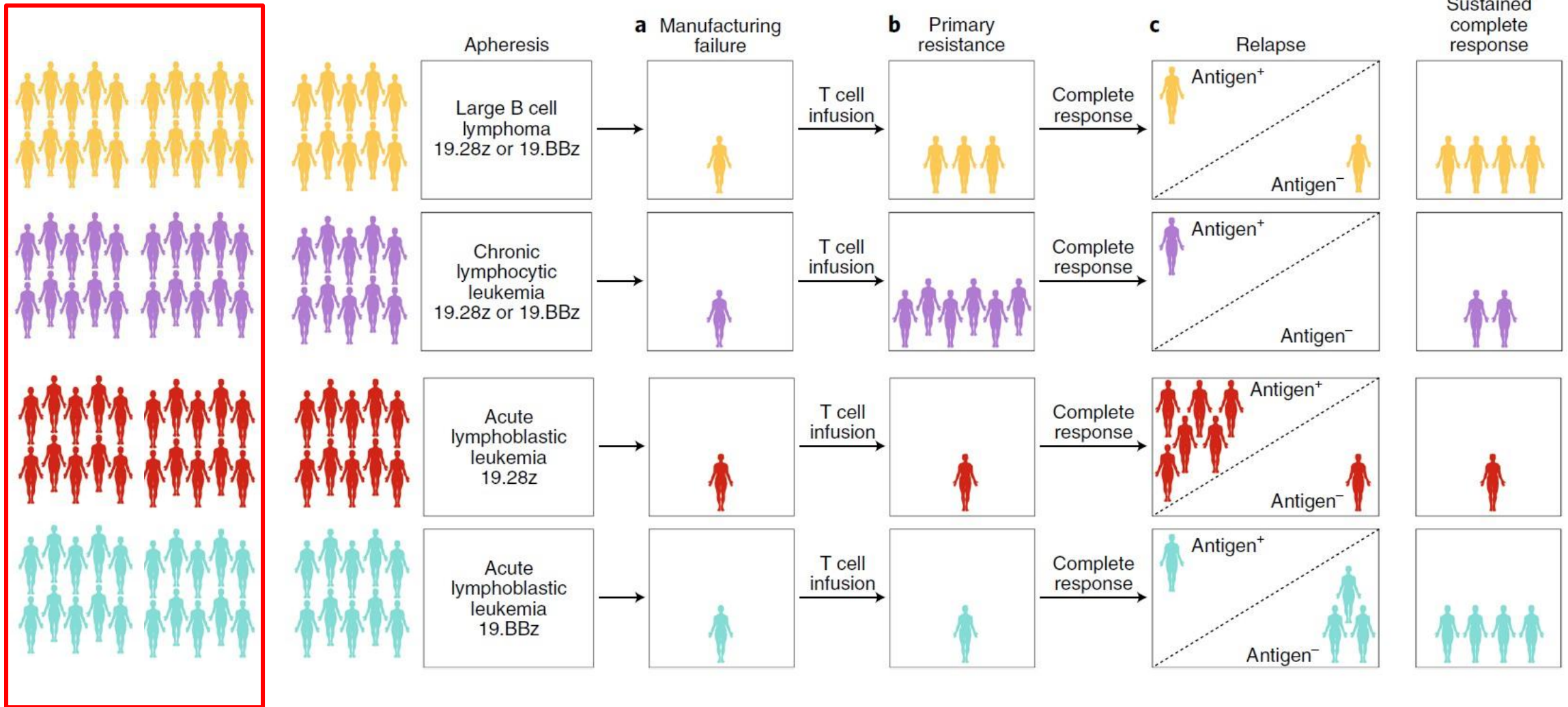
- Prof. Dr. Michael Hudecek, Fraunhofer IZI & Uniklinik Würzburg
- Prof. Dr. Dr. Ulrike Köhl, Fraunhofer IZI & Uniklinik Leipzig
- Dr. Sabrina Prommersberger, T-CURX GmbH, Würzburg
- Dr. Jan van den Brulle, T-CURX GmbH, Würzburg



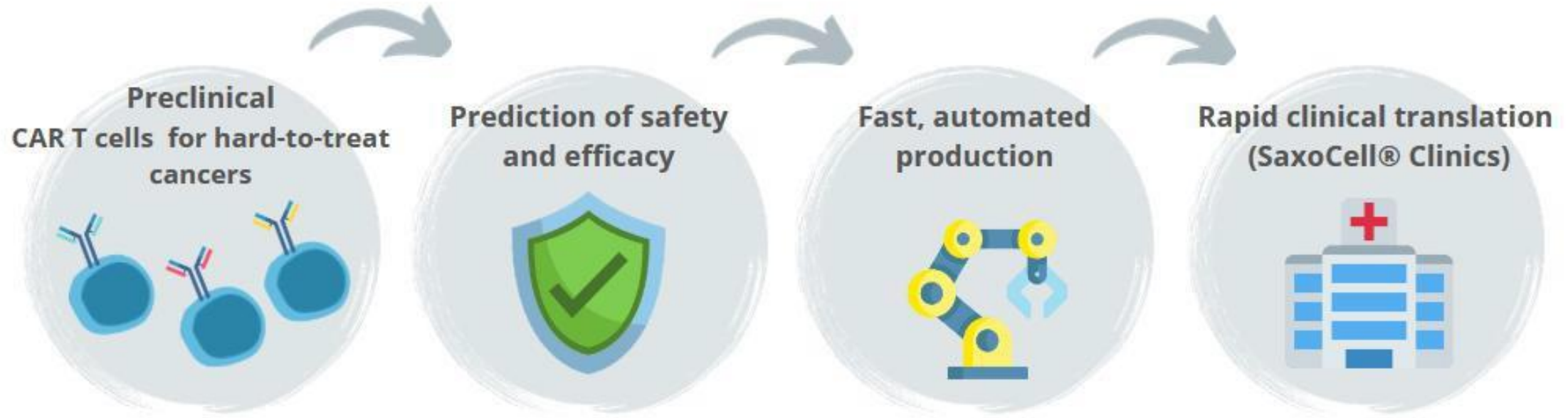
Major Pharma with marketed CAR-T



Outcome in B-cell leukemia/lymphoma



UltraCART – Objectives

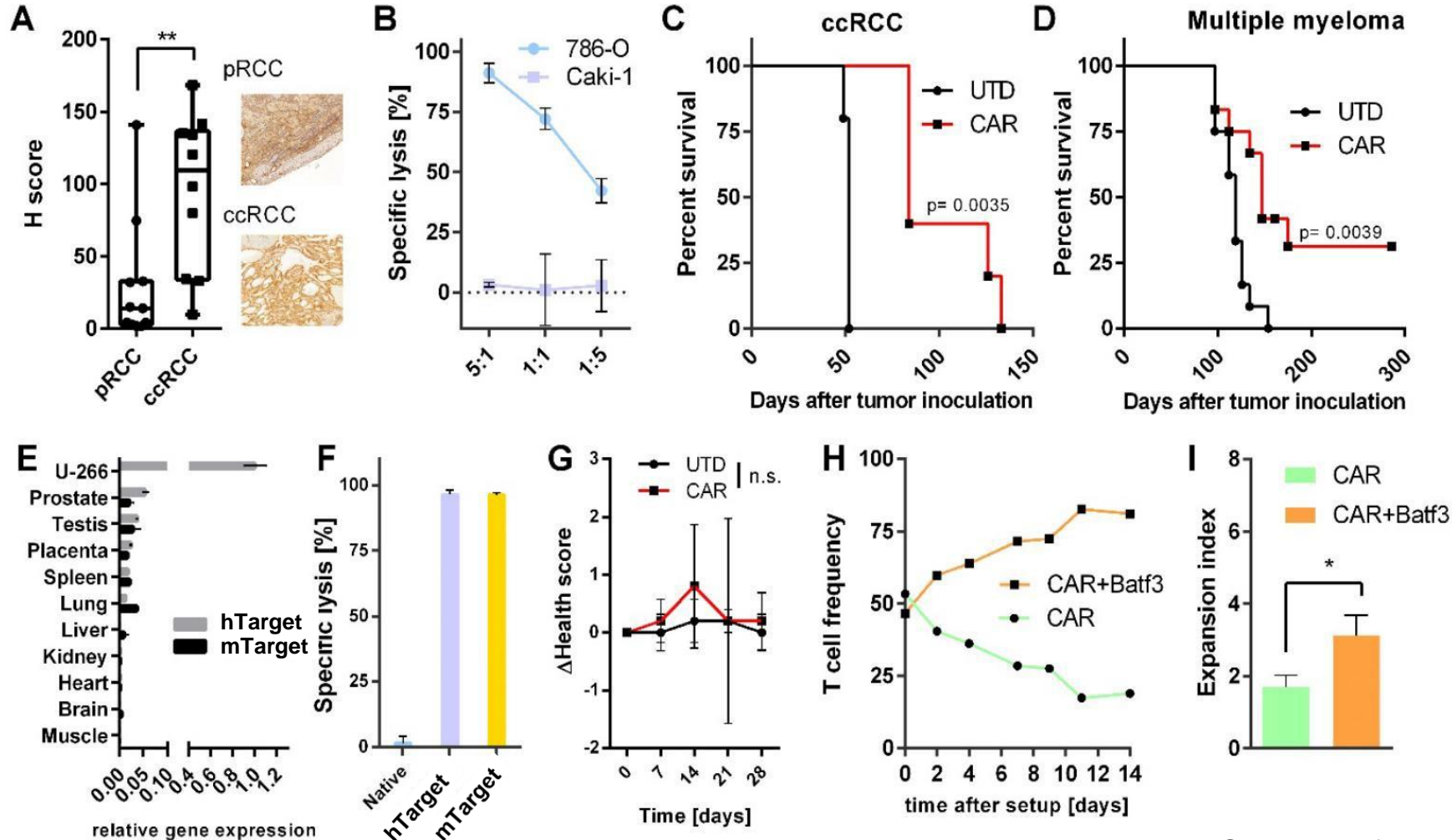


Deliver High-End CAR-T Products for Clinical Trials within SaxoCell

UltraCART – Results

WP 1: New Targets and CAR-T Products

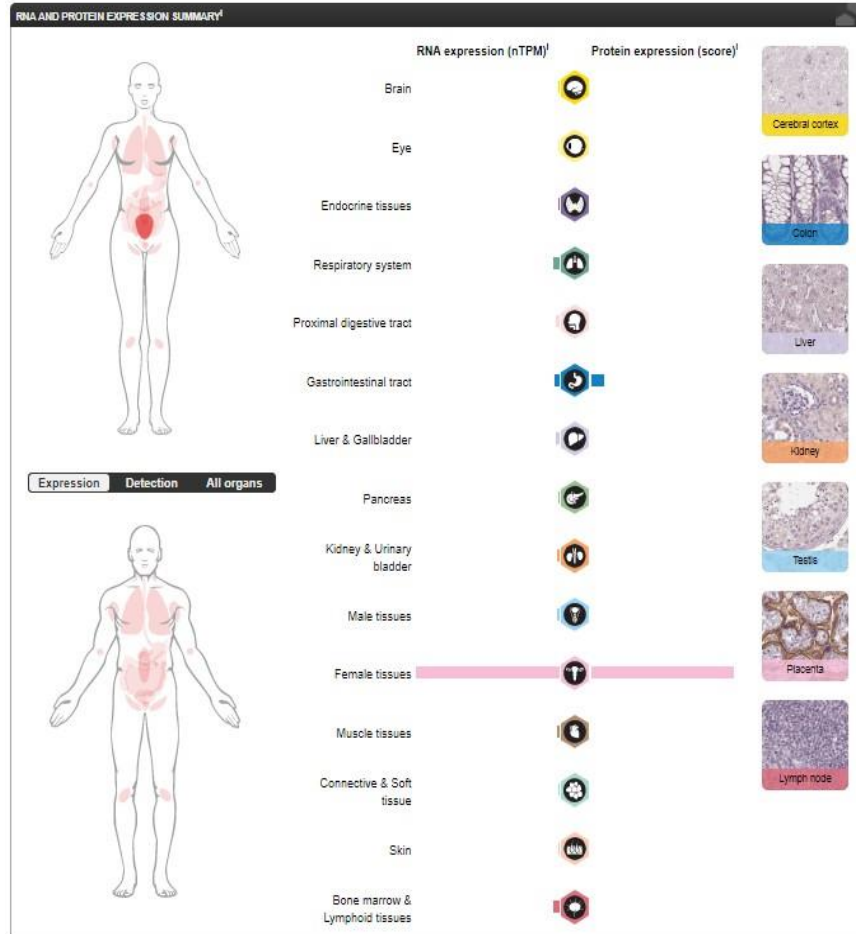
ROR2 – Oncofetal Antigen, Cross-Entity CAR Target in Hematology & Oncology



UltraCART – Results

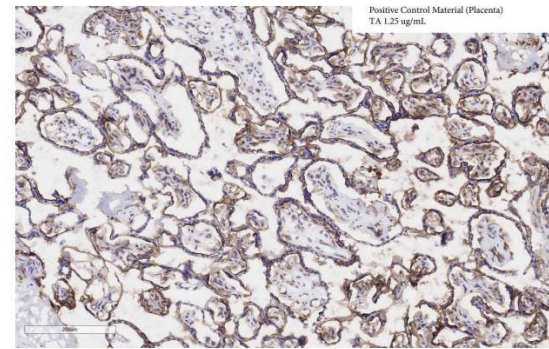
WP 1: New Targets and CAR-T Products

Undisclosed Target in Hematologic Malignancies, incl. AML

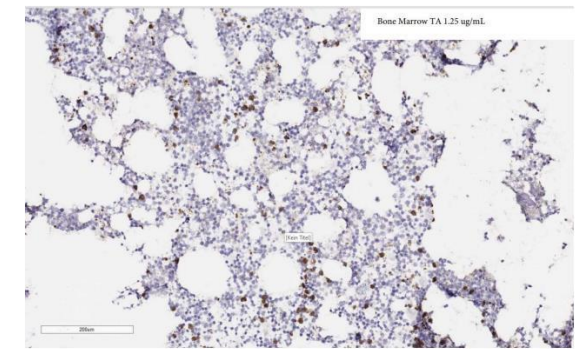


WP 2: New Models for Predicting Safety & Efficacy

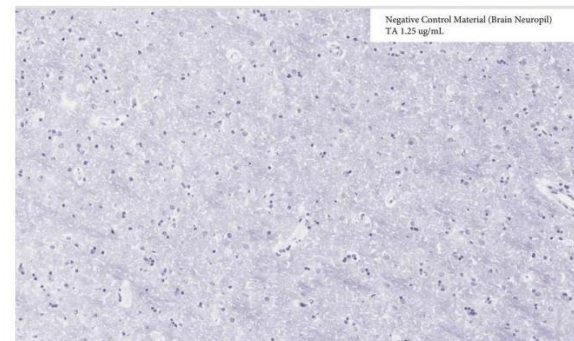
Tissue-Cross Reactivity Study to Assess Expression in Healthy Tissues



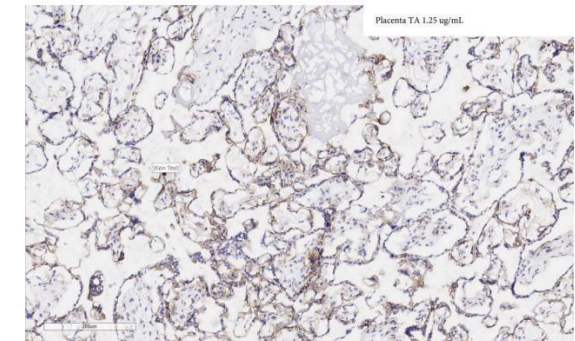
Placenta



Bone marrow



Neuropil

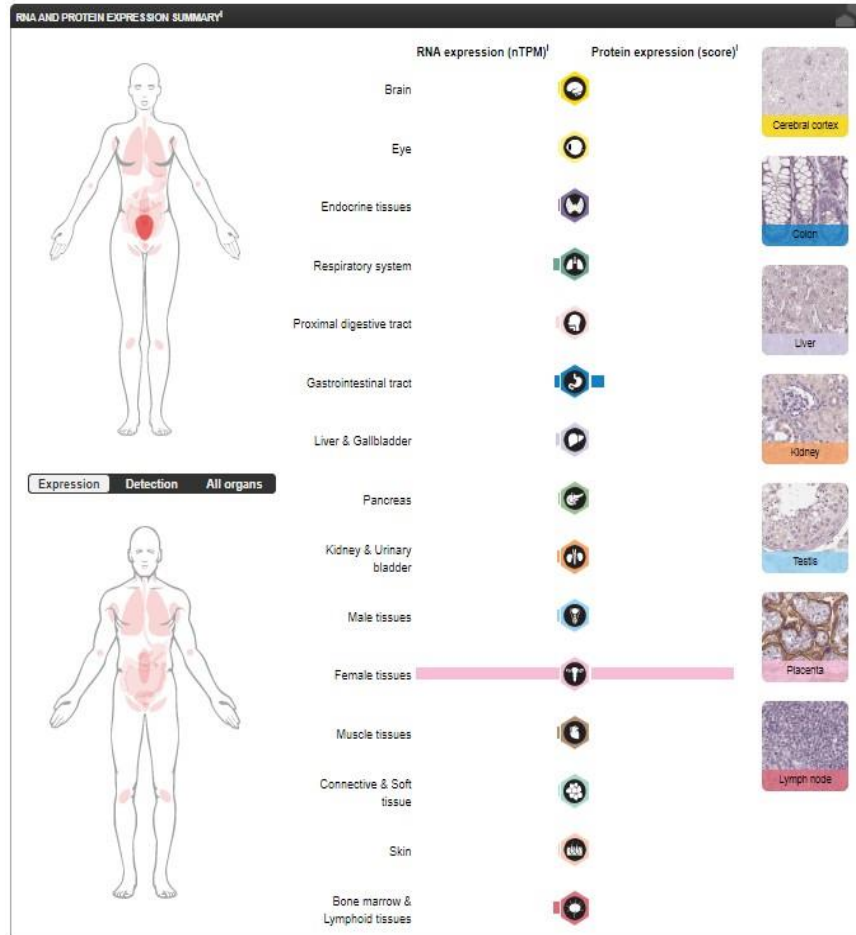


Placenta

UltraCART – Results

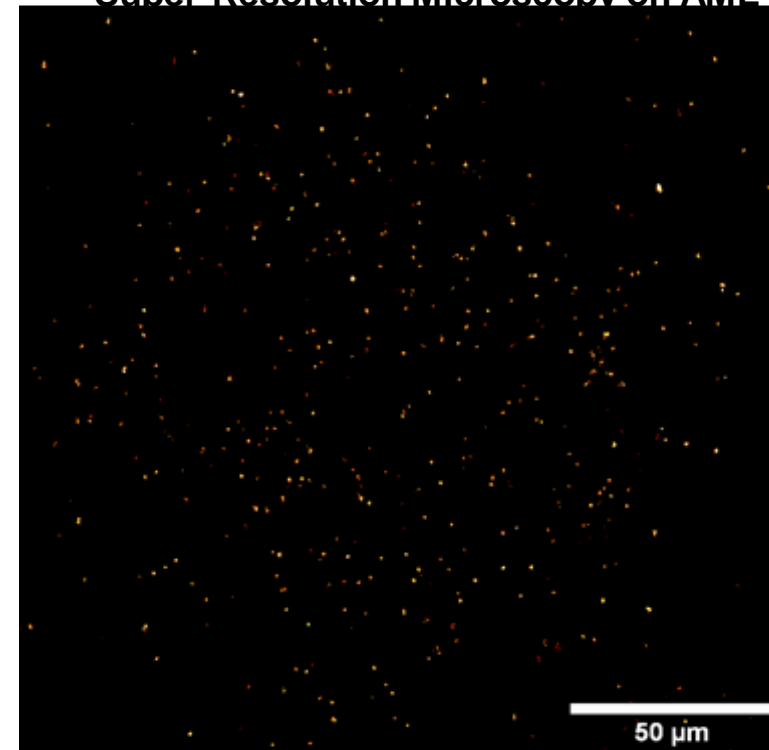
WP 1: New Targets and CAR-T Products

Undisclosed Target in Hematologic Malignancies, incl. AML



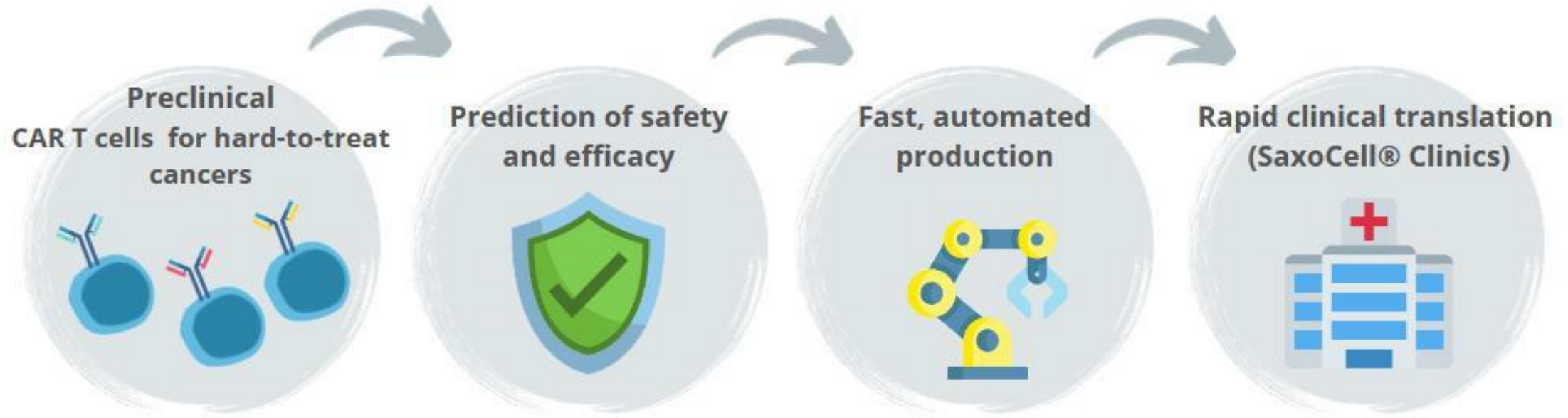
WP 2: New Models for Predicting Safety & Efficacy WP 4: High-Resolution Microscopy

Super-Resolution Microscopy on AML



AREA 1 – CAR-T

UltraCART – Objectives

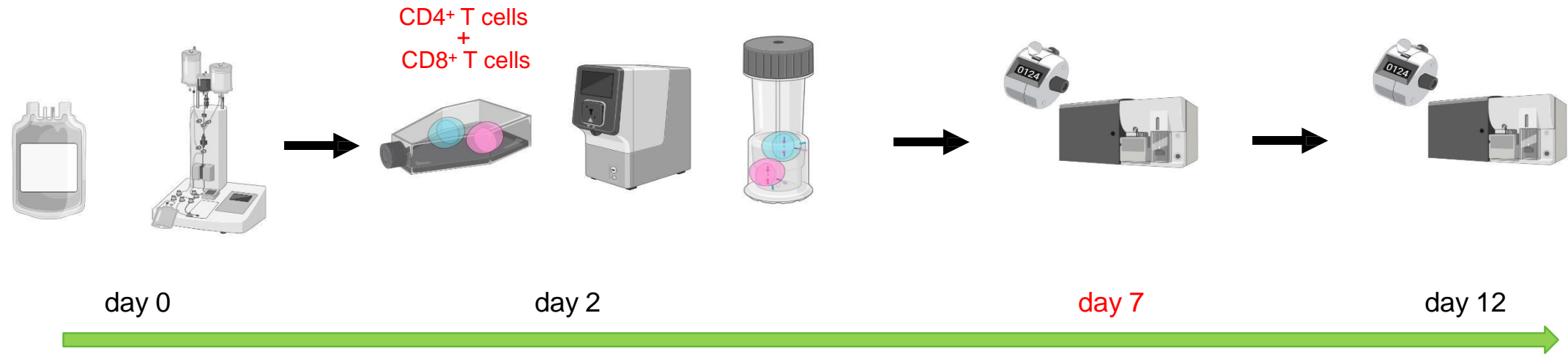


Deliver High-End CAR-T Products for Clinical Trials within SaxoCell

UltraCART – Results

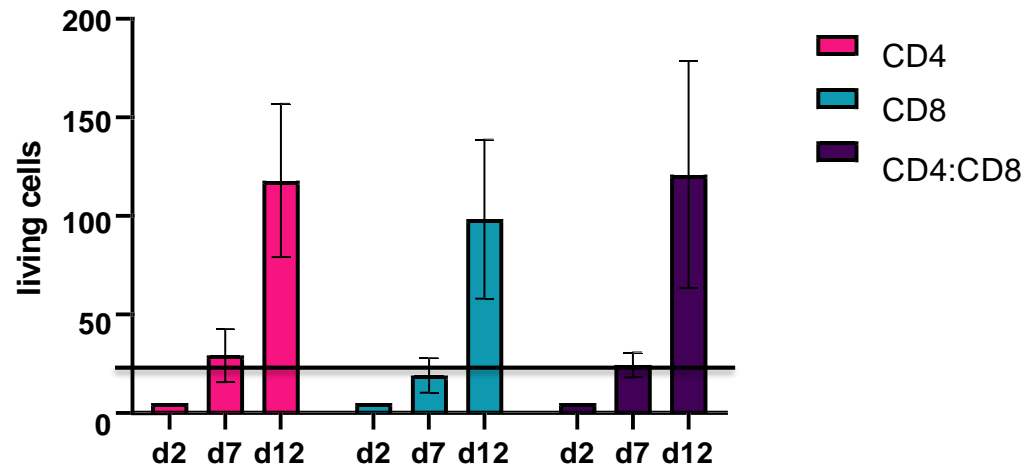
WP 3: Short Manufacturing and Automation

Starting Point: 12-day Manufacturing Process est'd in PoC Project, Virus-Free Transposon Gene Transfer

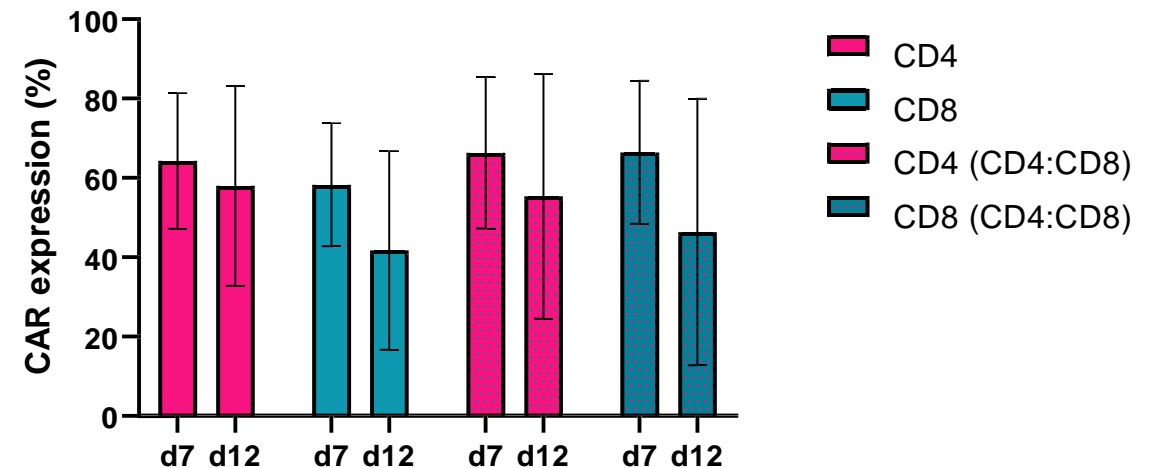


UltraCART – Results so far

WP 3: Short Manufacturing and Automation



Summary CAR-T Yield (n=3)



Clinical dose:

$2 \times 10^6 / \text{kg} \rightarrow 200 \times 10^6$ to treat a 100 kg patient

↓ *CAR T cells with greater fitness, expand in vivo*

$2 \times 10^5 / \text{kg} \rightarrow 20 \times 10^6$ to treat a 100 kg patient

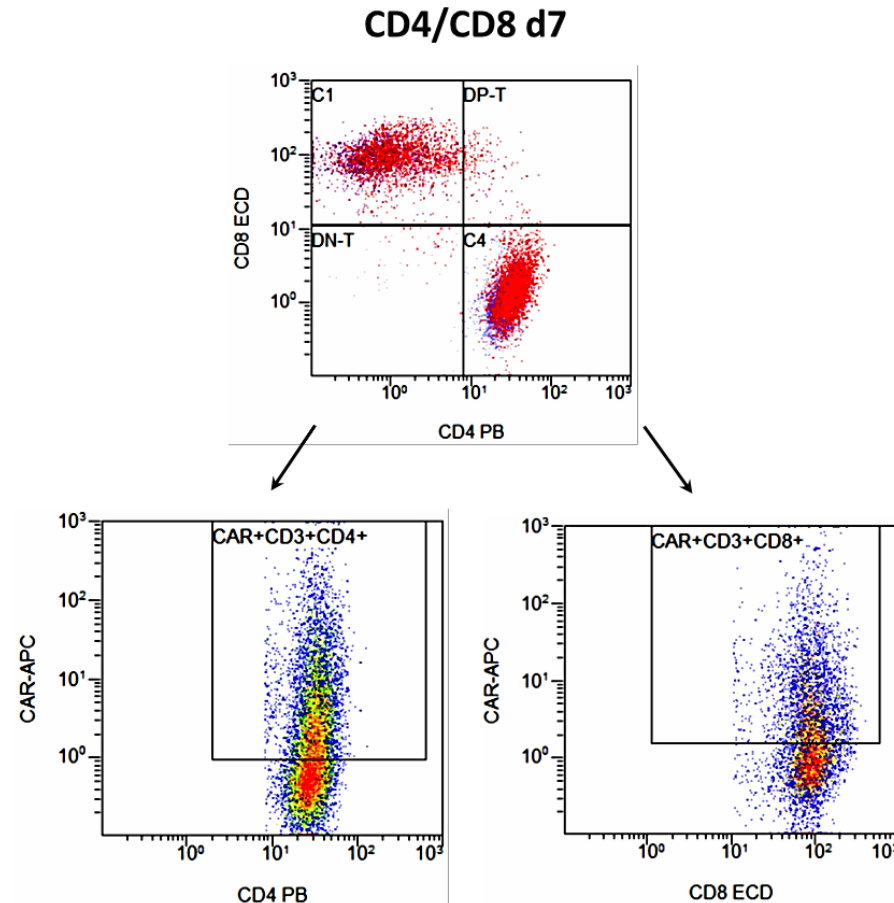
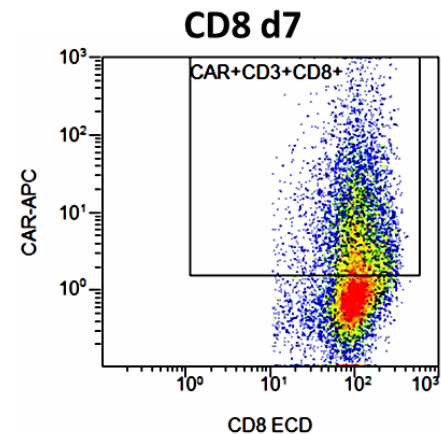
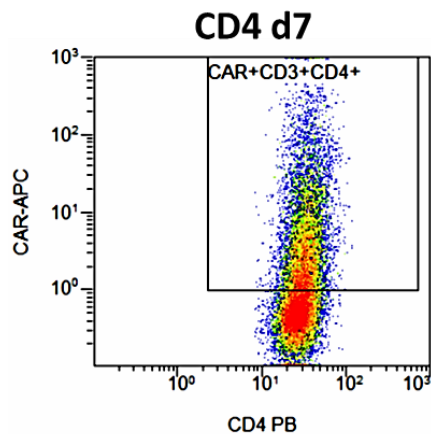
Higher yield easily achievable through scaling effect
(Seed not 1 but multiple G-Rex devices)

UltraCART – Results

WP 3: Short Manufacturing and Automation

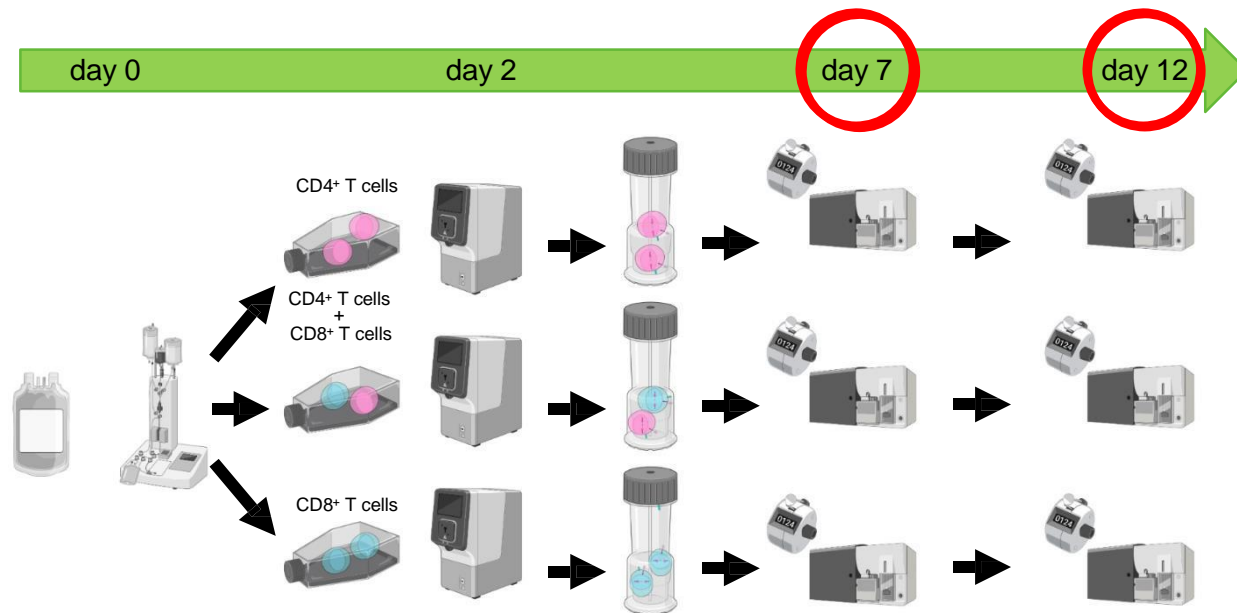
Harvest on Day 7 (Run 3)

