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CLUSTERS 4 FUTURE
Innovationsnetzwerke für unsere Zukunft

GEFÖRDERT VOM
Bundesministerium für Bildung und Forschung

LIVING DRUGS

PRECISION THERAPY CLUSTER FOR SAXONY

Welcome to our

SaxoCell Consortium Meeting 2022

20th June 2022 | CRTD Dresden

Ezio Bonifacio, Ulrike Köhl, Martin Bornhäuser, Uwe Platzbecker

TECHNISCHE UNIVERSITÄT DRESDEN

UNIVERSITÄT LEIPZIG

Fraunhofer IZI

KLINIKUM CHEMNITZ gGmbH

Partners from Research and Industry

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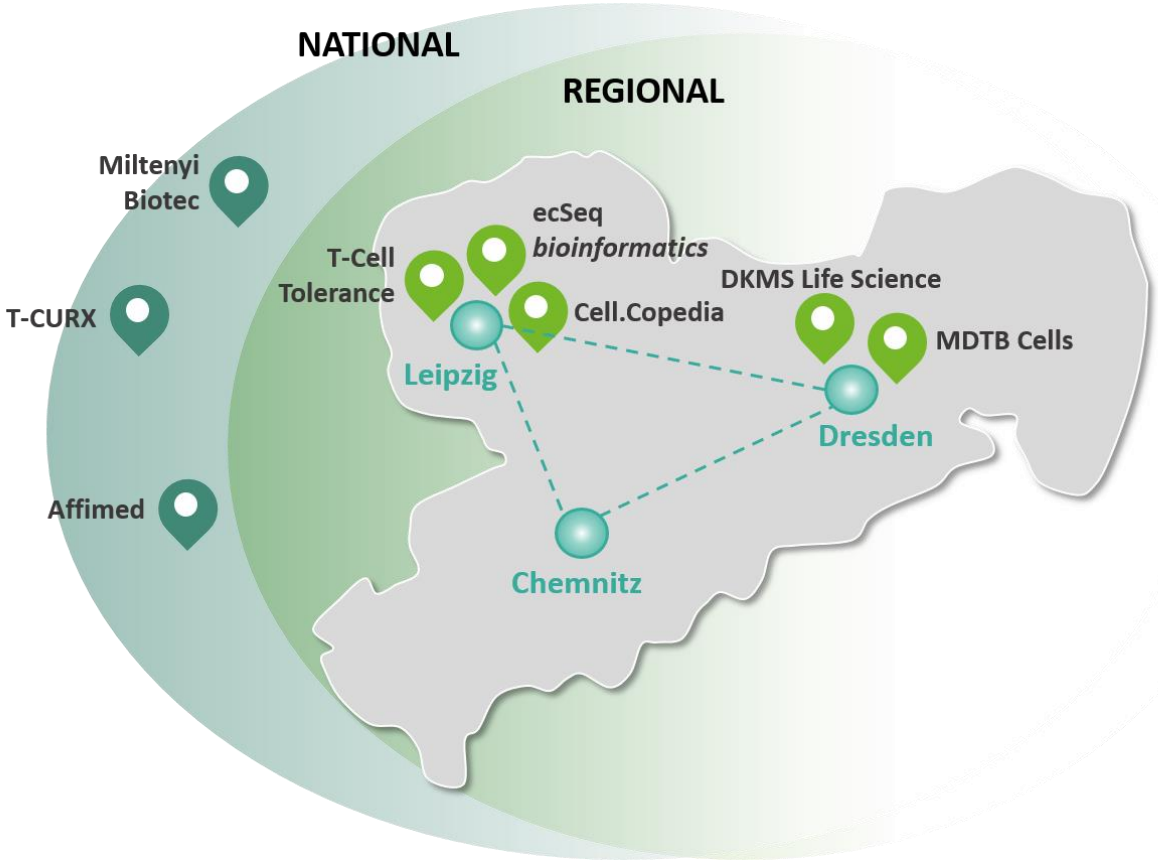
Research

38 academic PIs

Industry



Vision

SaxoCell will bring efficient, safe and affordable autologous and allogeneic Cell and Gene Therapies (CGTs) to patients who suffer from serious disease.

Core Partners

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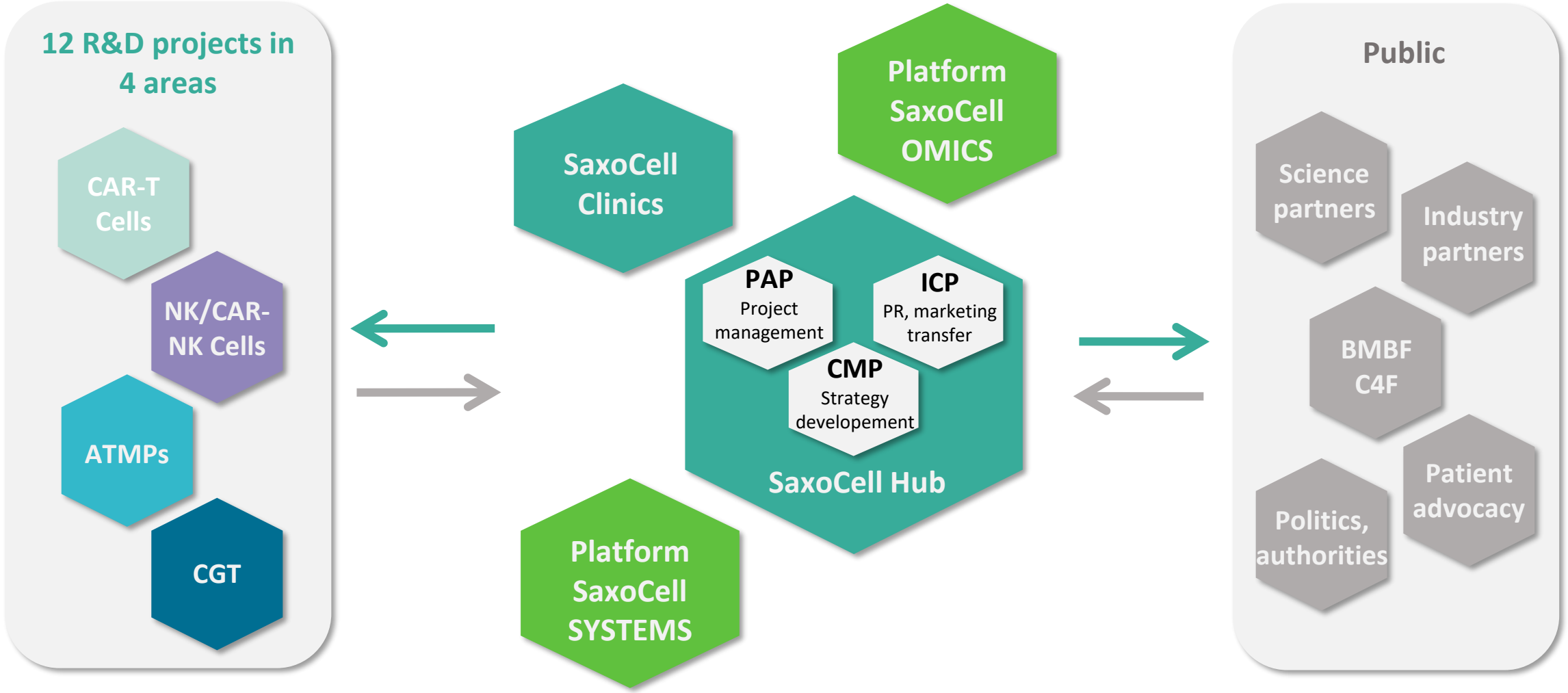
UNIVERSITÄT LEIPZIG

Fraunhofer IZI

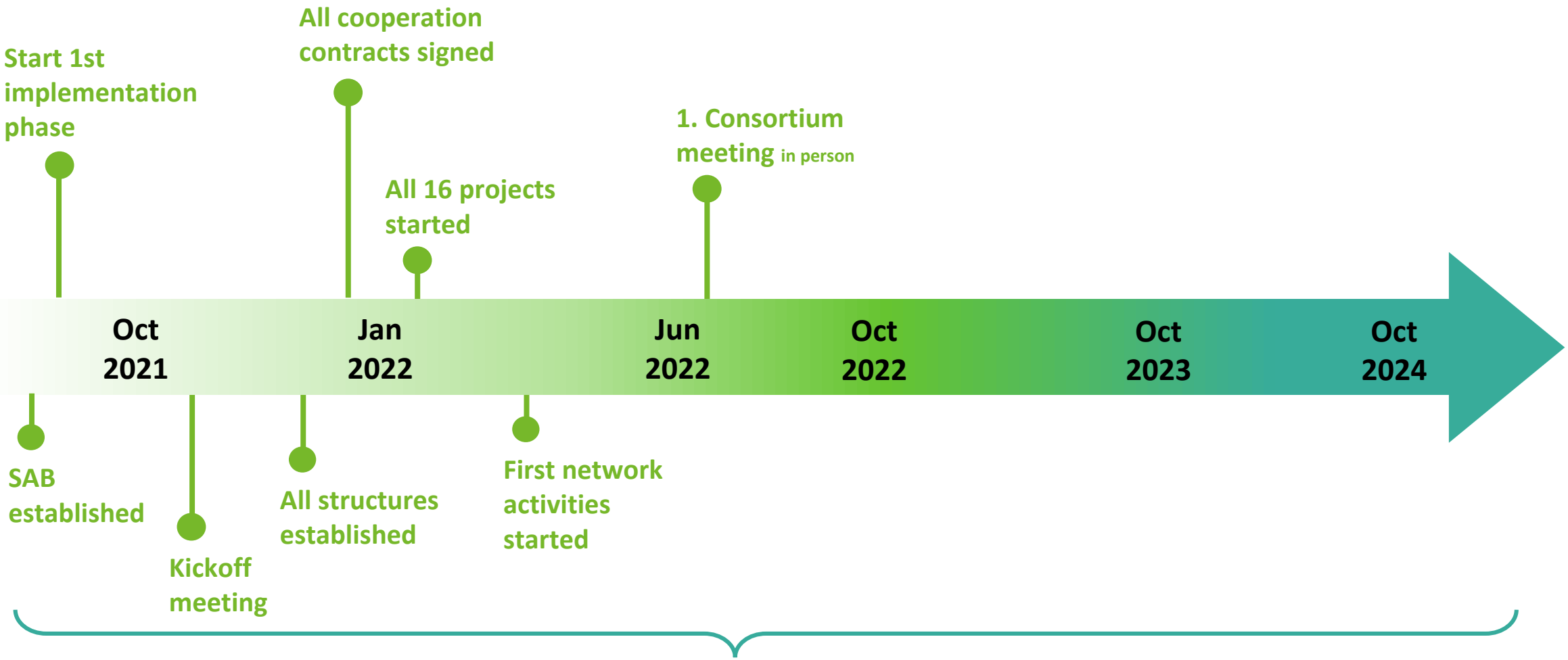
KLINIKUM CHEMNITZ gGmbH

Cluster-Structure

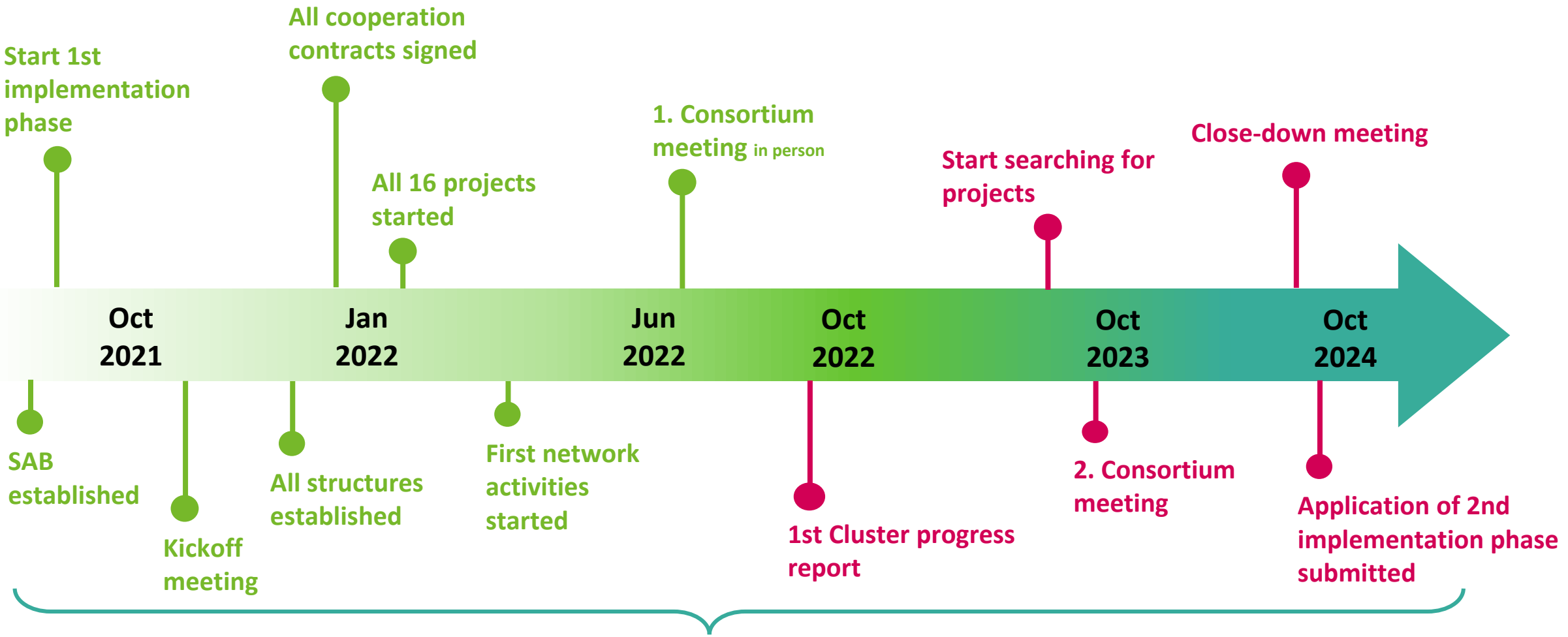


ATPMs: Advanced Therapy Medical Products | CGT: Cell and Gene Therapy| PAP: Pipeline Accelerator Programme | ICP: Innovation Culture Programme | CMP: Cluster Matching Programme

Activities so far



Activities so far and next steps



The region starts growing

- 1st start-up **RecTech** etablished**, winner of the Science 4 award;** Buchholz
- **ERC proof-of-Concept-grant;** Sieweke
- Fraunhofer lighthouse project: Automation technologies for the production of mRNA-based vaccines and gene and cell therapeutics; Köhl, Fricke
- Fraunhofer **ICON Grant "Natural killer cells for allogeneic cancer Immunotherapy" (DesingerNK) with University Hospital Oslo;** Köhl, Fricke, Blache
- **Life Center for Medicine Innovation** (CMI) is one of the 6 **finalists** in the competition for '**Großforschungszentrum**' of BMBF; Meiler, Neumuth, Beck-Sickinger, Köhl

Overall time schedule

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1st implementation phase

2021-2024

20% industry contribution

2nd implementation phase

2024-2027

35% industry contribution

3rd implementation phase

2027-2030

50% industry contribution

BMBF plans to avoid time gap between 1st and 2nd funding period

The jury will read all of the clusters' annual progress reports and provide feedback in between!

News from BMBF C4F meeting

- The BMBF/PtJ suggest to **meet once a year** for an exchange
- BMBF offered **additional cross topic** and **cross networking workshops** for all clusters
- Acquisition of **additional funding** to the cluster is important
- It is important to achieve **benefits for the region**
- BMBF will try to be more **flexible** with parts in the funding to react on new ideas or aspects in the future
- Interest from other clusters (e.g. **Proxidrug**) for **closer collaboration** (transfer, VC contacts, workshops,….) and cross-clustering

CLUSTERS 4 FUTURE
Next generation innovation networks

Federal Ministry of Education and Research

Communication is the ♥ of the Cluster!

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- Hub Meetings
- PAP Meetings
- Project Meetings
- Stammtisch
- ICP Meetings
- Area Meetings
- Consortia Meetings
- Meetings with SAB
- Meetings with BMBF/PTJ
- Steering Board Meeting
- Executive Board Meeting

AGENDA

CONSORTIUM MEETING 2022

Time	Topic	Responsible
10:00 – 10:20	Welcome	Ulrike Köhl + Ezio Bonifacio
10:20 – 10:55	Key note – Gene editing	Frank Buchholz 30min + 5min discussion
10:55 – 11:10	**Coffee break**	**All**
11:10 – 13:00	Project Pitches	5min + 5min discussion each
13:00 – 13:05	**Group picture**	**All**
13:05 – 14:00	**Lunch Break**	**All**
14:00 – 14:50	Presentation of Platforms and Hub	5min + 2min discussion
14:50 – 16:15	Area Meetings	All
16:15 – 16:35	**Coffee Break**	**All**
16:35 – 16:40	Results and Discusson Area 1	Area 1
16:40 – 16:45	Results and Discusson Area 2	Area 2
16:45 – 16:50	Results and Discusson Area 3	Area 3
16:50 – 16:55	Results and Discusson Area 4	Area 4
16:55 – 17:15	Discussion	All
17:15 – 17:30	Wrap up, outlook and Goodbye	All
17:30	**Get together**	**All**

KEY NOTE – Gene Editing

Genome editing tools to make the best and safest living medicines

Frank Buchholz
frank.buchholz@tu-dresden.de

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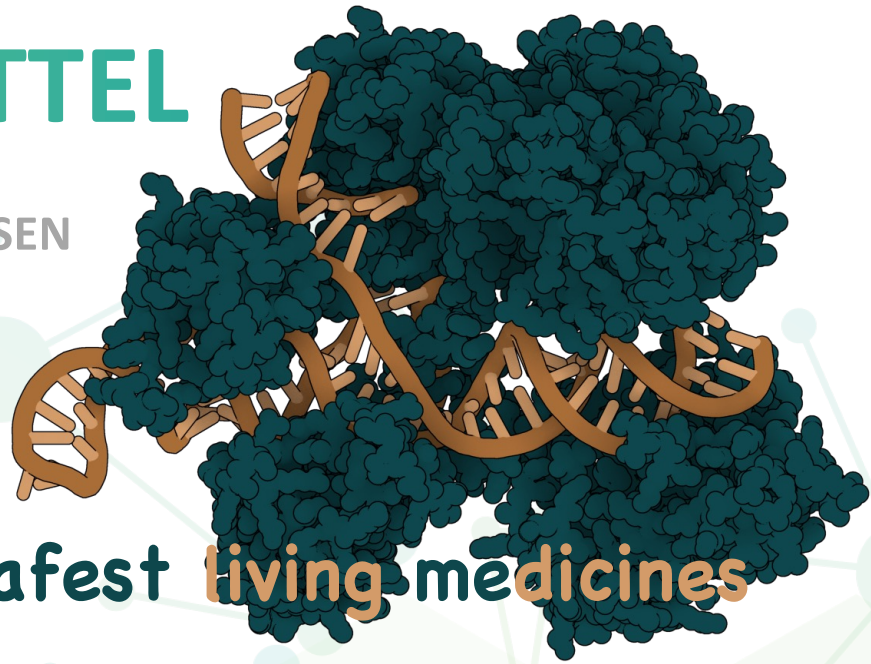
LEBENDE ARZNEIMITTEL