	CD4 d7	CD8 d7	CD4/CD8 d7
Total	45,7x10 ⁶	18,7x10 ⁶	31,3x10 ⁶
Viability	93,6%	92,8%	94,3%
Viable cells	42,7x10 ⁶	17,4x10 ⁶	29,5x10 ⁶
CD3+CD? ⁺	98,56%	92,70%	63,89%/34,17%
EGFR ⁺	48,26%	44,37%	52,83%/50,55%

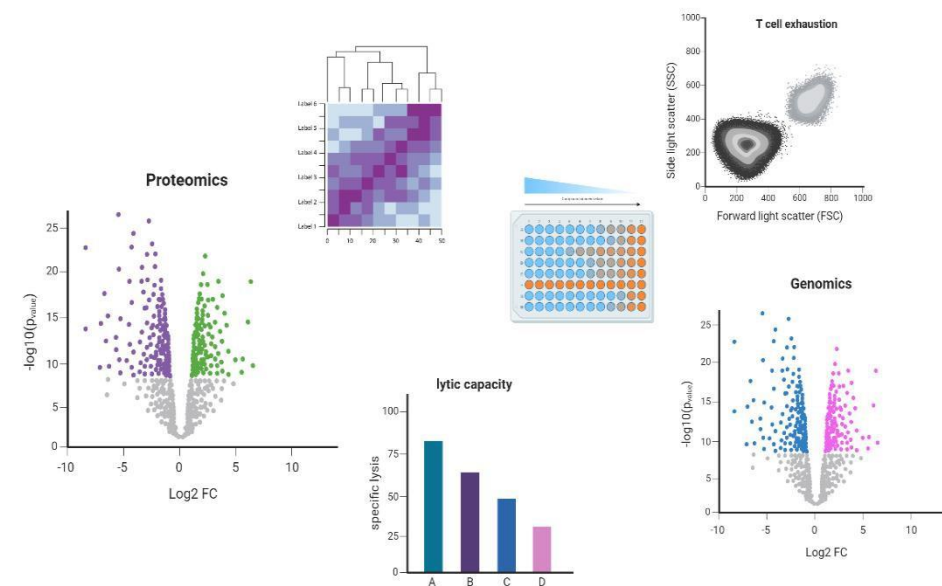


UltraCART – Results

WP 5: Omics and AI

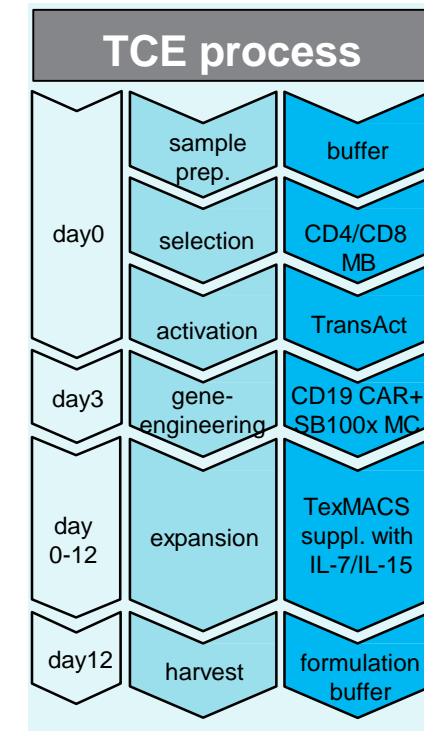
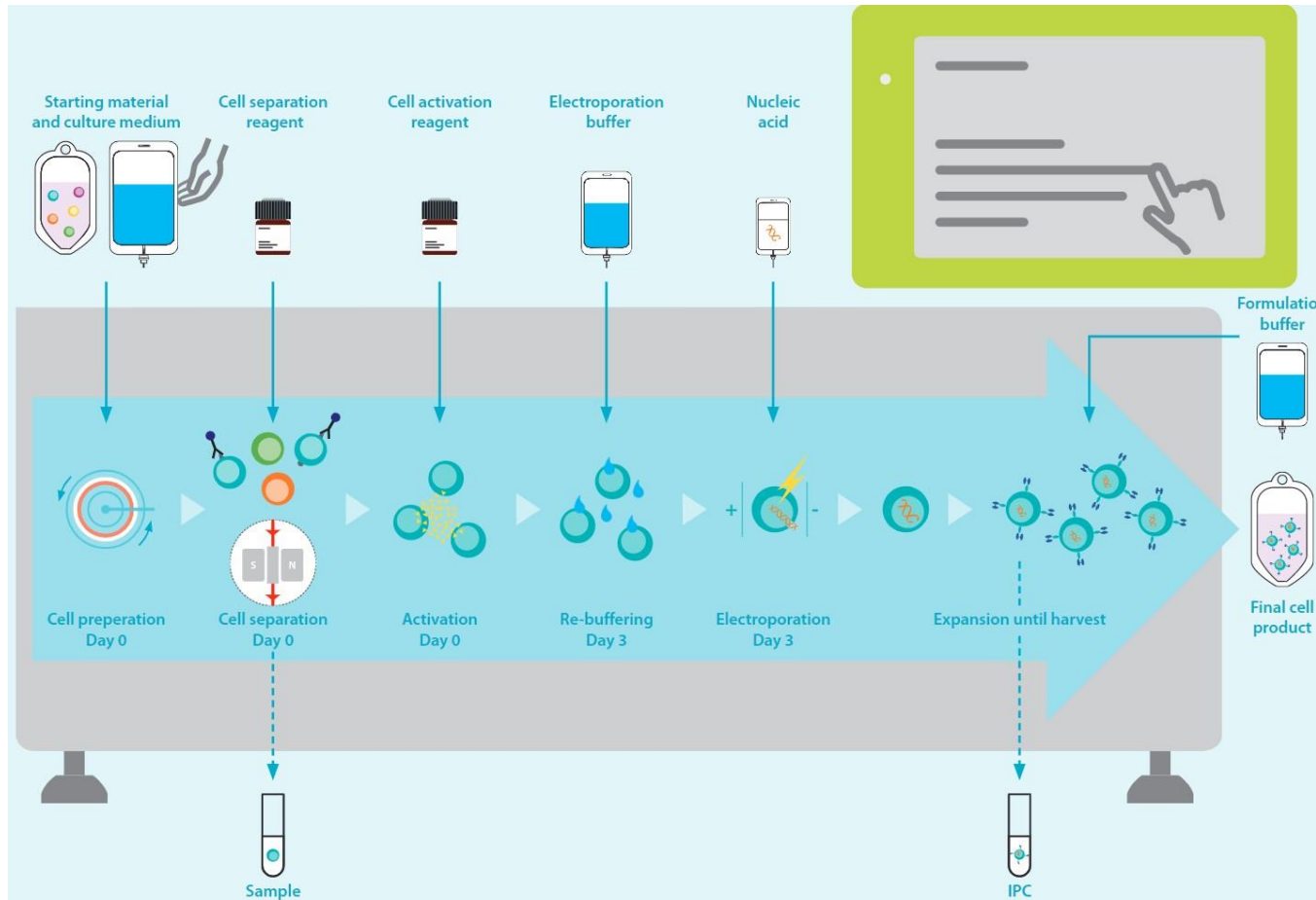


Analyse Anti-Tumor Function Analyse Genomics/Proteomics Profile



UltraCART – Results

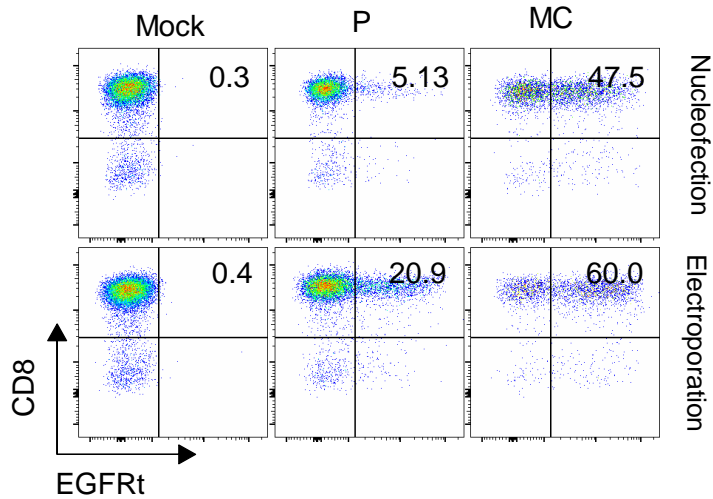
WP 3: Short Manufacturing and Automation



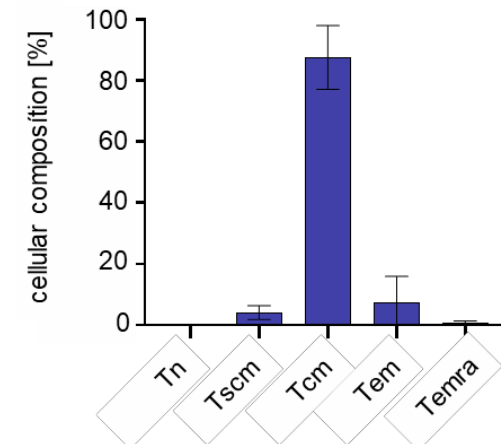
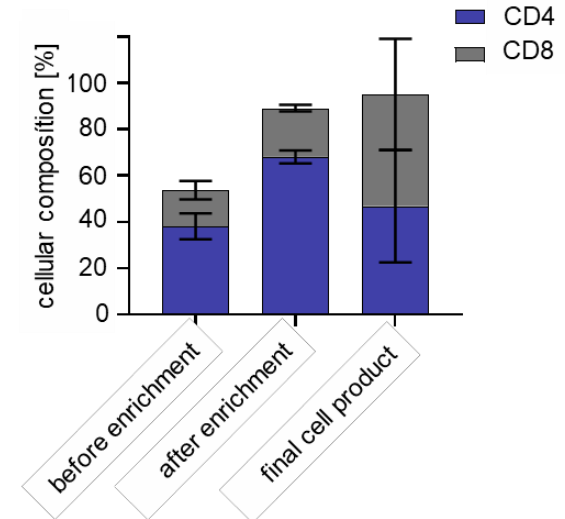
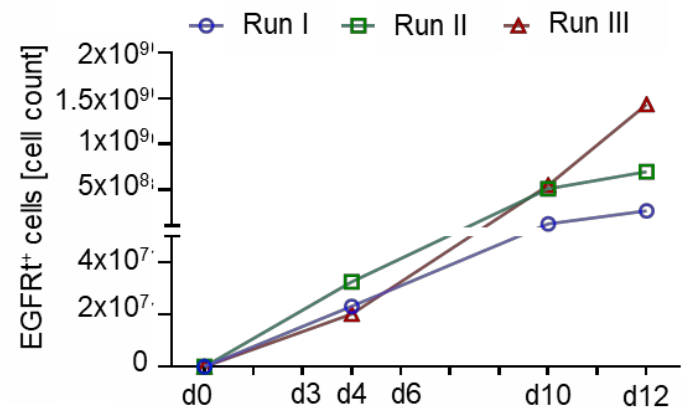
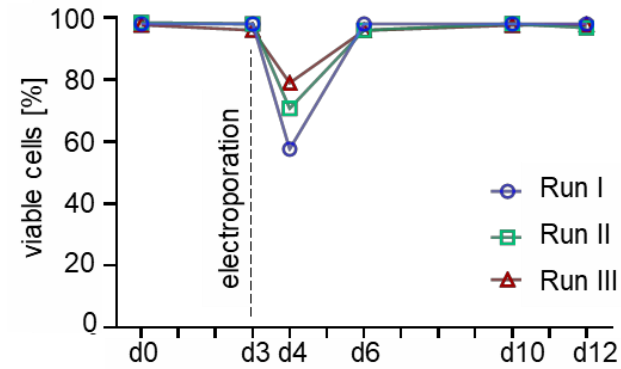
AREA 1 – CAR-T

UltraCART – Results so far

WP 3: Short Manufacturing and Automation



Gene Transfer Rate: 60%
 Therapeutic Dose
 T_{CM} Phenotype, CD4/CD8 Ratio 1:1

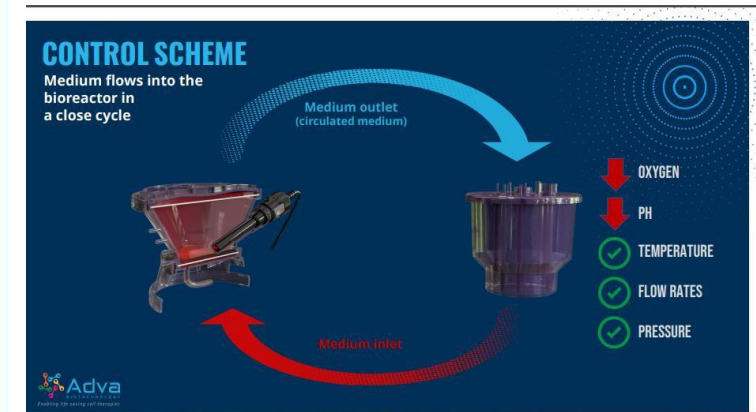


UltraCART – Results

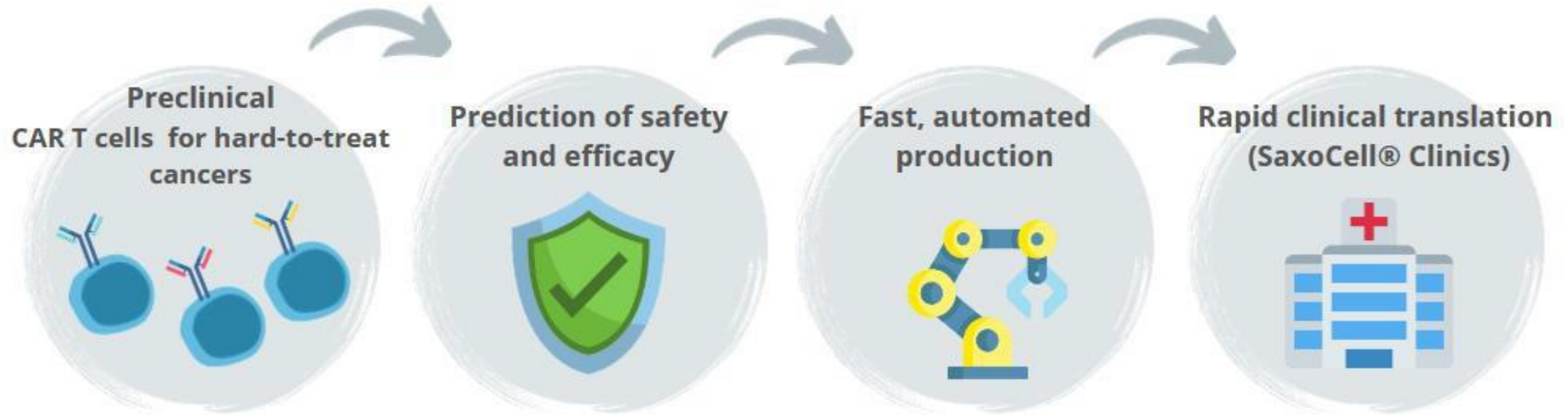
WP 3: Short Manufacturing and Automation



- d0 T cell isolation
- d0 Activation
- d2 Nucleofection
- d2 Seeding in Adva
- d7 Harvest



UltraCART – Objectives & Outlook



Deliver High-End CAR-T Products for Clinical Trials within SaxoCell

Expand work on fast, automated CAR-T manufacturing

UltraCART – Results



Clinical Trial Engine

ROR2 CAR-T: LION-2 Trial

Hematology: Multiple Myeloma Oncology: Renal Carcinoma (and Glioblastoma)

Partner: Uniklinik Würzburg, Uniklinik Leipzig, Fraunhofer IZI, T-CURX, Myeloma Patients Europe

*Supported by Federal Ministry for Education and Research
Program “Frühe Klinische Studien”, Project Duration: 2023 - 2028*



Bundesministerium
für Bildung
und Forschung

AML CAR-T: TCX-001

Hematology: AML

Sponsor: T-CURX

Partner: Uniklinik Würzburg, Uniklinik Dresden and selected other sites

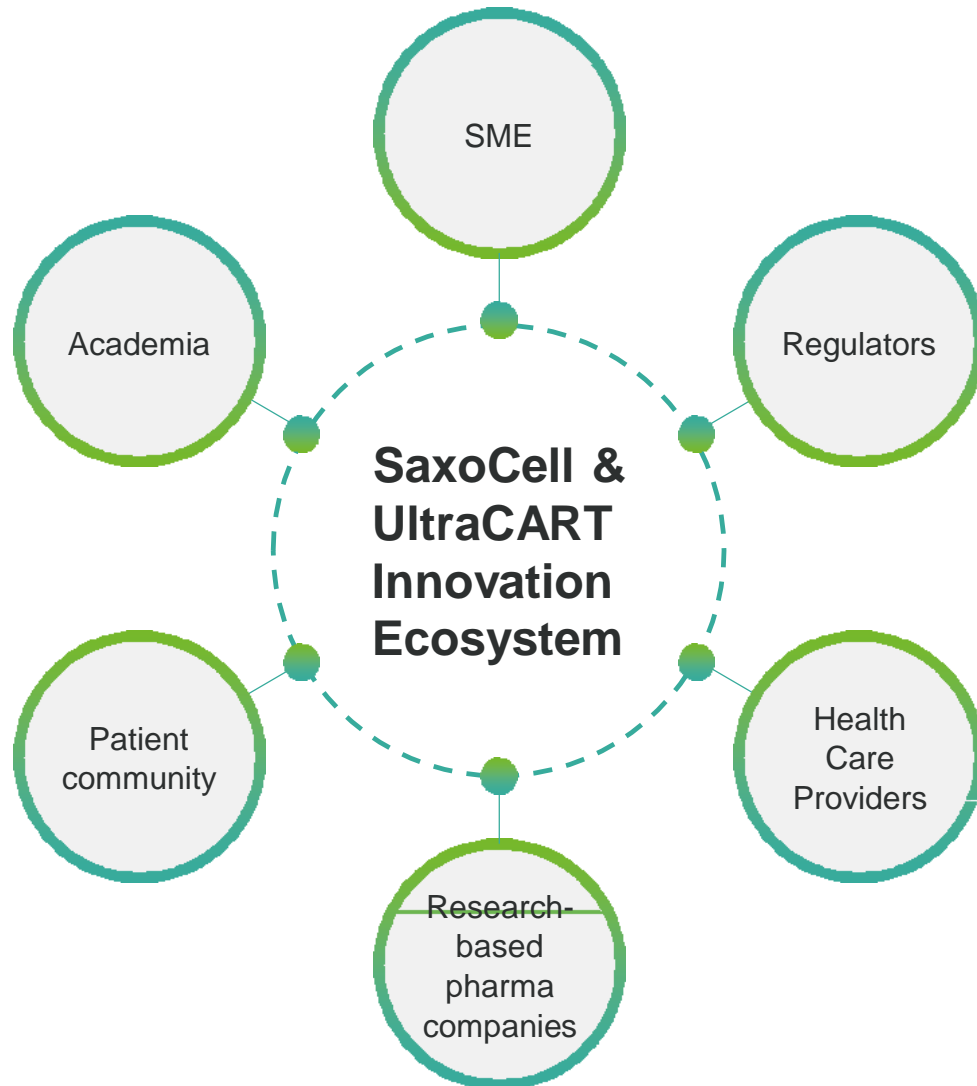
T-CURX Lead Program

The logo for T-CURX, featuring the text "T-CURX" in a blue sans-serif font. The letter "X" is stylized with a blue swoosh that extends from the bottom right of the letter.

UltraCART – Progress



UltraCART – Synergy



innovative
medicines
initiative

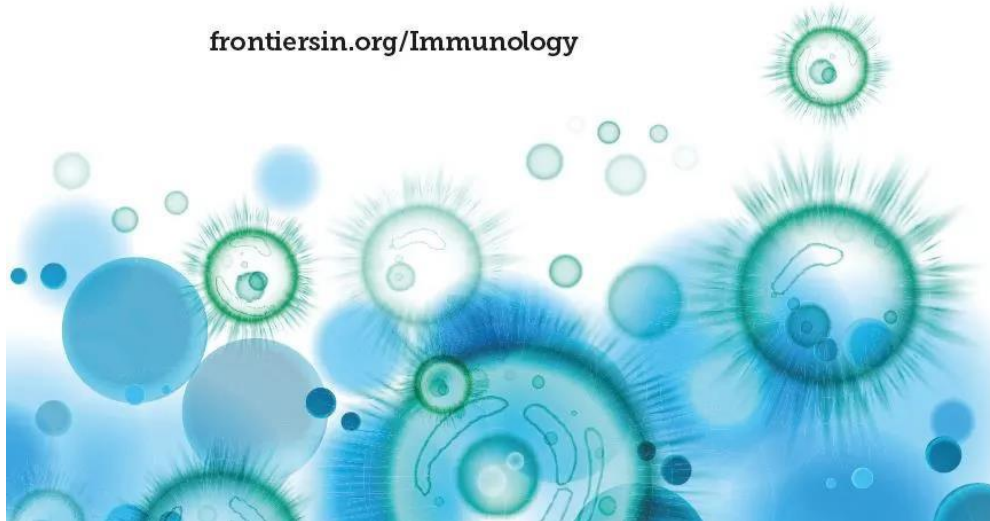
T²EVOLVE



UltraCART – Visibility



frontiersin.org/Immunology



Special Topic on Advances in Pre-clinical and Clinical Development of CAR-T cells

Editors: Ulrike Köhl, Michael Hudecek, Helèn Negré, Stephen Goldrick, Qasim Rafiq

7 Articles accepted/published

12 Articles in pipeline

Journal 2023 Impact Factor: 7.3

UltraCART – Visibility



Largest CAR-T Meeting in Europe, >1.000 Attendees

EBMT Chair: Anna Sureda (ESP), EHA Chair: Michael Hudecek (GER)

The poster features a blue background with several 3D-rendered T-cells of varying sizes. In the top left, the EBMT logo (a white circle with a line) and the EHA logo (three white stars above the text "EHA") are displayed. In the top right, a white circle contains the text "15-17 February 2024". In the bottom right, a dark blue square contains a white QR code and the text "SIGN UP HERE" in white. The main title "6th European CAR T-cell Meeting" is written in large white font, with "Valencia, Spain" in a smaller white font below it.

EBMT | **EHA**

15-17
February
2024

**6th European
CAR T-cell Meeting**
Valencia, Spain

SIGN UP HERE

UltraCART – Outlook

Standardisation of

1. Translational development
2. Clinical development
3. Data collection

WP 1: New targets and CART products. Lead: T-CURX. ✓

WP 2: New models for predicting safety & efficacy. Lead: Fnh-IZI.

WP 3: Short manufacturing and automation. Lead: Fnh-IZI.

WP 4: High resolution microscopy. Lead: T-CURX.

WP 5: Omics analytics and KI. Lead: Fh-IZI.

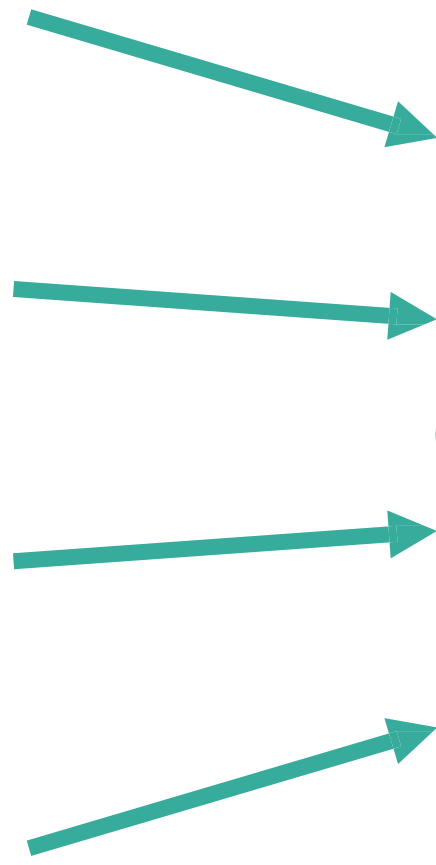
UltraCART – Objectives

Validation of novel target antigens and corresponding CART products with optimal anti-tumor efficacy

Shortening of development time by optimization of novel pre-clinical models to assess safety and efficacy of CART products

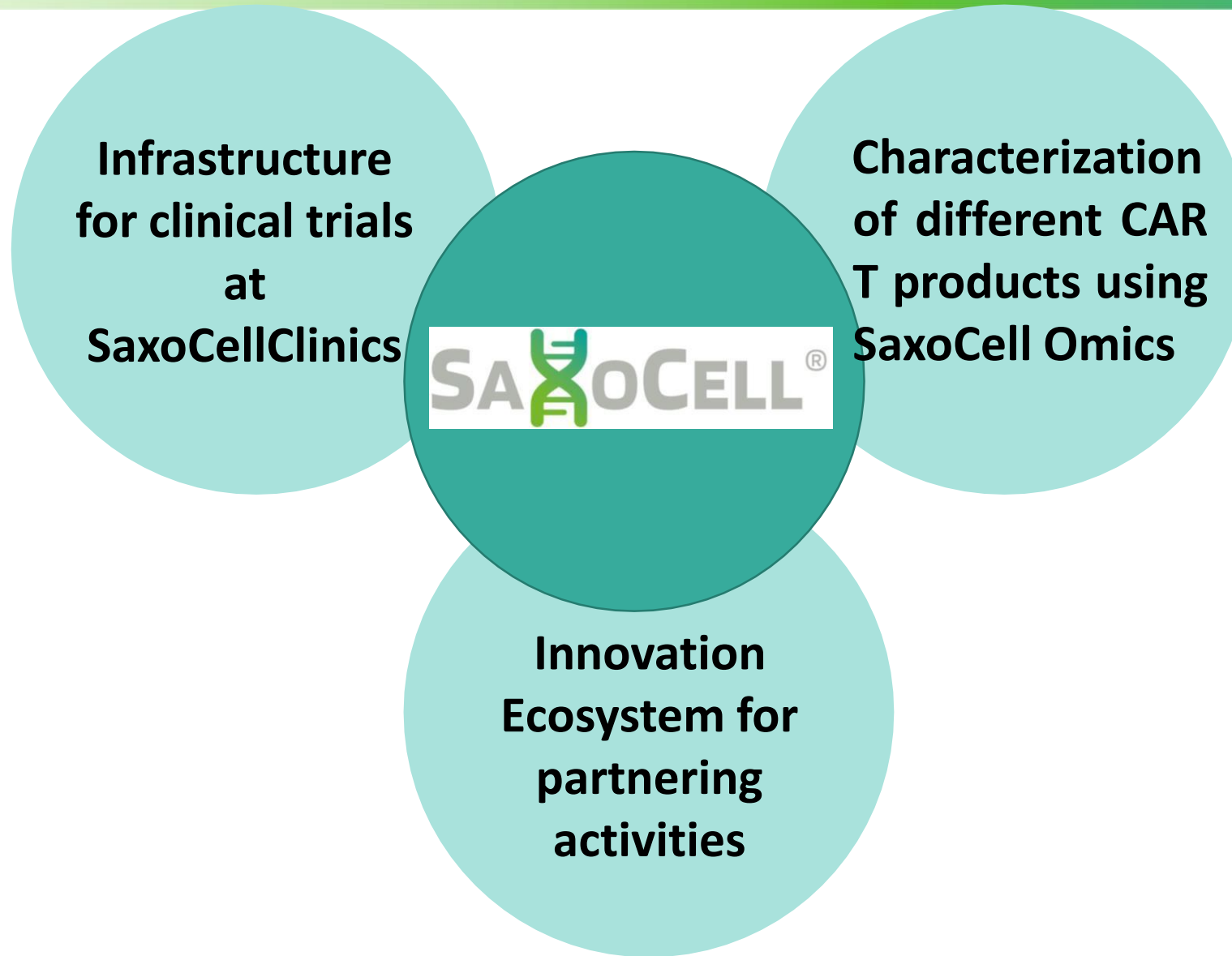
Shortening of delivery time by application of optimized scalable manufacturing processes

Standardization of therapeutic management and monitoring to allow for the deployment of artificial intelligence



Innovative CAR-T products are developed and transferred into clinical application to open up high-value chains along the translational and commercial development of novel genetically-modified cellular immunotherapies.

UltraCART – Synergy

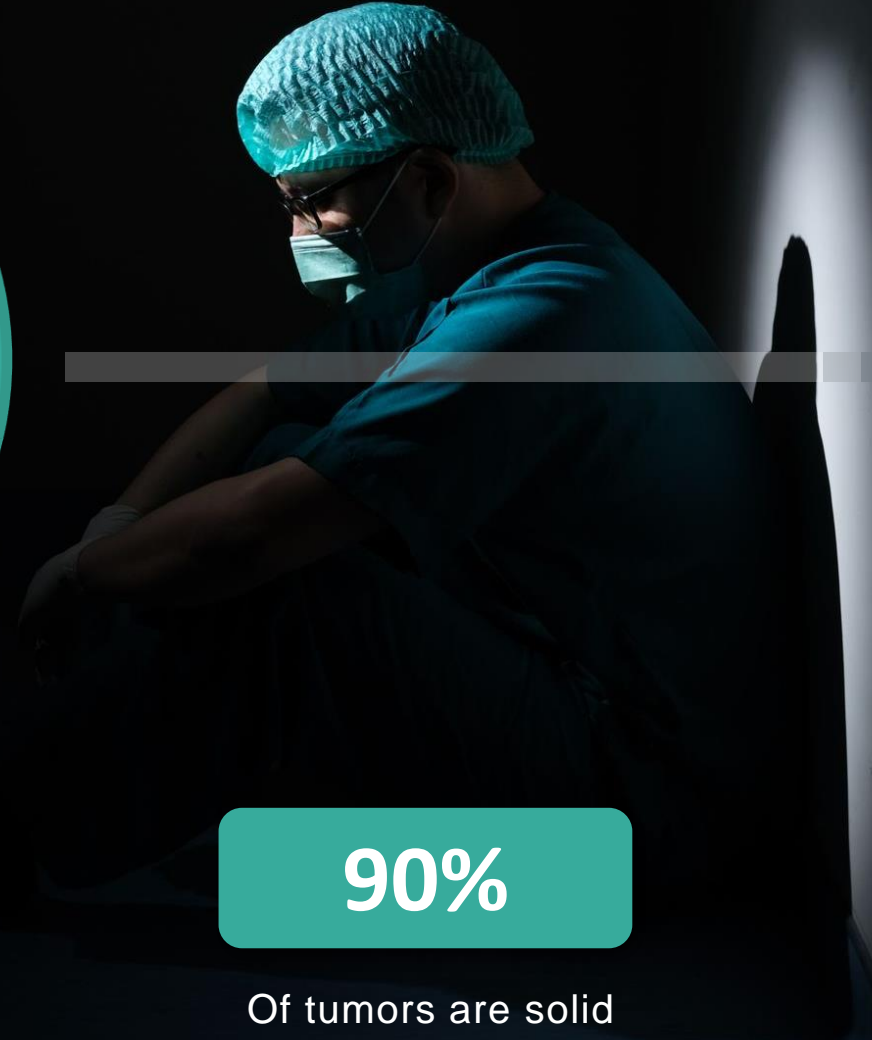
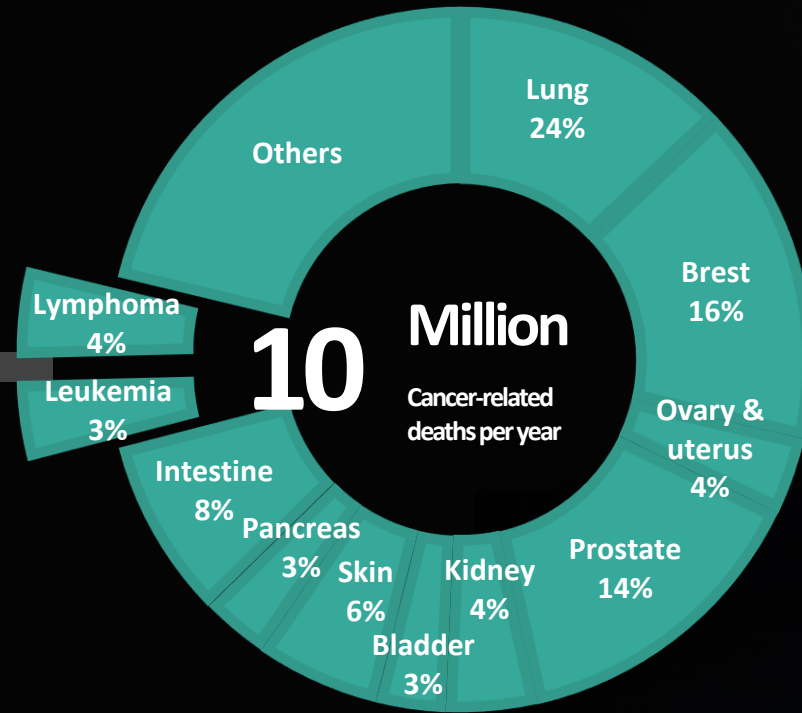


xMac – Project Overview

SAXOCELL



Michael H. Sieweke
Saxocell Symposium
Leipzig, 11. 09. 2023



10%

targetable with autologous immune cells

CAR T-cells against breast cancer

90%

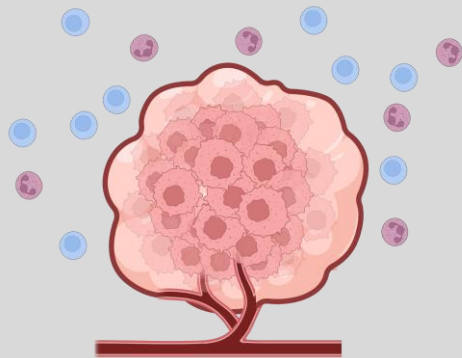
Of tumors are solid

T cells cannot infiltrate

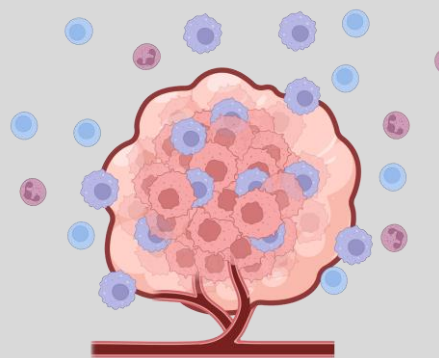


New cellular therapy

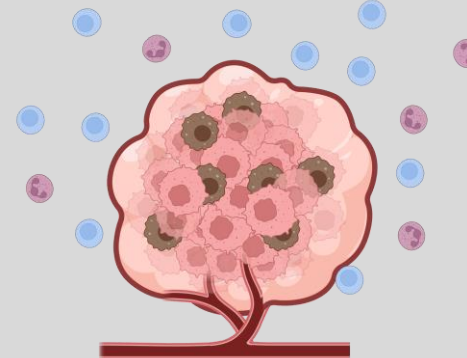
**Human macrophages
against solid tumors**



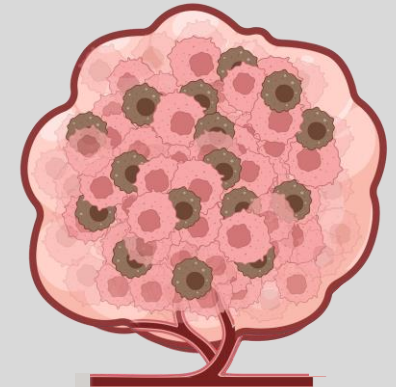
Tumor encapsulates



Macrophages infiltrate tumor



...but become reprogrammed by the tumor



Tumor continues to grow

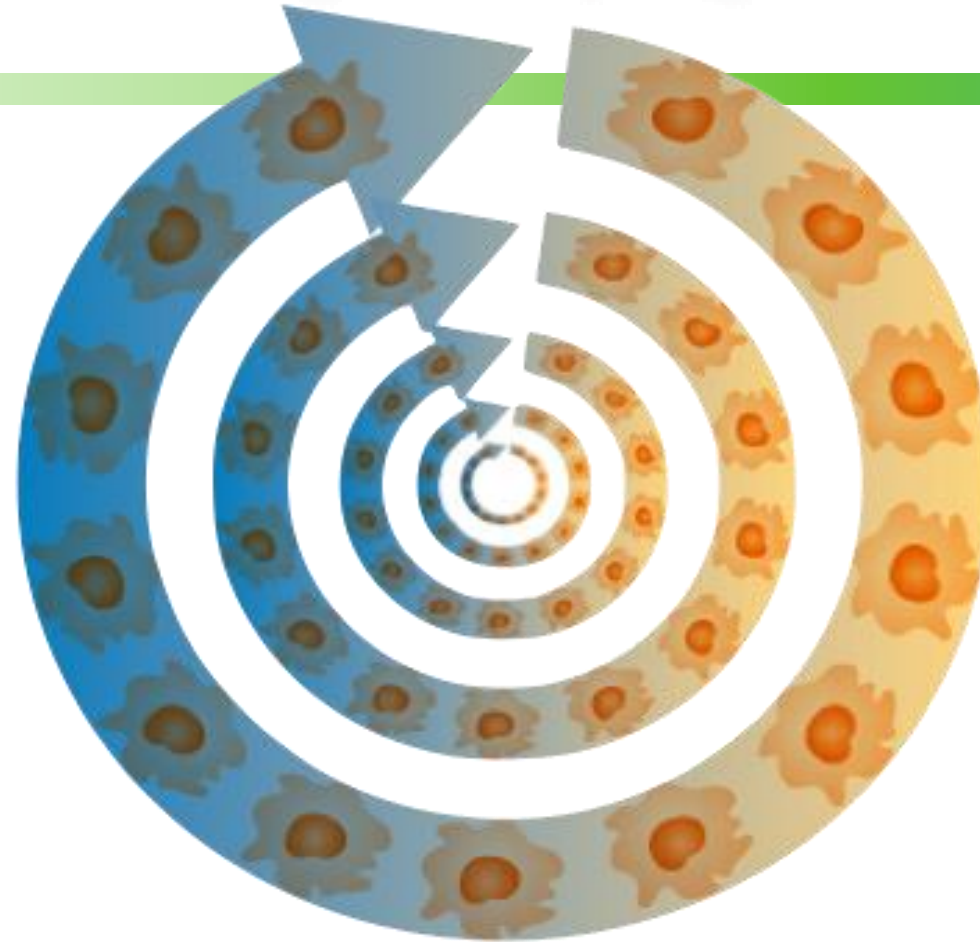
Probleme #1

Macrophages are not expandable in culture

Probleme #2

Reprogrammed macrophages act pro-tumorigenic

Our solution: Self renewing macrophages



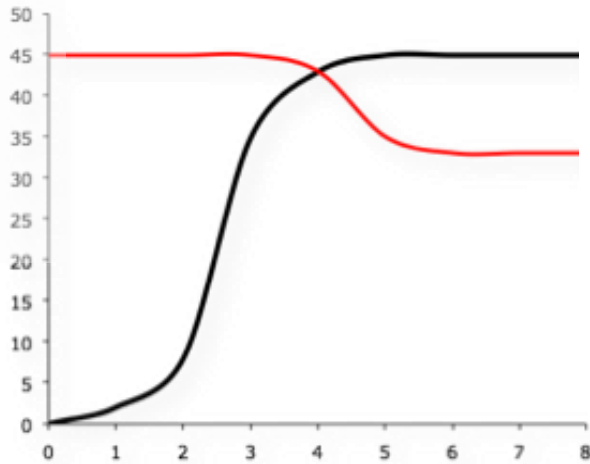
Probleme #1

Macrophages are not expandable in culture

Probleme #2

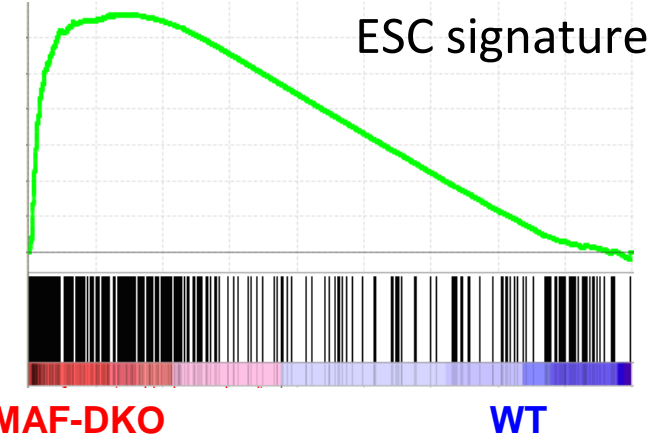
Reprogrammed macrophages act pro-tumorigenic

Dissociate differentiation and cell cycle arrest



Differentiation

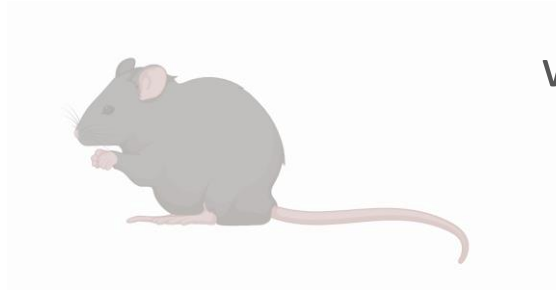
Proliferation



MafB/c-Maf DKO macrophages

Aziz et al. , Science, (2009)
Soucie et al. , Science, (2016)

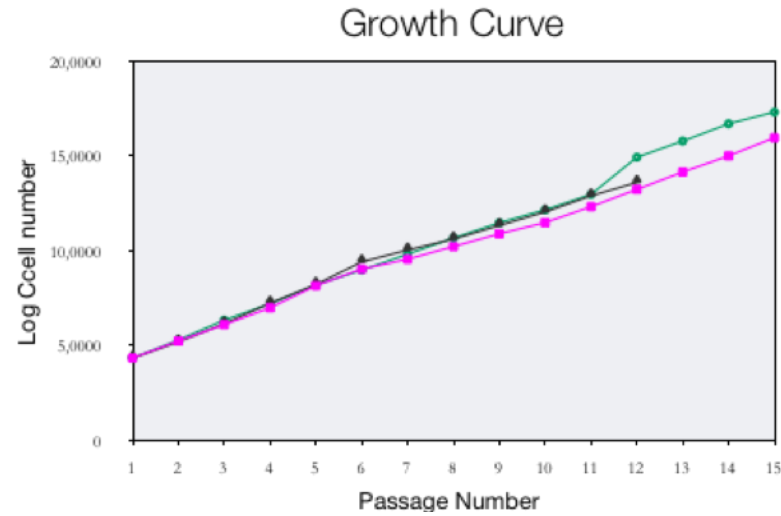
Self-renewing Maf-DKO macrophages



wt



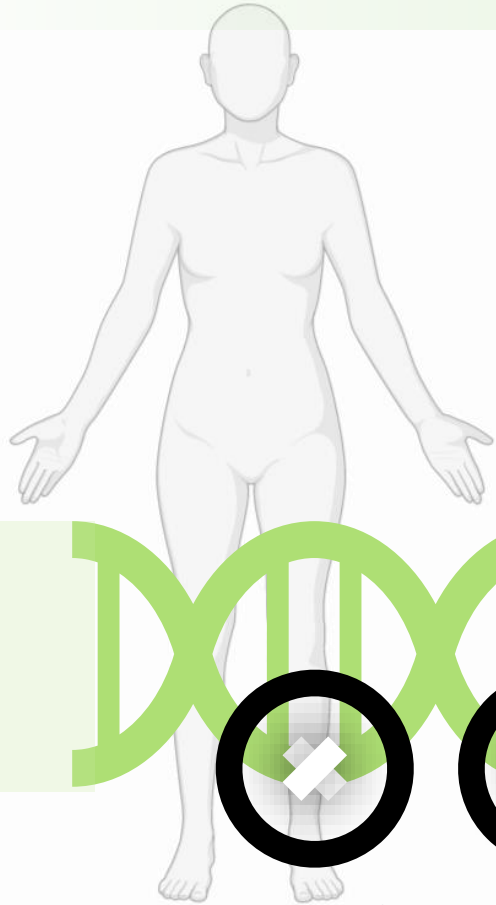
Maf-DKO



- Long term self expansion in culture
- Not transformed
- Macrophage identity

Aziz et al. , Science, (2009)
Soucie et al. , Science, (2016)

Transfer to HUMAN : MAF DKO macrophages



Deletion of MAF and MAFB
Transcription factors



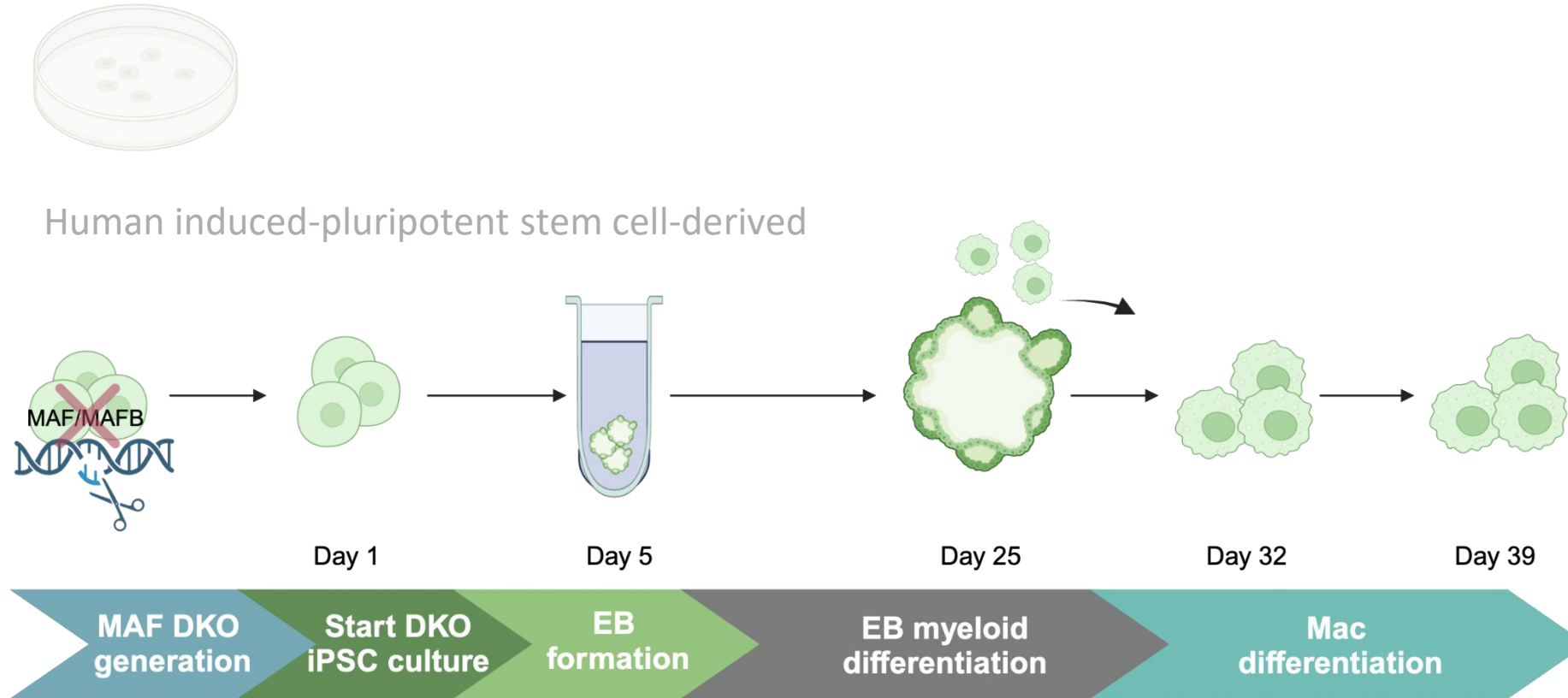
DKO
macrophages

xMac – work program



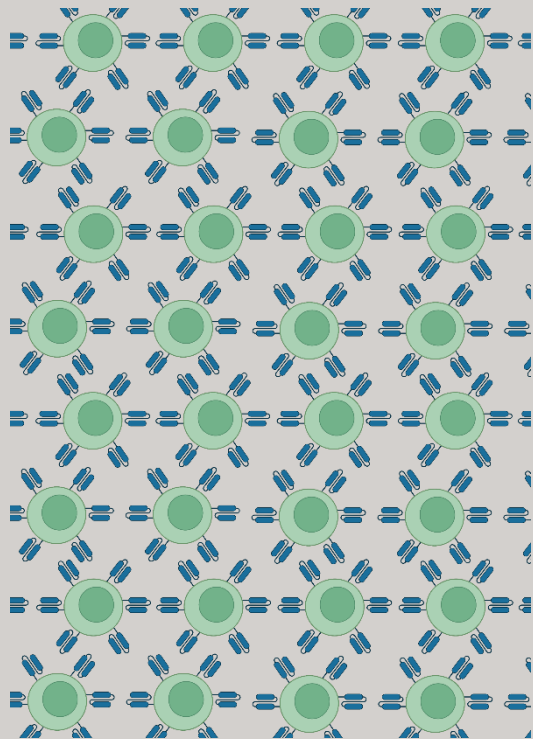
- establish and optimize culture conditions
- characterize macrophage differentiation
- characterize tumor-induced macrophage reprogramming
- first steps to universal, broadly applicable macrophages
-

Work package 1: production pipeline of human MAF DKO macrophages

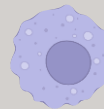


Work package 1: Culture optimization

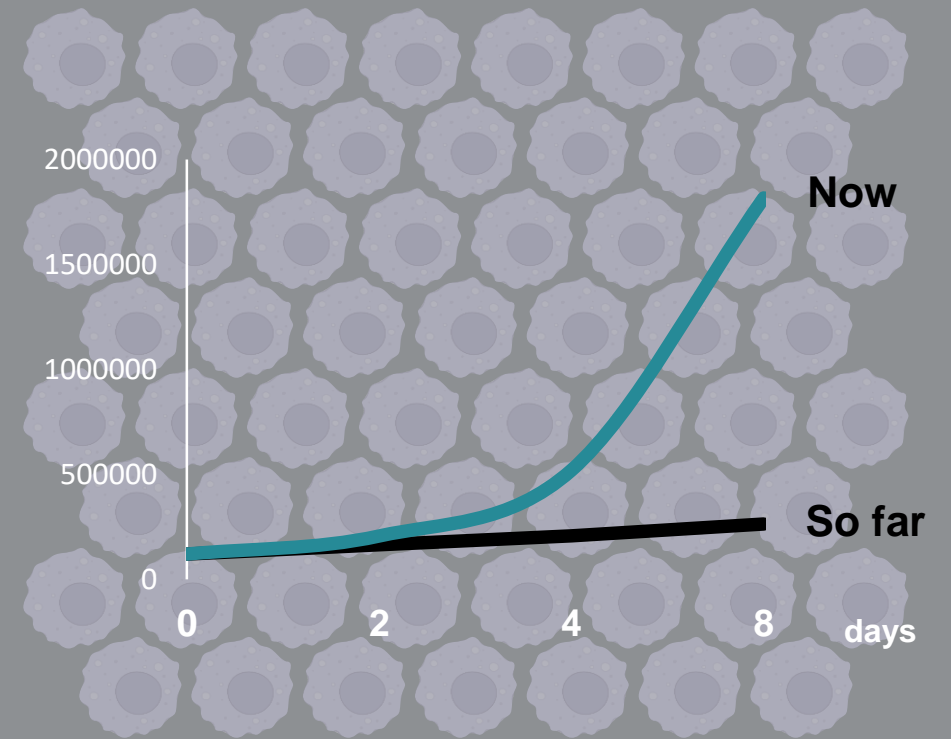
Ex Vivo



CAR T-cells

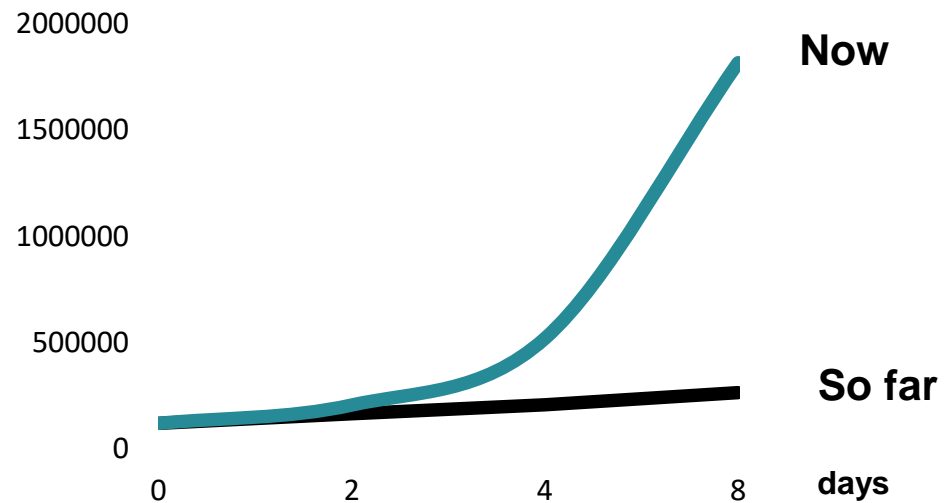


Macrophages

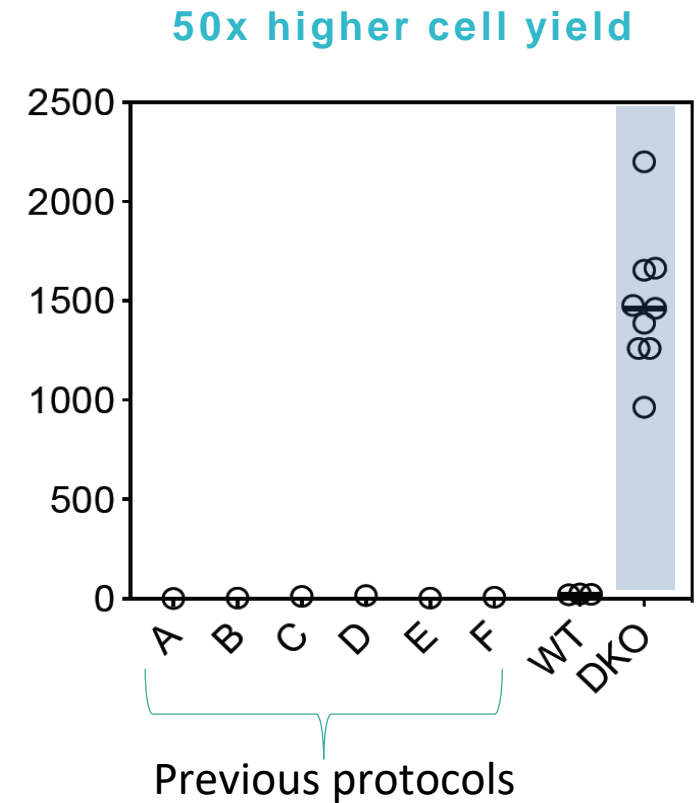


Solution: MAF DKO macrophages

Work package 1: Culture optimization



Solution: MAF DKO macrophages

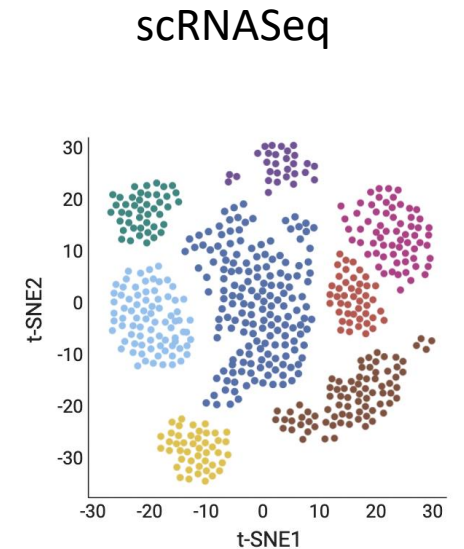
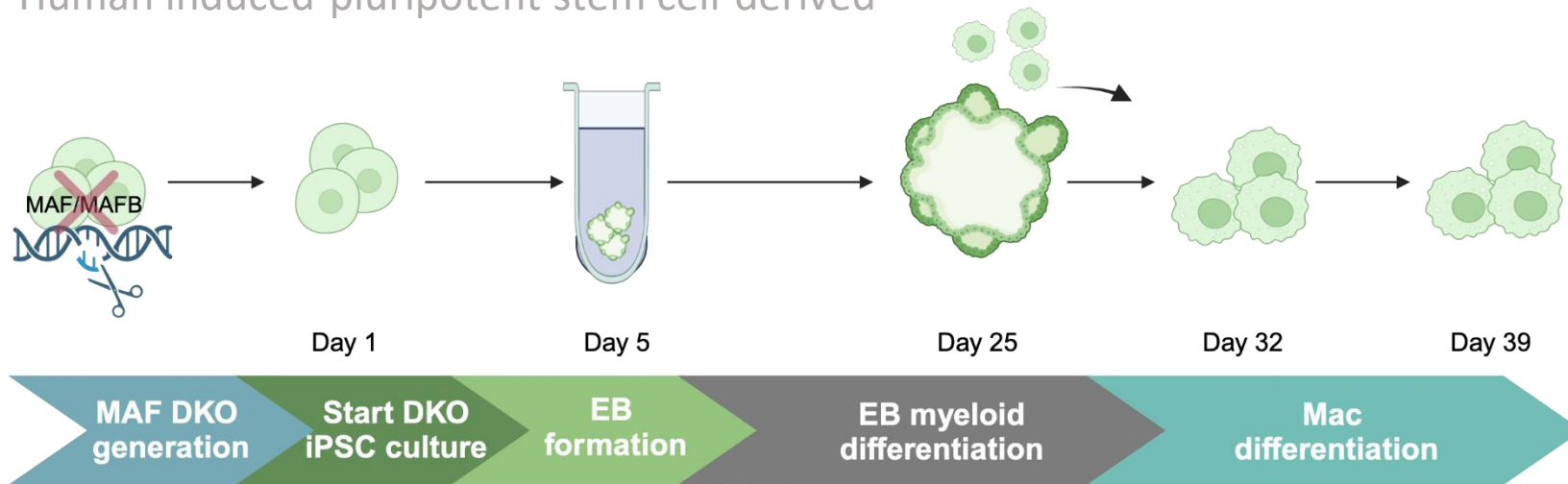


Work package 2:

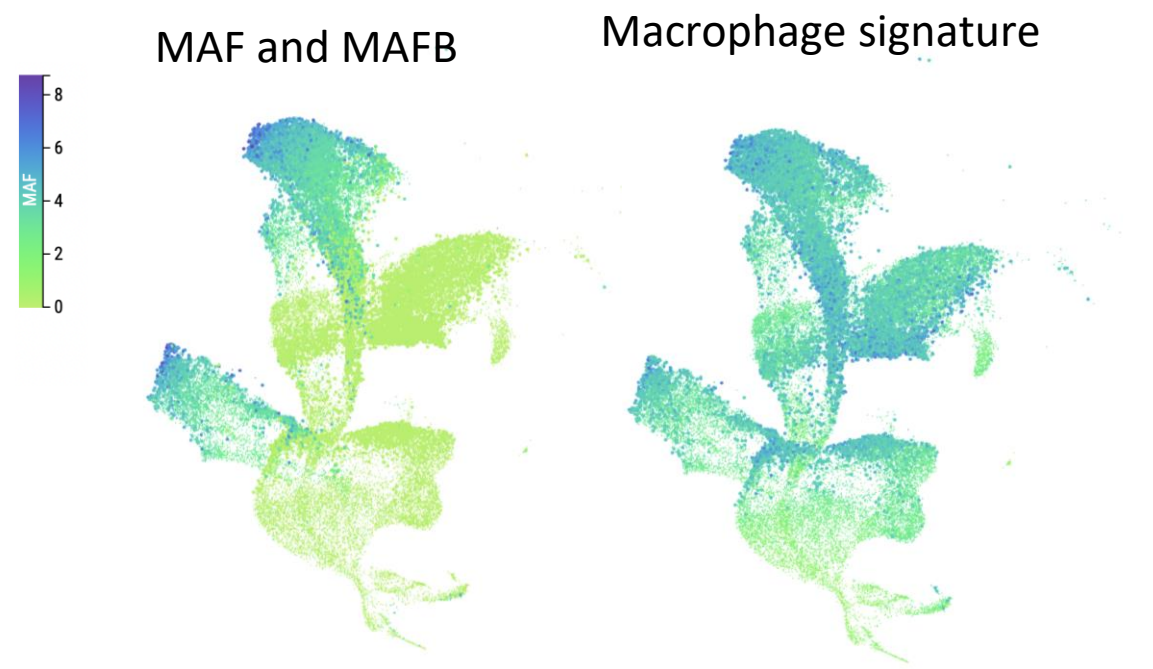
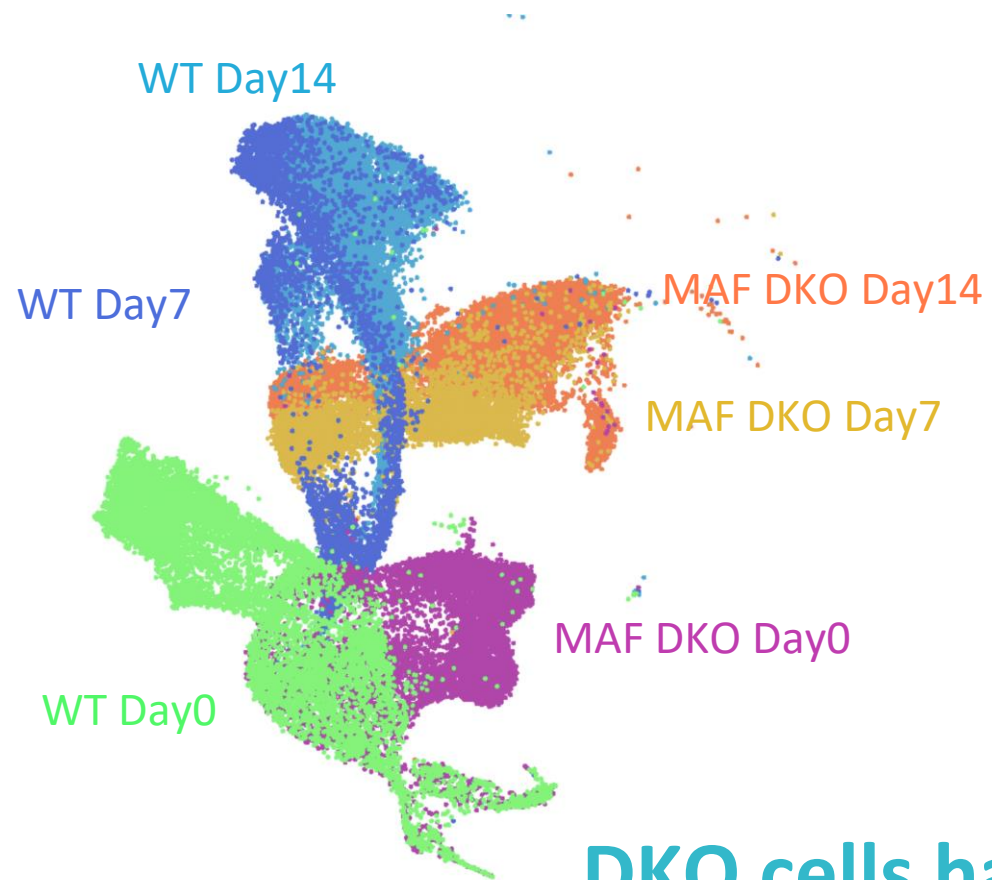
Macrophage characterization