PRÄZISIONSTHERAPIE-CLUSTER IN SACHSEN



Genome editing tools to make the best and safest living medicines

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From Surgery to Genome Surgery

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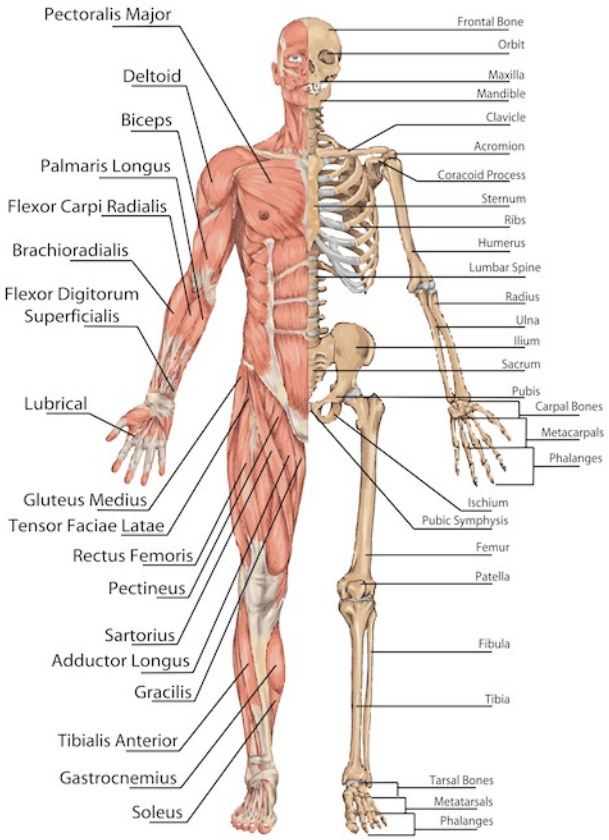
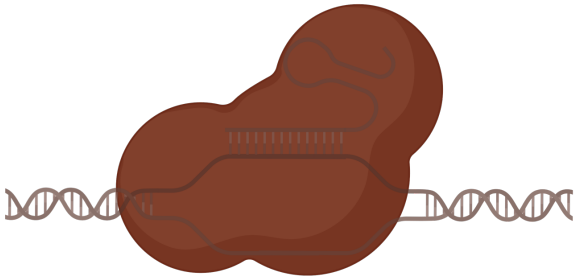
"Anatomy is the Basis of Surgery"



"Genomics is the Basis of Genome Surgery"

We know the genetic basis for many diseases, but how can we repair them?

The CRISPR revolution



CRISPR Knockout / In

↓

RNA-based programable nuclease

↓

Great research tool, but…

Letter | Published: 18 May 2020

Cas9 activates the p53 pathway and selects for p53-inactivating mutations

Article | Open Access | Published: 06 October 2021

Whole chromosome loss and genomic instability in mouse embryos after CRISPR-Cas9 genome editing

Brief Communications Arising | Published: 08 August 2018

Large deletions induced by Cas9 cleavage

NEWS | 15 July 2021

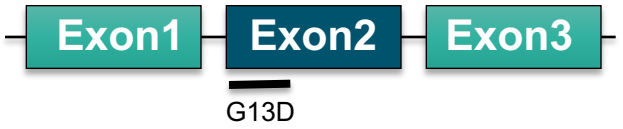
CRISPR therapies march into clinic, but genotoxicity concerns linger

Article | Open Access | Published: 11 November 2021

A systematic genome-wide mapping of oncogenic mutation selection during CRISPR-Cas9 genome editing

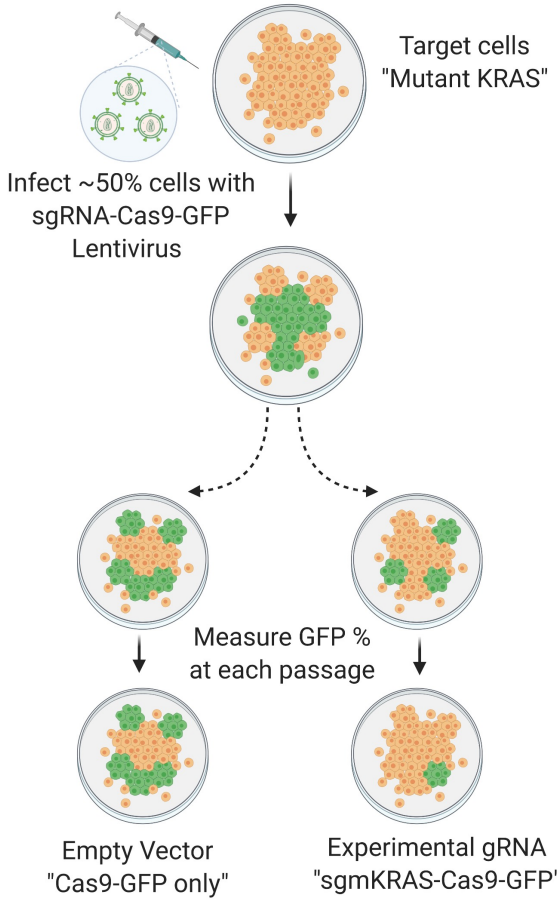
… not ideal for (cell) therapies

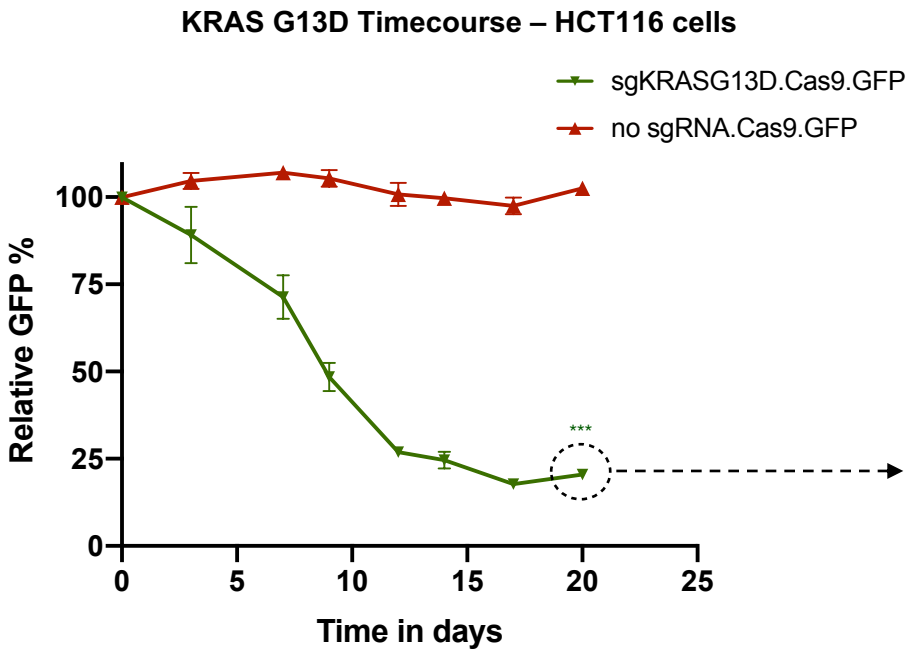
Inactivation of KRAS mutations with CRISPR/Cas9 nuclease

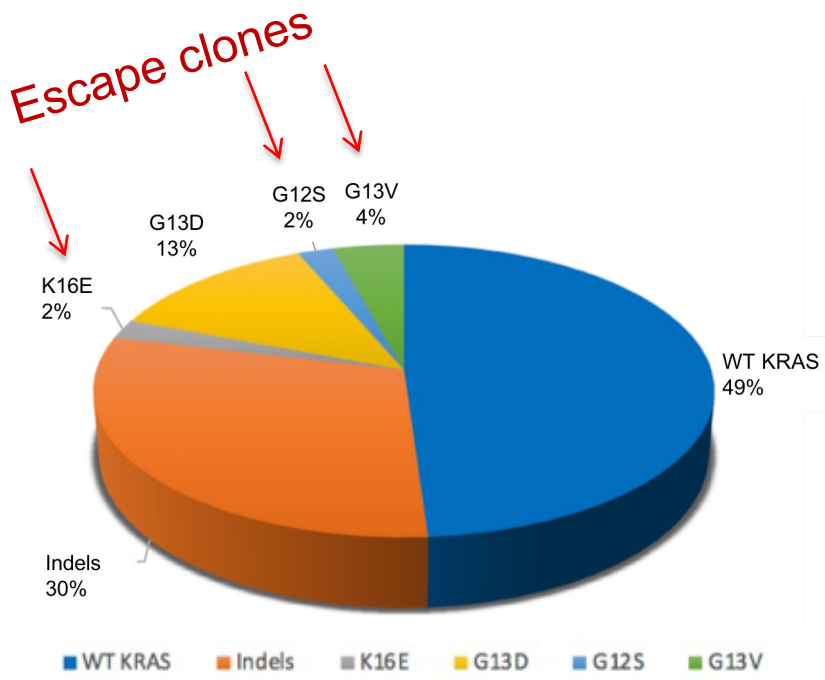


KRASwt
5′-GTAGTTGGAGCTGGTGGCGTAGG-3′
3′-CATCAACCTCGACCACCGCATCC-5′

KRASG13D
5′-GTAGTTGGAGCTGGTGACGTAGG-3′
3′-CATCAACCTCGACCACTGCATCC-5′

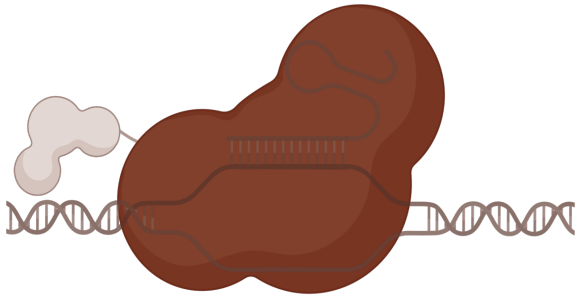






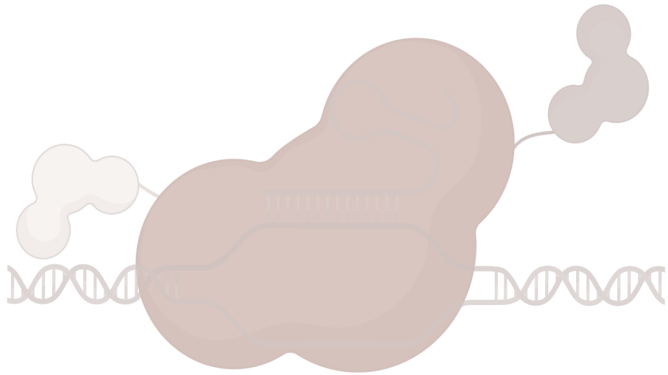
Sayed et al., in press

Gene editing without DNA breaks

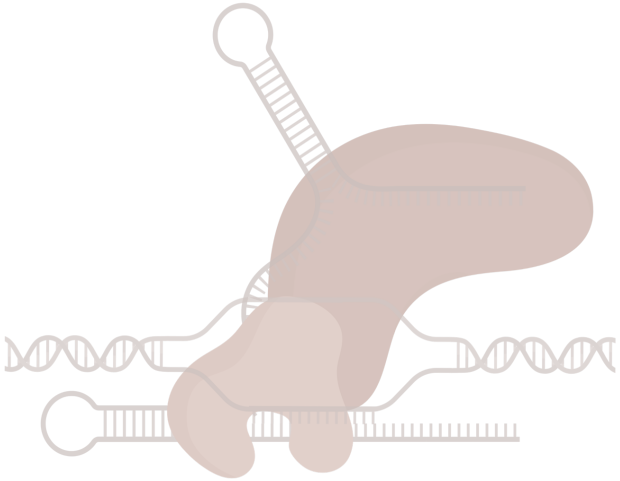


Base Editing

CRISPR
Tool box

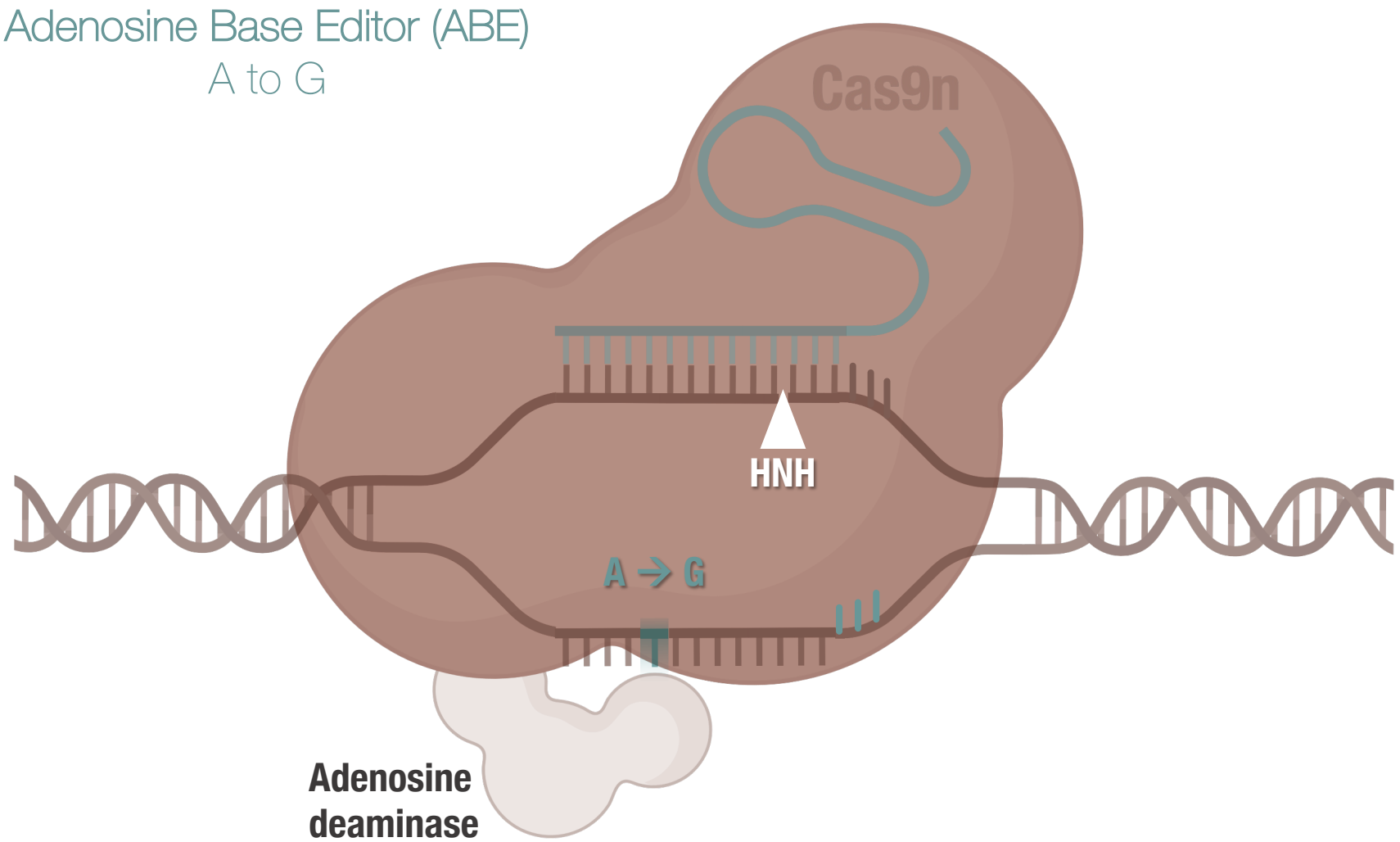


Epigenetic Editing



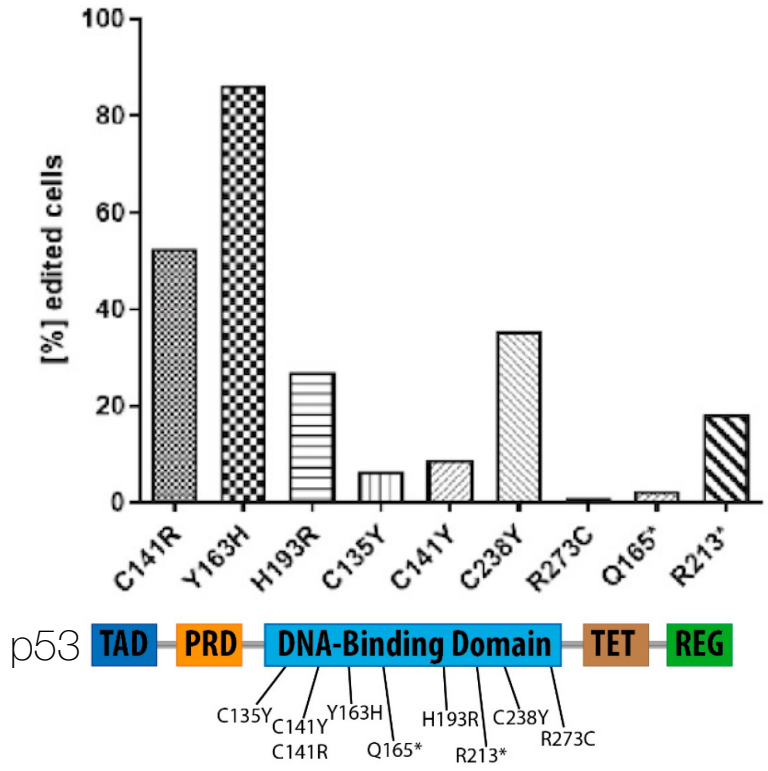
Prime Editing

Base editors induce precise single base mutations



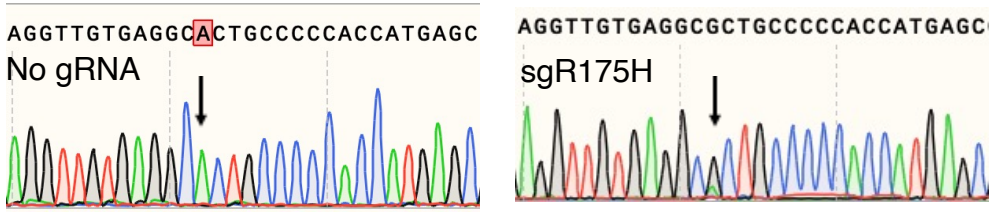
Base editors for cancer research/therapy

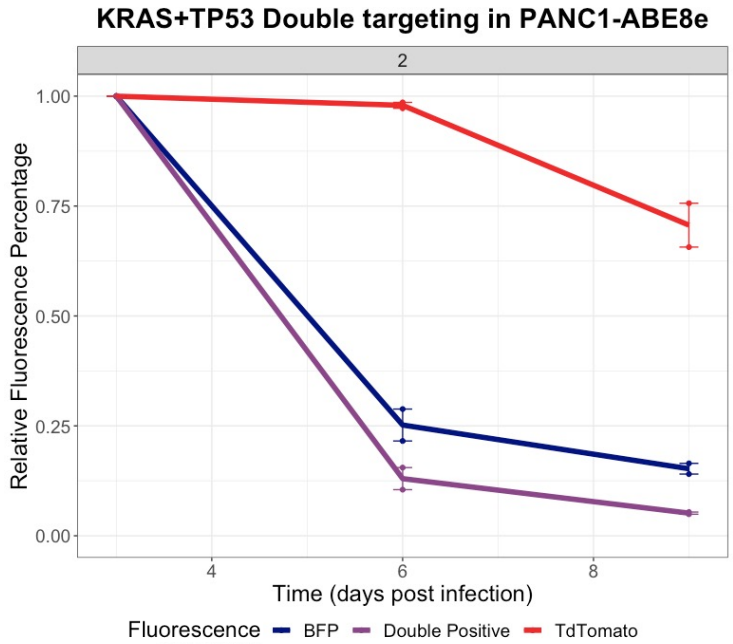
p53 mutant hiPS cell lines to study cancer associated mutations in an isogenic background



Dürün et al., Genes, 2020

P53 + KRAS mutantion correction

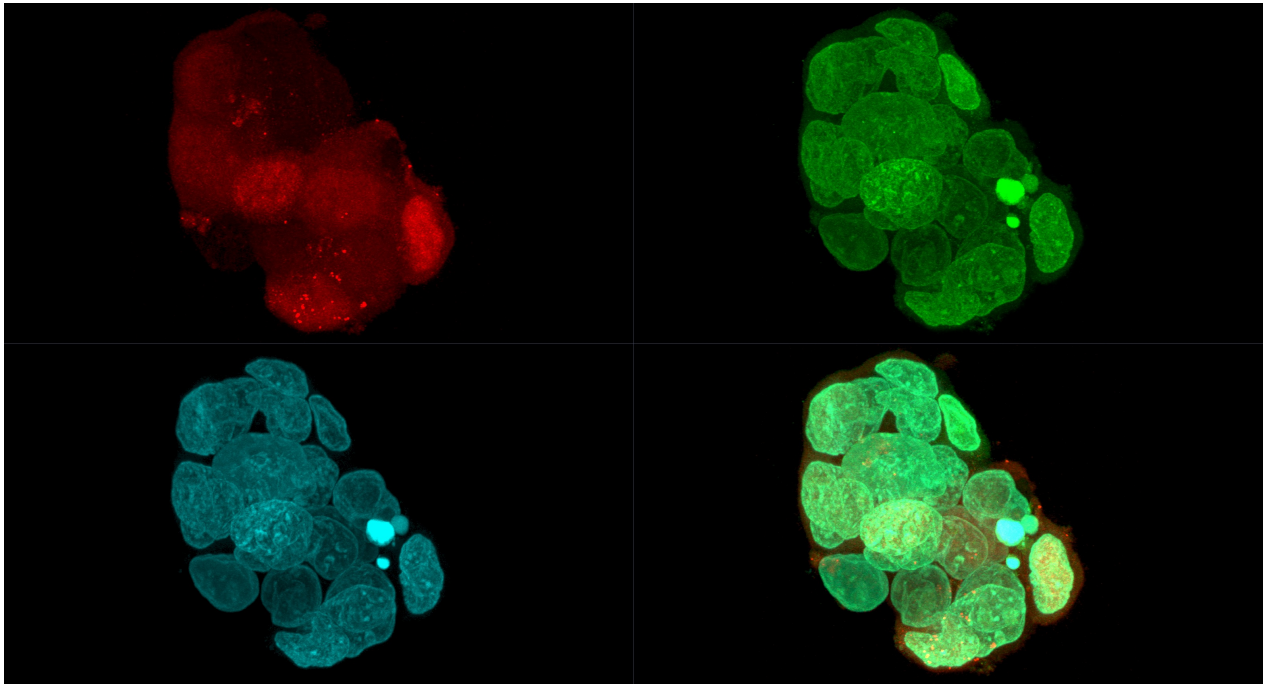




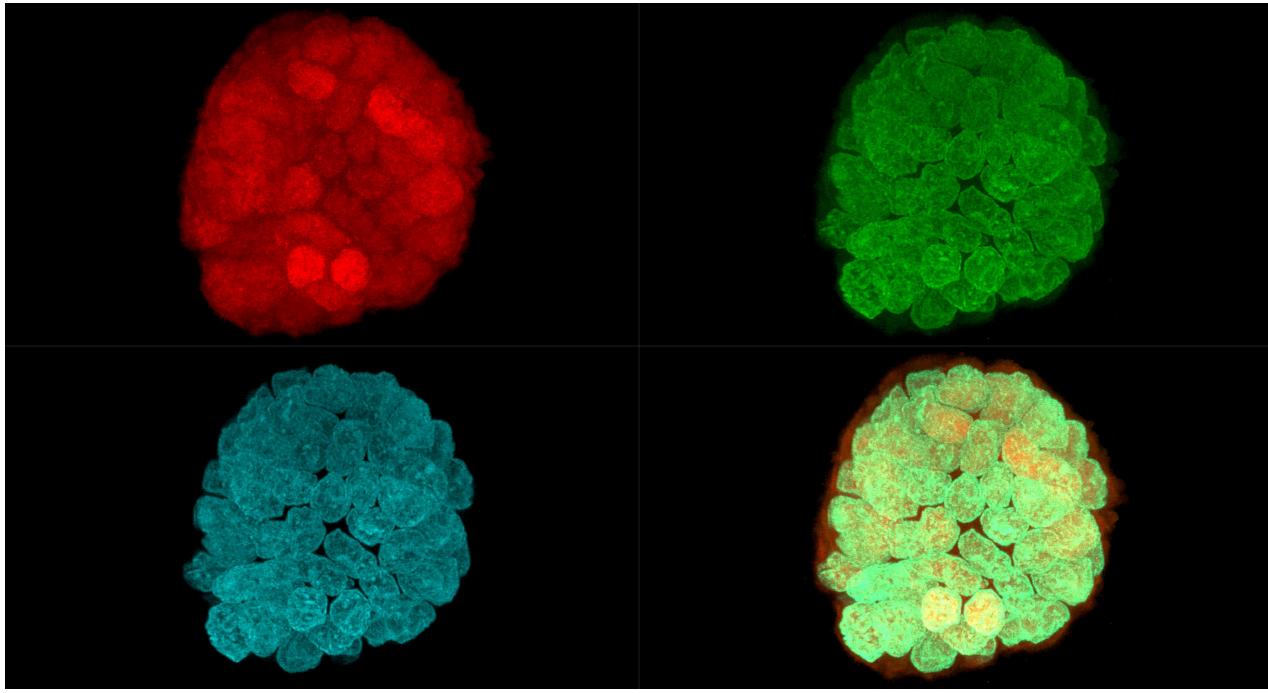
Sayed et al., Cancer Research, in press

Correction of TP53 mutation in patient organoids

P53_sg175H



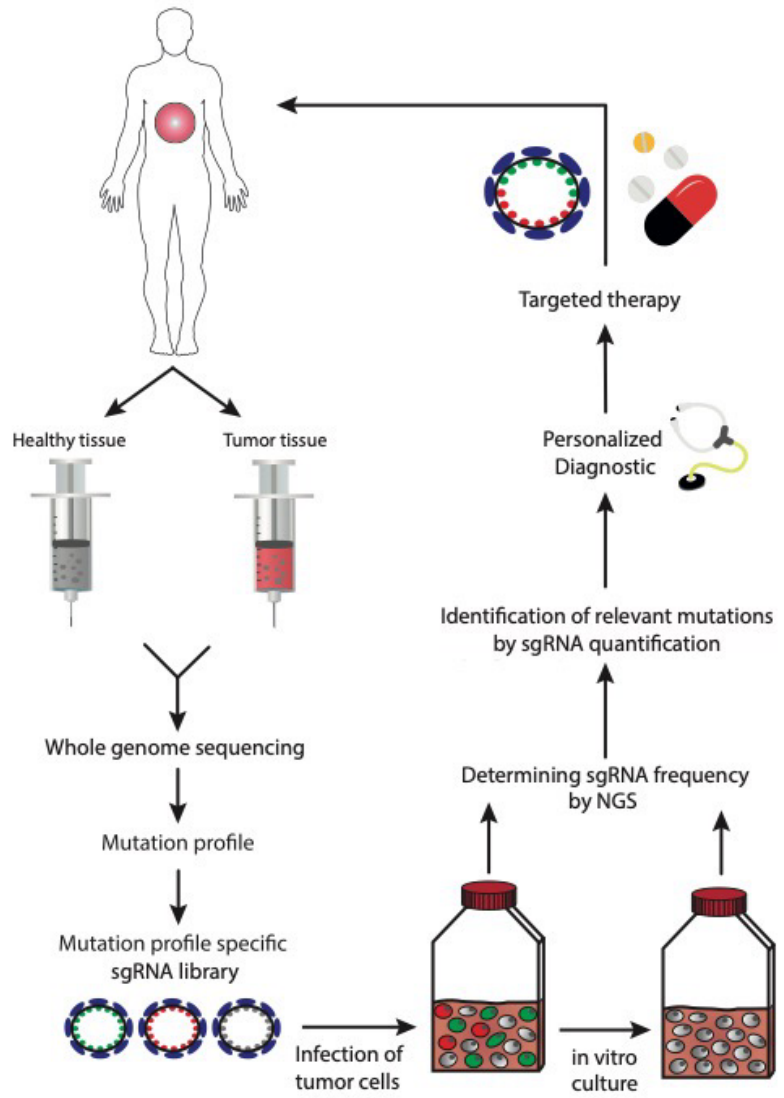
P53_sgControl



functional interrogation of vulnerabilities in a personalized manner for precision oncology

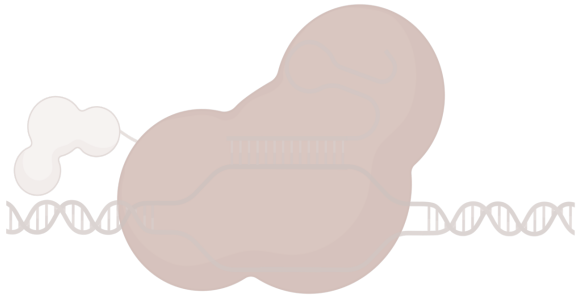
Vision of cancer genome surgery

The ultimate precision oncology approach



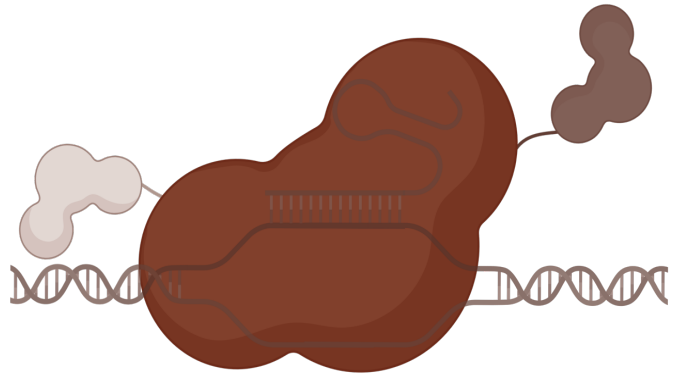
Delivery challenge

Gene editing without DNA breaks

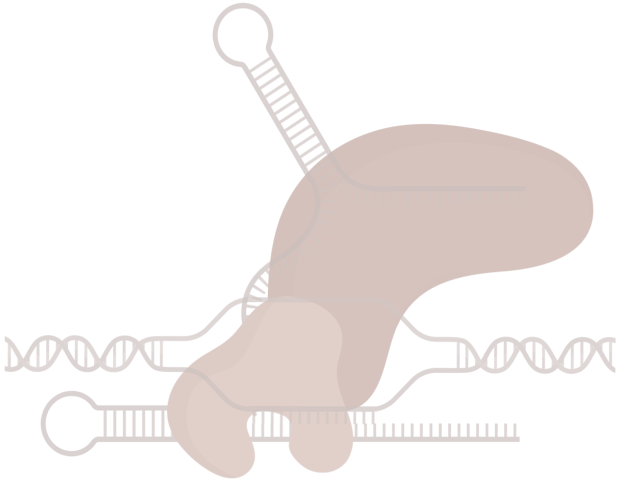


Base Editing

CRISPR
Tool box

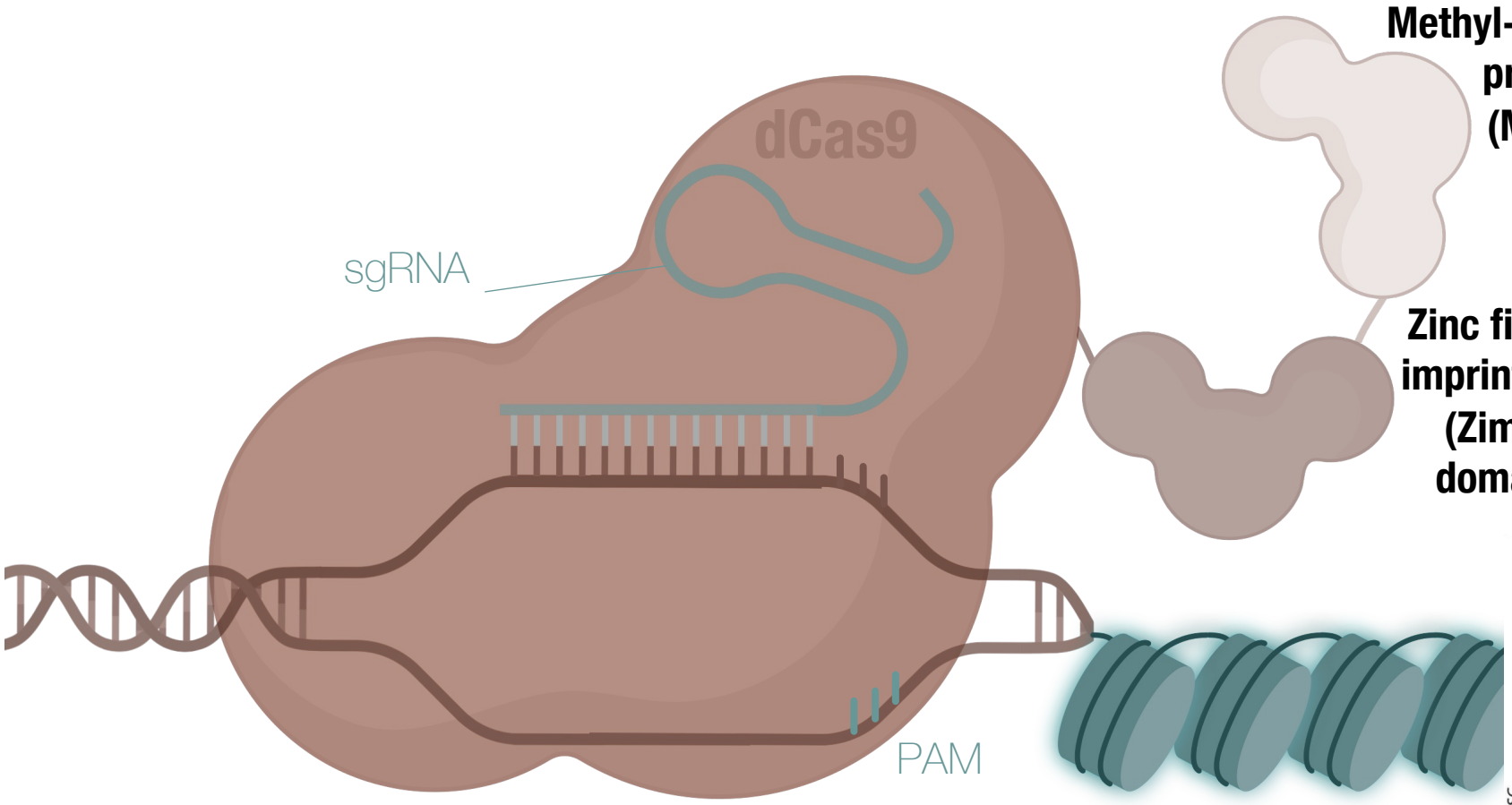


Epigenetic Editing



Prime Editing

Long-term gene silencing with epigenetic editors

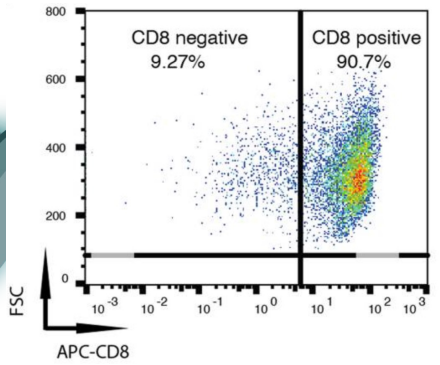


Methyl-CpG-binding protein 2 (MeCP2)