Human induced-pluripotent stem cell-derived

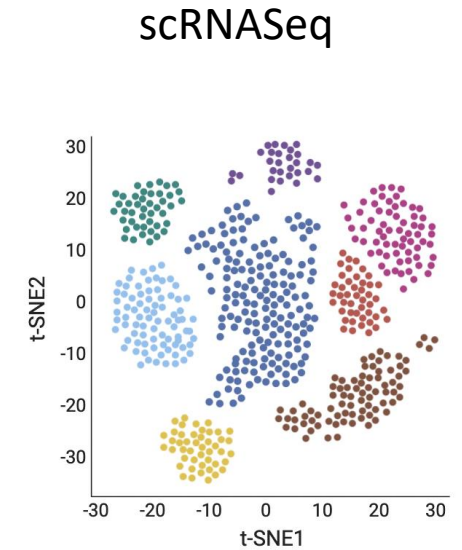
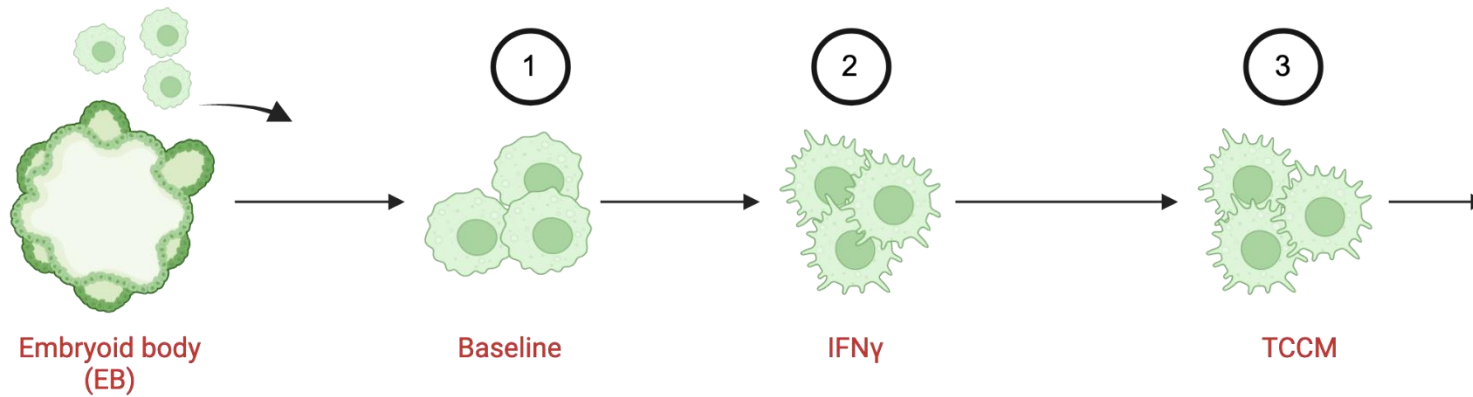


scRNASeq: Macrophage maturation

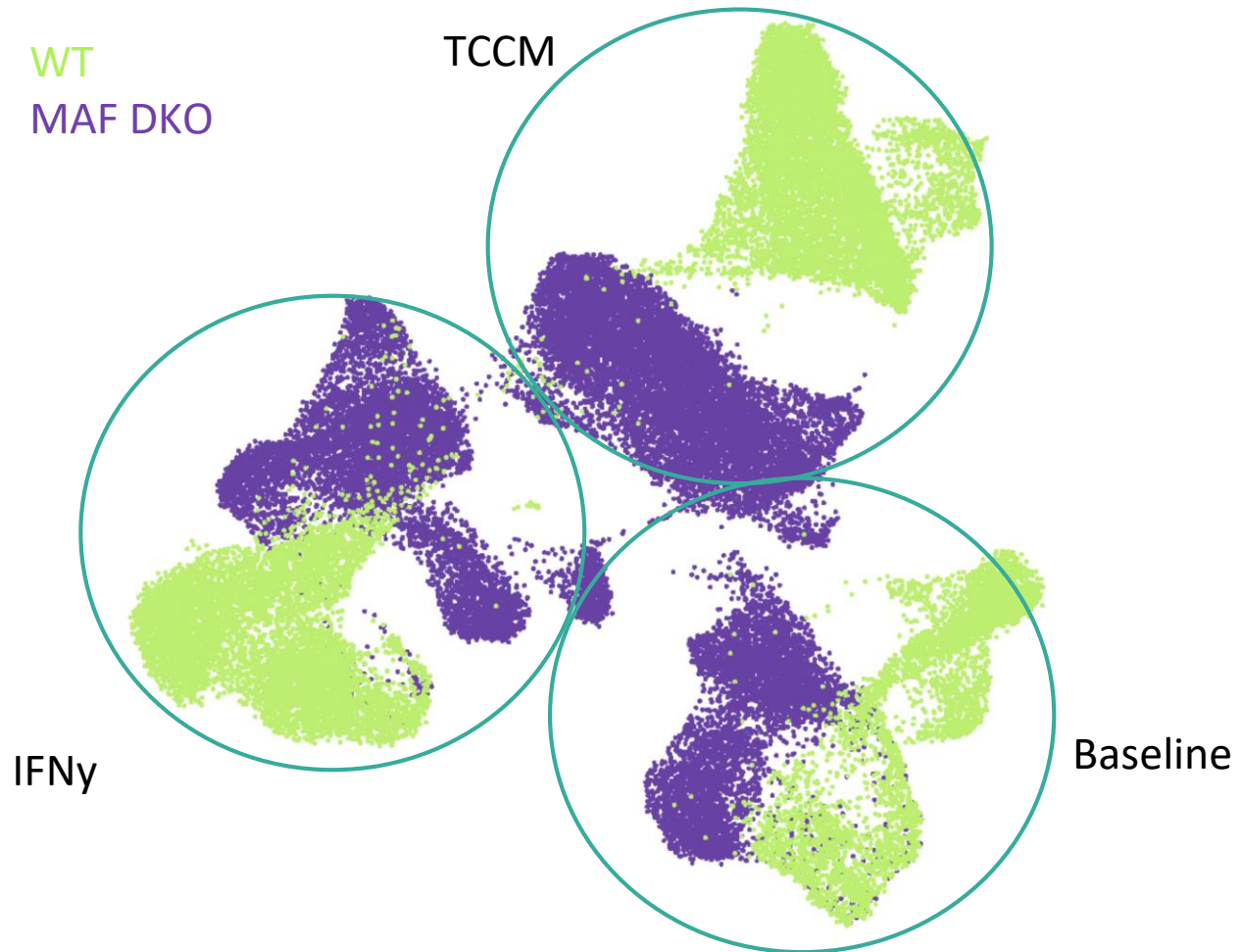


DKO cells have mature Macrophage signature

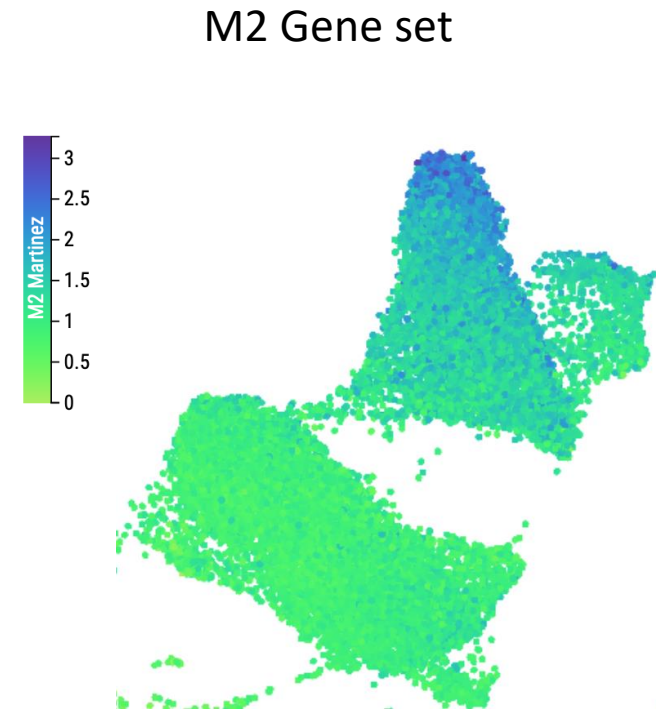
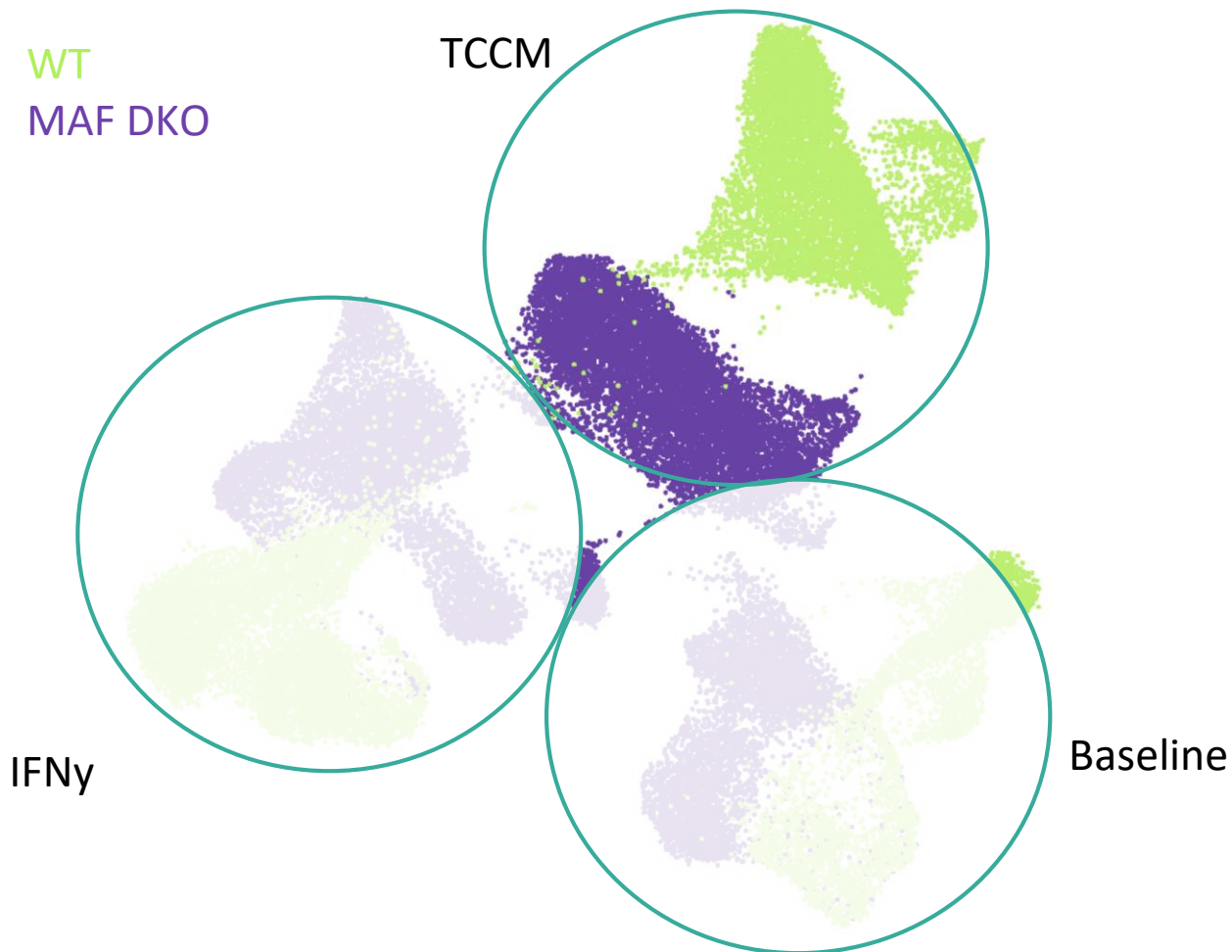
Work package 3: characterization of tumor induced macrophage polarisation



Macrophage polarization: scRNASeq

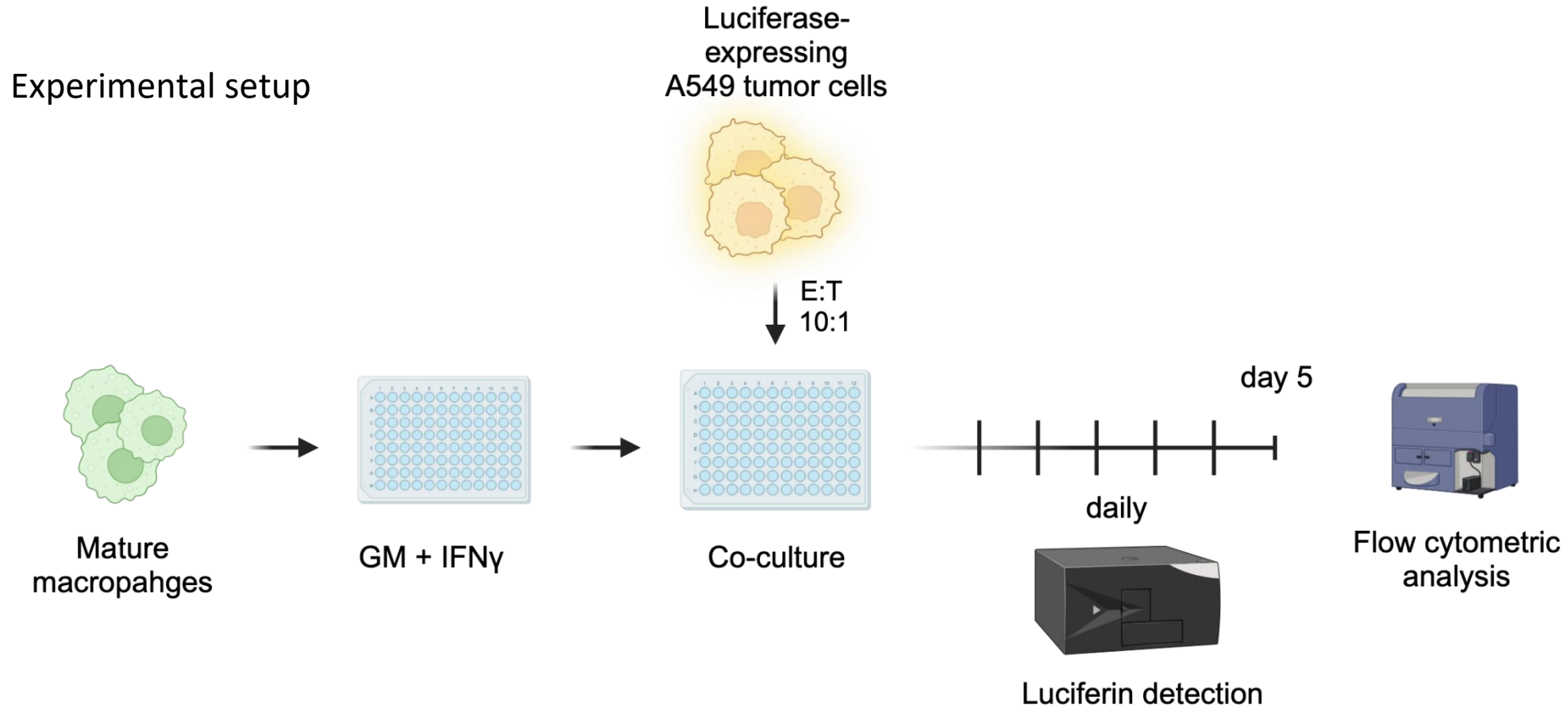


Macrophage polarization: scRNASeq

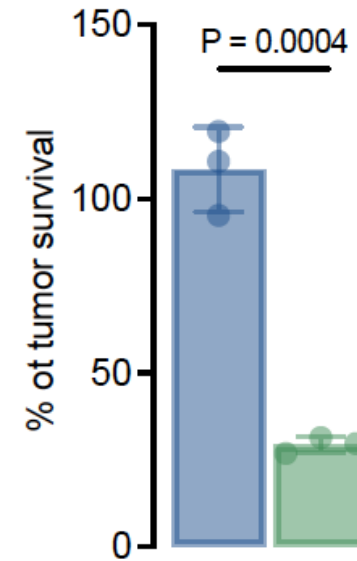
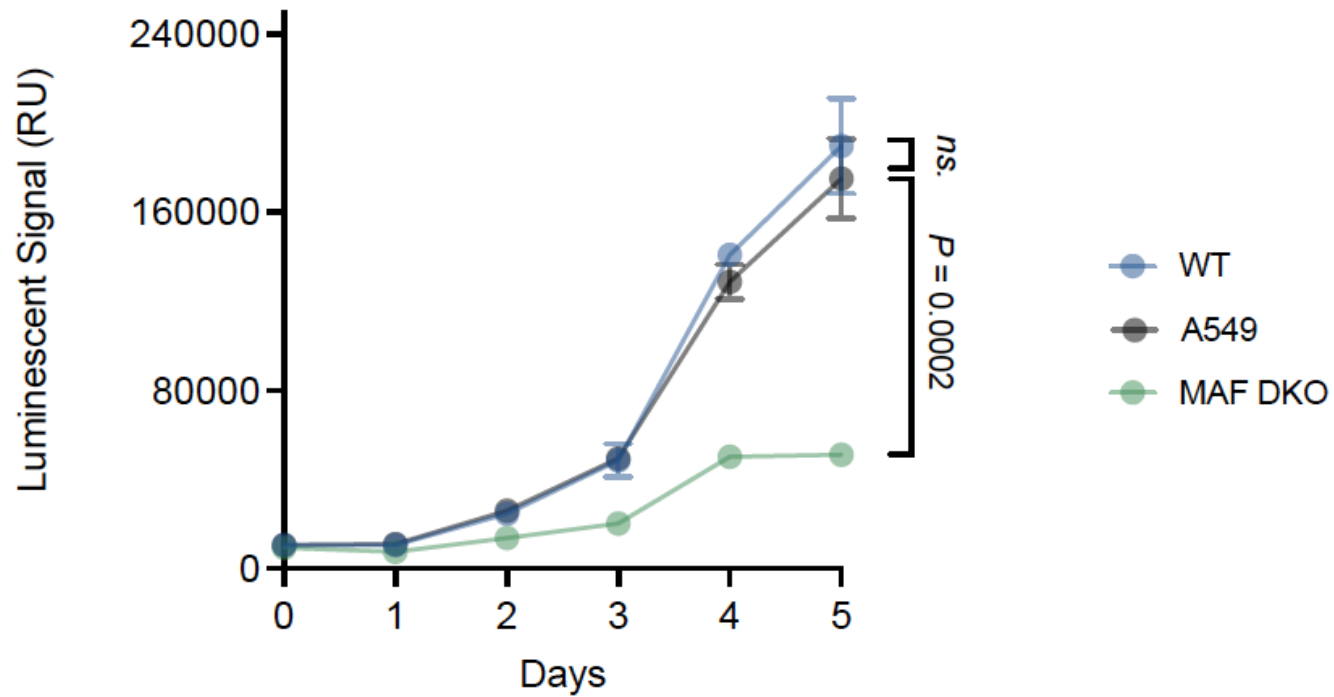


DKO macrophages resist tumor-repolarization

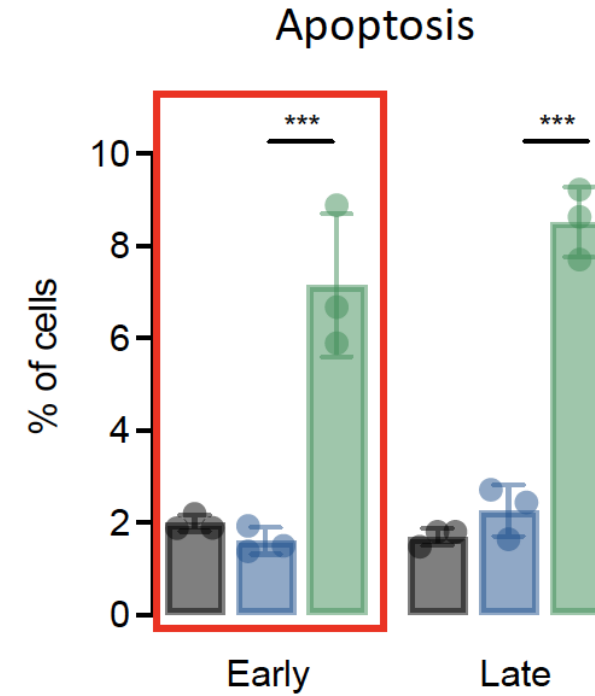
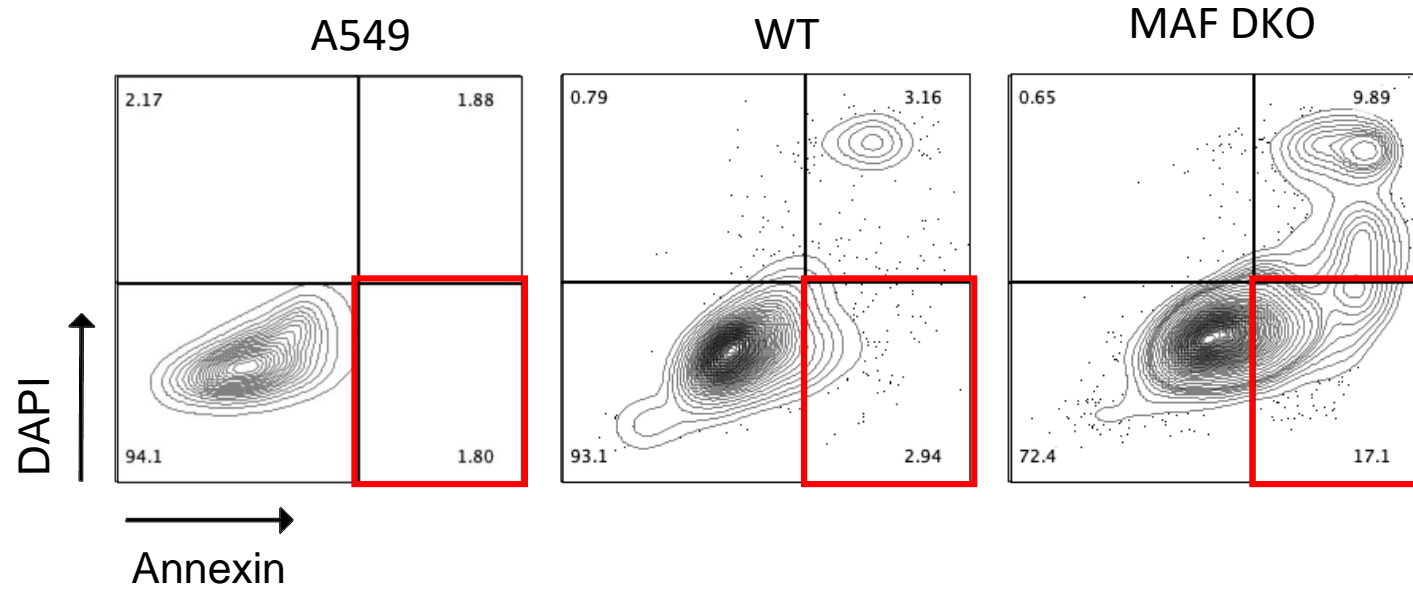
Tumor cell killing by DKO macrophages



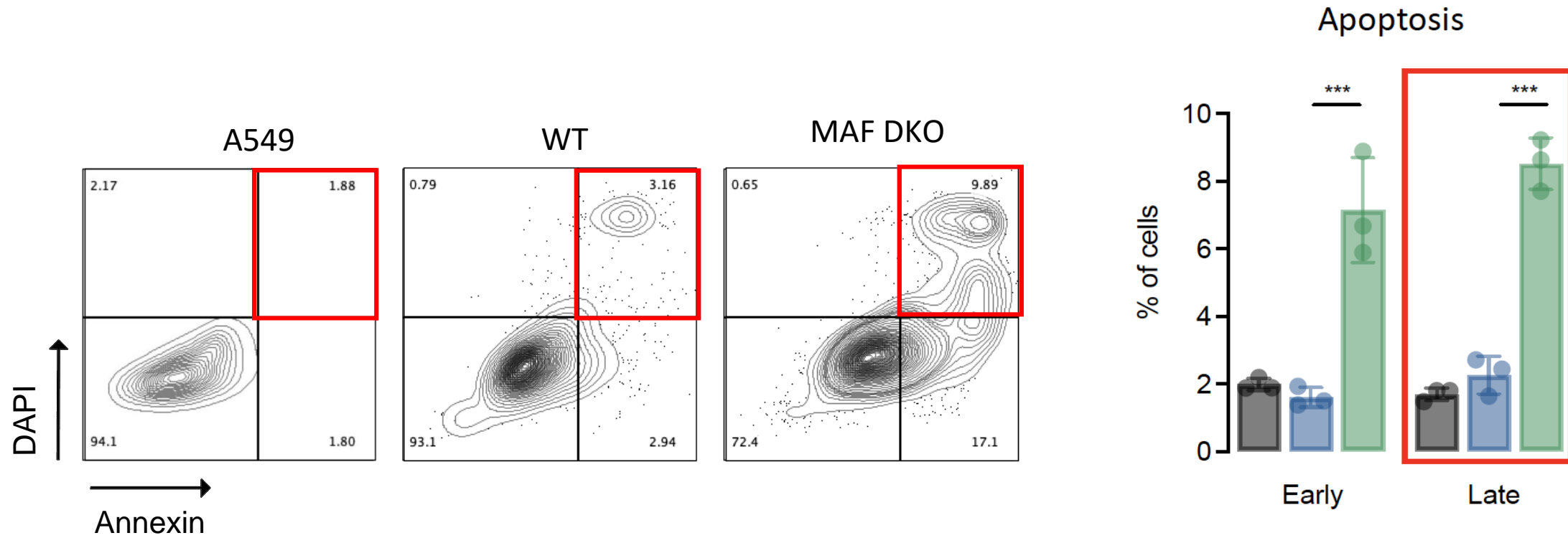
Tumor cell killing by DKO macrophages



Tumor cell killing by DKO macrophages



Tumor cell killing by DKO macrophages



Maf-DKO macrophages kill tumor cells

- Anja Feldmann/Michael Bachmann: CAR-Macs (RevCAR/UniCAR)
- Anke Fuchs: Process optimization/ scaling / GMP / regulatory
- Frank Bucholz: Alternative silencing systems > new cell sources / genes
- NK cell projects: combination therapy

.....

xMac – Outlook

- Spin-Out planed 2024: Macrophagen 2.0



Saxocell II

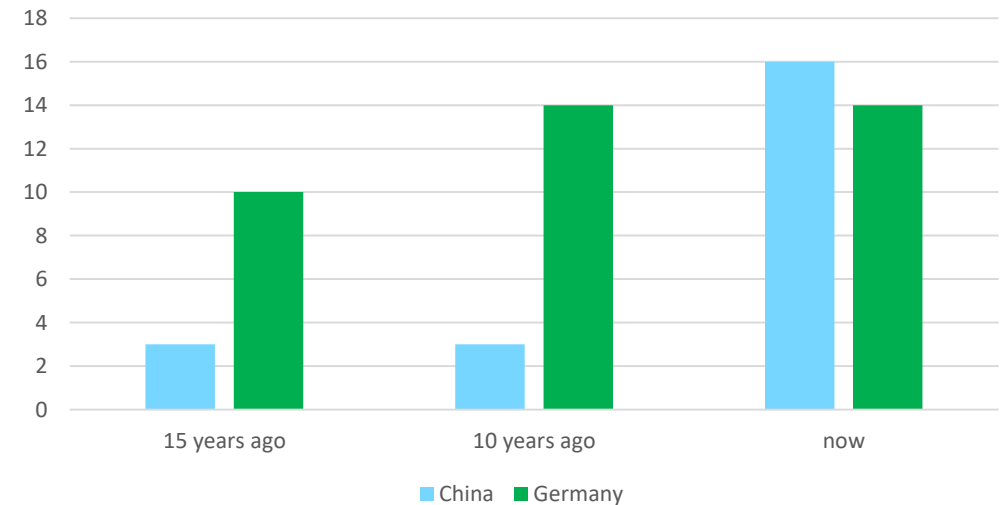
- Universal off-the shelf allogenic macrophages
- immune cell Interaction (macrophage/T-cell/NK-cell)
 - > Combination therapy?
- Haplotype matching
 - > homozygous haplotype iPS: Saxocell support ?

Research in Germany



Land of Ideas

Last author papers in NI over 2 year period



Research in Germany



- Install and operate an irradiator **4.5 years**
- Establish a lentivirus protocol **4.5 years**
- Acquire a rotating incubator **1 year**
- Acquire a spectral cell sorter **1 year + ?**
- Obtain an iPS cell line **0.5 year + ?**
- Recruit a technician **0.5 years**
- Apply for **2.5M** European funds in 3 months **> Failed**
- Recruit a monocyte junior group leader **> Failed**
- Reporting+ Resource management **> loss of momentum**

Land of Over-Regulation

Day 1: Monday 11.9.23
14:10-14:50

OPTIX

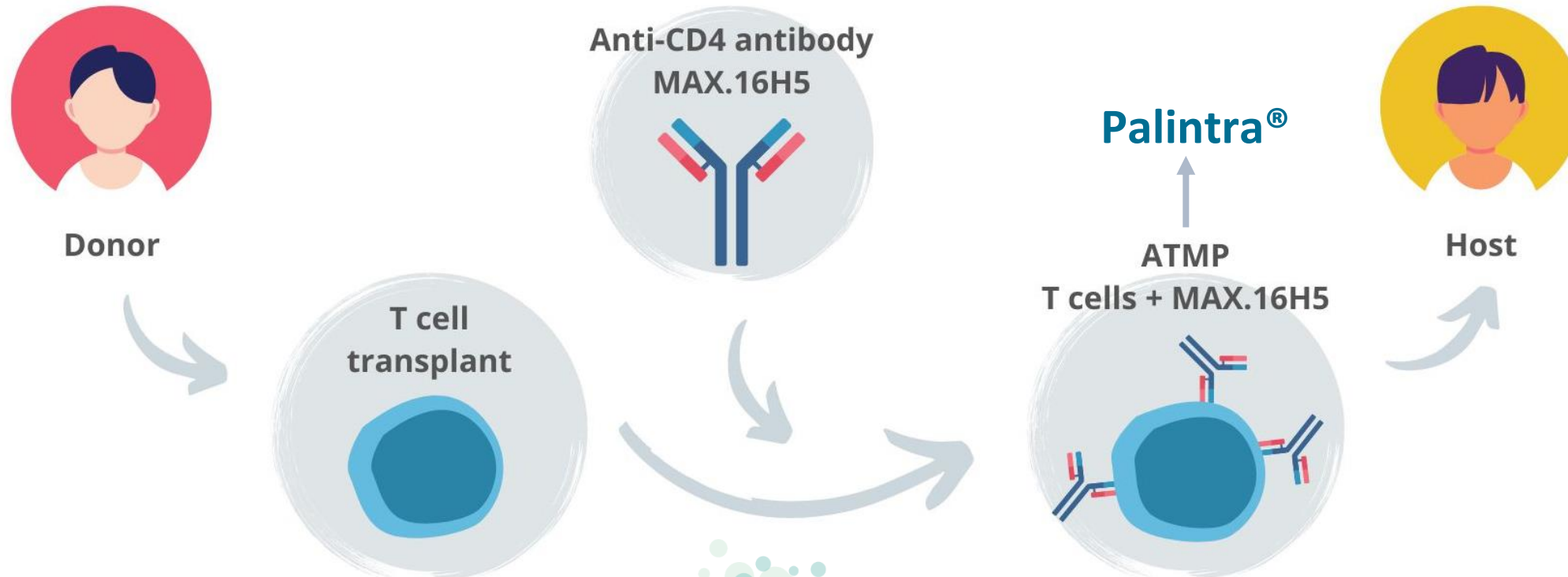
Sandy Tretbar (IZI), sandy.tretbar@izi.fraunhofer.de

CAR-NK 4.0/ NK4 Therapy

Dominik Schmiedel (IZI) & Susanne Michen (TUD)
dominik.schmiedel@izi.fraunhofer.de ; susanne.michen@ukdd.de

OPTIX – Project Overview

OPTIX - Optimized allogeneic hematopoietic cell transplantation (Tx):



OPTIX – Objectives - or: Why Palintra®?

Hematopoietic Cell Transplantation (HCT)

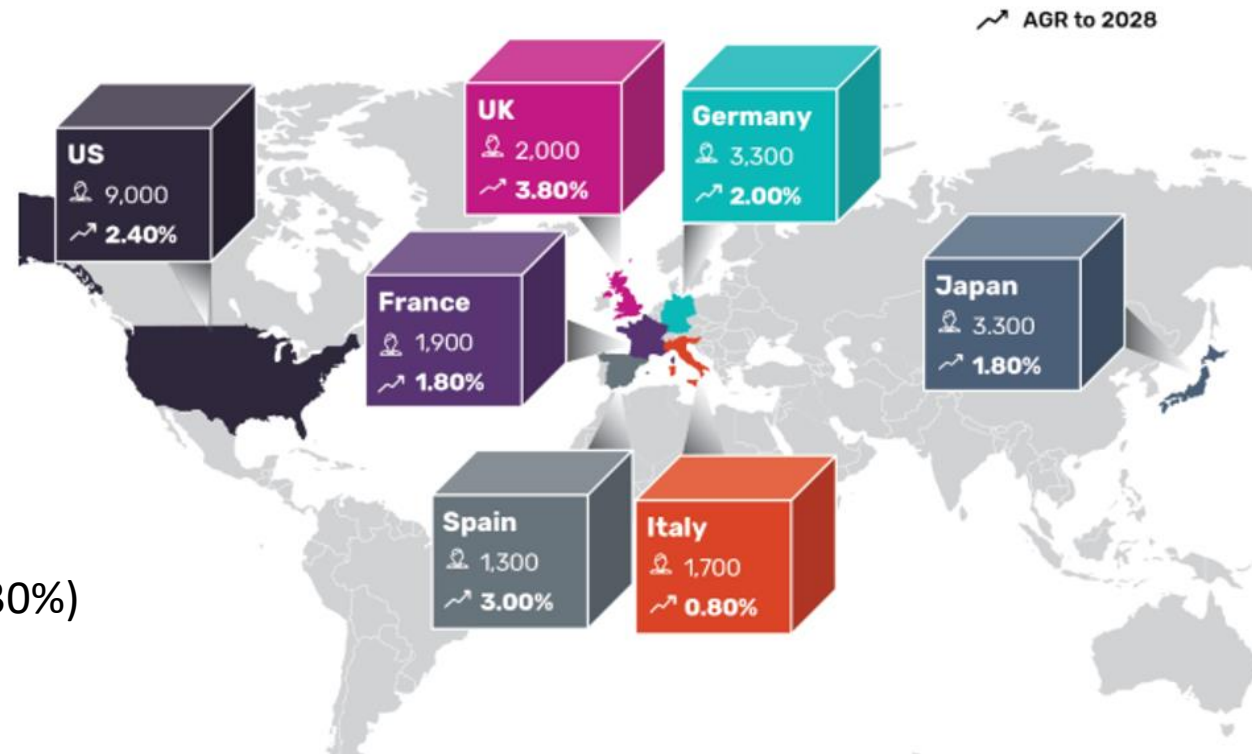
- ❖ Only curative approach for many hematologic malignancies
- ❖ Worldwide > 50.000 transplantations annually

Graft-versus-Host-Disease (GvHD)

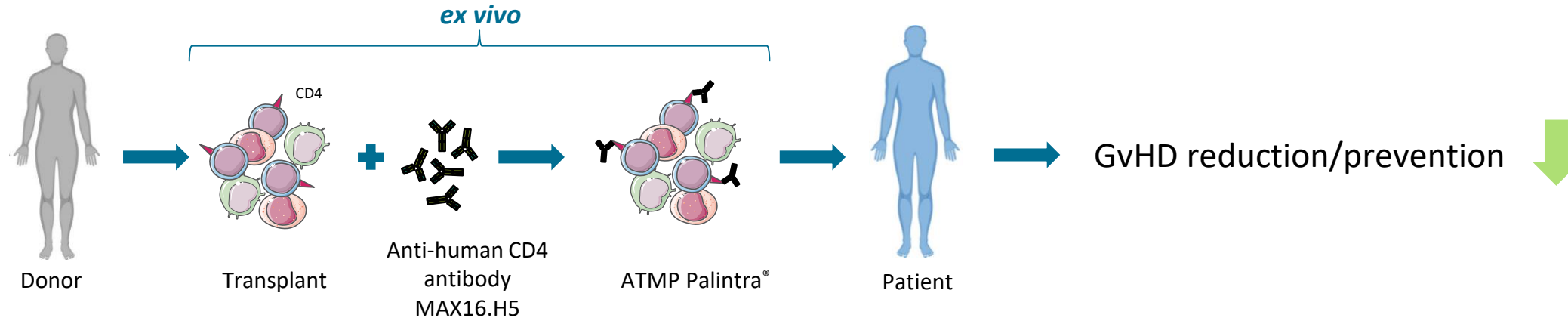
- ❖ 30-60% of HCT patients develop GvHD
- ❖ leading cause of non-relapse mortality (15-30%)
- ❖ Annual costs for treatment of acute GvHD ~ 160,000 US \$ per patient

Diagnosed incident cases of GvHD, men and women, all ages, 2028

GlobalData.