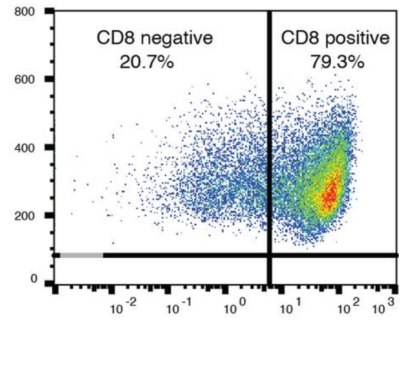
Zinc finger imprinted 3 (Zim3) domain

human CD8+ primary T lymphocytes

dCas9-Zim3-MeCP2 + non targeting sgRNA



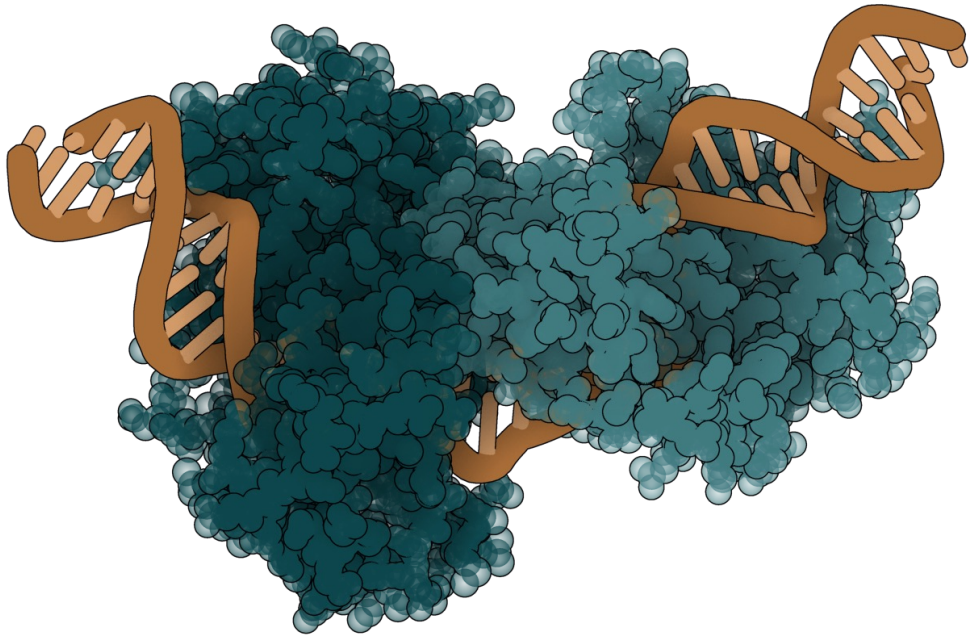
dCas9-Zim3-MeCP2 + sgCD8



Ding et al., Life Sci Alliance, 2022

The Swiss knife of genome editing tools

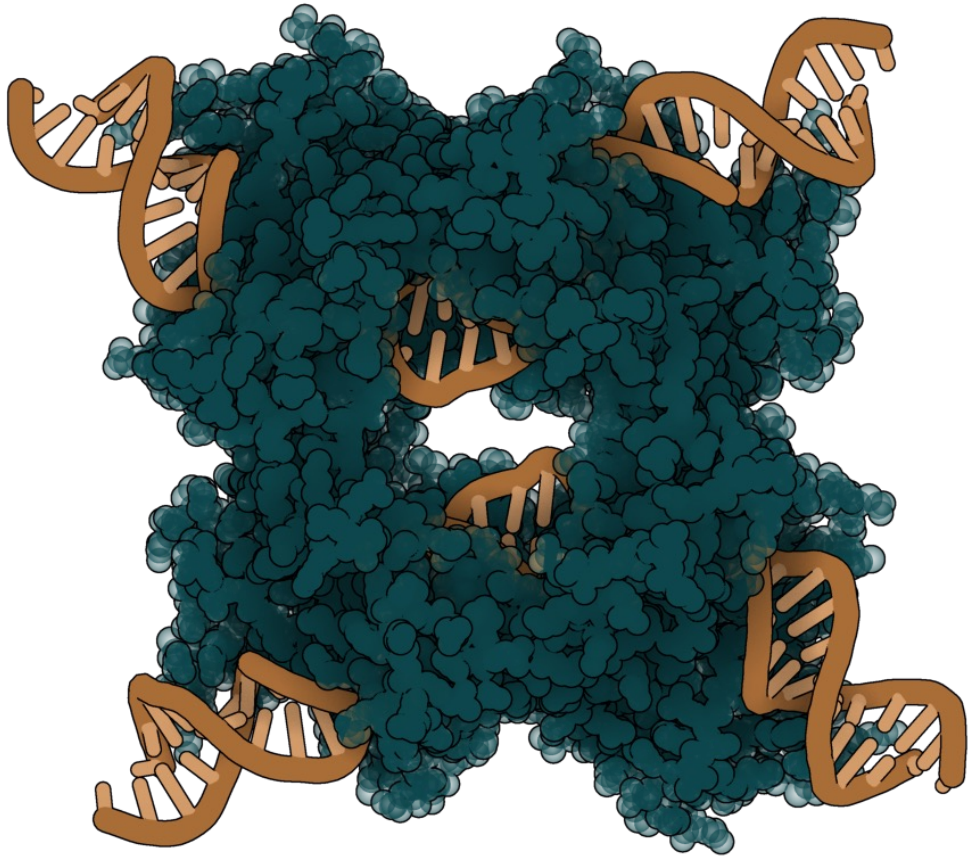
Site-specific recombinases (SSR)



half-site spacer half-site

ATAACTTCGTATA-ATGTATGC-TATACGAAGTTAT

TATTGAAGCATAT-TACATACG-ATATGCTTCAATA



Recombinases – Next Generation Editing

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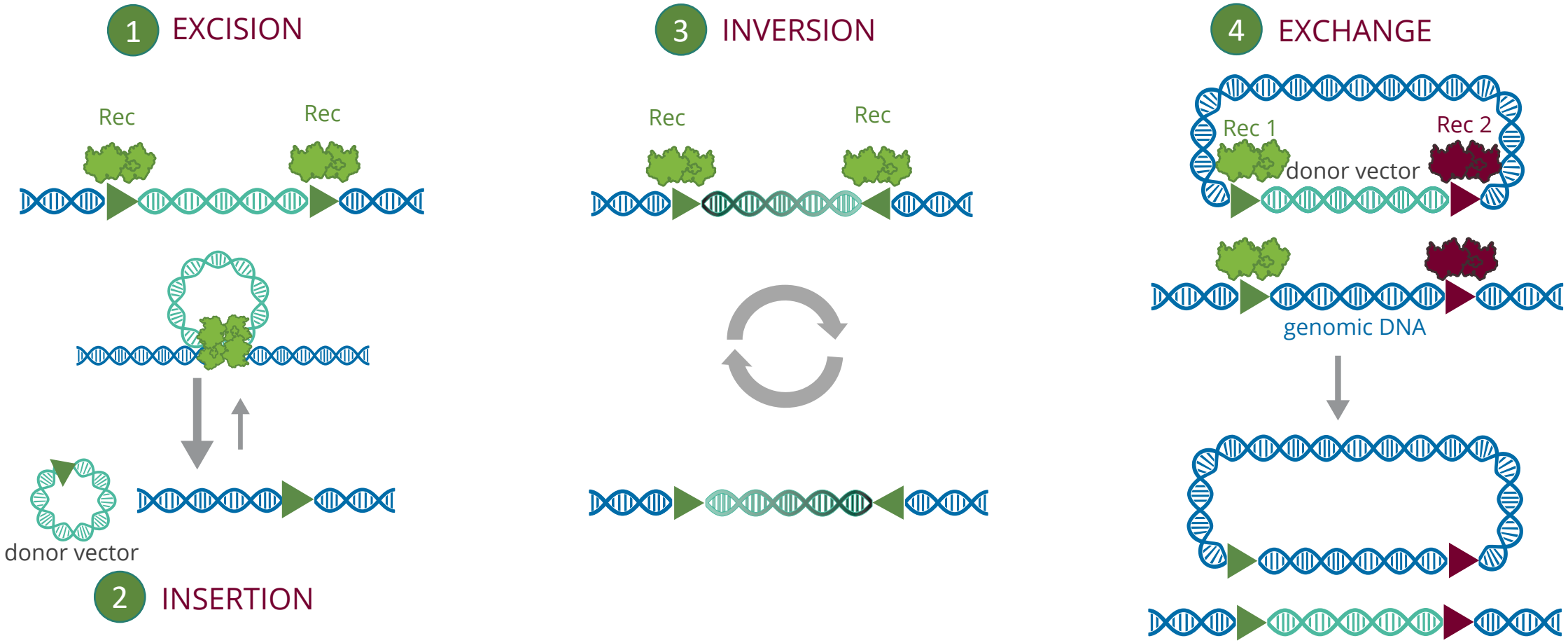


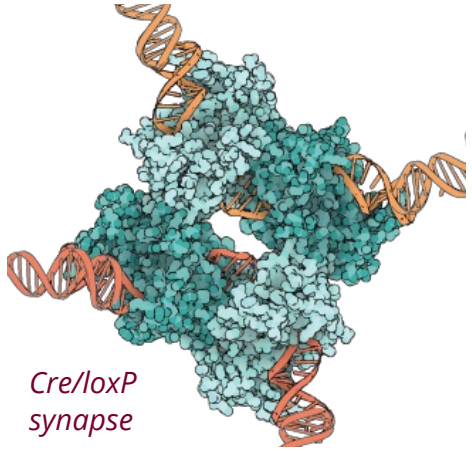
PRECISE RECOMBINATION

▶ = lox-like target site

= Cre-like recombinase

Why are recombinases not used by everyone for gene editing?

Programming Recombinases to new target sites

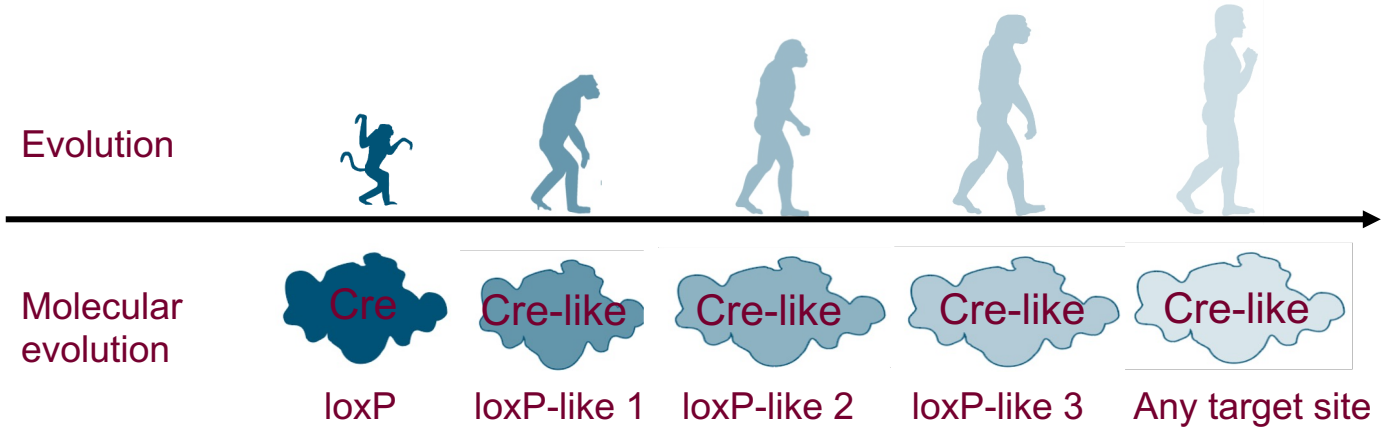


Cre/loxP synapse

- No DNA binding domain
- Need of tetramer formation
- Need of DNA bending
- Consecutive strand cleavage
- Formation of holliday junction intermediate
- Isomerization
- Resolution

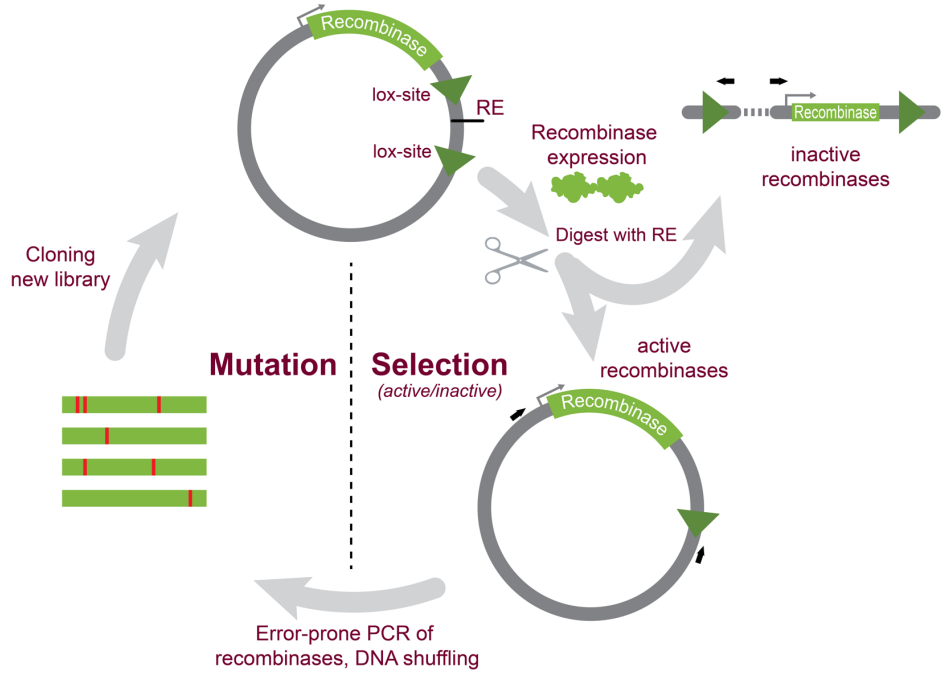
All of these hard-coded into the protein therefore it is difficult to program recombinases

Our solution – Directed Evolution



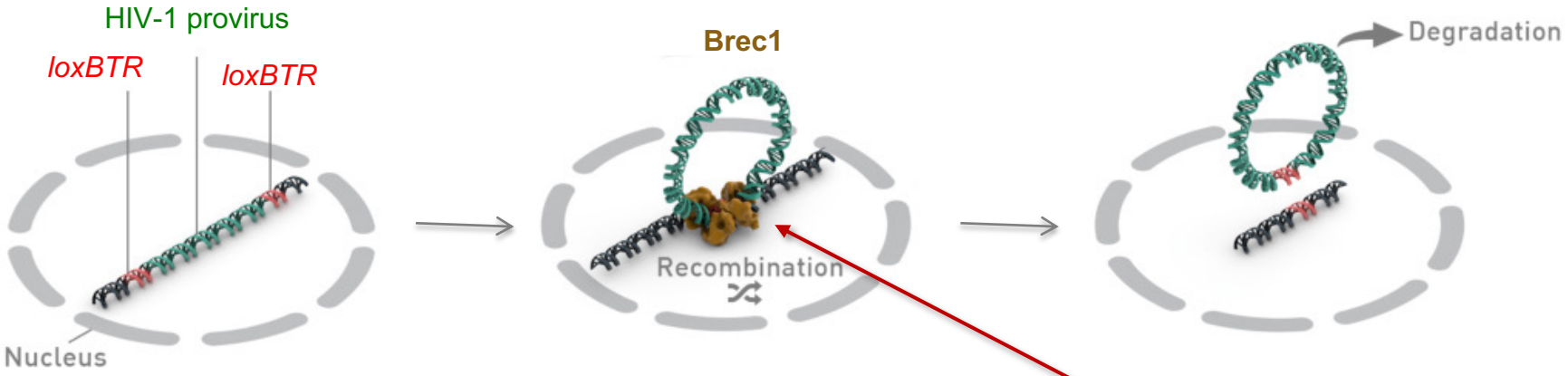
Substrate **li**nked **d**irected **e**volution (**SLiDE**)

Way to program recombinases



Lansing F. et al., NAR. 2020
Meinke G. et al. Chem Rev 2016
Buchholz F. et al. Nat Biotechnol 2001

Brec1 as a clinical SSR candidate to treat HIV-1 infections



nature biotechnology

Article | Published: 22 February 2016

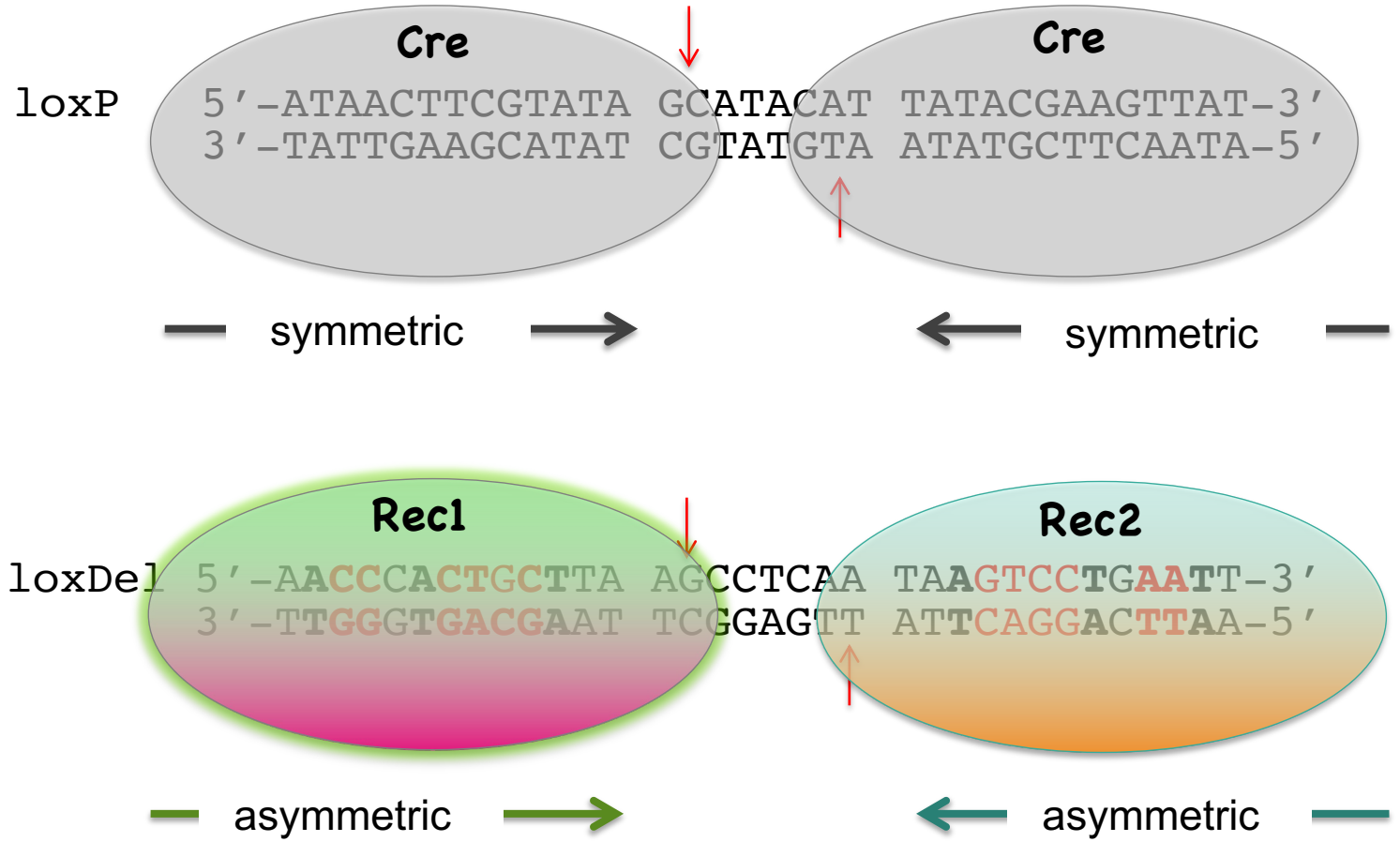
Directed evolution of a recombinase that excises the provirus of most HIV-1 primary isolates with high specificity

Janet Karpinski, Ilona Hauber, Jan Chemnitz, Carola Schäfer, Maciej Paszkowski-Rogacz, Deboyoti Chakraborty, Niklas Beschorner, Helga Hofmann-Sieber, Ulrike C Lange, Adam Grundhoff, Karl Hackmann, Evelin Schrock, Josephine Abi-Ghanem, M Teresa Pisabarro, Vineeth Surendranath, Axel Schambach, Christoph Lindner, Jan van Lunzen, Joachim Hauber & Frank Buchholz