OPTIX – Objectives - or: Why Palintra®?



Academic attractiveness:

- ❖ 1st approach of *ex vivo* antibody incubation with graft
- ❖ Explorative studies, assay development, process development

Attractiveness for industry:

- ❖ Patented process
- ❖ Industry-driven GvHD projects at Fh IZI besides Palintra®:
 - EVs for GvHD prevention and/or treatment (*in vivo* studies)
 - Immunomodulation by cytokine treatment (*in vivo* studies)
 - Kinase inhibitors for GvHD treatment (*in vivo* studies)

OPTIX – Objectives - or: Why Palintra®?

GvHD is not an old hat:

Table 1. Summary graft-versus-host disease (GVHD) preventative strategies.

GVHD prophylaxis	Outcome
Calcineurin inhibitor (CSA/TAC) plus MTX/MMF (standard GVHD prophylaxis)	Reduces aGVHD and cGVHD
Addition of sirolimus to standard GVHD prophylaxis	Reduces aGVHD but no difference in cGVHD
Addition of abatacept to standard GVHD prophylaxis	Reduces aGVHD
Post-transplant cyclophosphamide	Reduces aGVHD and cGVHD
<i>In vivo</i> TCD using ATG	Reduces aGVHD and cGVHD
<i>In vivo</i> TCD using alemtuzumab	Reduces aGVHD and cGVHD (increased infection and relapse risk compared with ATG)
<i>Ex vivo</i> TCD - CD3+TCRαβ+/CD19+ lymphocyte removal	Reduces aGVHD and cGVHD
<i>Ex vivo</i> TCD - removal of naïve T-lymphocytes	Reduces cGVHD but not aGVHD
<i>Ex vivo</i> TCD - CD34+ selection with infusion of Tregs (regulatory T-lymphocytes) and conventional T-lymphocytes	Reduces aGVHD and cGVHD

aGVHD, acute graft-versus-host disease; ATG, anti-thymocyte globulin; cGVHD, chronic graft-versus-host disease; CSA, cyclosporin; MMF, mycophenolate mofetil; MTX, methotrexate; TAC, tacrolimus; TCD, T-cell depletion.

Fac Rev. 2023; 12: 4.

Published online 2023 Mar 6. doi: [10.12703/r/12-4](https://doi.org/10.12703/r/12-4)

Recent advances in graft-versus-host disease

Aisling M. Flinn^{1,2} and Andrew R. Genney^{1,2*}

Immunosuppression / T cell depletion

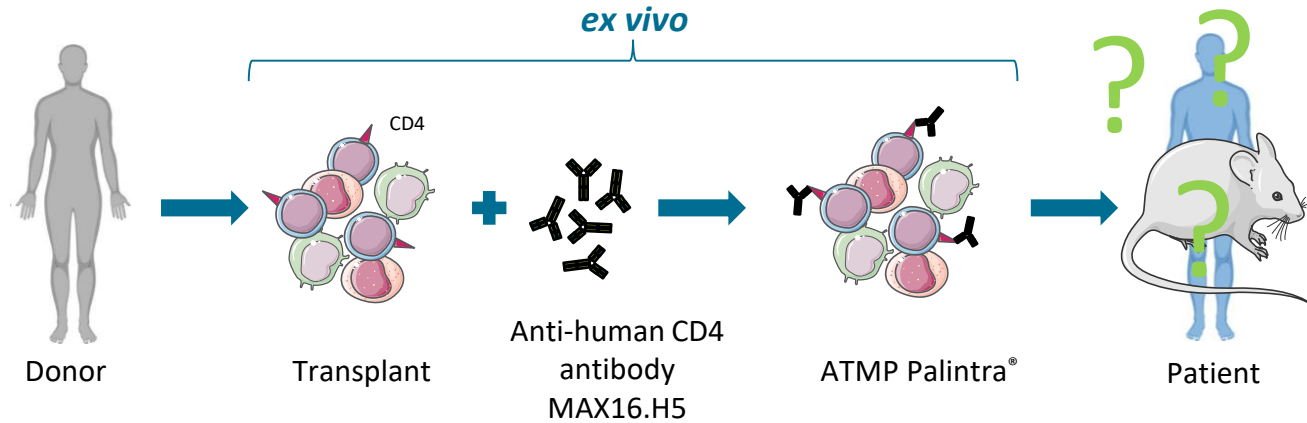
- Infections
- Relapse

Summary

Despite significant advances, aGVHD and cGVHD continue to be significant challenges and causes of HSCT-related morbidity and mortality, particularly for patients with corticosteroid-refractory disease. Even when GVHD is controlled by corticosteroids, many patients have adverse side effects and die from infections related to immunosuppression. Barriers to pro-

→ Most attractive approach for GvHD reduction by preserving T cell function → lowered risk of infections and relapse

OPTIX – Results so far



Has been shown in 3 mouse models +/- tumor cells (GvHD/GvL)

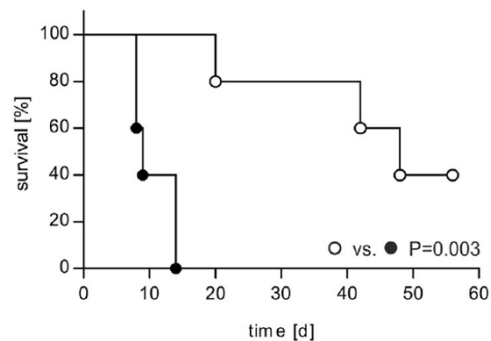
- Donor TTG-C57Bl/6 (USP) → Balb/c mice
- Donor TTG-C57Bl/6 (USP) → C3H/HeN mice
- Donor huPBMC in NOD/SCID mice

GvHD reduction/prevention



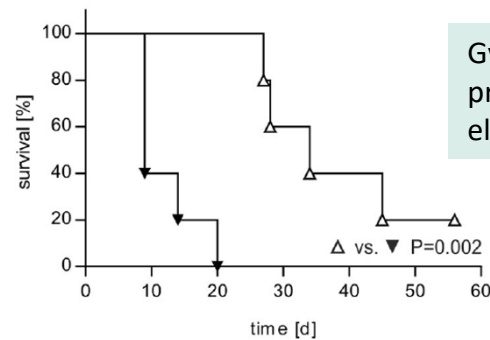
Recent data from ongoing experiments using GMP sample batch antibody:

GvHD mouse model



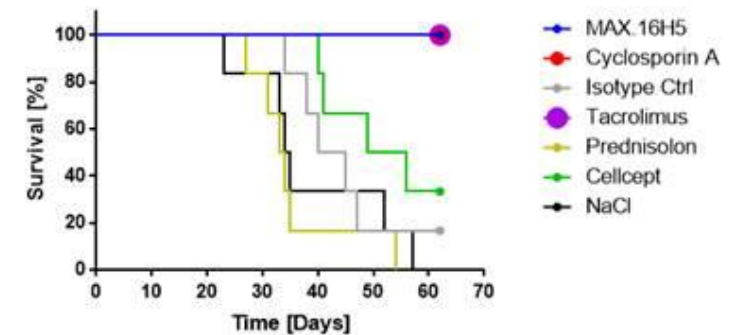
- Cell transplant
- Cell transplant incubated with MAX.16H5

GvHD mouse model including AML



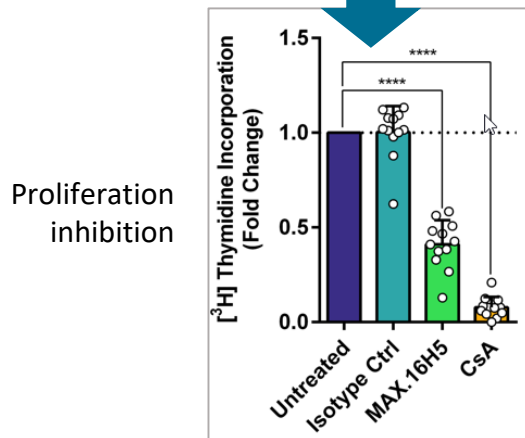
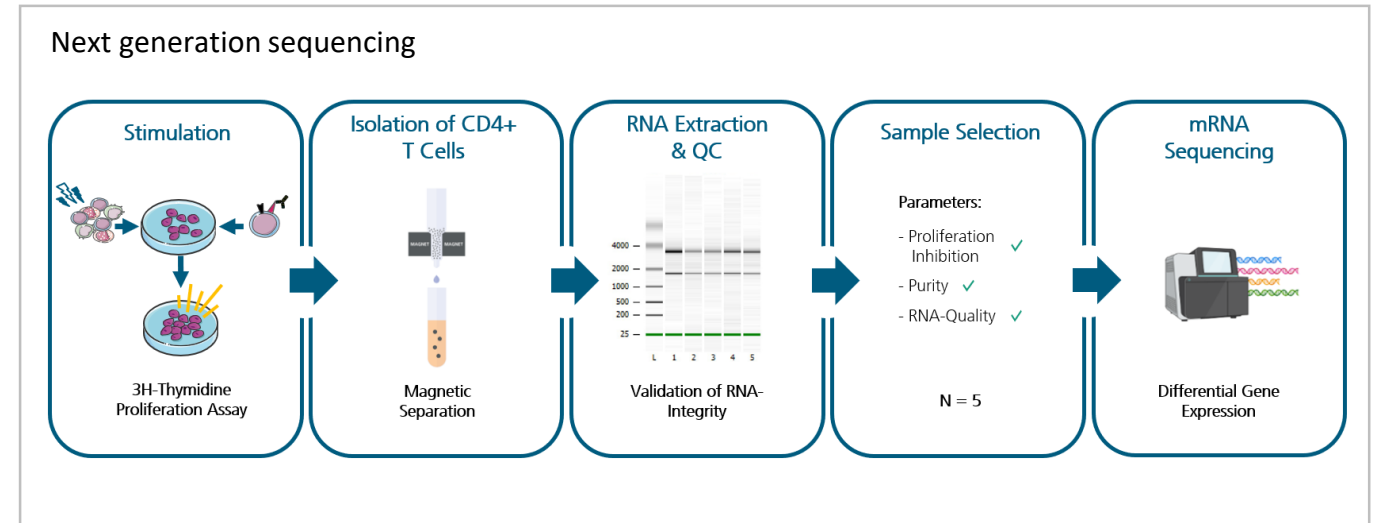
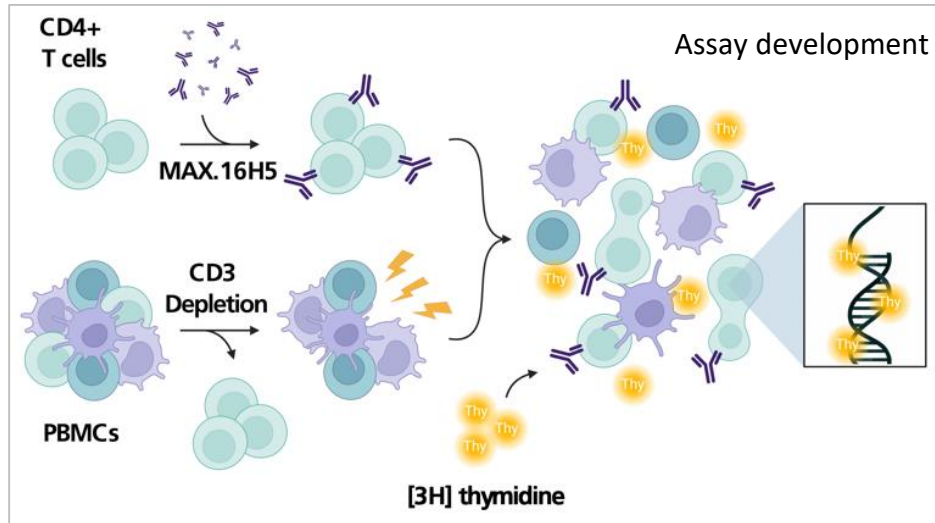
GvHD prevention by preservation of tumor elimination

- ▼ Cell transplant
- Δ Cell transplant incubated with MAX.16H5



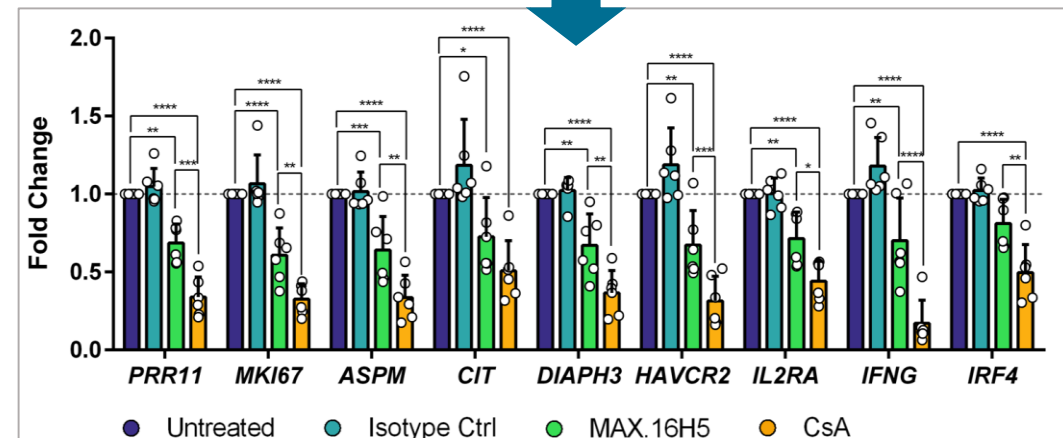
OPTIX – Results so far

Why is Palintra® functional?



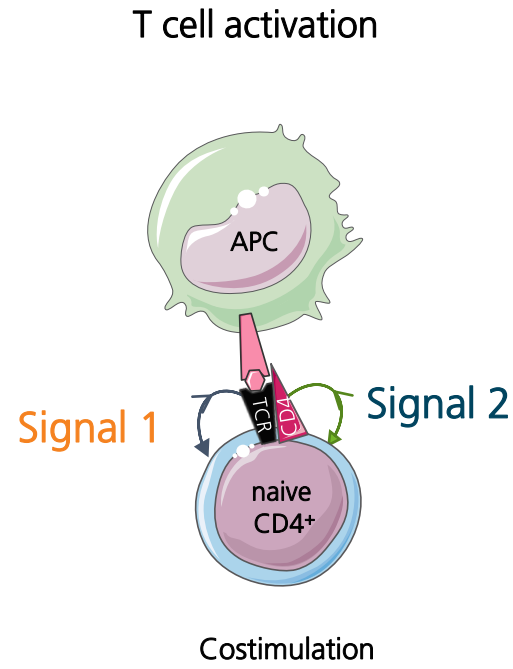
Differentially expressed genes involved in proliferation/T cell activation

Roth et al., *Front Immunol*, under review

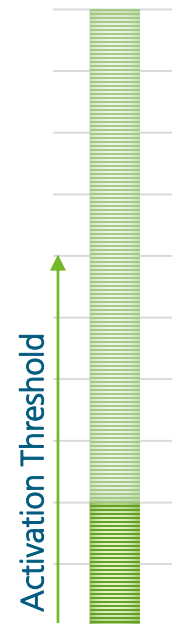


OPTIX – Results so far

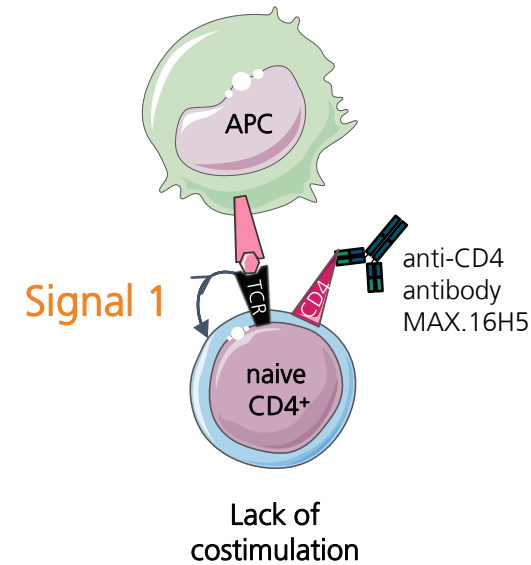
Why is Palintra® functional? → Induction of immune tolerance



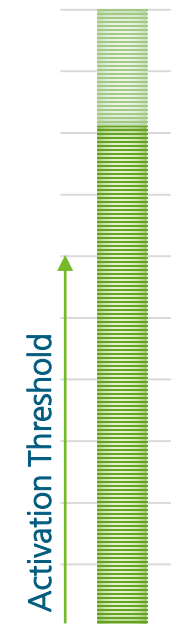
GvHD



Blockade by anti-CD4 antibody



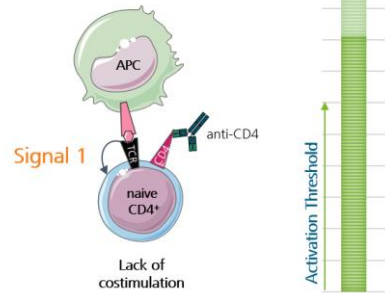
Hyporesponsiveness to alloantigens



OPTIX – Results so far

Palintra® mode-of-action

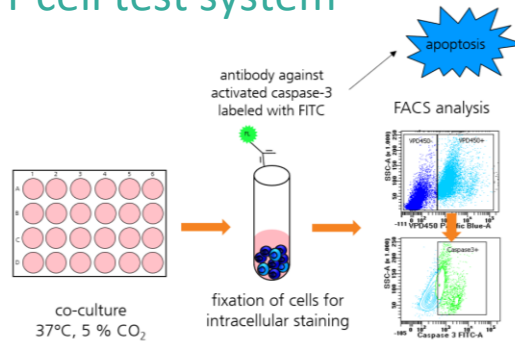
Blockade by anti-CD4 antibody



Hyporesponsiveness to alloantigens

→ Roth *et al.*, *Front Immunol*, under review

T cell test system



European and US patent published:
EP20757340.3/US2022283145A1

→ Zönnchen and Heimer *et al.*, in preparation

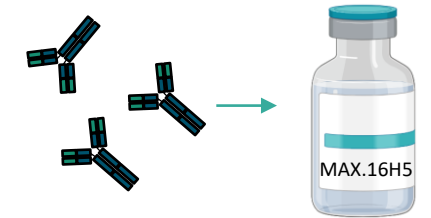
Ethical approvals for biobanking



Patient material from hematological indications:

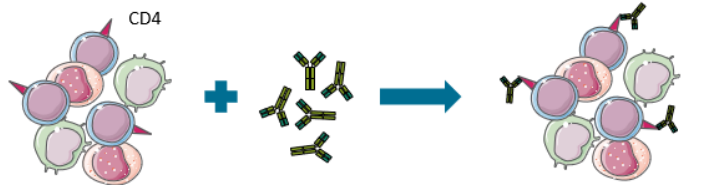
- Initial diagnosis
- After HCT

Master cell bank and GMP sample batch



MAX.16H5 antibody production

Process development for Palintra® production



Transplant

Anti-human CD4
antibody
MAX16.H5

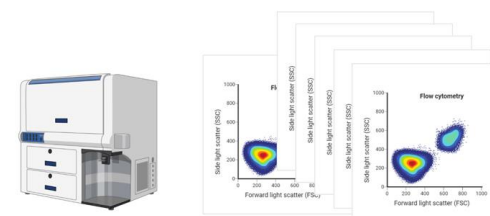
ATMP Palintra®

- Implementation of quality by design
- With wash/without wash
- Antibody saturation studies
- Shortened process
- 4th Scientific Advice 11/23

Paul-Ehrlich-Institut

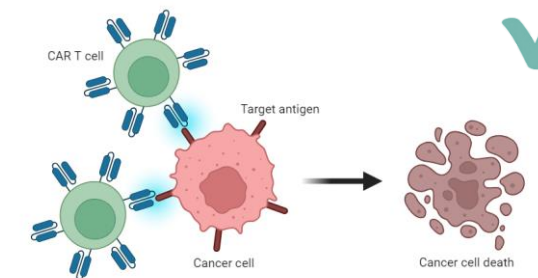


Software for AI-analysis flow cytometric data

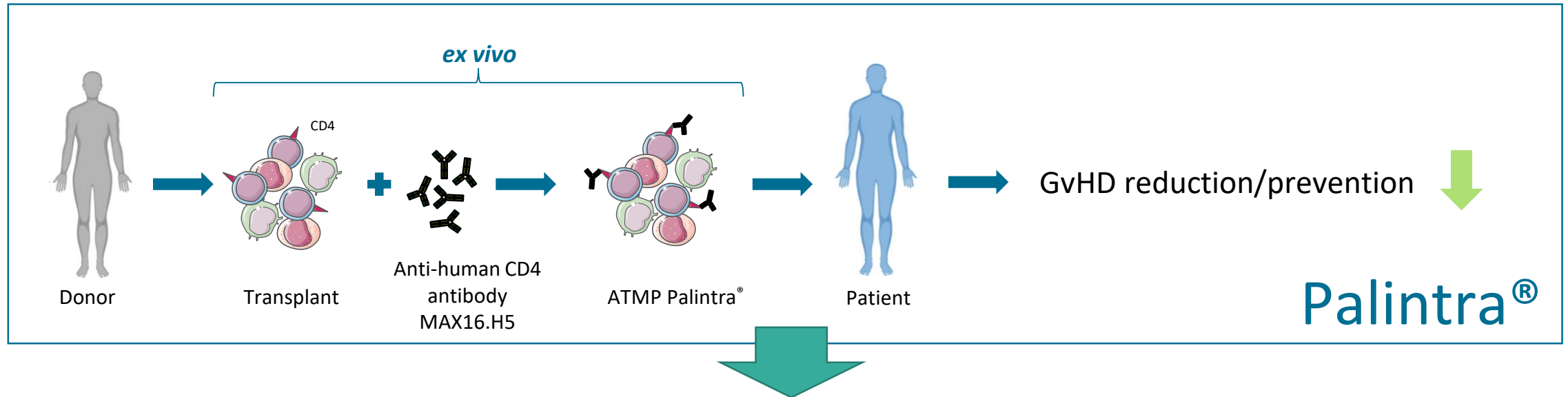


→ Popp *et al.*, *ISSRE*, submitted

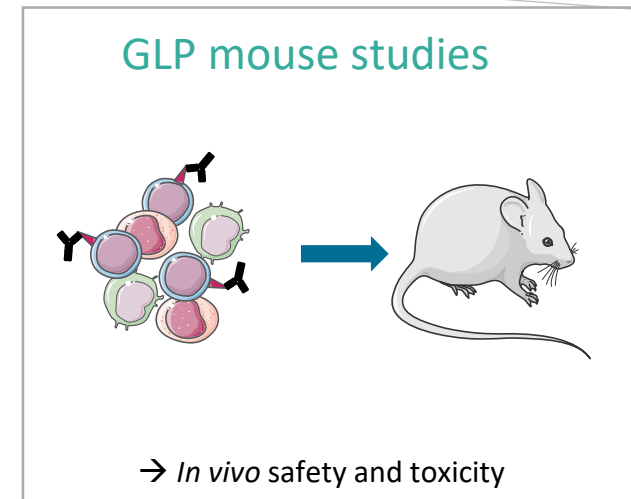
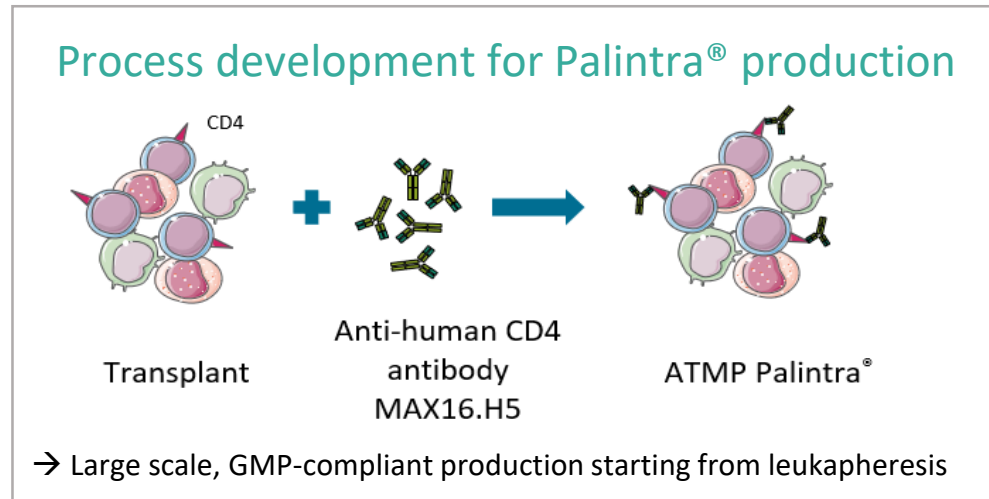
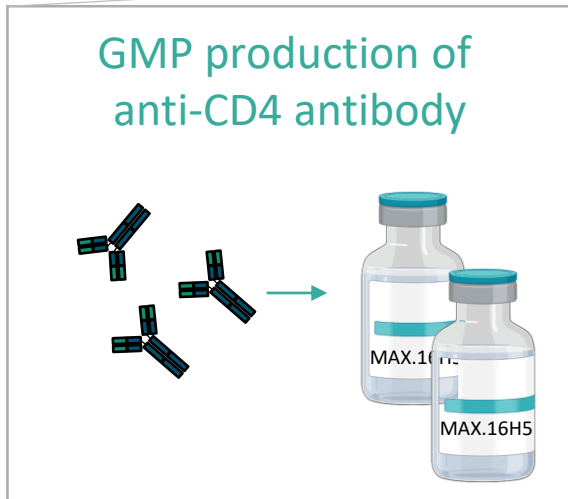
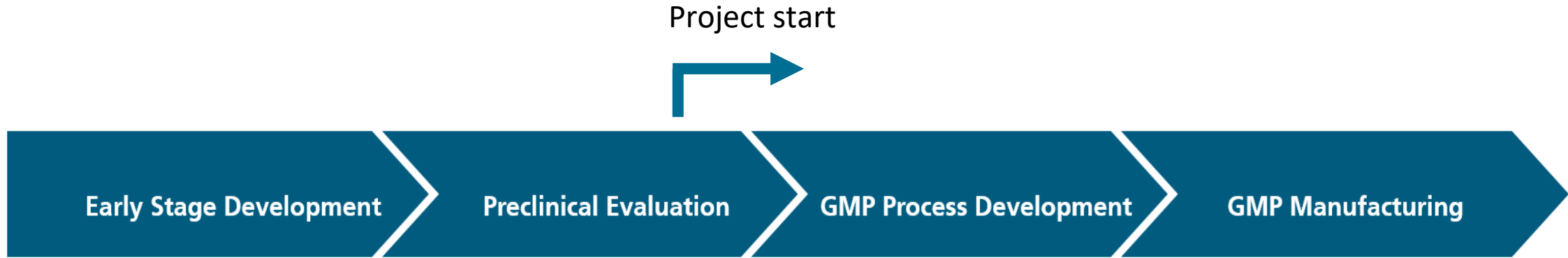
Approval for CAR-T cell application



OPTIX – Synergies



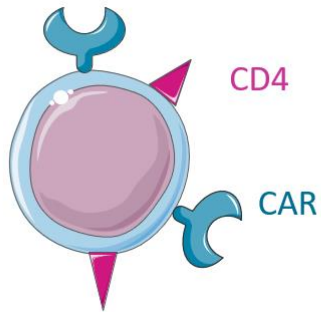
OPTIX – Outlook



- GMP production of Palintra[®] for phase I/II study (SaxoCell[®] Clinics)

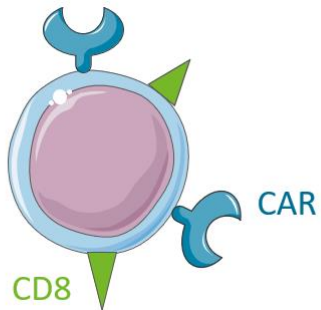
Indication extension

„CAR-Palintra®“



Matched donor,
allogeneic CAR-T cells?

Reduction of cytokine
release syndrome?