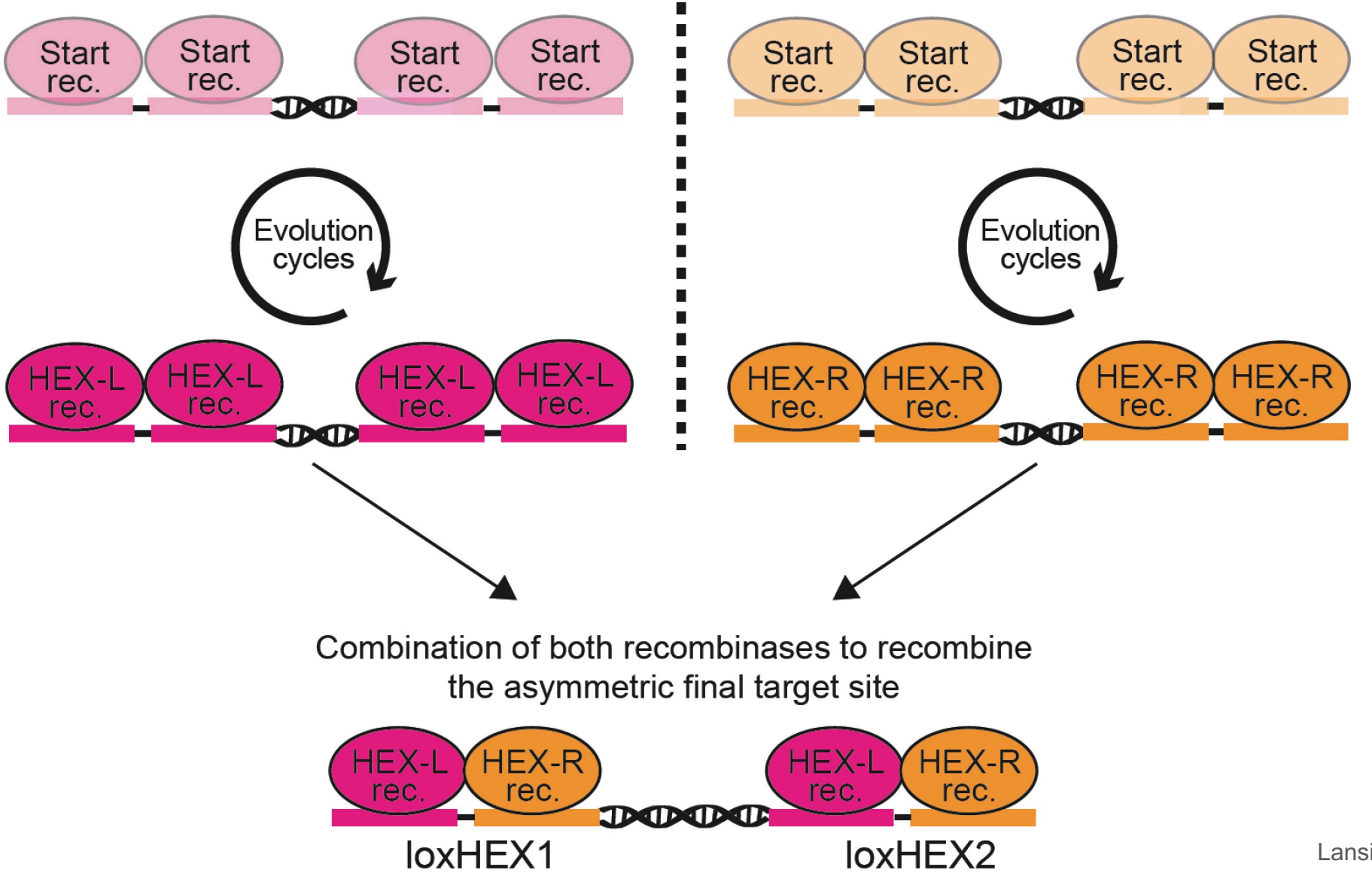
PROVIREX
Genome Editing Therapies GmbH

Sarkar *et al.*, **Science** (2007)
Karpinski *et al.*, **Nat. Biotechnol.** (2016)

Dual recombinases targeting asymmetric sites

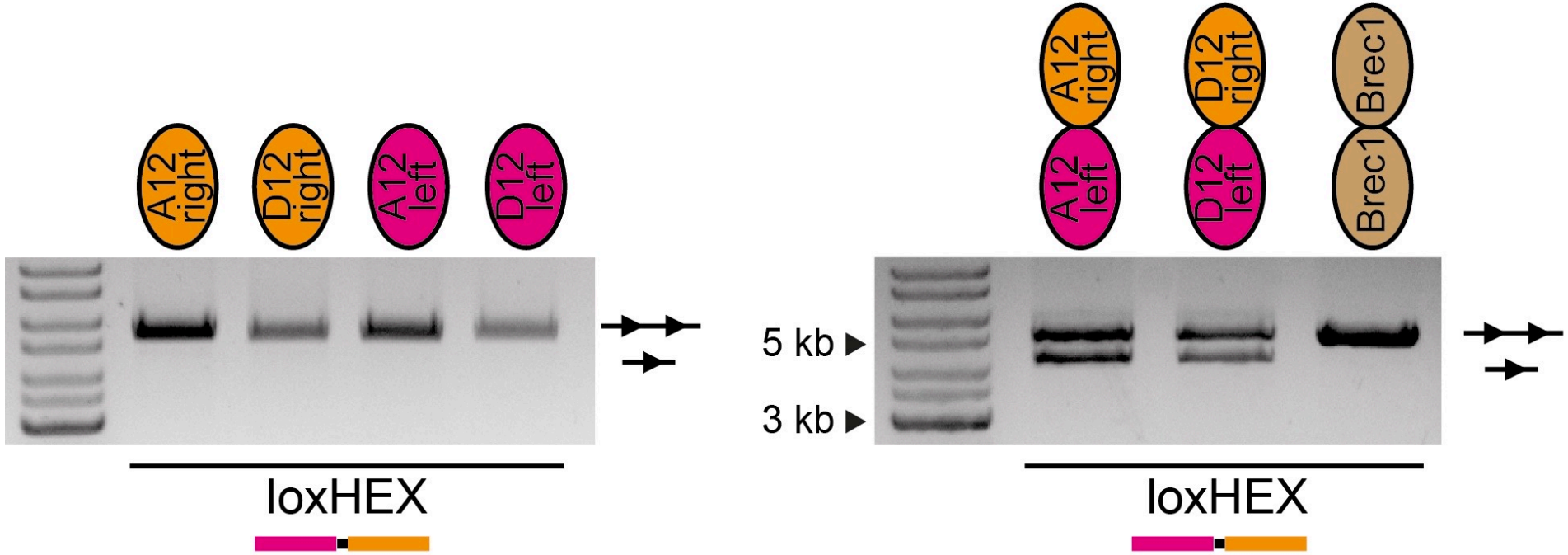


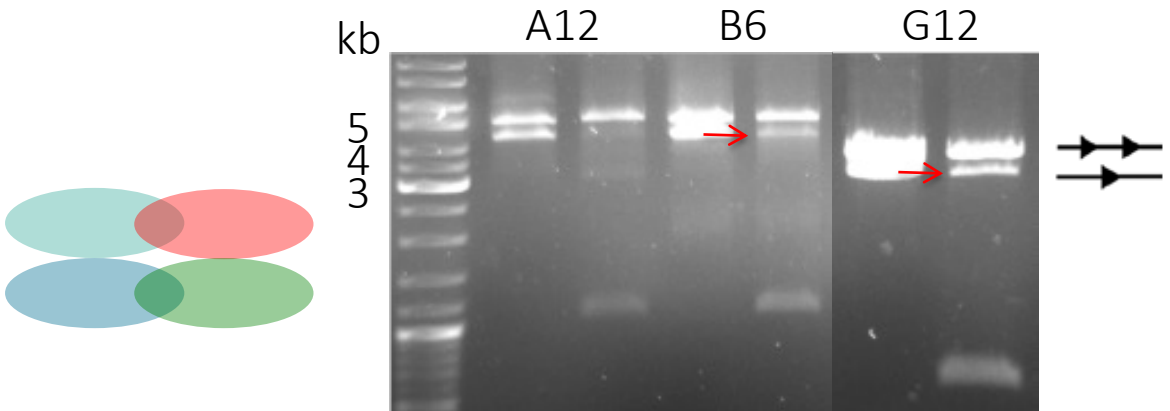
Dual SLiDE strategy



Lansing *et al.*, **NAR** (2020)

Liberating SSRs from target site restrictions





Lansing *et al.*, **NAR** (2020)

Example for a therapeutic heterospecific designer-recombinase: Hemophilia A

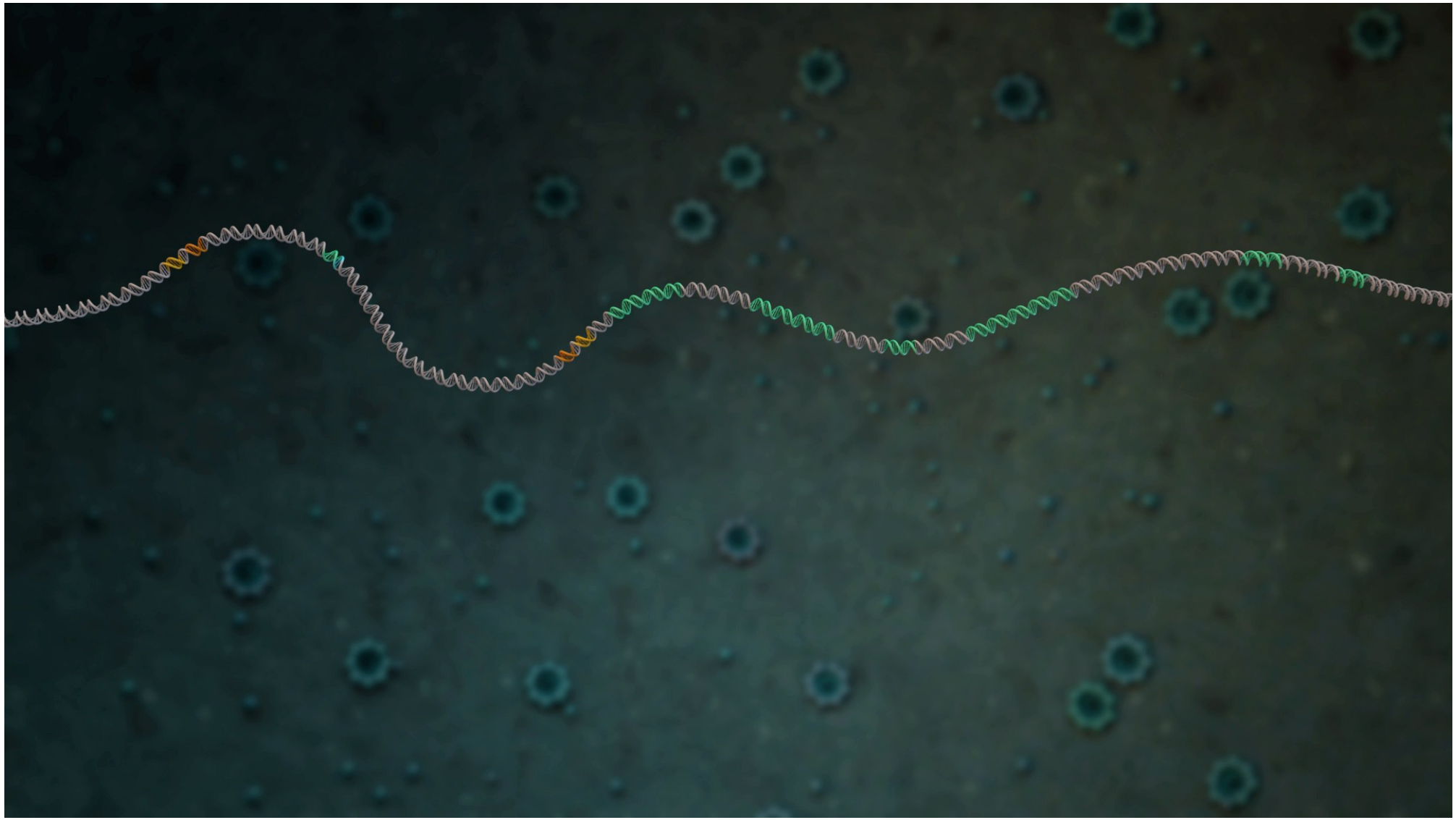
Hemophilia A in a nutshell

- Monogenetic X-linked disease (disruption of the F8 gene)
- Most common blood clotting disorder (**1:5000** new born males)
- Current treatment option - injections of recombinant Factor VIII (2-8 times a month - **100,000€ - 600,000€**/year)
- Problem I: Stable Factor VIII level (**short half-life**)
- Problem II: Formation of **antibodies** against recombinant Factor VIII

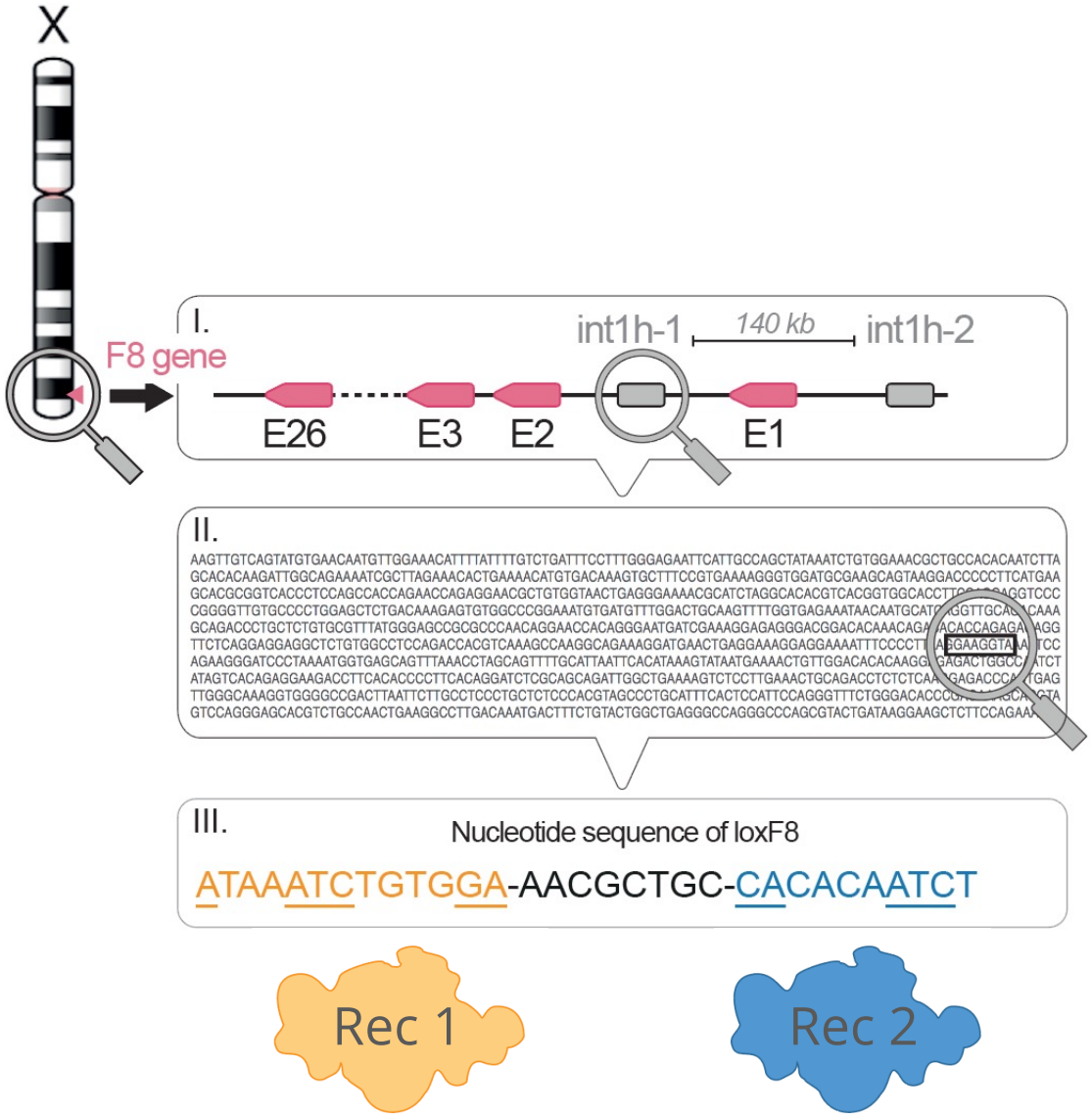
Gene therapy for treating Hemophilia?