Acknowledgements

OPTIX Project Partners:

Dr. Uwe Krasselt
Lilly Stahl
Florian Koch



Fraunhofer

IZI



Tcell
Tolerance



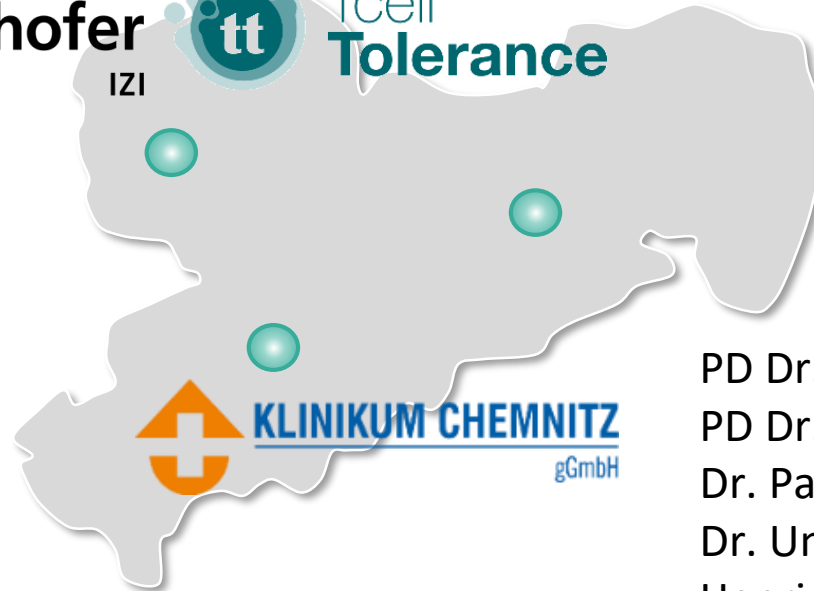
**CLUSTERS
4 FUTURE**
Innovationsnetzwerke
für unsere Zukunft



GEFÖRDERT VOM

Bundesministerium
für Bildung
und Forschung

PD Dr. Stephan Fricke
Dr. Ulrich Blache
Nadja Hilger
Kristina Roth
Bianca Zönnchen



KLINIKUM CHEMNITZ
gGmbH

SaxoCell Advisory Board

SaxoCell Hub

SaxoCell Speakers

PD Dr. Mathias Hänel
PD Dr. Stephan Fricke
Dr. Paul Warncke
Dr. Undine Meusch
Henriette Auerswald
Nadine Heimer



LIVING DRUGS

PRECISION THERAPY CLUSTER FOR SAXONY

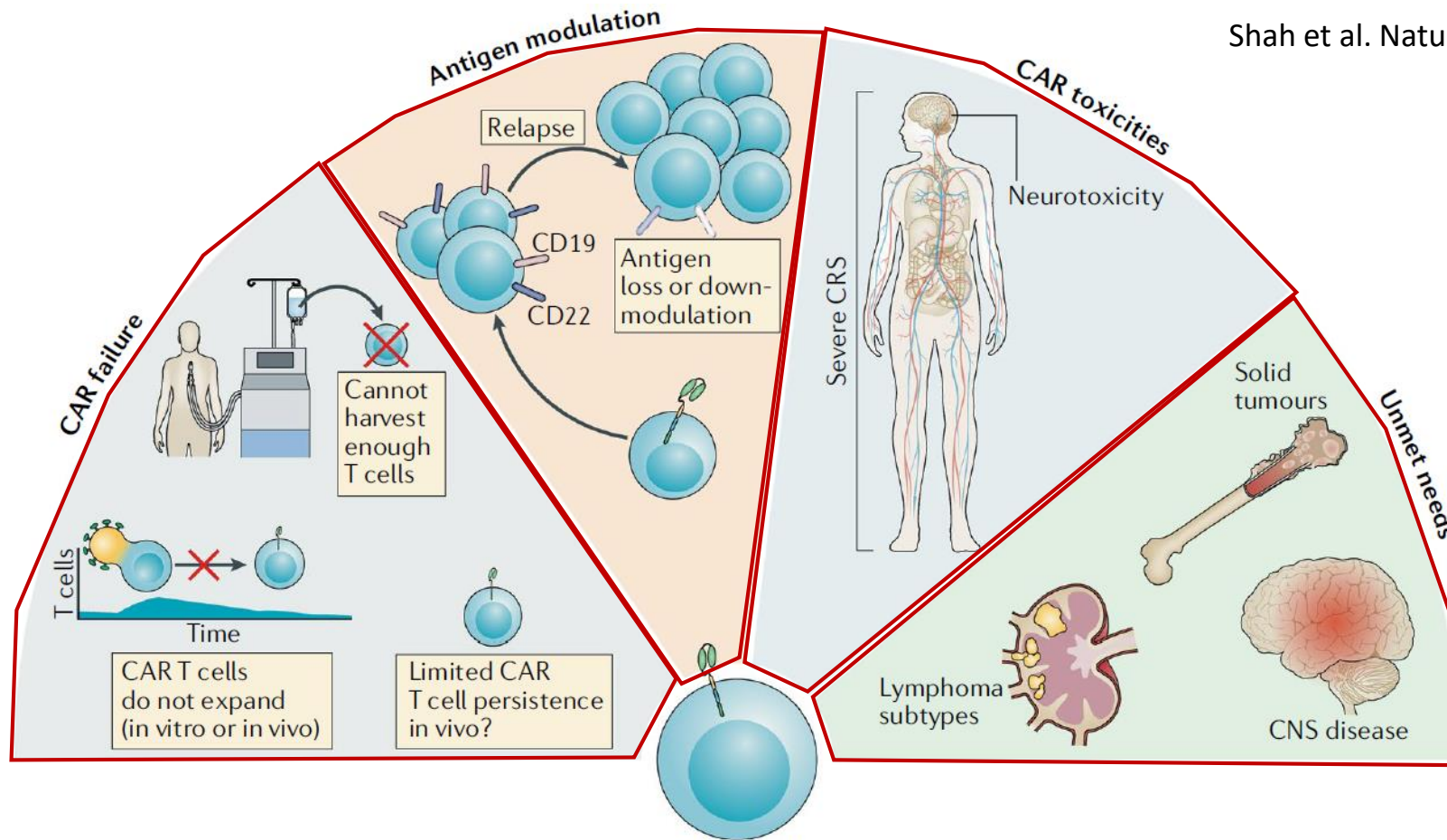
Empowering NK cell immunotherapy of cancer

CAR-NK4.0 / NK4Therapy (PIs: Ulrike Köhl / Achim Temme)

Dominik Schmiedel & Susanne Michen

Limitations of current cell therapies

Shah et al. Nature Reviews Clinical Oncology 2019



Failure of CAR T cell production

- Limited bone marrow function
- Exhausted T cell repertoire

Lack of CAR T cell function

- Low *in vivo* proliferation
- Antigen loss

CAR T cell

CAR toxicities

- CRS
- ICANS

Limited spectrum of diseases

- Mixed results in solid tumors and hematological malignancies apart from the B cell lineage

NK cells for immunotherapy of cancer

General information about Natural Killer (NK) cells

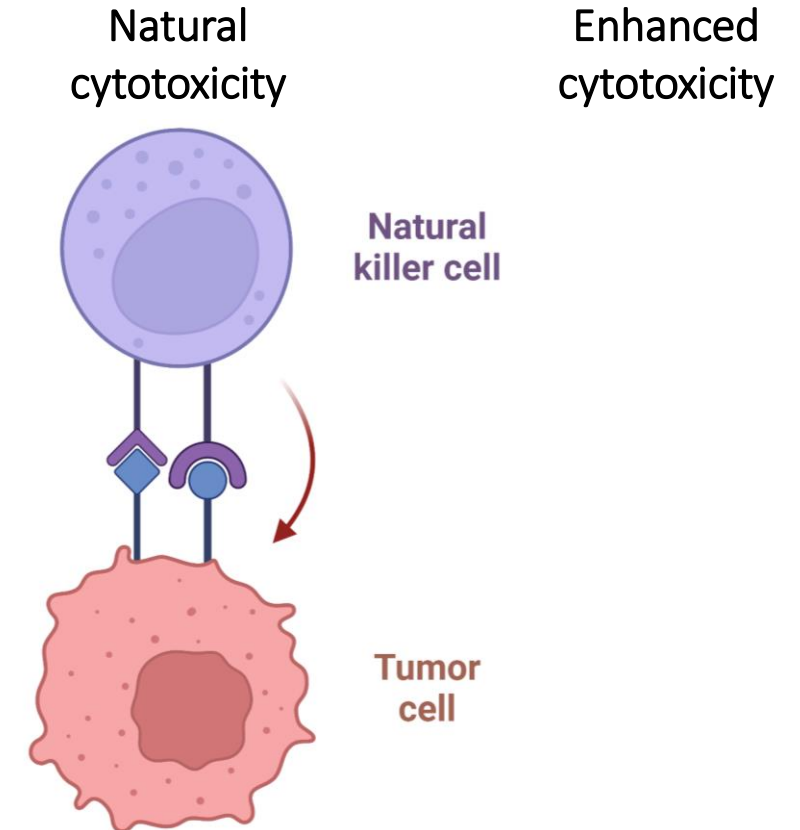
- Innate, cytotoxic lymphocytes
- Activating and inhibitory signals through a diverse and polymorphic innate receptor repertoire
- Natural recognition and killing of transformed cells
- Safe transplantation across HLA barriers (“off-the-shelf” cell therapy)

Limitations of NK cell immunotherapies

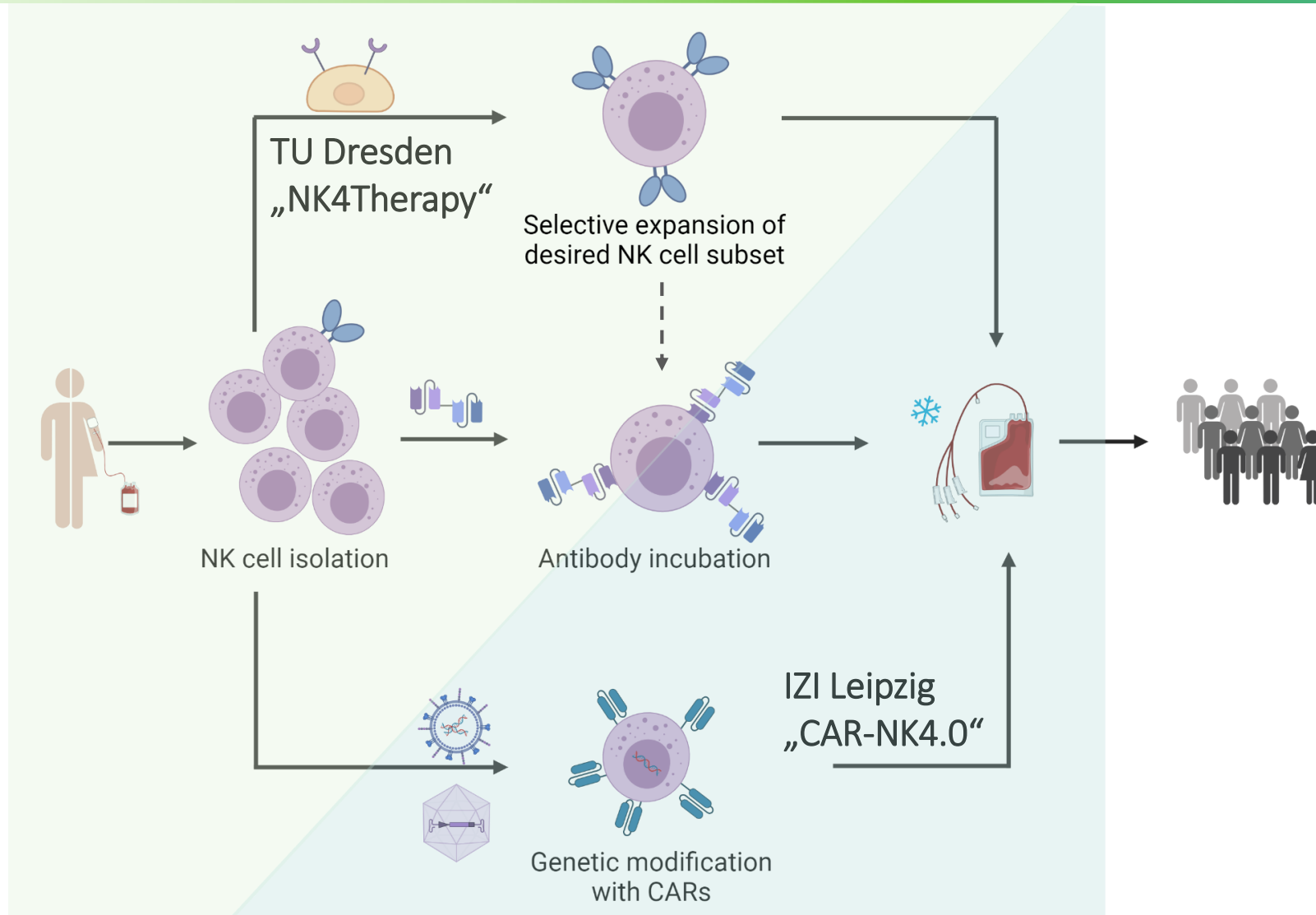
- Intrinsic resistance to genetic modification
- Insufficient expansion of modified NK cells

Enhancement of natural NK cell functions

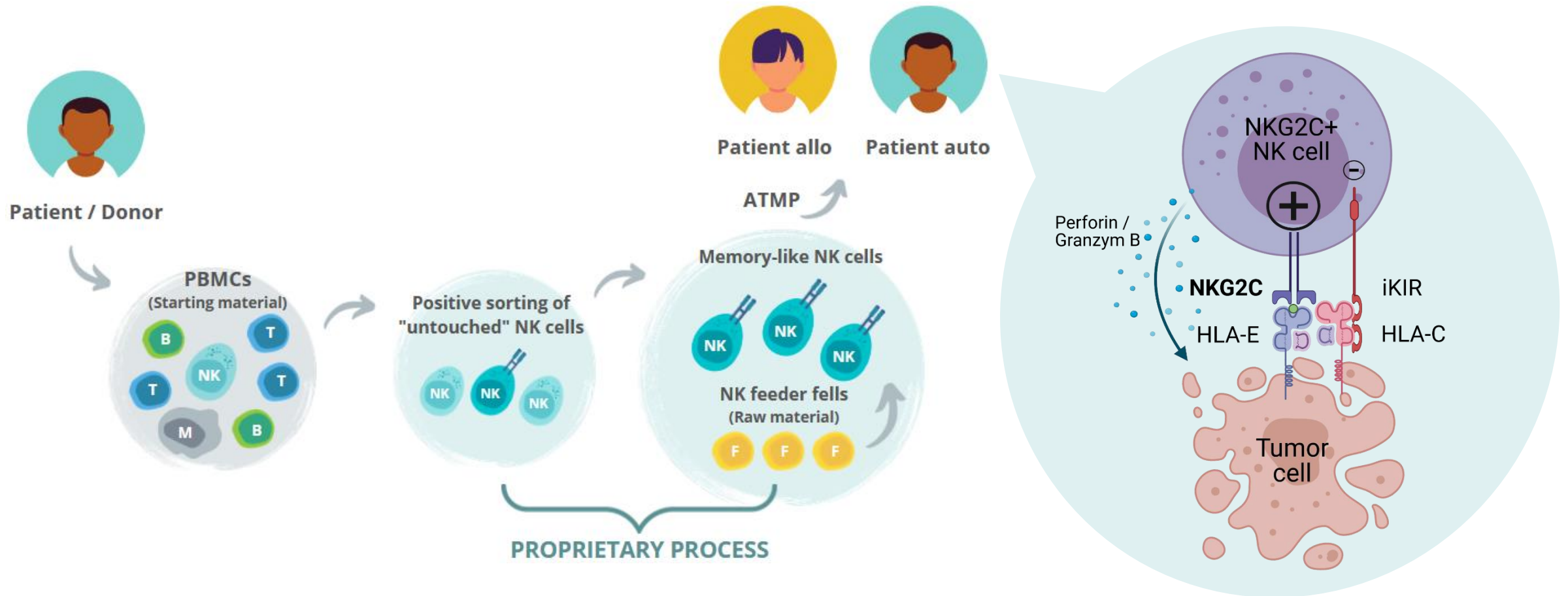
- Selective expansion of NK cell subsets, e.g. NKG2C+ NK cells with superior function
- Synergistic combination of NK cells and (bispecific) antibodies
- Genetic engineering, e.g. chimeric antigen receptors (CARs)



Empowering NK cells for cancer therapy



NK4Therapy: Establishment of GMP-compliant process for production of NKG2C+ NK cells

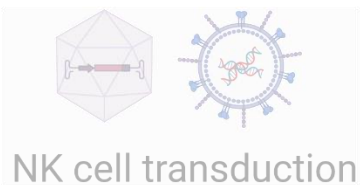
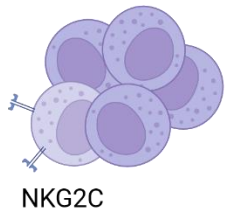


NK cell expansion via PC-3-based feeder cells

NK cell isolation

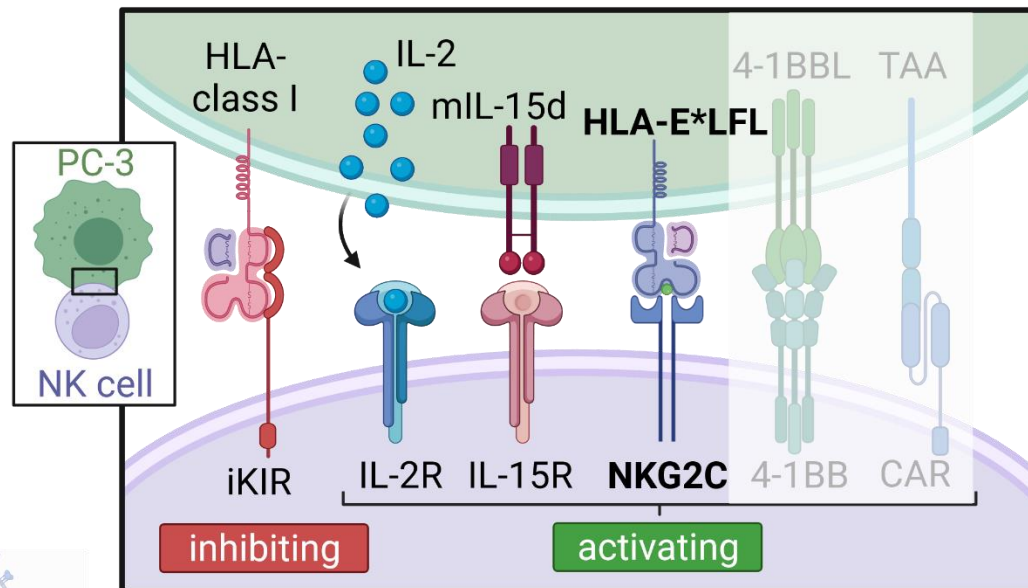


NK cells

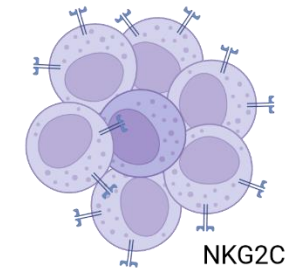


NK cell transduction

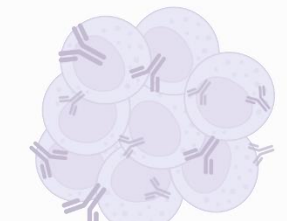
Expansion with PC-3-based feeder cells in bioreactors



NKG2C+ NK cells

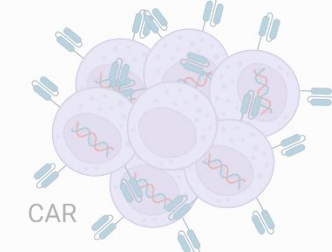


NK cells for ADCC

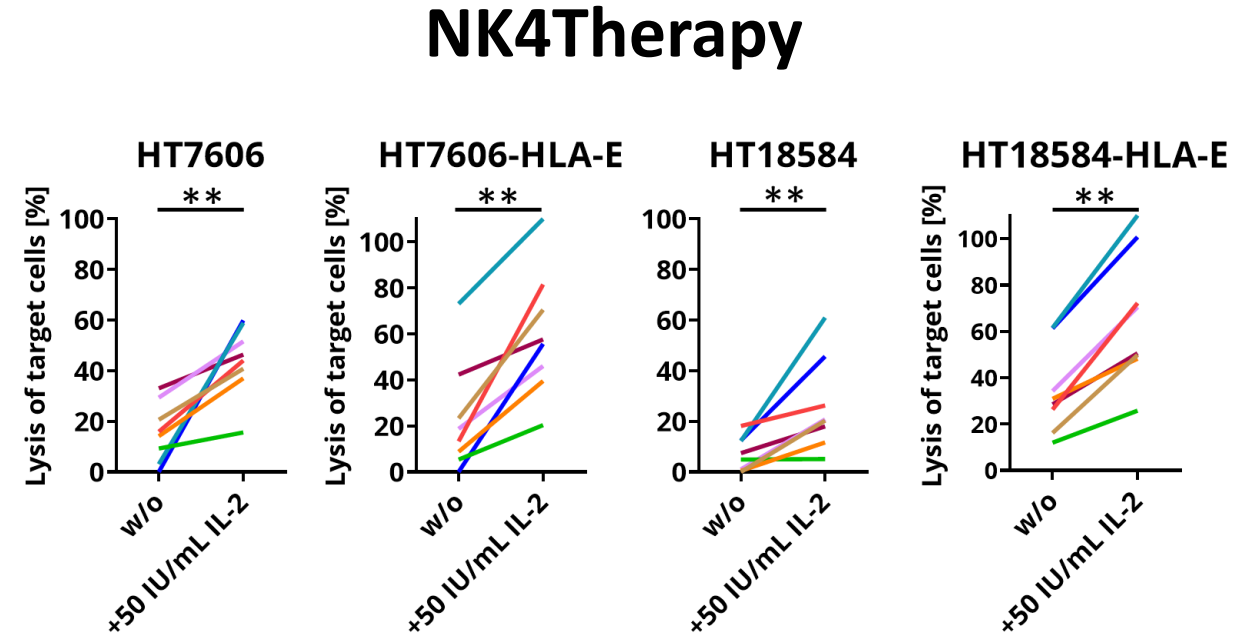
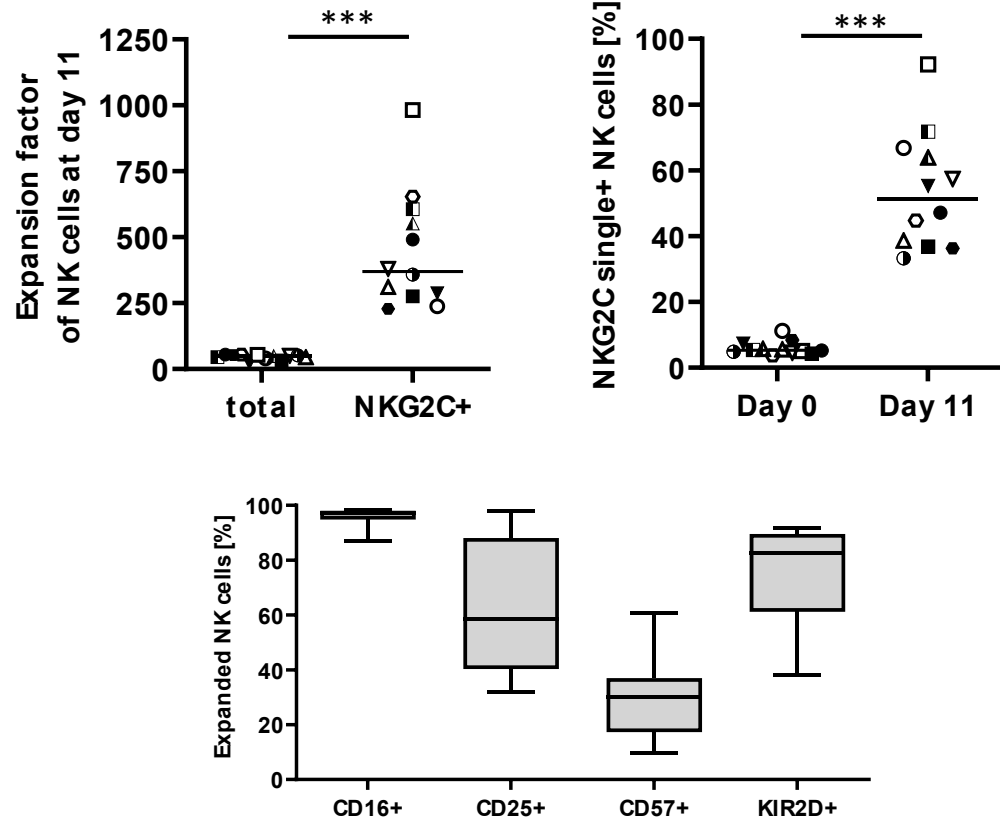


therapeutic antibodies

CAR-NK cells



Large-scale expansion of NKG2C+ NK cells



Murad et al., Int J Mol Sci., 2022
Michen et al., manuscript in preparation

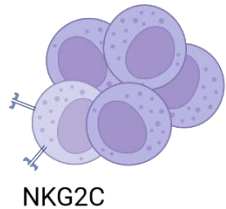
- PC-3-IL-2-mIL-15d-HLA-E*LFL feeder cells selective expand NKG2C+/CD25+ "memory-like" NK cells with cytotoxicity against HLA-E-overexpressing primary glioblastoma cells

NK cell expansion via PC-3-based feeder cells

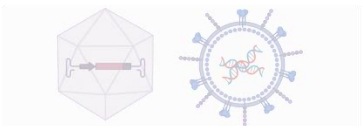
NK cell isolation



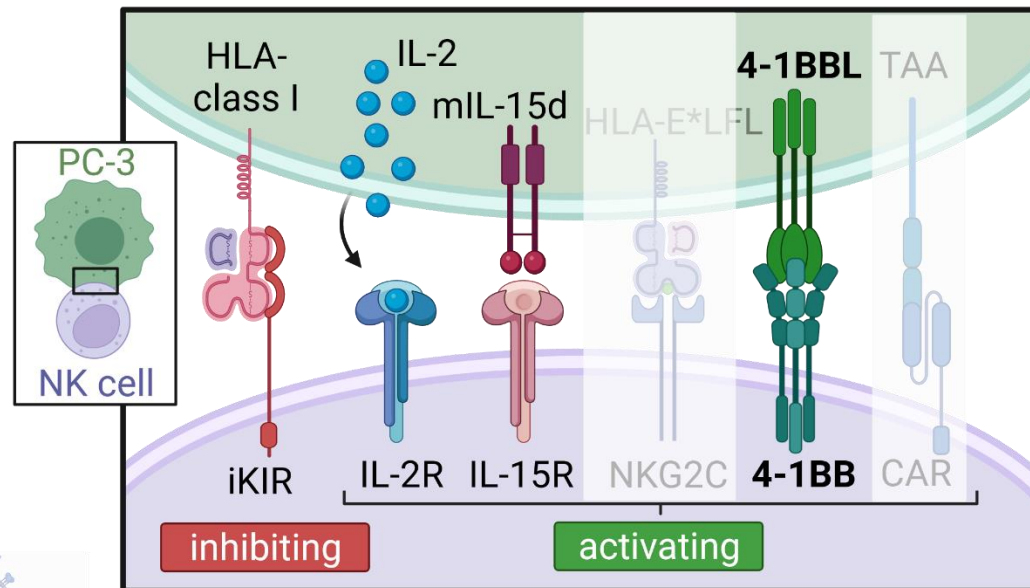
NK cells



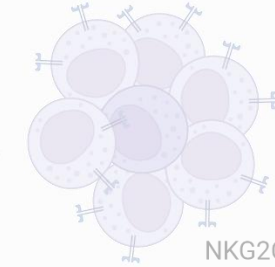
NK cell transduction



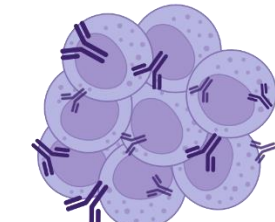
Expansion with PC-3-based feeder cells in bioreactors



NKG2C+ NK cells



NK cells for ADCC

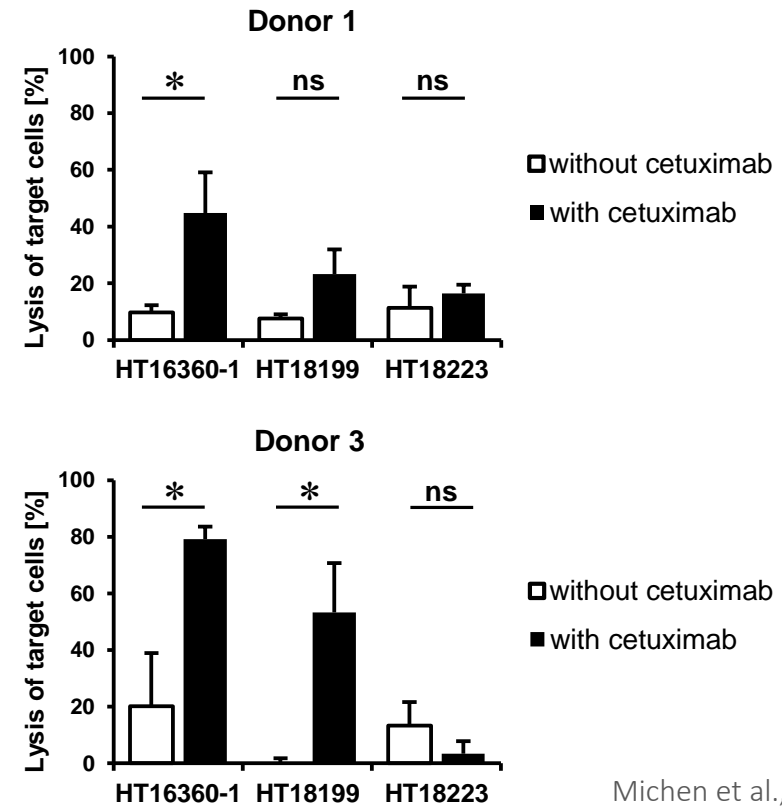
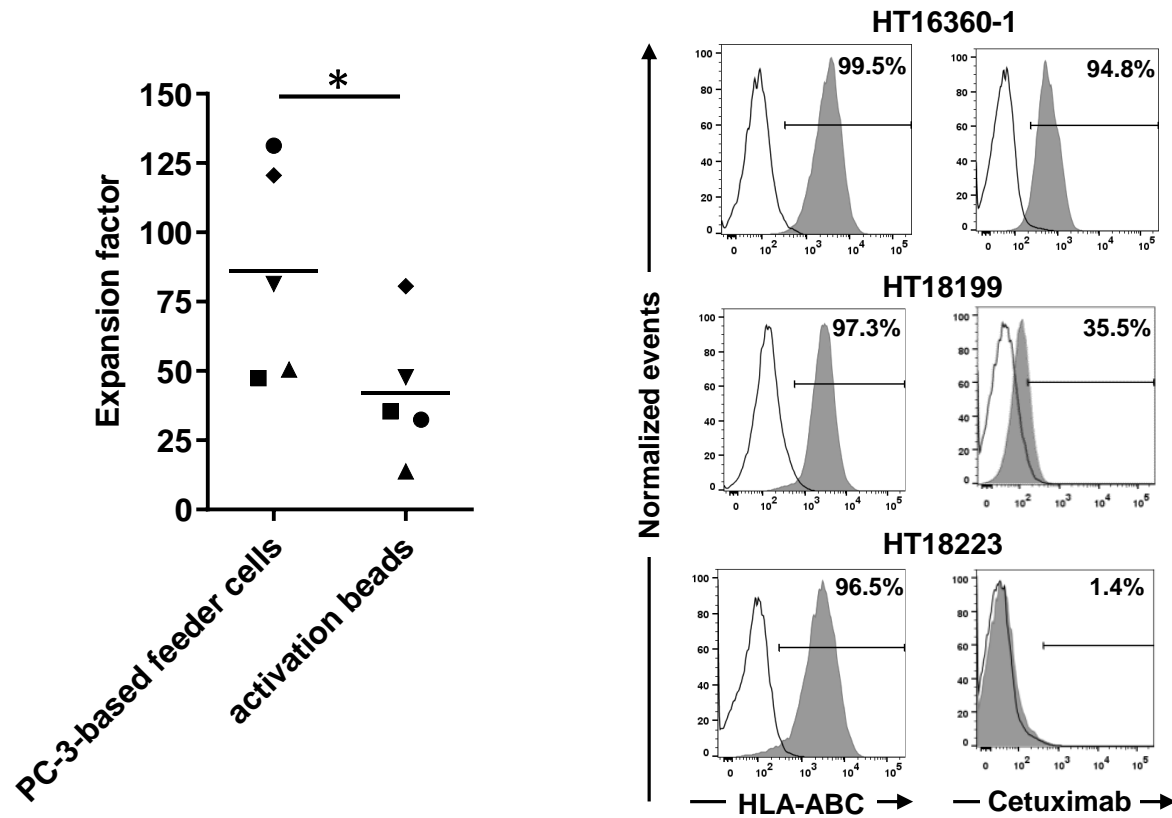


therapeutic antibodies

CAR-NK cells



ADCC of PC-3 feeder cell-expanded NK cells



Michen et al., Cytotherapy, 2020

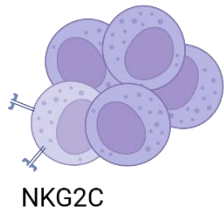
- NK cells expanded via PC3-IL-2-mIL-15d-4-1BBL feeder cells show marked antibody-dependent cellular cytotoxicity against EGFR-expressing primary glioblastoma cells when combined with cetuximab

NK cell expansion via PC-3-based feeder cells

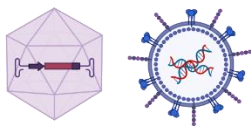
NK cell isolation



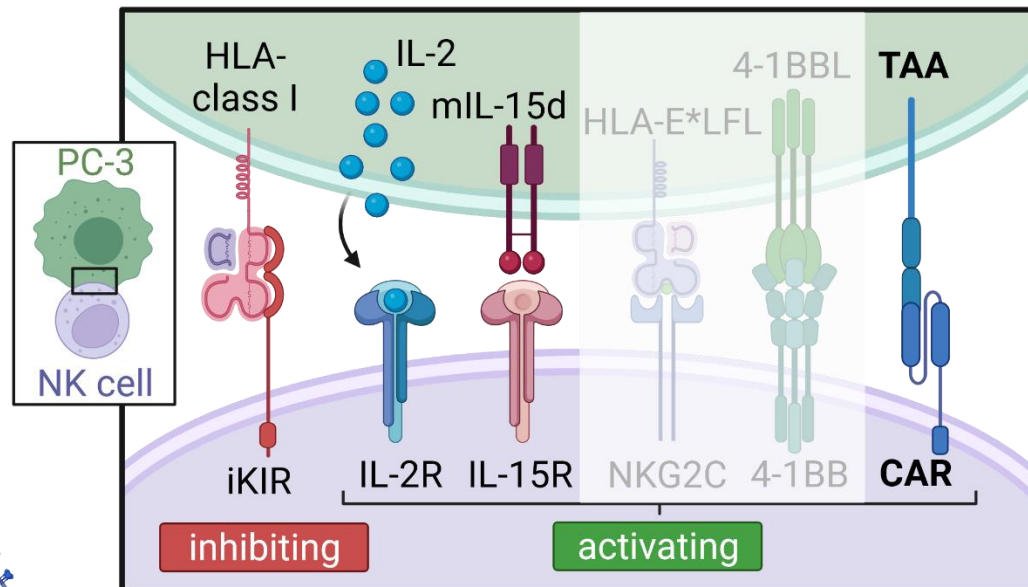
NK cells



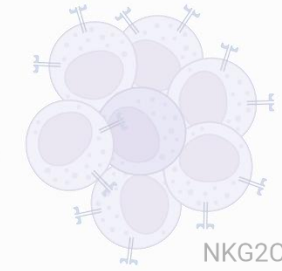
NK cell transduction



Expansion with PC-3-based feeder cells in bioreactors

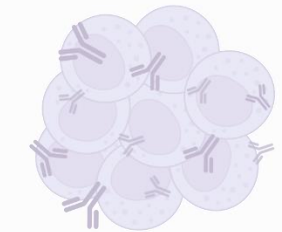


NKG2C+ NK cells



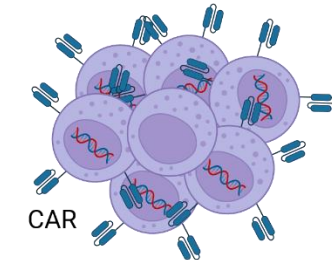
NKG2C

NK cells for ADCC



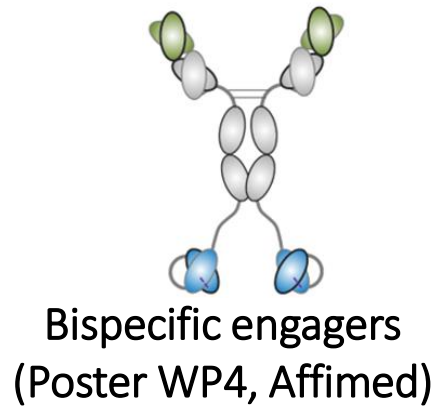
therapeutic antibodies

CAR-NK cells



see poster presentation
CARENK-AID
project/Anna
Possidente

CAR-NK4.0: generation of highly efficient NK effectors for clinical applications



Research to enhance cytotoxicity of effector cells

Development of bispecific CAR constructs

Combination CAR NK & multispecific ICES

AAV vector mediated delivery system into NK cells

Patents/
Publications

Optimization of CAR constructs & automated CAR NK cell manufacturing

SaxoCell®
SYSTEMS

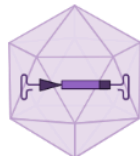
Study plan design
CAR NK cells in MDS

SaxoCell®
CLINICS

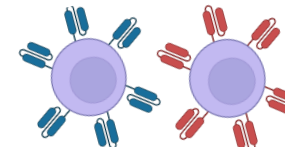


Clinical Manufacturing
(Poster WP1, Miltenyi)

Enhanced transgene delivery
(Poster WP5)

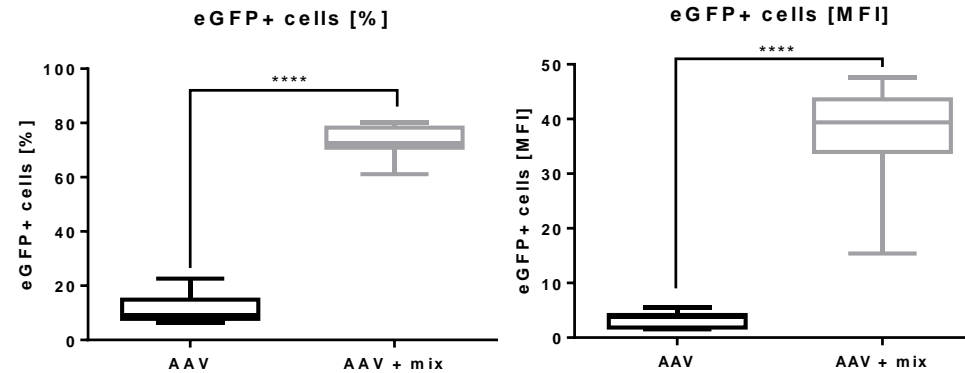
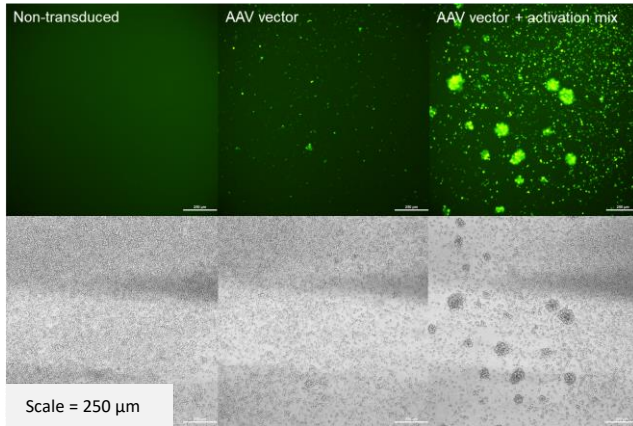


Tumor analysis & dual-specific CAR-NK cells
(Poster WP3)



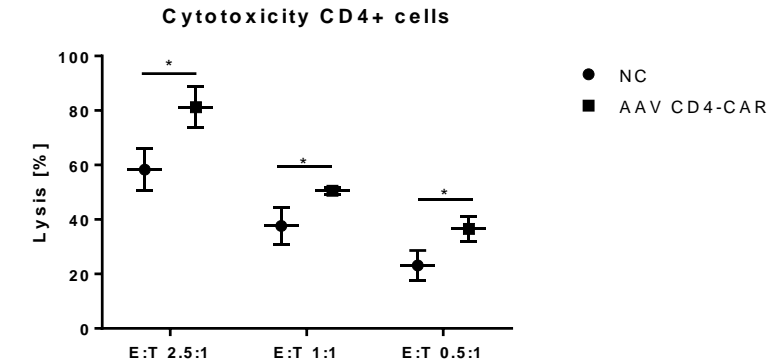
AAV vectors for primary human NK cells

AAV vector selection and optimized transduction



- First successful and efficient direct transgene expression of human primary NK cells with AAV vectors
- Basal transgene expression level of AAV vectors is highly donor-dependent
 - Mainly around 10-30%
- Addition of activation mix increases transgene expression level to ~80%
 - Independently of the donor!
- First AAV-CAR constructs (CD19-CAR, CD4-CAR) are produced and currently tested

CD4-CAR in NK cells



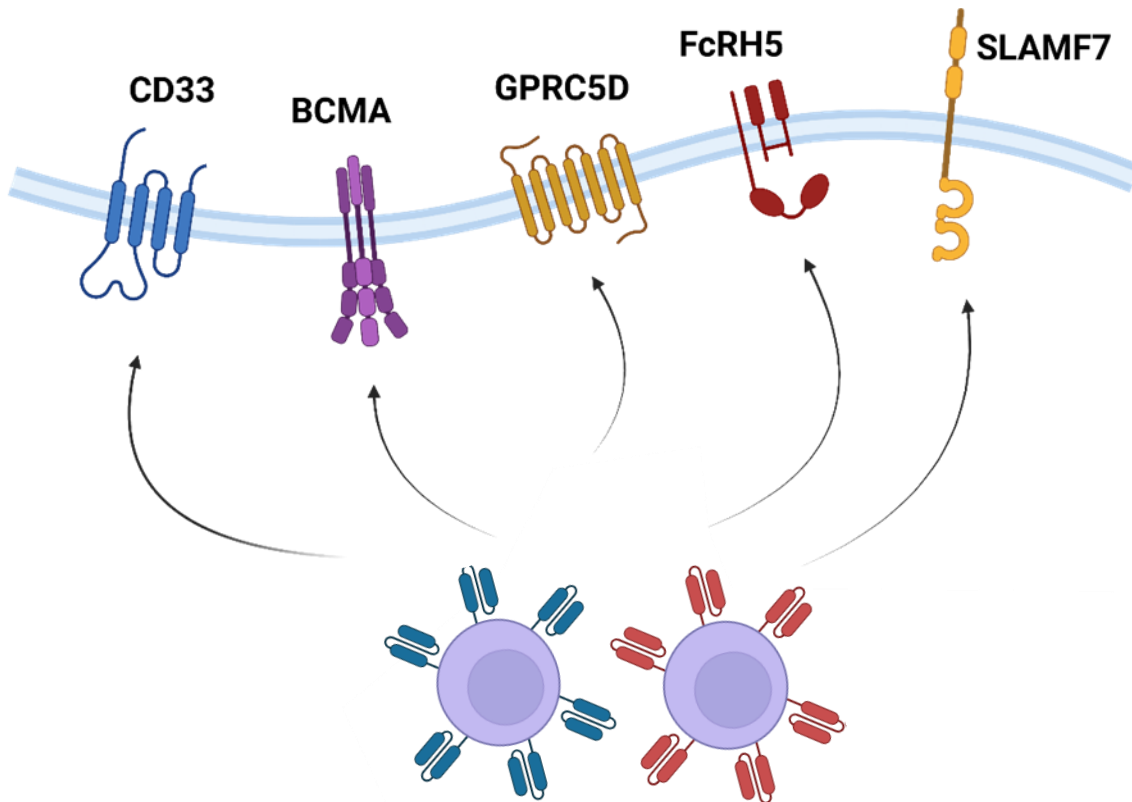
Project:

Prof. Dr. Hildegard Büning, MHH
Prof. Dr. Ulrich Hacker, UKL
Dr. Claire Fabian, Fraunhofer IZI

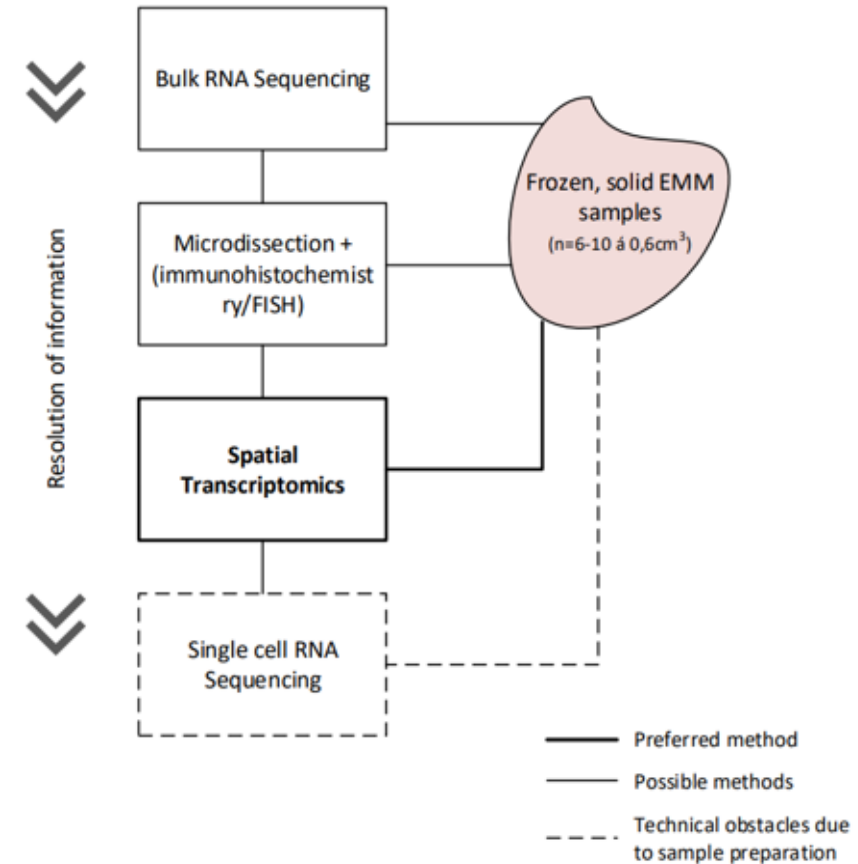


Dual CAR-NK cells targeting multiple myeloma

Generation of an array of monospecific CAR-NK cells

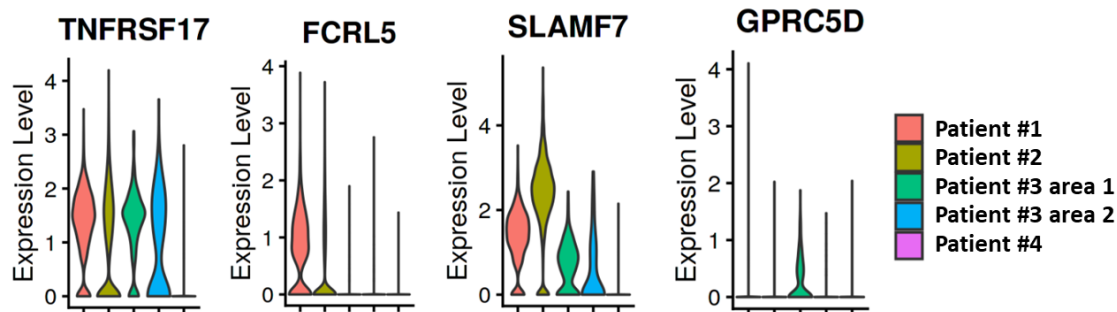


EMM sampling and spatial transcriptomics

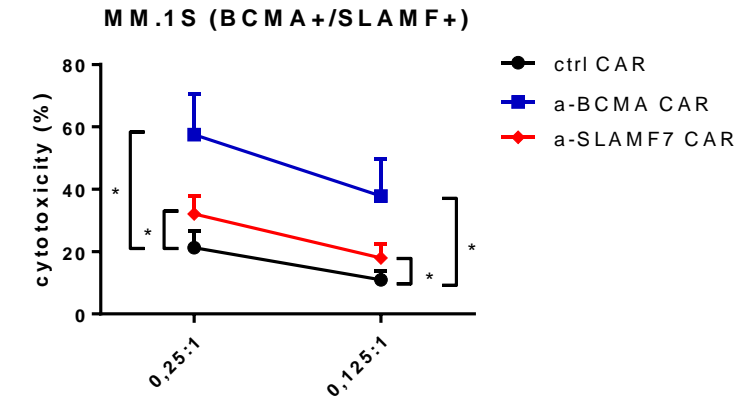
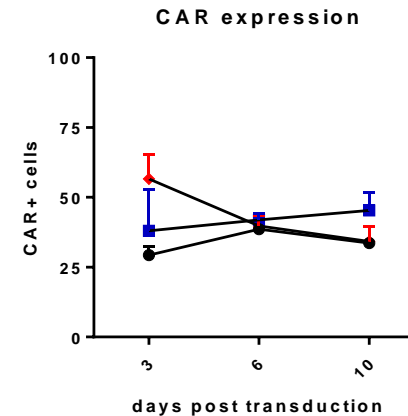


CAR-NK cells targeting multiple myeloma

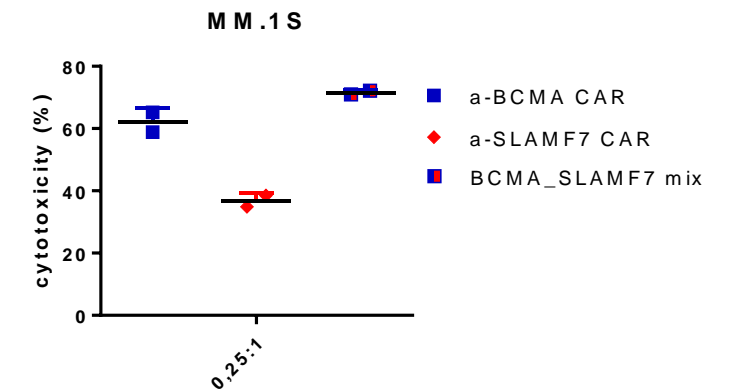
EMM sampling and spatial transcriptomics



Expression tests and functional validation



- Next steps: testing of cytotoxicity towards multiple myeloma patient samples using mono- and multi-specific CAR-NK cells



Synergies: Bridging SaxoCell and the NK Fraunhofer cluster of excellence → patent on NK transduction method

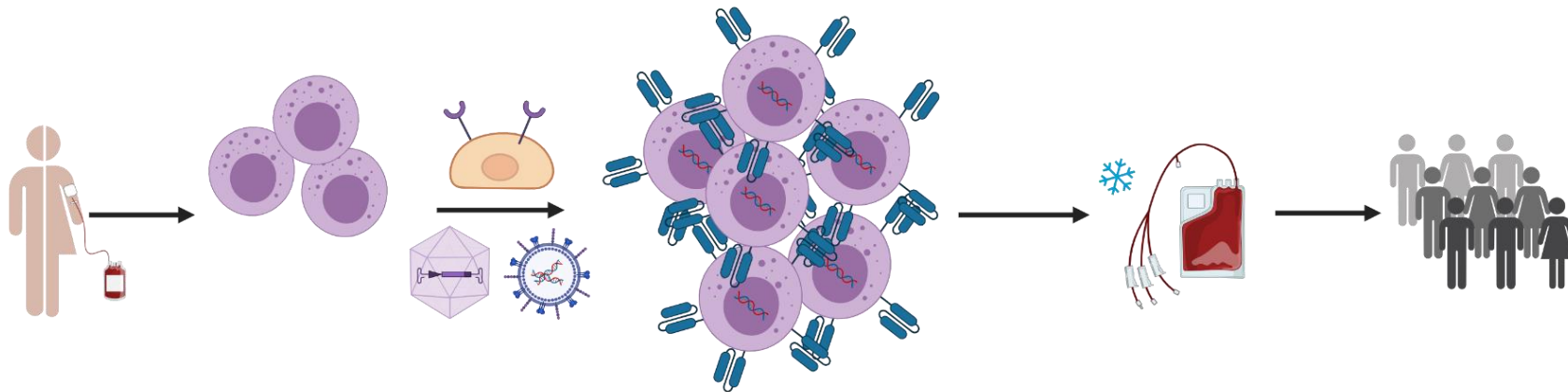
NK cells for immunotherapy of cancer

Achievements

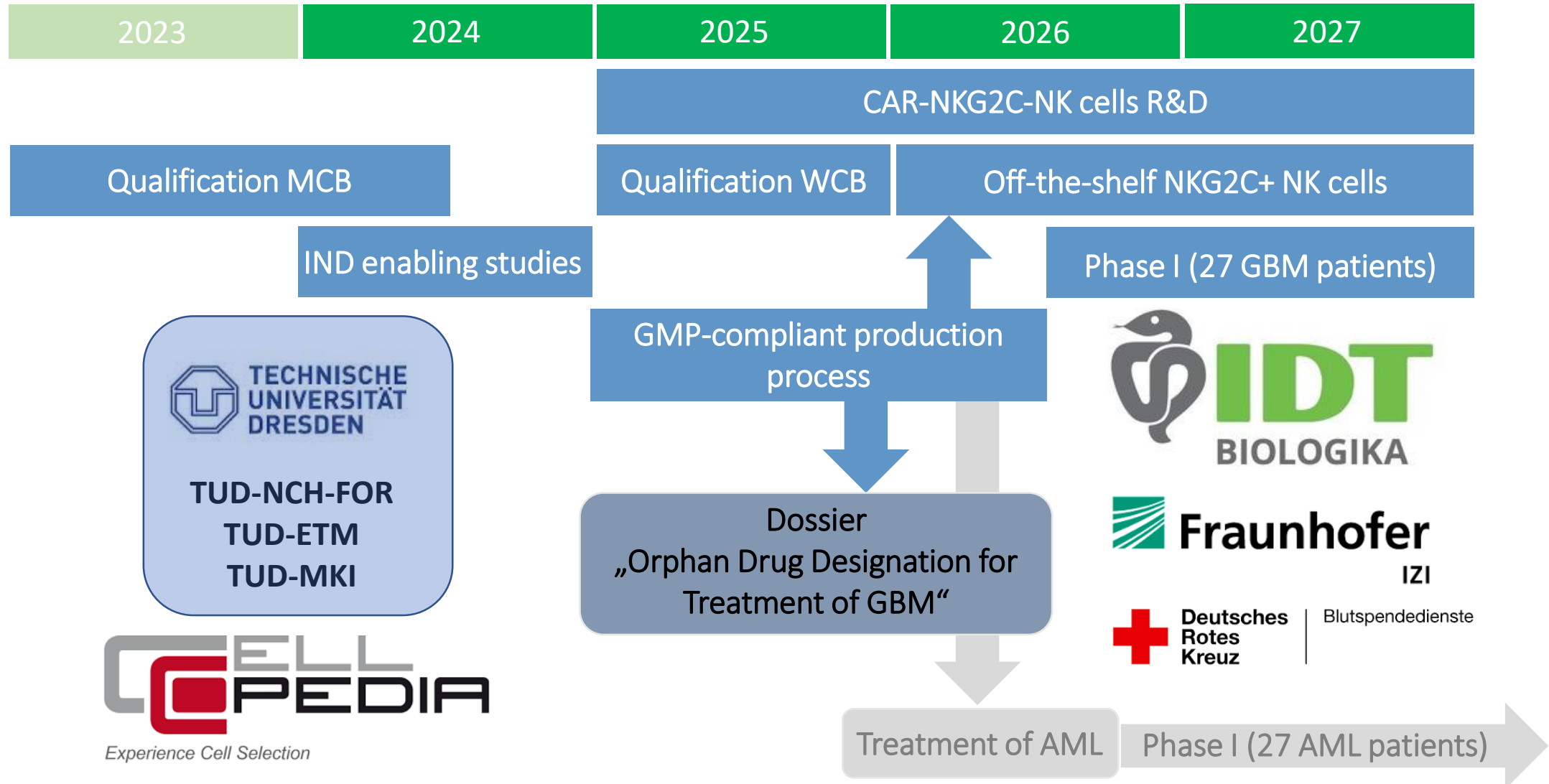
- Improved NK cell isolation and expansion
- Production of NK cells in clinical scale, progress in manufacturing automation (Blache et al., 2022)
- Significant progress in the generation of CAR-NK cells using viral vectors
→ Patent pending for transduction of non-dividing immune cells
- Significant enhancement of natural, antibody-, or CAR-based anti-cancer effects (Michen et al., 2020; Murad et al., 2022; Feigl et al., 2023; Ruppel et al. 2023)

Tying the ends of CAR-NK4.0 / NK4Therapy

- Selective expansion of CAR-NK cells via PC-3 feeder cells for clinical use



NK4Therapy: Outlook



CAR-NK4.0: Outlook

2022 -2024

Technology development

Clinical manufacturing protocols

Efficacy enhancement



2025 -2027

GMP readiness

Tech transfer from lab to manufacturing scale of application-specific gene transfer technologies



2028 - 2030

Clinical implementation

Automated manufacturing of NK cells using high-end gene engineering for clinical studies



Thank you for your attention!

For questions and further information please contact:

Dr. Dominik Schmiedel
dominik.schmiedel@izi.fraunhofer.de

Dr. Susanne Michen
susanne.michen@ukdd.de

Platforms: Systems, Omics, Clinics; Hub



Day 1: Monday 11.9.23

14:50-15:20

Systems

Tino Hammer (TUD) & Dr. Alexander Oeser (UL, ICCAS)

tino.hammer@mdtbcells.com, Alexander.Oeser@medizin.uni-leipzig.de

Omics

Juliana Roscito (TUD), juliana.rosquito@tu-dresden.de

Clinics

Silke Gloaguen (Uni Leipzig), Silke.Gloaguen@medizin.uni-leipzig.de

Hub

Dorit Teichmann (TUD) & Ilka Henze (IZI)

dorit.teichmann@tu-dresden.de ; ilka.henze@izi.fraunhofer.de

PLATFORM – SYSTEMS

Prof. Dr. Rüdiger, Dr. Freund
TU Dresden



Prof. Dr. Neumuth
Uni Leipzig, ICCAS



Prof. Dr. Rahm
Uni Leipzig, ScaDS.AI



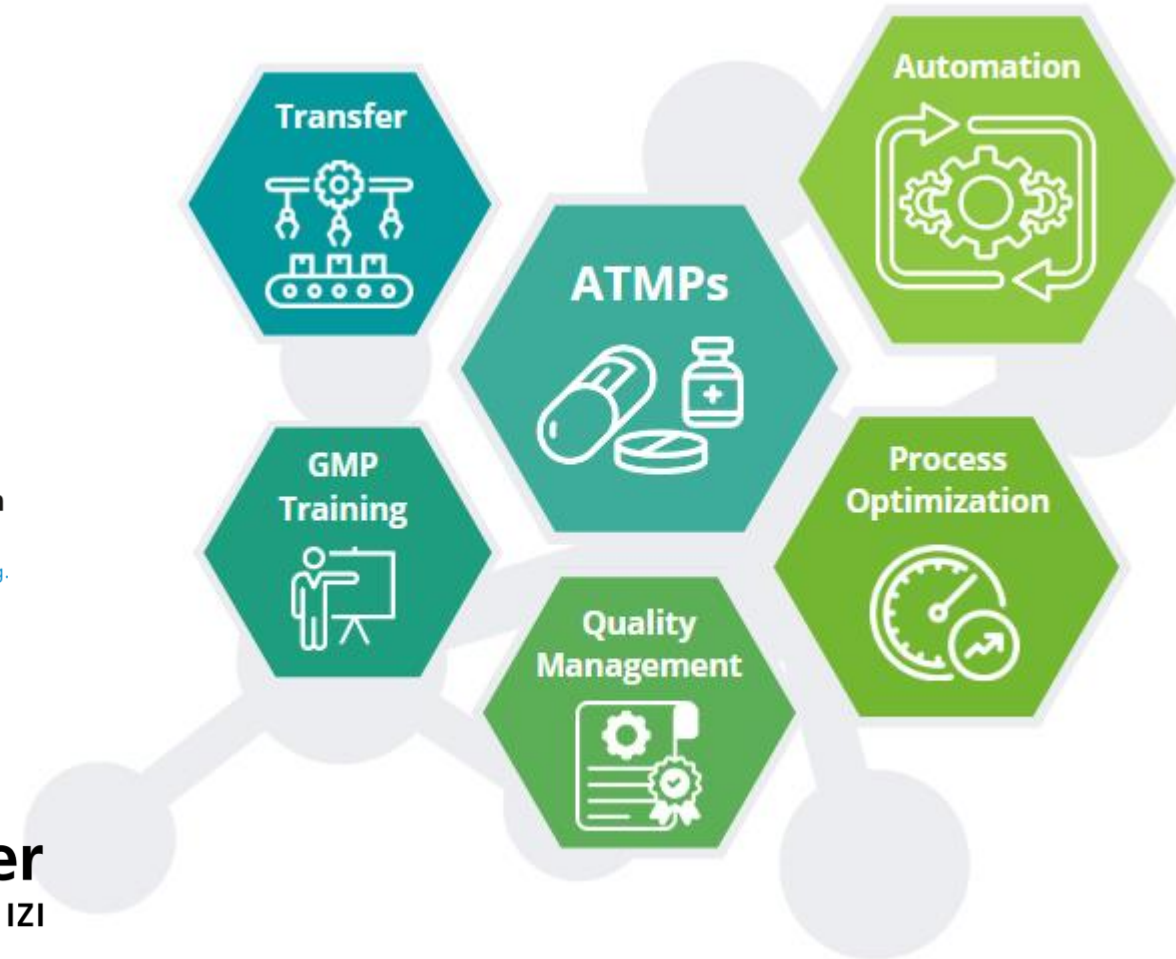
Prof. Dr. Henschler
Uni Leipzig, UKL



Prof. Dr. Pompe, Dr. Jahnke
Uni Leipzig, BBZ



PD Dr. Fricke, Dr. Blache
Fraunhofer IZI, Coordination



SYSTEMS – Objectives

General Objectives:

Establish leading ATMP-Infrastructure

- Automated production equipment for upscaling
- Qualified personnel

Phase I Objectives:

Develop ATMP solution modules

- **GMP automation concept** using 3D bioreactors
- **Artificial Intelligence concept** using sensors
- **GMP Quality Management concept** using supply-chain-management
- **GMP training concept**

SYSTEMS – Results so far

✓ WP1

- **Use case MSC:** from manual small scale to automated large scale

as planned – Daniel Freund
CRTD

✓ WP2

- **GMP Quality Management** concept using supply-chain-management

see next slides – Alexander
Oeser
ICCAS

✓ WP3

- **Artificial Intelligence** concept using sensors

see next slides – Maximilian
Joas
ScaDS.AI

✓ WP4

- **Technical GMP-Training** concept

see last meeting – Ulrich Blache
FhG IZI

✓ WP5

- **Online GMP-Training** concept

next meeting

✓ WP6

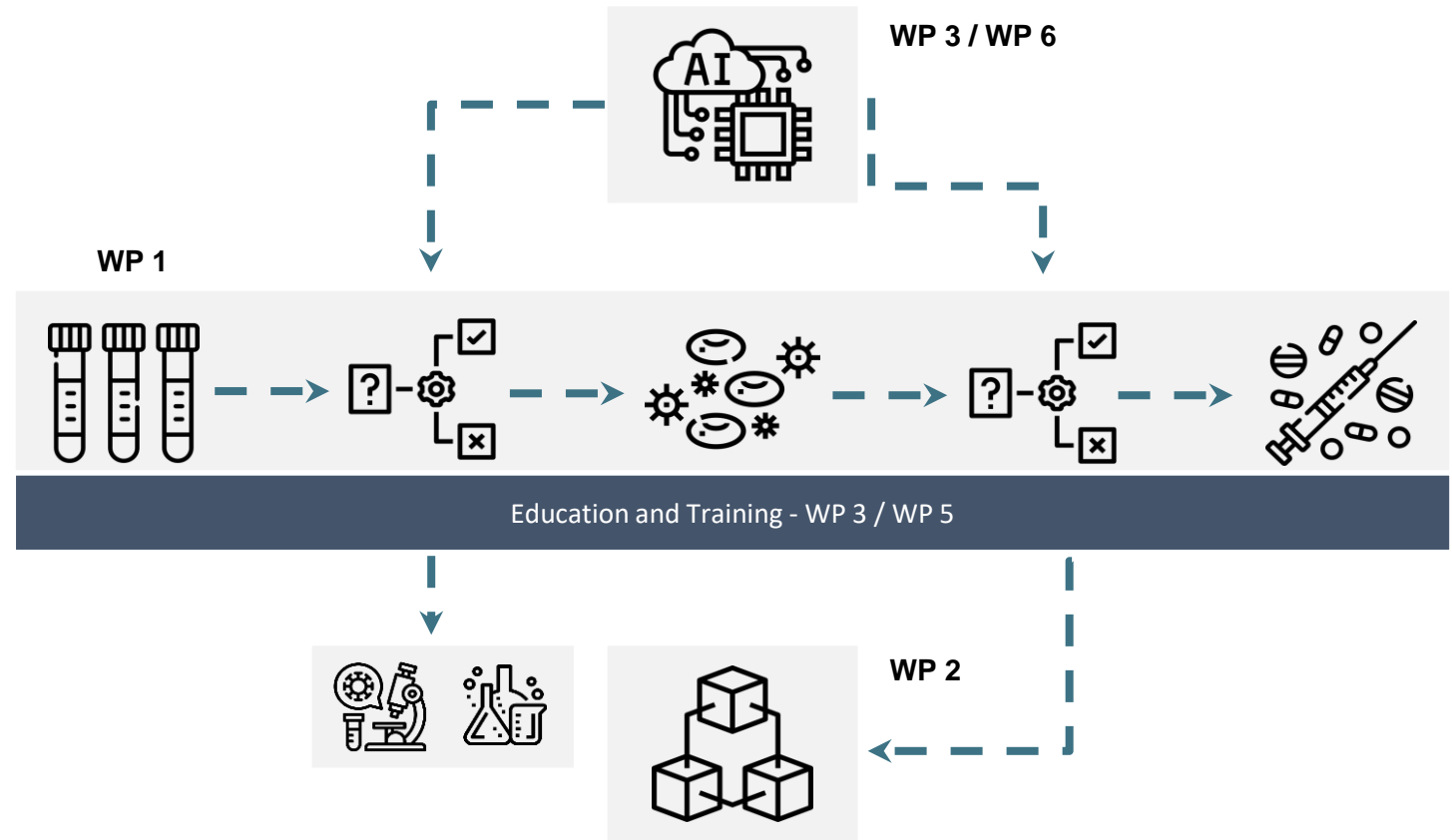
- bioelectronic **Cell analysis** concept

next meeting

SYSTEMS — focus: QM and AI

The overarching goal of SaxoCell SYSTEMS is to provide a **proof-of-principle platform** for sensor- and AI-assisted quality control in cell therapeutics manufacturing.

Work packages focus on information- and process modeling, system development and integration, AI-enriched monitoring components and holistic education and training along the manufacturing pathway.




SYSTEMS — Result: AI confluence estimation



SaxoCell Confluence Detection

Upload Cell Image

 Drag and drop files here
Limit 200MB per file

[Browse files](#)

[Predict all](#)

A sample use case of our confluence* estimation support platform:

Users can upload images and our AI models will run confluence prediction and visualizations.

The results can be downloaded as a CSV file with the estimated confluence per image.

*surface coverage (MSC are adherent cells)

SYSTEMS – Result: QM demonstrator

We first modeled the process and the associated components (hardware, substances) using interoperable standards (HL7 FHIR).

We then formalized GMP-aligned rulesets as computable inputs for aligned with actual sensor-based measures.

The derived knowledge-base will now be fused with a browser-based client application and a mocked-up process to provide a representative showcase.

The screenshot displays the 'SaxoCell Systems' web interface. On the left, there is an 'Auftragsliste' (Order List) with four entries:

- Auftrag: #CND849302, UK Leipzig, Start: 06.06.2023 - 16.41 Uhr, Status: Vorbereitung
- Auftrag: #ABC49382, UK Dresden, Start: 06.06.2023 - 14.22 Uhr, Status: Kultivierung
- Auftrag: #FJDH73829, UK Dresden, Start: 06.06.2023 - 13.12 Uhr, Status: Kultivierung
- Auftrag: #FBD430898, UK Leipzig, Start: 06.06.2023 - 15.17 Uhr, Status: Freigabe

The main area shows a detailed view for 'Auftrag: #ABC49382':

- Leiter der Herstellung:** James T. Kirk
- Sachkundige Person:** Christopher Pike
- Leiter der Qualitätskontrolle:** Hikaru Sulu
- Beauftragter der Qualitätssicherung:** Dr. Leonard McCoy
- Produkt:** Obnitix®
- Hersteller:** Medac
- Ansprechpartner:** Montgomery Scott

The process flow is shown as a timeline:

- Adhärenzprüfung (06.06.2023 - 16:21 Uhr) by Nyota Uhura
- Konfluenzbestimmung (06.06.2023 - 17:02 Uhr) by KI Modell (ScaDS AI)
- Kontrolle Mykoplasmen (06.06.2023 - 17:24 Uhr) by Nyota Uhura
- Vitalitätsbestimmung (Aktueller Prozess) by Wesley Crusher

Buttons at the bottom include: 'Auftragsdaten bearbeiten', 'Dokumentation hinzufügen', 'Prozessabschnitt abschließen', 'Foto aufnehmen', and 'Konfluenzbestimmung'. A large image of a cell culture dish is visible in the background.