- Severely affected individuals (**<1%** activity) would profit the most
- A clinical benefit could be achieved by reconstitution of **3-5%** of F8 activity
- Severe Hemophilia A is often caused by genomic inversions (**50%** of the cases)

Designer-Recombinase induced Genomic Inversion (DRiGI)

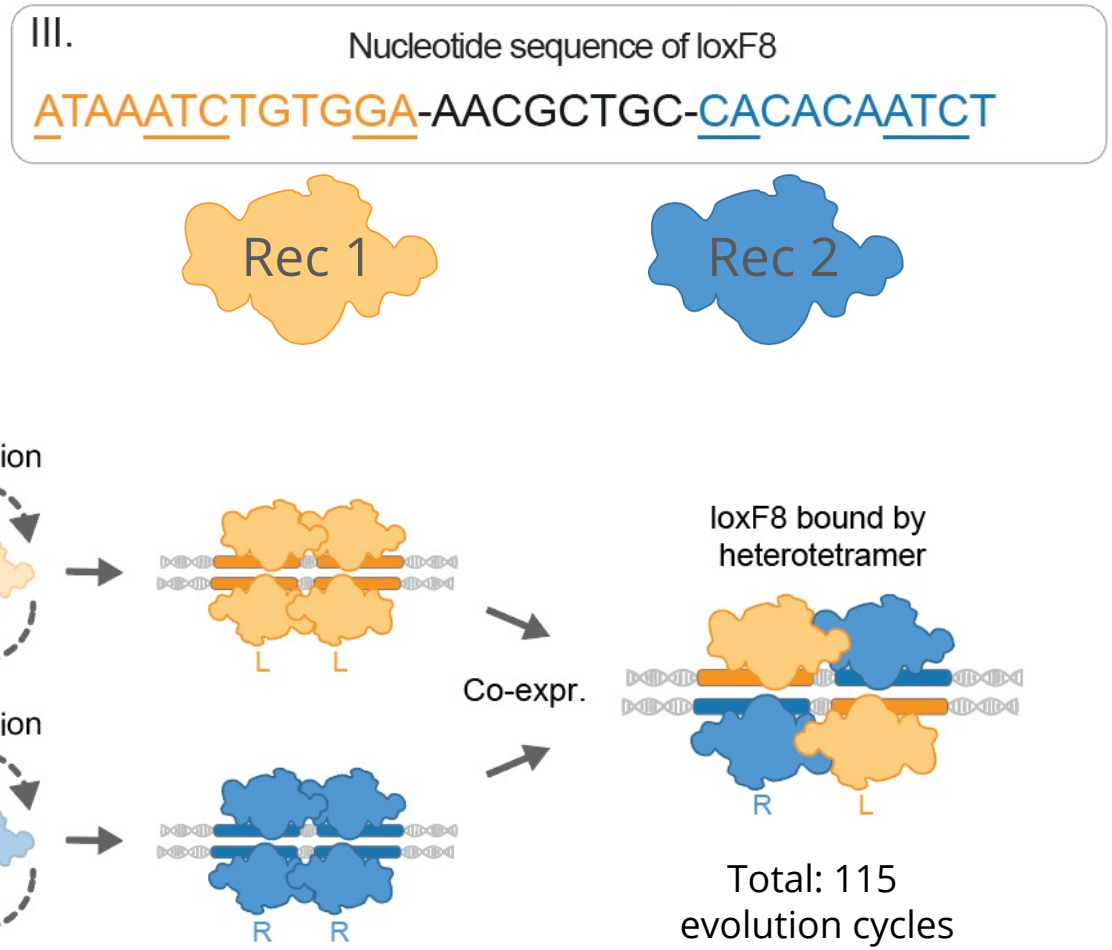


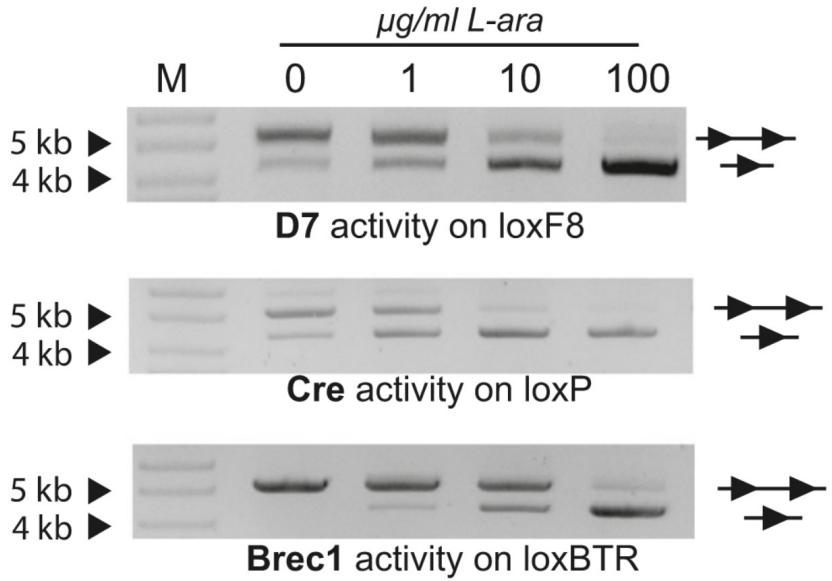
Finding a target site



Lansing F. et al., *Nat. Com.* 2022

Making a heterospecific RecF8 recombinase

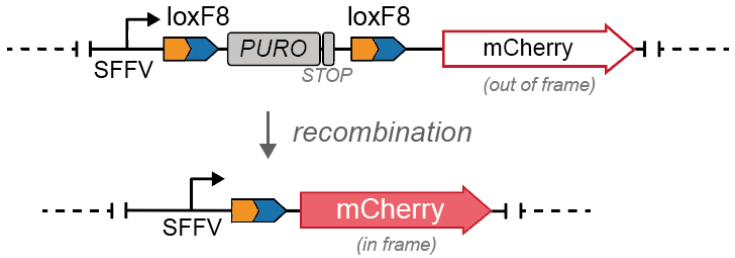


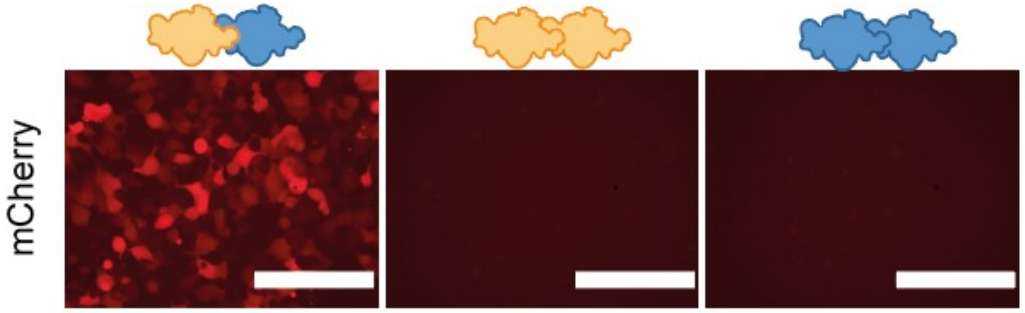


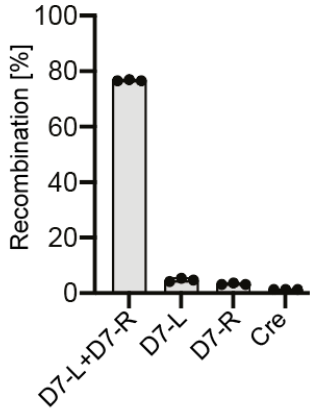
Lansing F. et al., *Nat. Com.* 2022

RecF8 in reporter cells

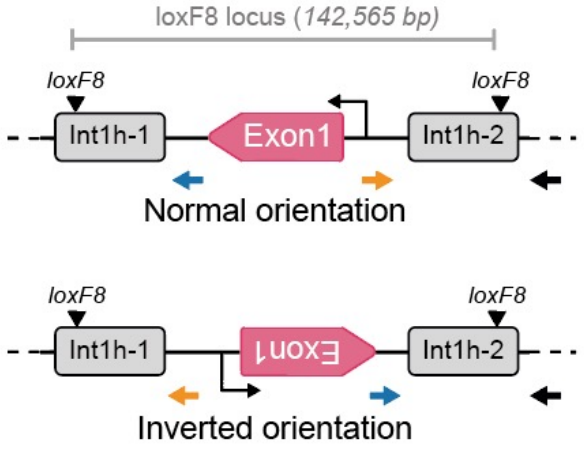
Reporter cell line

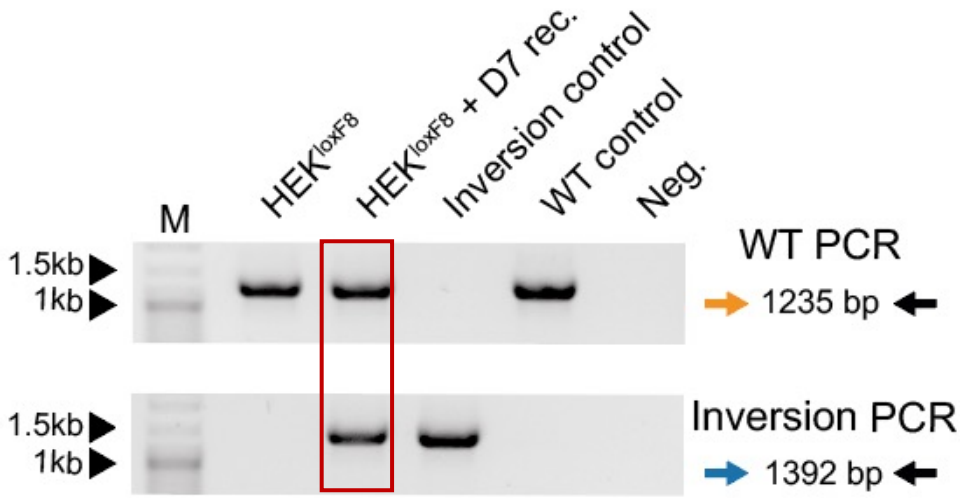


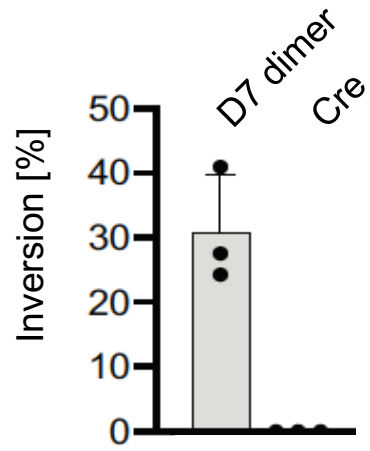




Genomic loxF8 locus

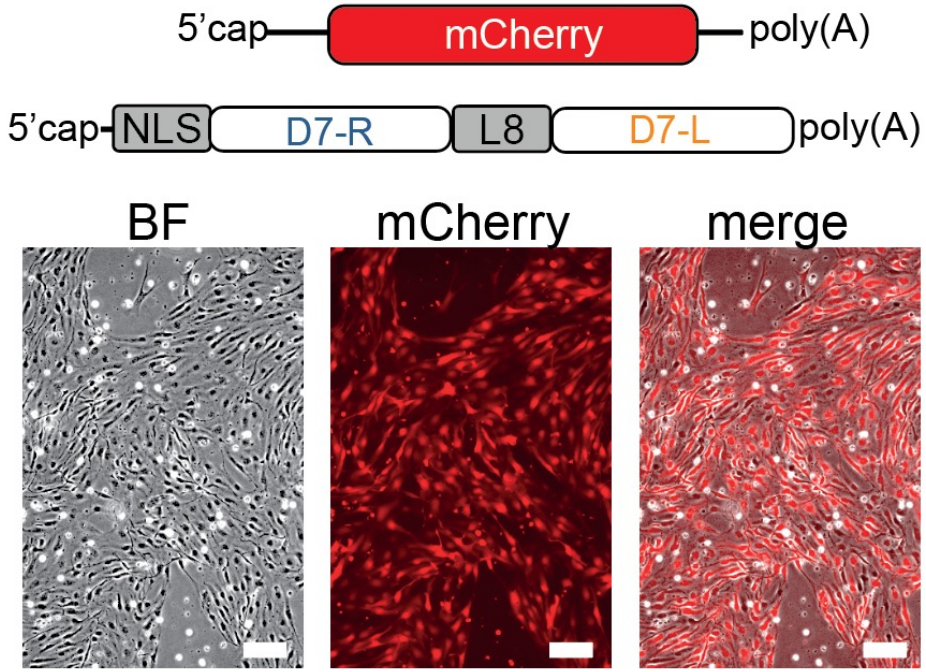




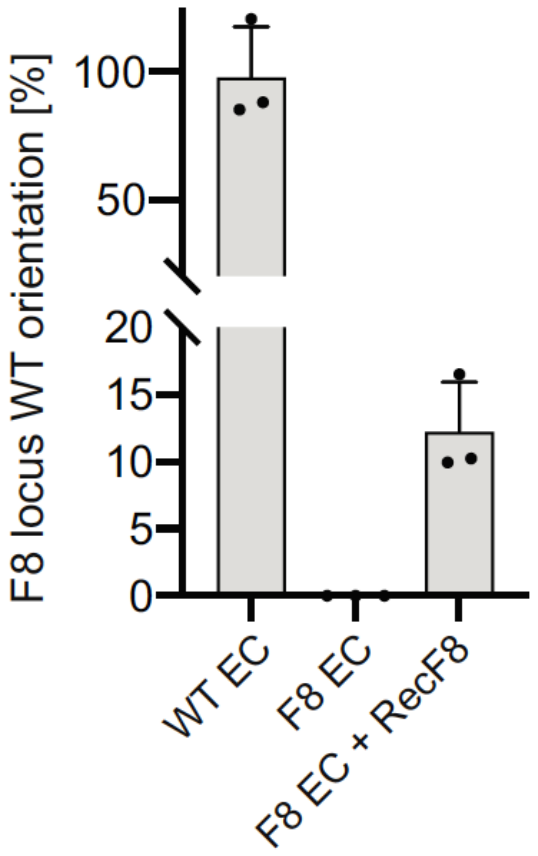


Lansing F. et al., *Nat. Com.* 2022

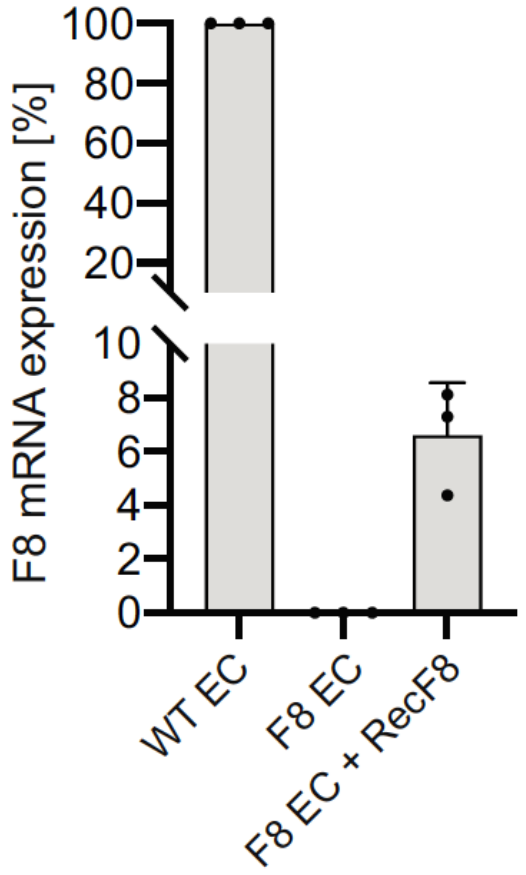
RecF8 corrects the inversion in patient cells



Genomic inversion

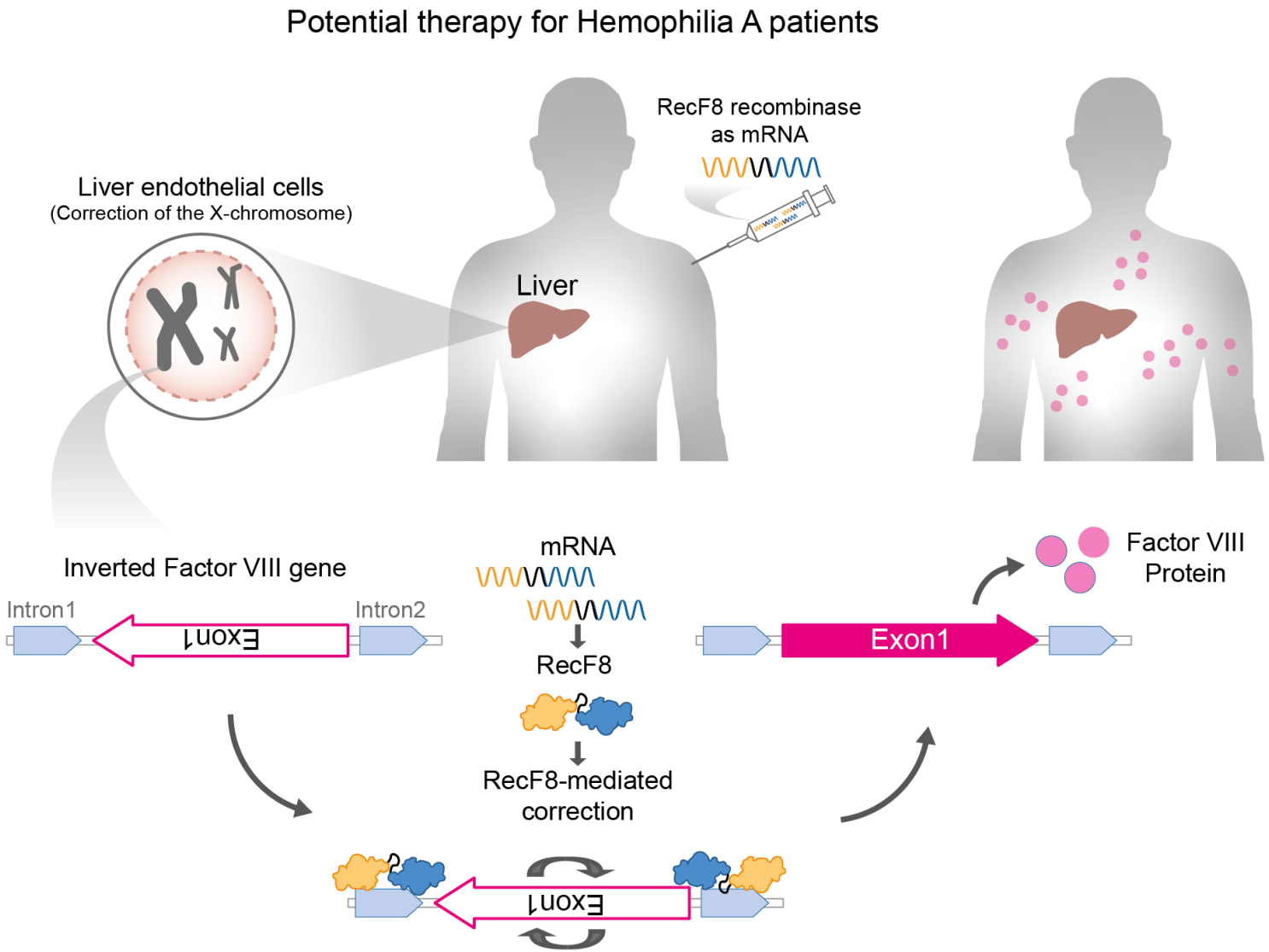


mRNA expression



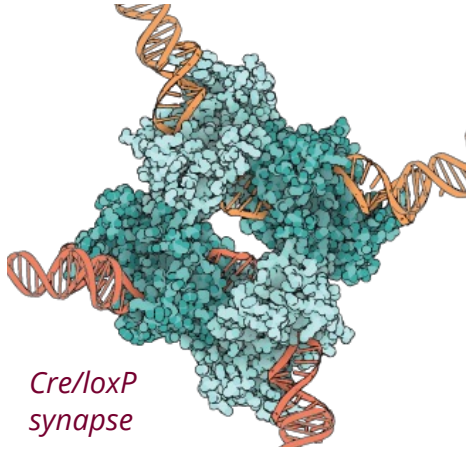
Lansing F. et al., *Nat. Com.* 2022

Envisioned RecF8 therapy



Lansing F. et al., *Nat. Com.* 2022

Are there better ways of programming Recombinases to new target sites?

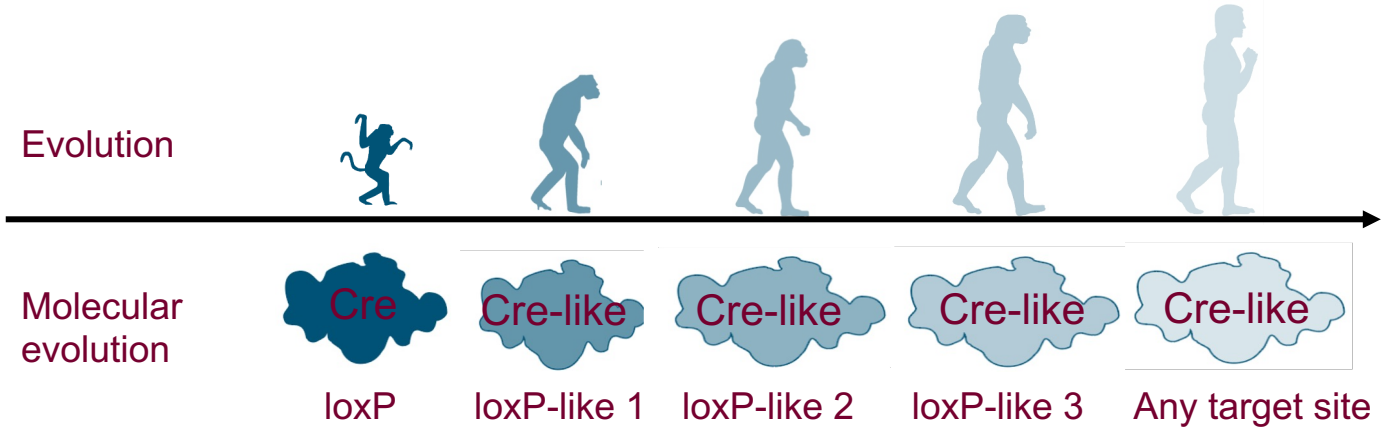


Cre/loxP synapse

- No DNA binding domain
- Need of tetramer formation
- Need of DNA bending
- Consecutive strand cleavage
- Formation of holliday junction intermediate
- Isomerization
- Resolution

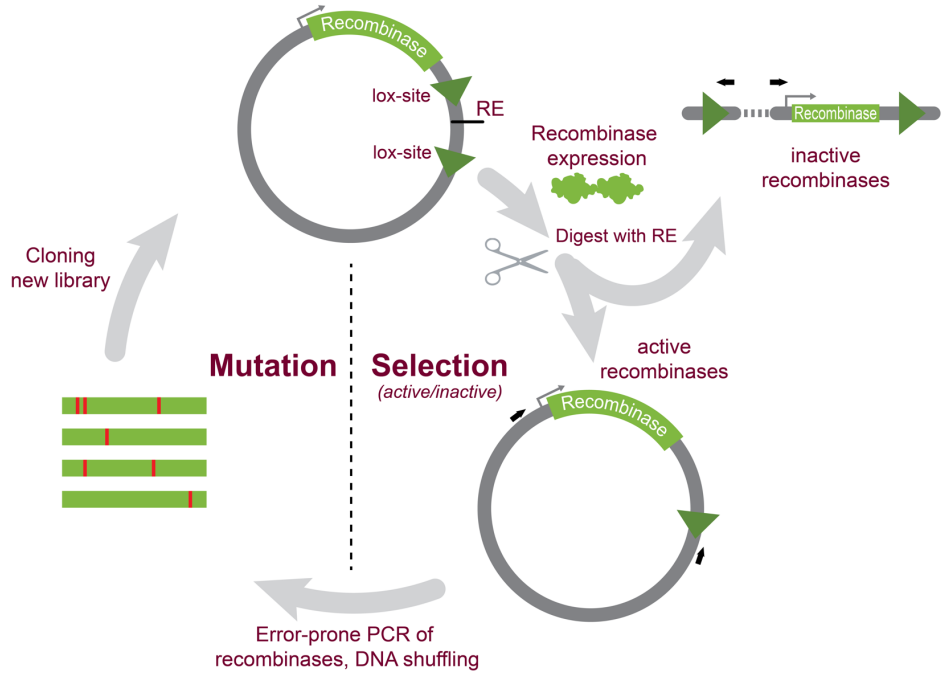
All of these hard-coded into the protein therefore it is difficult to program recombinases

Our solution – Directed Evolution



Substrate **li**nked **d**irected **e**volution (**SLiDE**)

Way to program recombinases

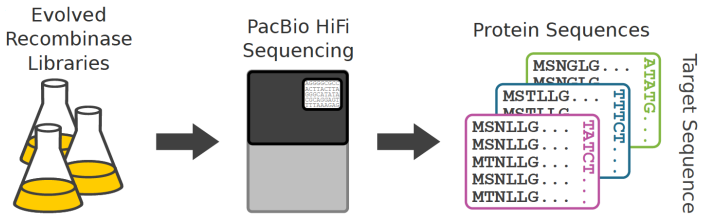


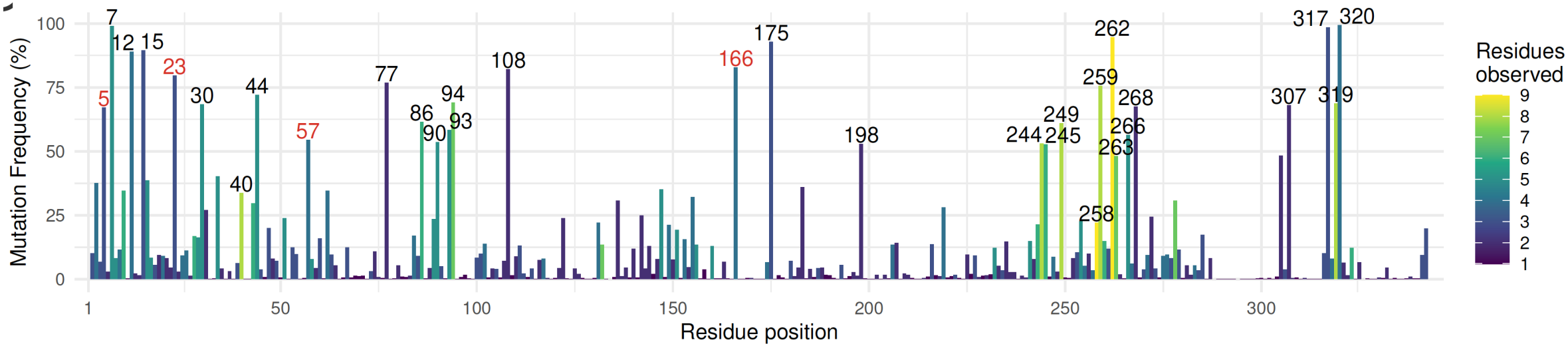
→ 89 evolved recombinase Libraries targeting different sites

Lansing F. et al., NAR. 2020
Meinke G. et al. Chem Rev 2016
Buchholz F. et al. Nat Biotechnol 2001

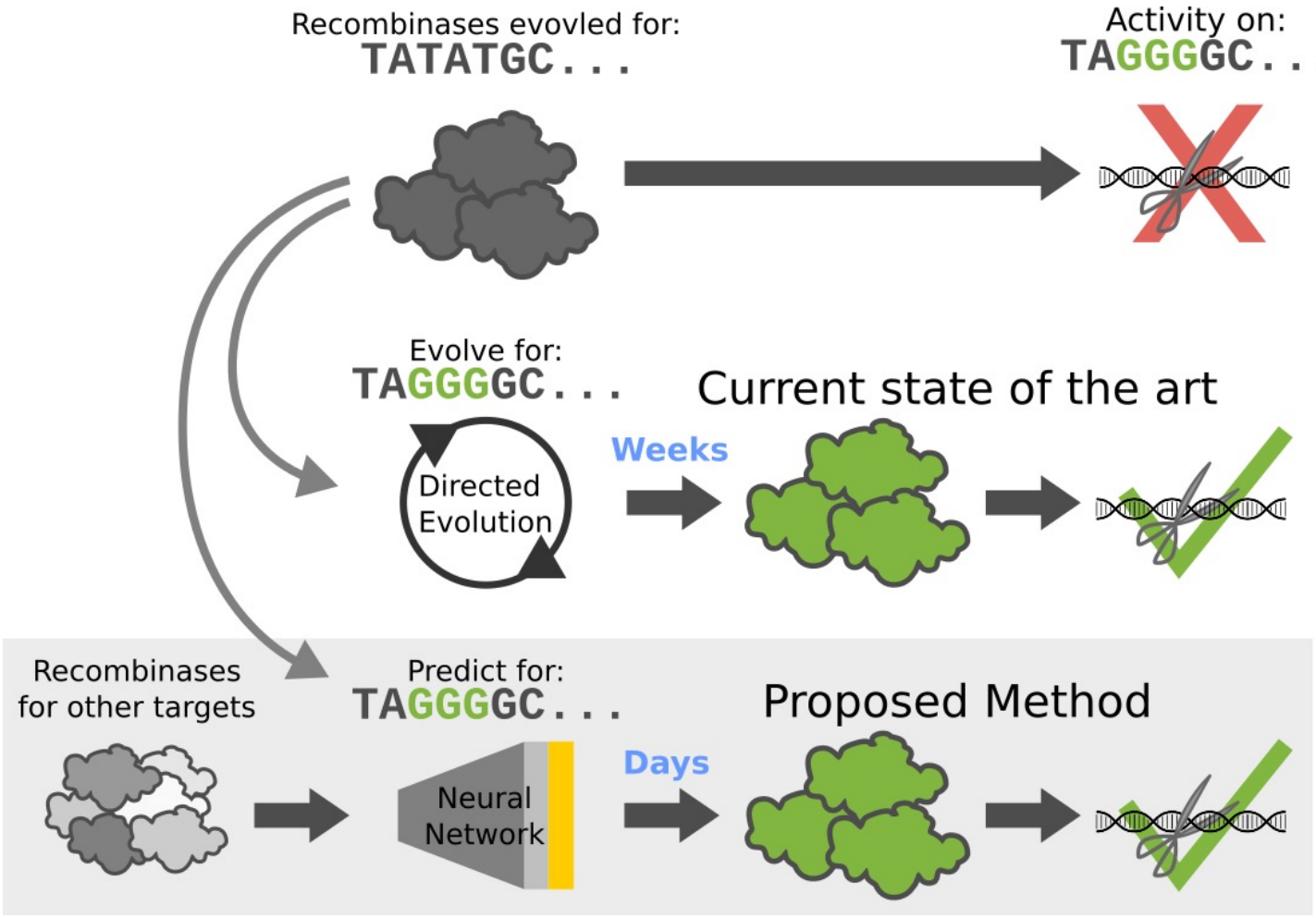
Rational design of designer-recombinases is out of reach

- **89 evolved recombinase Libraries targeting different sites**
- **Deep sequencing > 2 Mio. full-length recombinases**





RecGen: an AI-based algorithm to predict designer-recombinases



Schmitt *et al.*, under review

Summary

- Non-nuclease approaches are likely safer for therapeutic genome editing
- Base editors are excellent tools to correct cancer mutations
- Epigenetic editors allow long-term silencing of genes
- Designer-Recombinases are efficient, versatile and safe genome editing tools
- RecF8 seamlessly corrects int1h inversion with potential for clinical use
- RecGen is an AI-based algorithm to accelerate the generation of new designer-recombinases

Acknowledgments

Janet

Felix

RECTECH
PRECISION GENOME SURGERY

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erc
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UPGRADE Unlocking Precision Gene Therapy

Joachim Hauber, HPI, Hamburg
M. Teresa Pisabarro, Biotec, DD
Daniel Stange, DD
Ralf Knöffler, DD
Takanori Takebe, Cincinnati, USA

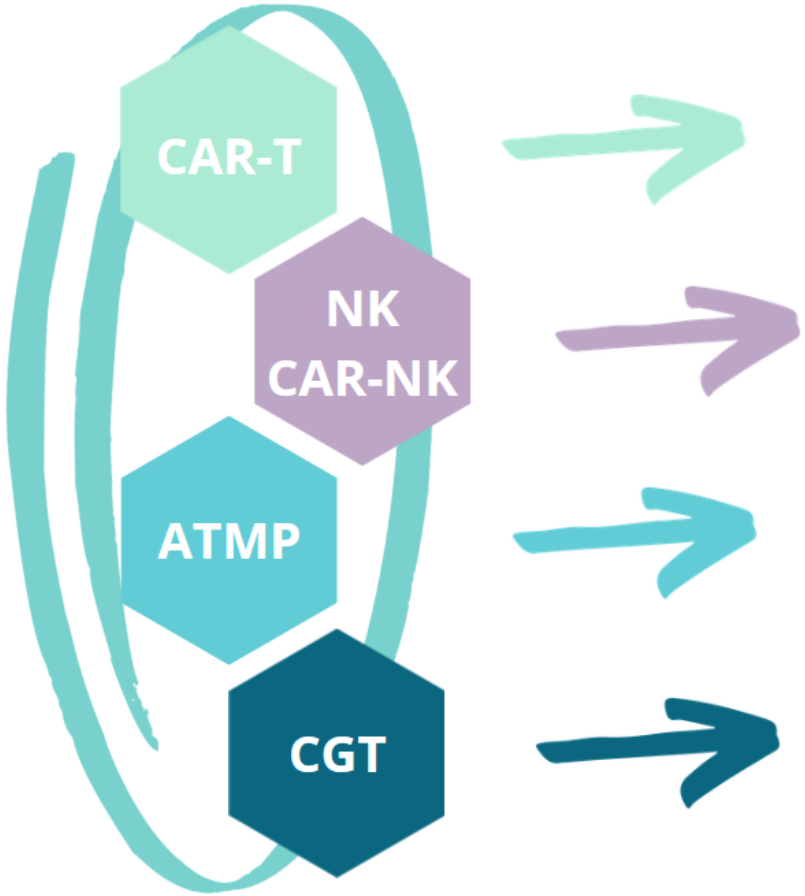
Lansing F. et al., *Nat. Com.* 2022

Coffee Break

Time	Topic	Responsible
10:00 – 10:20	Welcome	Ulrike Köhl + Ezio Bonifacio
10:20 – 10:55	Key note – Gene editing	Frank Buchholz 30min + 5min discussion
10:55 – 11:10	**Coffee break**	**All**
11:10 – 13:00	Project Pitches	5min + 5min discussion each
13:00 – 13:05	**Group picture**	**All**
13:05 – 14:00	**Lunch Break**	**All**
14:00 – 14:50	Presentation of Platforms and Hub	5min + 2min discussion
14:50 – 16:15	Area Meetings	All
16:15 – 16:35	**Coffee Break**	**All**

PROJECT PITCHES

SAXOCELL®



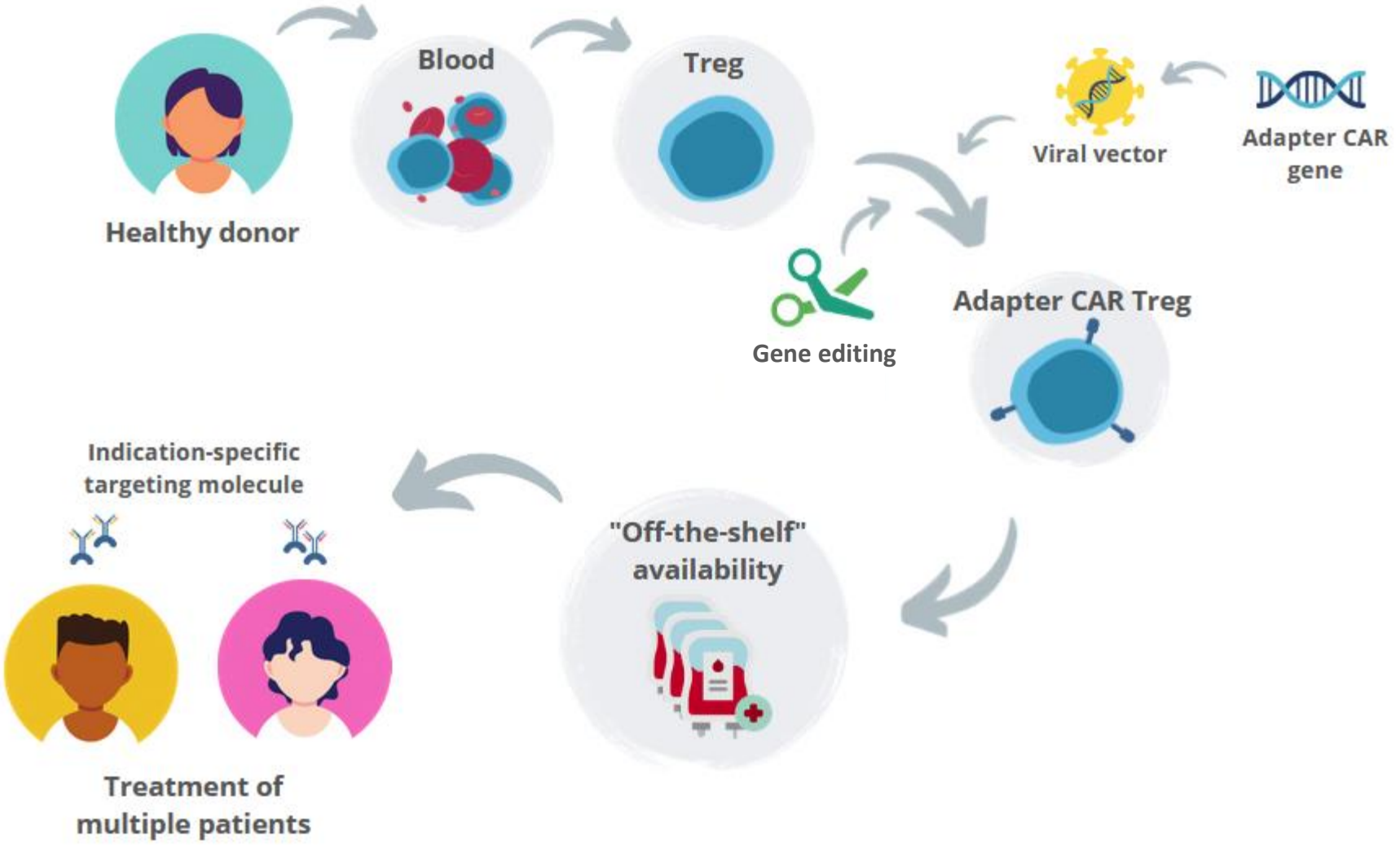
AlloCART & UltraCART

CAR-NK 4.0, CAReNK-AID
& NK4Therapy

HemRec, ZellTWund,
xMac & MSC-PreStiGe

OPTIX, ECP-CAR
& TheraSTAR

AlloCART*reg* – Project Overview



AREA 1 – CAR-T

AlloCART*reg* – Results so far

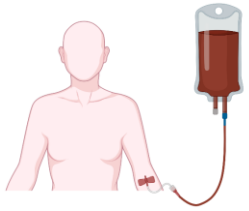
SAXOCELL®

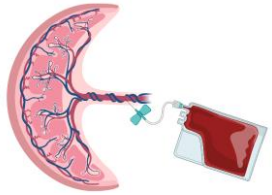
AREA 1 – CAR-T

Samikshya

Treg source

Adult vs cord blood



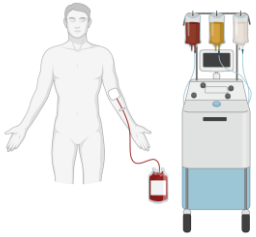


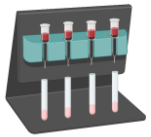
- Collaboration with UKD maternity ward ✓
- Ethics approval ✓
- Panels for 20 Treg markers ✓