SYSTEMS – Synergies to other SaxoCell Projects



✓ to MSC-Prestige

- concepts to scale-up MSC-Manufacturing and Value Chain

✓ to SaxoCellHub

- GMP training concepts for Qualified personnel

SYSTEMS – Outlook Phase I

✓ Target Achievements Phase I

1) High-tech Concept Pack: **GMP automation concept using 3D bioreactors, AI concept using sensors, GMP QM concept using supply-chain-management**

2) GMP training concept

⇒ SaxoCell-Goals ATMP Cost Efficiency/ ATMP Industrialisation

⇒ Continuity => Phase II

SYSTEMS – Outlook Phase II

⇒ Goal Phase II

Combine the high-tech concept elements of phase I to a **complete modular ATMP inline system** (demonstrator)

- **Vision: World leading cost-efficient ATMP cell manufacturing**
- **Industrial Value Chain**
- **ATMP Quantity Scaling**
- **ATMP Cost Reduction**
- **ATMP Quality Assurance**

✓ **Programme Phase II: proposed**

✓ **1.7-2 million EUR industrial contribution: confirmed**

⇒ Programme Phase II

- Combine high-tech concept elements to a **complete modular ATMP inline system** (demonstrator)
- Configure it to a concrete ATMP (MSC product Desacell) = the CellMaster (tbd) configuration
- Develop a cost-effective GMP installation environment for the ATMP production (class D)
- Build the cost-effective environment and install and test the ATMP inline system = **high scaled ATMP manufacturing** ... up to 15,000 doses p.a. per [full] system
- Design an additional packaging module (using an industrial robot)
- Create a **new start-up** for the CellMaster

PLATFORM – OMICS

Dr. Kristin Reiche, Dr. Ulrike Weirauch
Fraunhofer IZI, Leipzig

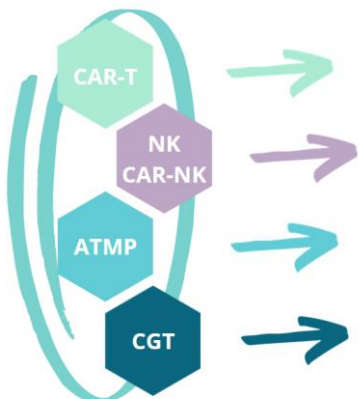
Prof. Dr. Ezio Bonifacio, Dr. Juliana Roscito
CRTD / TU Dresden

Dr. Jan Ewald, Max Joas
ScaDS.AI / Uni Leipzig

Dr. David Langenberger, Dr. Mario Fasold
ecSeq Bioinformatics, Leipzig



OMICS – Objectives



Specific needs of „Living drugs“

- Understand mechanisms of action, resistance and side effects (molecular and cellular)
- Assess quality of novel targets (e.g. target-specificity)
- Identify the right patient at the right time for treatment
- Characterize cells prior to manufacturing and final product



SaxoCell Omics

Improved evaluation of cell and gene therapies through standardized and documented high-throughput measurements & cutting-edge ex-vivo tools

- CONSULTATION & GUIDANCE
- OPERATING PROCEDURES
- PROCESS STANDARDIZATION

- Support on experimental design, guidance on available technologies, and SOPs for sample collection & processing
- Standardization of procedures across sites guarantees:
 - data quality and comparability, and
 - paves the way for multi-centric studies



- Versatile & scalable analysis platform
- Data storage and management following FAIR principles; full compliance with ethical and privacy aspects; infrastructure for storage and analyses servers
- Training in data analysis and statistics

OMICS – Results so far



1. Map of the available infrastructure and expertise in Saxony

Technology offers

Areas of competence offered by Fraunhofer IZI

Areas of competence offered by Klinikum Chemnitz

Areas of competence offered by TU Dresden

Areas of competence offered by Universität Leipzig

Areas of competence offered by SaxoCell Systems and partners



2. SOPs and guidelines for relevant OMICS methods (sample collection and processing)



3. Planned Ringversuch – method harmonization across production sites Dresden and Leipzig



4. Validation of experimental methods to detect CAR T cells with single-cell transcriptomics



5. Data Management Plan: GDPR compliance for metadata collection and storage, data sharing and analysis



6. Human OMICS data to be integrated into GHGA, the German National Infrastructure for FAIR storage and sharing of human data



7. Data Analysis support tailored to the needs of SC projects:

- web-based Galaxy Server

 **Galaxy** *check out our poster
PROJECT

- tailored pipelines and workflows
- direct support and collaboration on advanced AI analysis methods

- join us at the Spakt Meeting (22/sept)!



8. Bioinformatic courses offered regularly by ecSeq Bioinformatics



9. Strategic partnership with industry

OMICS – Synergies to SaxoCell Projects



SaxoCell Projects are already benefitting from our activities:

Projects **ECP-CAR**, **UltraCAR-T** and **CAR NK 4.0** already took advantage from offers from our partners for **data production** (omics measurements on ATMPs or samples from clinical studies), using assays such as bulk and single-cell RNA-seq and spatial transcriptomics.

In addition, we are actively looking for supporting projects with omics **data analysis**, either via our newly implemented Galaxy server or via collaborations for tailored advanced analyses.

OMICS – Outlook

SaxoCellOmics will support the technological development of Cell and Gene Therapies in Saxony by creating a **unified network of regionally-developed and available service offers and IPs** for high-throughput analysis of CGT products in research and clinical settings.

- **OMICS as a mediator**, advising and facilitating omics-related work for SaxoCell (and associated) projects.
- **Strategic partnerships** with relevant academic, clinics and industry players aimed at strengthening the local/regional value chain for the production of safe & affordable ATMPs.
- **Advanced data analysis pipelines** designed to uncover new action mechanisms of ATMPs and identify new targets and resistance dynamics for development of improved quality criteria for ATMP production.
- **Training opportunities** will be further adapted to specific needs of projects.

SaxoCellOmics aims at being the first point of contact for projects that plan on generating and/or analysing omics data of ATMPs and for cell or patient monitoring. Through the consultancy and knowledge expertise built over the first funding phase, we are fully ready to support projects in experimental and budget planning.



Get in touch, we are ready to support you!



CONTACT US



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ulrike.weirauch@izi.fraunhofer.de
alexander.scholz@izi.fraunhofer.de



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LEITUNG



Prof. Dr. Uwe Platzbecker
University Hospital Leipzig



Prof. Dr. Martin Bornhäuser
University Hospital Dresden

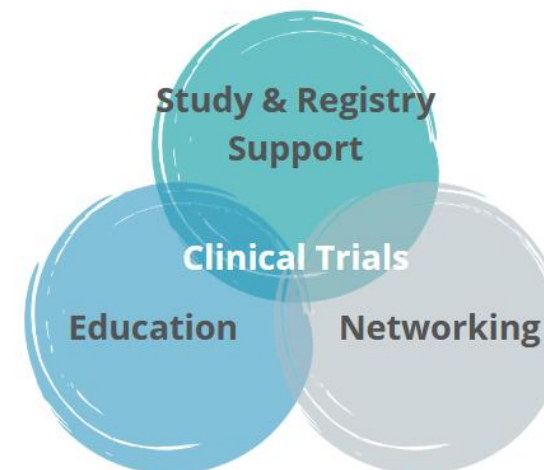


PD Dr. Mathias Hänel
Hospital Chemnitz

KOORDINATION



Silke Gloaguen
University Hospital Leipzig

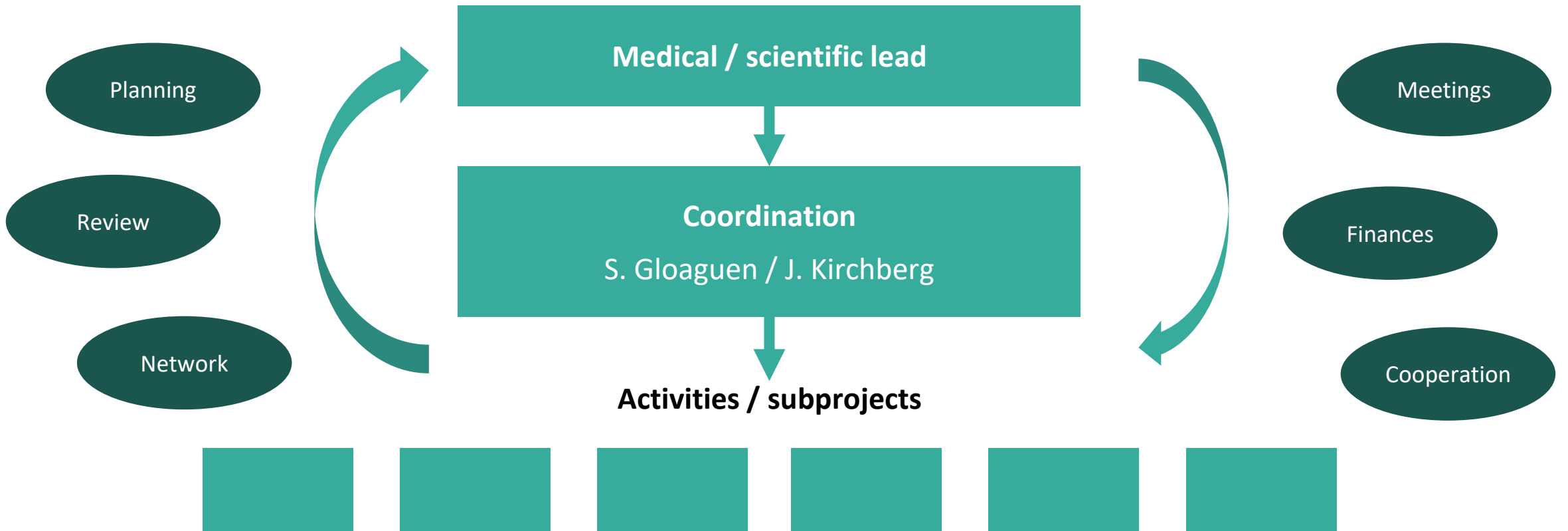


Goals were set as follows:

1. Establishment of a **central coordinating structure** for clinical and regulatory aspects in the field of gene and cell therapy within the SaxoCell cluster
2. Optimizing the **translation** of phase 1-3 **clinical trials** in cell and gene therapy
3. Provide **advice** and **networking**
4. Development of a **registry** and harmonization of biobanking (SaxoCell-Bio) for cell and gene therapies in Saxony within the three SaxoCell locations (Leipzig, Dresden, Chemnitz)

Clinics – results to date, cont'd

- Establishment of the SaxoCell Clinics coordination team
 - Organizational structure, processes




Clinics – results to date, cont'd



- Establishment of the SaxoCell Clinics coordination team
 - Organizational structure, processes
- **Contact with authorities, network expanded**
 - Clinics workshop on ATMPs – speakers from PEI and state authorities
 - Two Scientific Advices (PEI) carried out (on the PHOTOCAR study, November 2022 and May 2023)



 Landesdirektion Sachsen

Paul-Ehrlich-Institut 

Bundesinstitut für Impfstoffe
und biomedizinische Arzneimittel

Clinics – results to date, cont'd



- **Establishment of the SaxoCell Clinics coordination team**
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- **Advisory/Training Function**
 - Clinics workshop on ATMPs conducted

Workshop „clinical studies with ATMPs“

- 16-17 March 2023 at the University Hospital in Leipzig
- In collaboration with the HUB, ZKS Leipzig and KKS Dresden
- Conducted in a hybrid format
- Speakers from PEI, Landesdirektion, academia and industry
- More than 100 participants and good feedback
- Possibly continuation in 2024



Clinics – results to date, cont'd



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 - Two Scientific Advices (PEI) carried out (on the PHOTOCAR study, November 2022 and May 2023)
- **Advisory/Training Function**
 - Clinics workshop on ATMPs conducted
 - Consultations held on regulatory issues
 - Working paper on ATMPs



- Definitions
- ATMP classes and their characteristics
- Regulatory aspects

Clinics – results to date, cont'd



- **Establishment of the SaxoCell Clinics coordination team**
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- **Advisory/Training Function**
 - Clinics workshop on ATMPs conducted
 - Consultations held on regulatory issues
 - Working paper on ATMPs
- **Clinical trials / support for study preparation**



Support preparation of PHOTOCAR study

(the study should have provided samples for ECP-CAR)

- Collaboration with project team / Dr. Vucinic and regulatory bodies
- Supported 2 PEI advices for the study
 - November 2022 and May 2023
- Outcome: Regulatory hurdles / objections too high to conduct the trial at this time
 - Strategy:
 - Collect the samples required for the ECP-CAR project outside a trial → approved by BMBF



Support in preparation of the study protocol

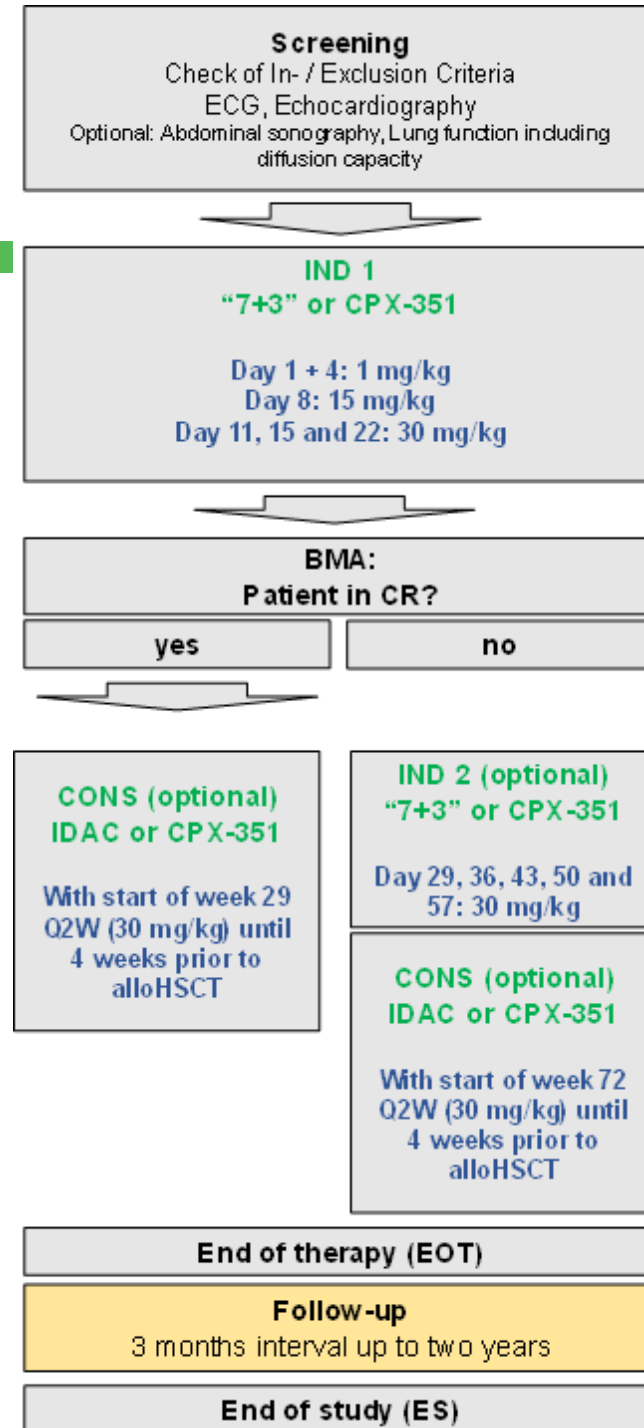
- Main work carried out by team in Chemnitz

Clinics – results to date, cont’d

MAGROLIC trial

Magrolimab plus intensive chemotherapy in newly diagnosed “ELN 2022 intermediate or adverse-risk” AML or high risk MDS patients intended to undergo allogeneic stem cell transplantation, a Phase 2, Single-arm, Open-Label Study

- **Magrolimab:**
 - humanized anti-CD47 mAb that blocks the interaction of CD47 with its receptor and enables phagocytosis of human cancer cells
- **Objective:**
 - To show the efficacy and safety of magrolimab in combination with intensive chemotherapy.
 - Primary efficacy endpoint: Best CR/CRi/CRh during induction chemo
- **Financier:** Gilead
- **Status:**
 - Regulatory approval obtained
 - Finalize contracts
 - Finalize IMP distribution



Clinics – results to date, cont'd



- **Establishment of the SaxoCell Clinics coordination team**
 - Organizational structure, processes
- **Contact with authorities, network expanded**
 - Clinics workshop on ATMPs – speakers from PEI and state authorities
 - Two Scientific Advices (PEI) carried out (on the PHOTOCAR study, November 2022 and May 2023)
- **Advisory/Training Function**
 - Clinics workshop on ATMPs conducted
 - Consultations held on regulatory issues
 - Working paper on ATMPs
- **Support for study preparation**
- **Biobank / Registry**
 - Set up successfully and first samples/data included (SHIMMER registry)

SHIMMER biobank

- Registry / biobank of patients treated with ATMPs and/or SCT.
- Status as of beginning of September 2023:

Baseline: **47** patients FU28d post Tx: **46** patients

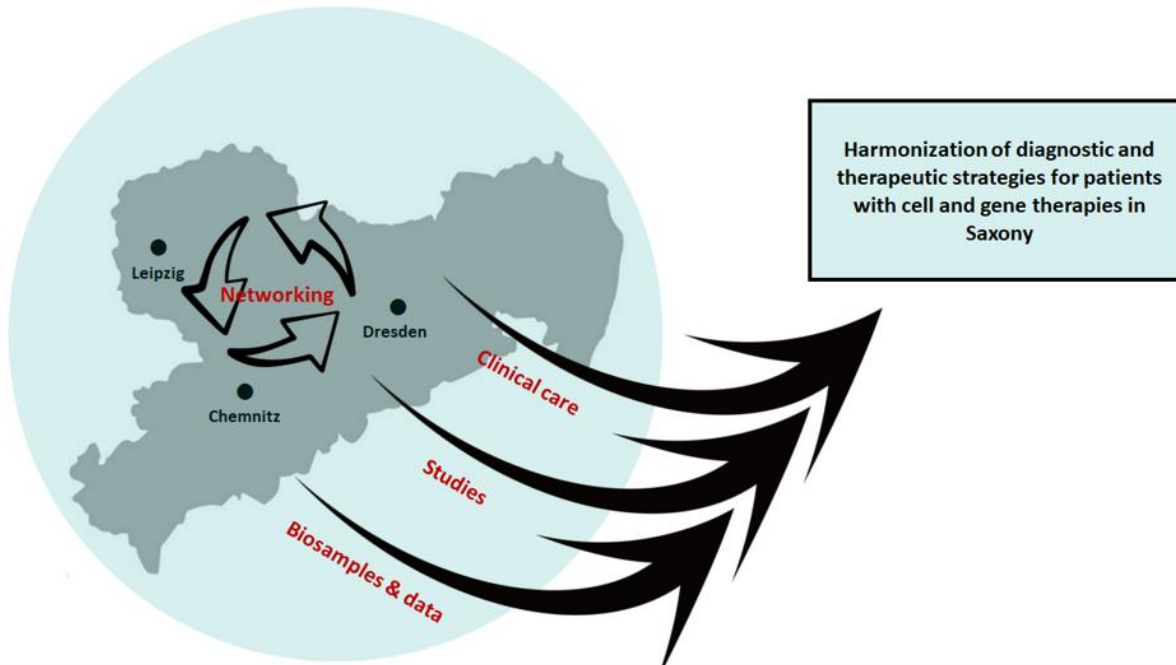
Clinics – outlook & ideas for next phase



Possibly 2nd editions of...

- ATMP Workshop
- Working Paper

Pooling of resources clinical studies & process and biosampling harmonization at the three locations **Leipzig, Dresden and Chemnitz**

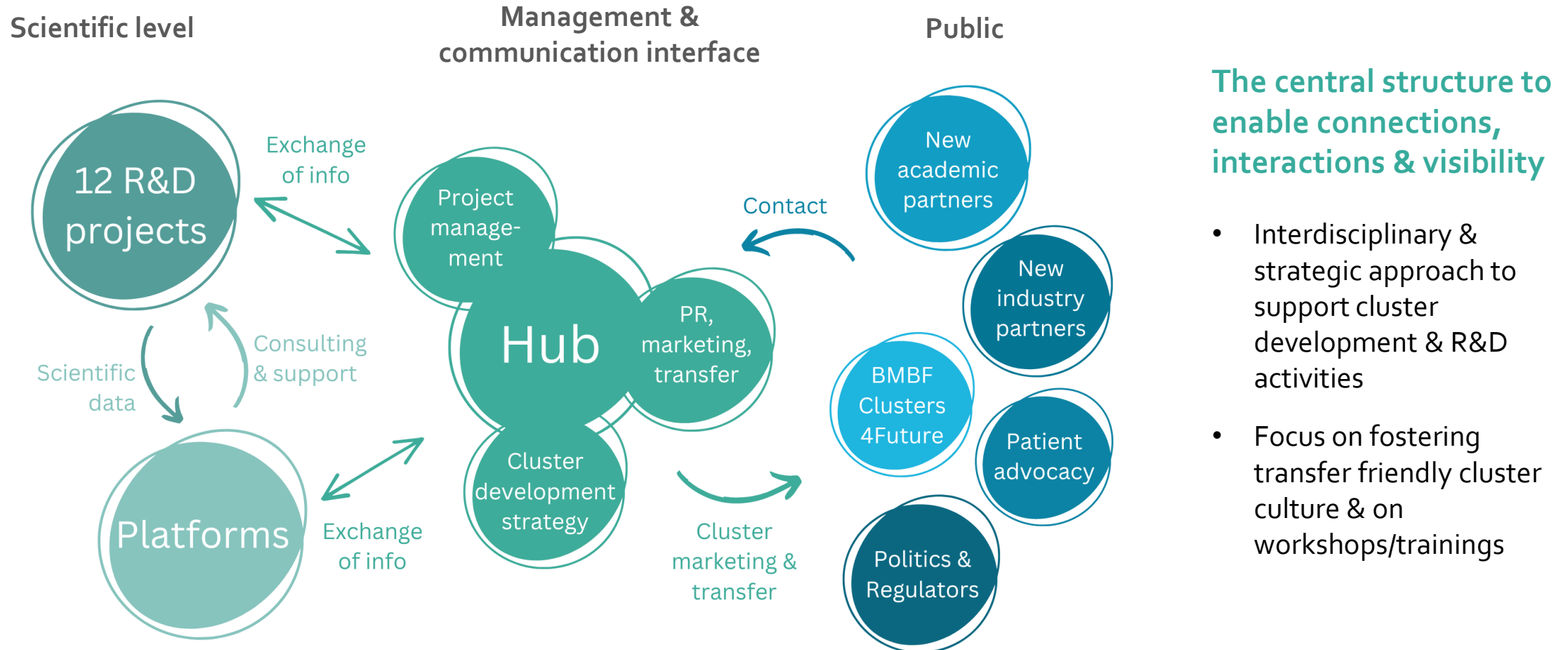


- Main site & satellite centers



- Use of entity-specific expertise of the sites (corresponding choice of the main site), resource-saving study implementation, optimized comparability of the clinical processes

SaxoCell's Innovation Hub



The central structure to enable connections, interactions & visibility

- Interdisciplinary & strategic approach to support cluster development & R&D activities
- Focus on fostering transfer friendly cluster culture & on workshops/trainings

Hub Team



Core contacts



Anette
Bartsch



Alexander
Funkner

Project lead: Ilka Henze



Core contacts



Franziska
Friebe-Viebach



Ira
Illgen



Stephanie
Wieneke



Luisa Brückner
(Maternity leave)

Project lead: Dorit Teichmann
Supporting Activities: Maren Henneken



UNIVERSITÄT
LEIPZIG

Core contacts



Stefanie
Binder



Nicole
Modler

Project lead: Beatrice Berneck

What we did in the last year

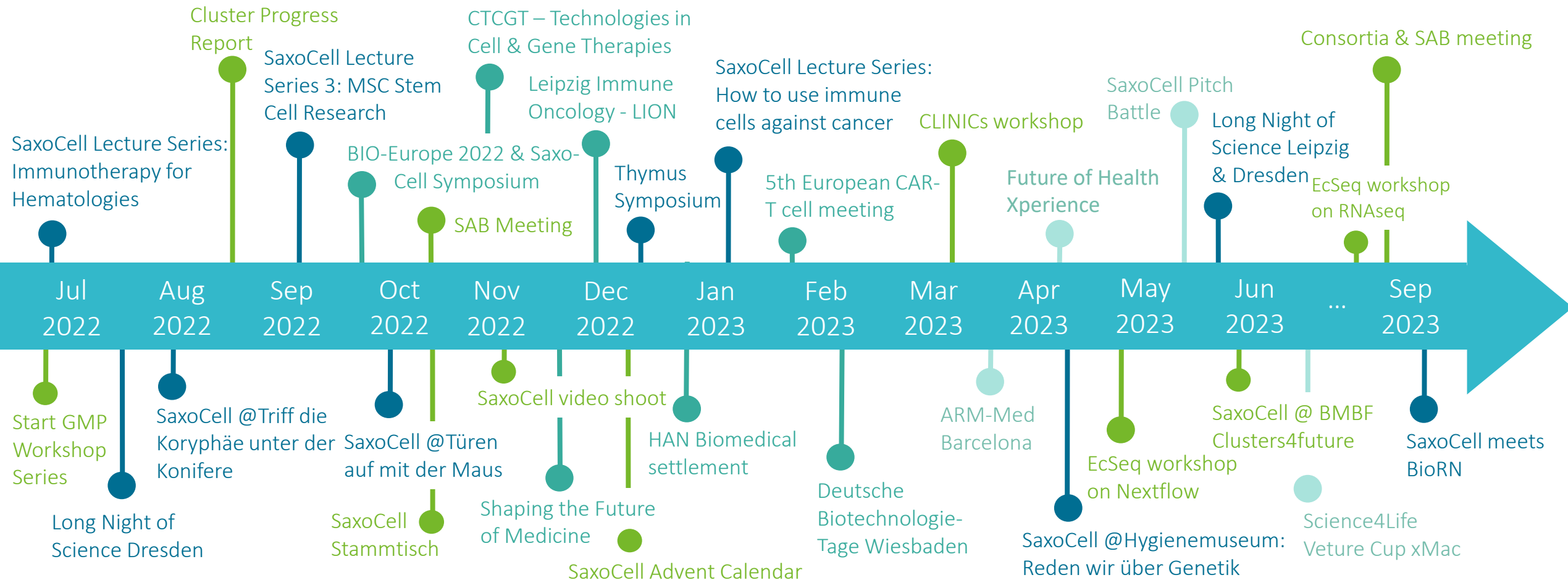


Transfer

Conferences

Public event

Cluster-internal



A closer look at...



BIO-EUROPE 2022 in Leipzig



Türen auf mit der Maus @CRTD



1st SaxoCell Pitch Battle in Dresden

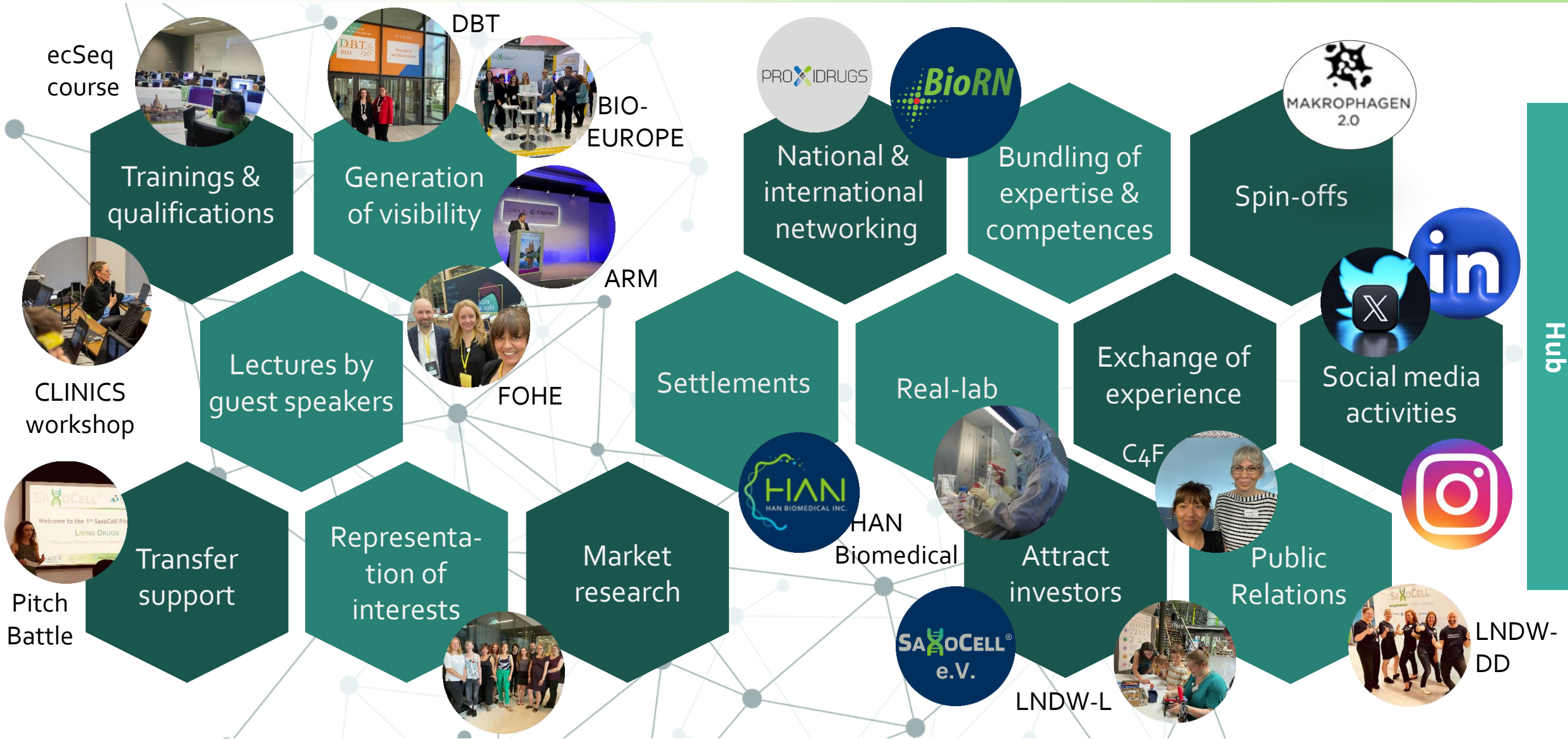


CLINICS workshop in Leipzig

We support you!



We support you!



News

News in the members area of the website



Miltenyi Biotec

Special offer
(check it out!)

Participation in raffle here on site

Tickets to

25th ANNUAL INTERNATIONAL PARTNERING CONFERENCE
BIO-EUROPE®

&

TAGESSPIEGEL | **BIH**
Future Medicine
Science Match

SaxoCell
publications
with affiliation



Annual
Report
22/23

Outlook

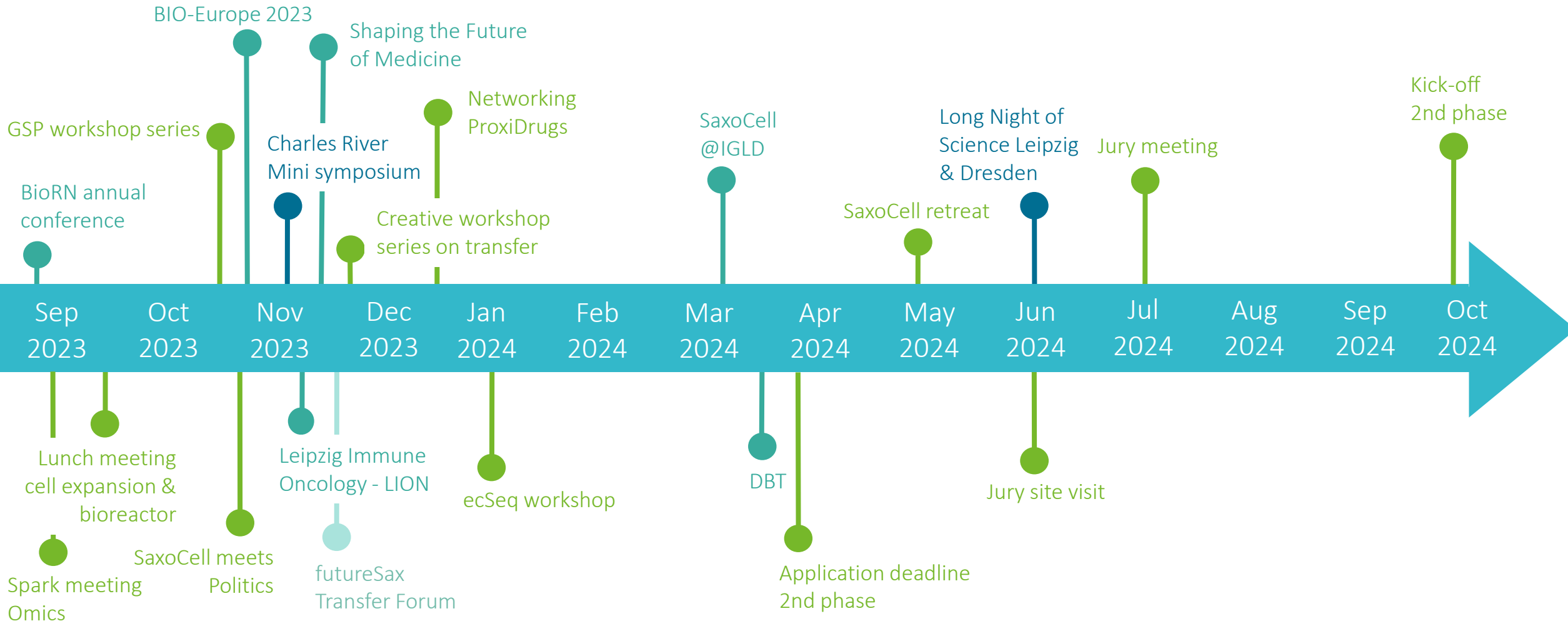


Transfer

Conferences

Public event

Cluster-internal



Broad visibility of SaxoCell!

Spread the word!



Website + Members Area

<https://www.saxocell.de>



LinkedIn

<https://www.linkedin.com/company/saxocell-cluster/>



Twitter / X

<https://www.x.com/saxocell>



Instagram

<https://www.instagram.com/saxocell/>



Day 1: Monday 11.9.23, IZI



Key note lecture

Christof von Kalle, BIH

17:15 – 18:00

Day 1: Monday 11.9.23, IZI

SAXOCELL®



Get together



Location tomorrow: Biocity