Kavitha

Treg isolation

Optimizing purity





Pre-enrichment

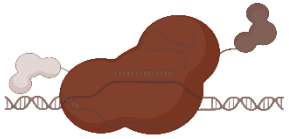
GMP compatible sort

- Phenotype ✓
- Expansion potential ✓

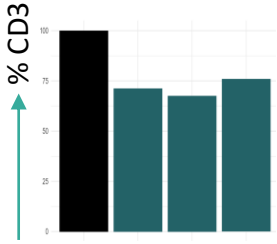
Pascal

T cell receptor knockdown

Proof of concept



Epigenetic knockdown



- T cell lines ✓
- Tool comparison ✓
- Testing different gRNAs ✓

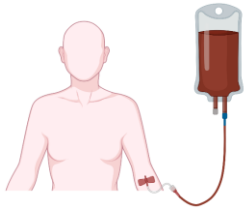
AlloCART$_{reg}$ – Outlook

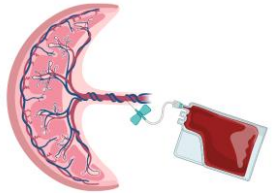
SAXOCELL®

AREA 1 – CAR-T

Samikshya

Treg source
Adult vs cord blood

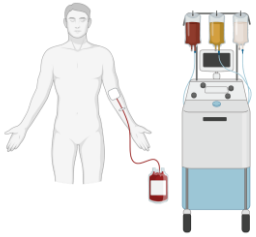


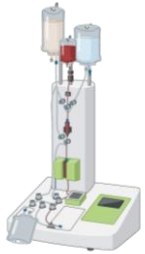


Expansion potential
Transduction efficiency
Stability & function

Kavitha

Treg isolation
Optimizing purity





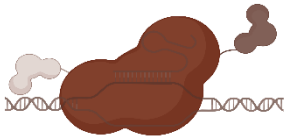
Clinical pre-enrichment

GMP compatible sort

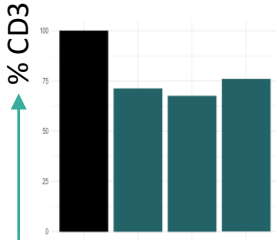
CAR transduction
Functionality
Stability

Pascal

T cell receptor knockdown
Proof of concept

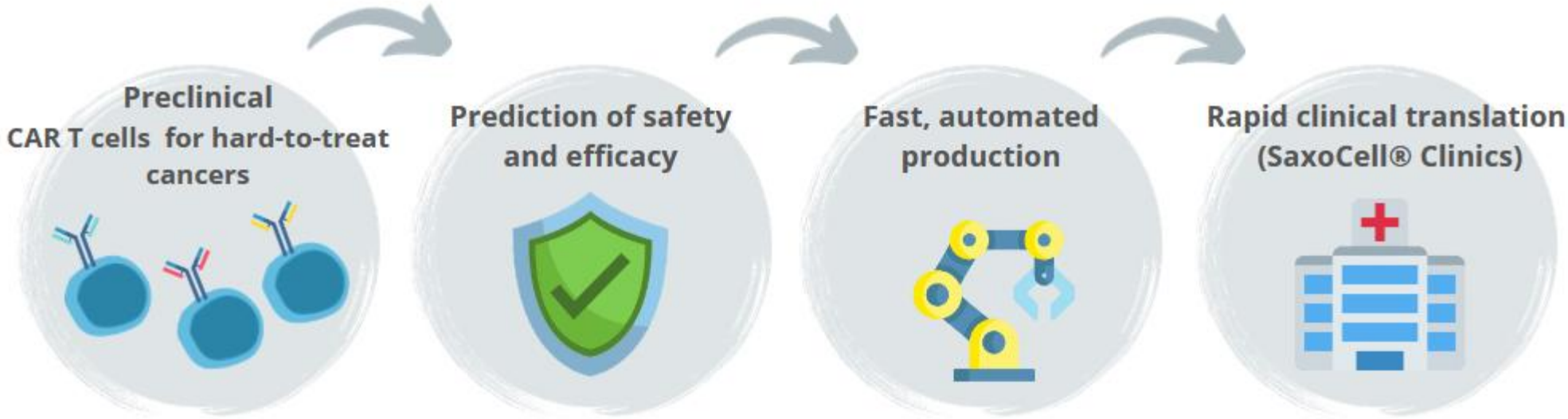


Epigenetic knockdown



Identify best editing system
Search for epigenetic repressors
→ Primary T cells → Treg

UltraCART – Project Overview

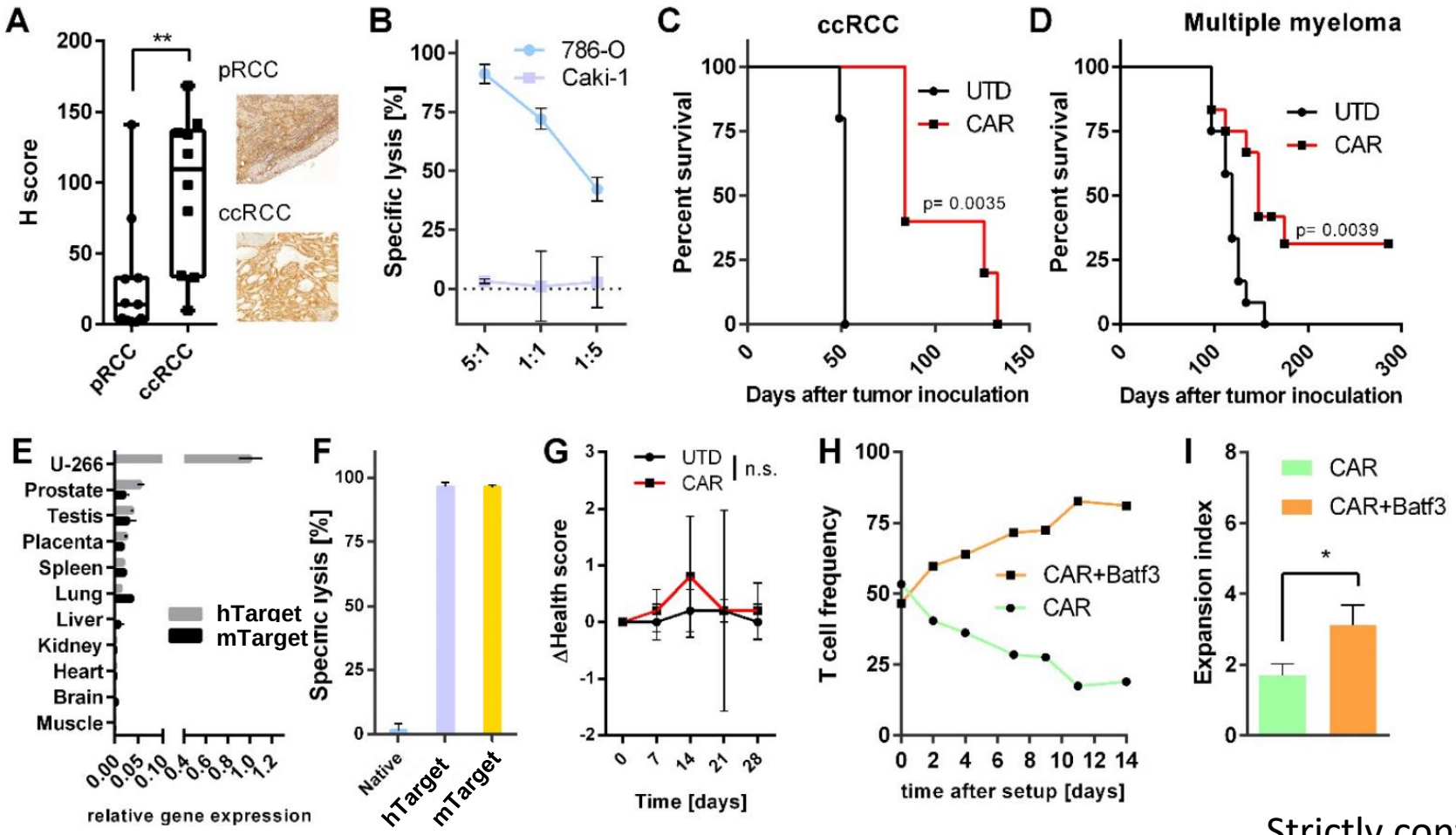


Strategisches Ziel: Klinische Translation des ersten Lead-CAR T Zell Produktes aus der Innovationspipeline von T-CURX und Initiierung einer klinischen Studie der Phase I/IIa im Programm SaxoCellClinics.

AREA 1 – CAR-T

UltraCART – Results so far

Arbeitspaket 1: Neue Targets und CAR-T Zell Produkte. Lead: T-CURX.
→ Neues Top Target für CAR-T, adressiert liquide und solide Tumore

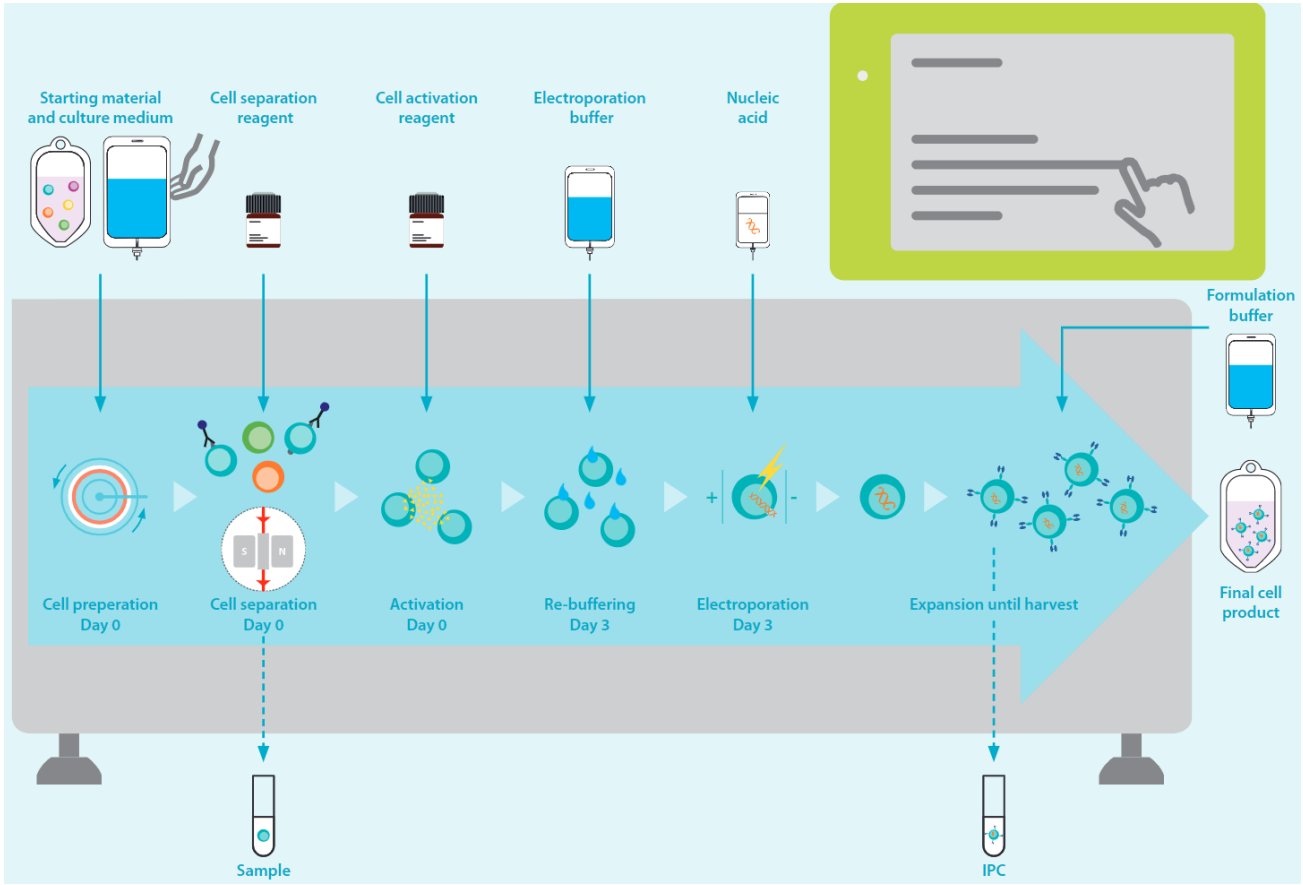


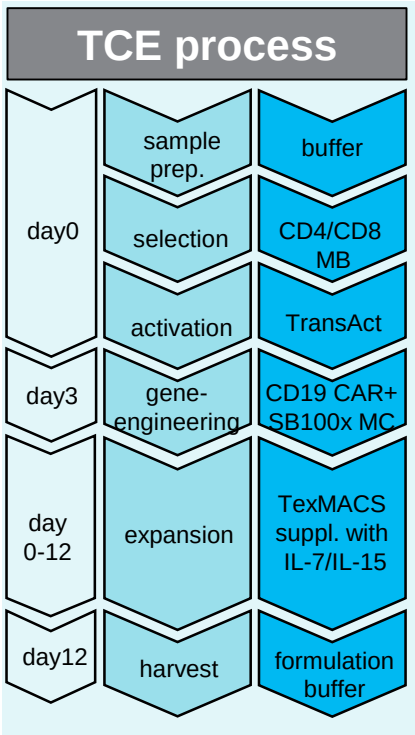
AREA 1 – CAR-T

UltraCART – Results so far

Arbeitspaket 3: Herstellung & Automation. Lead: Fnh-IZI

→ Automatisierter Herstellungsprozess für virus-freie Transposon basierte CAR-T auf Miltenyi Prodigy (+ EP)





AREA 1 – CAR-T

UltraCART – Results so far

Arbeitspaket 3: Herstellung & Automation. Lead: Fnh-IZI

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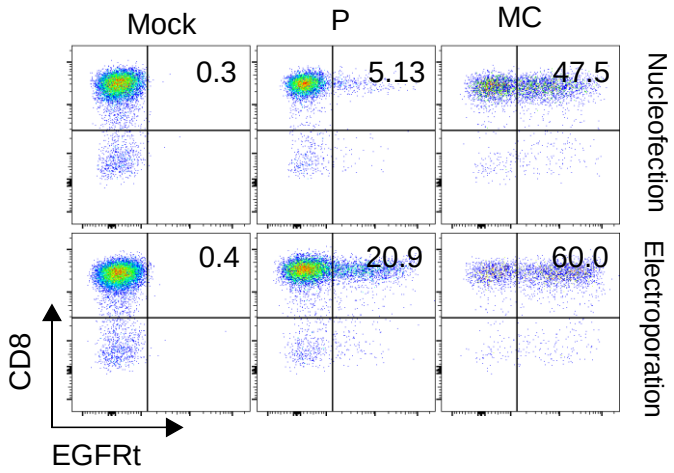
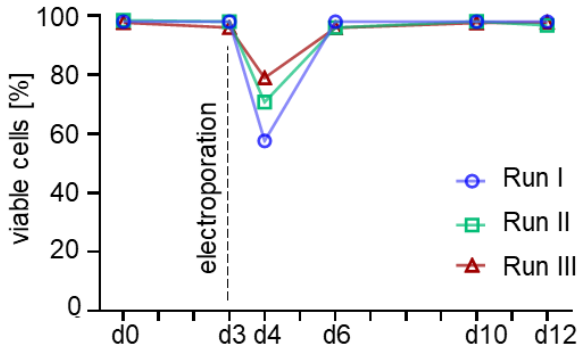
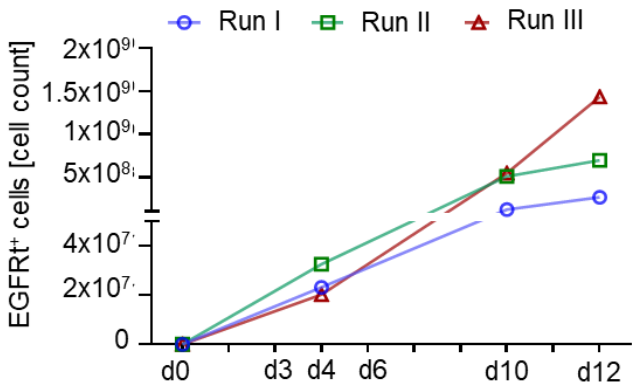
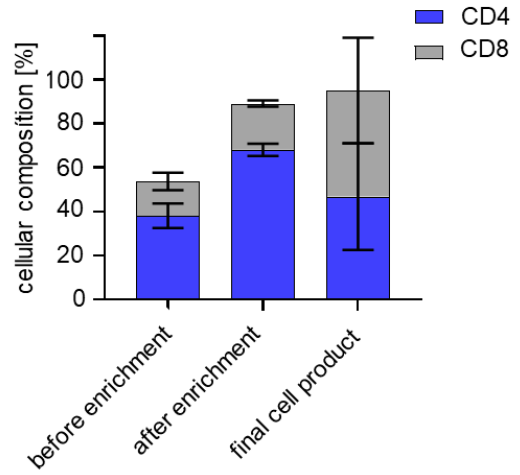
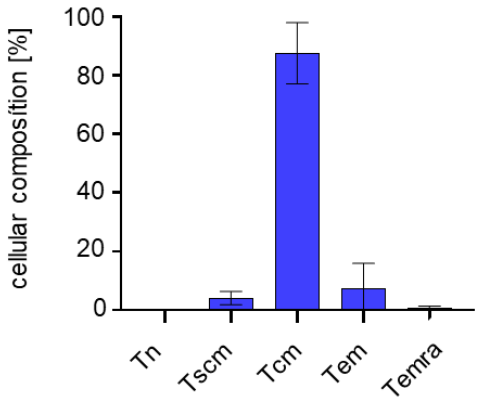










Gentransfer Rate: 60%

Therapeutische Dosis

TCM Phänotyp, CD4/CD8 Ratio 1:1

AREA 1 – CAR-T

UltraCART – Outlook

Arbeitspaket 1: Neue Targets und CAR-T Zell Produkte. Lead: T-CURX.

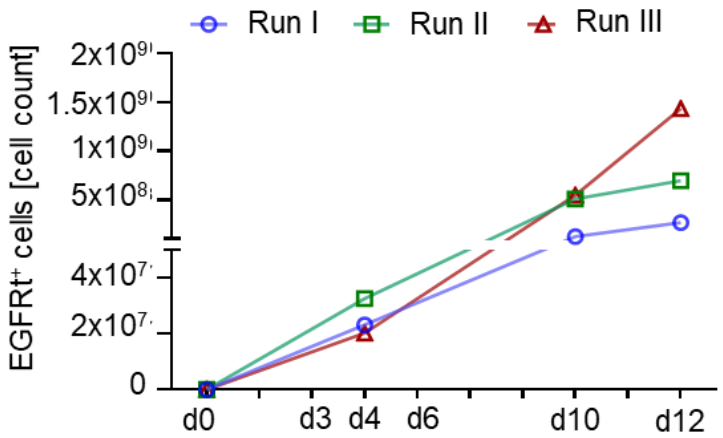
Arbeitspaket 2: Neue Modelle für die Prädiktion von Sicherheit & Wirksamkeit. Lead: Fnh-IZI.

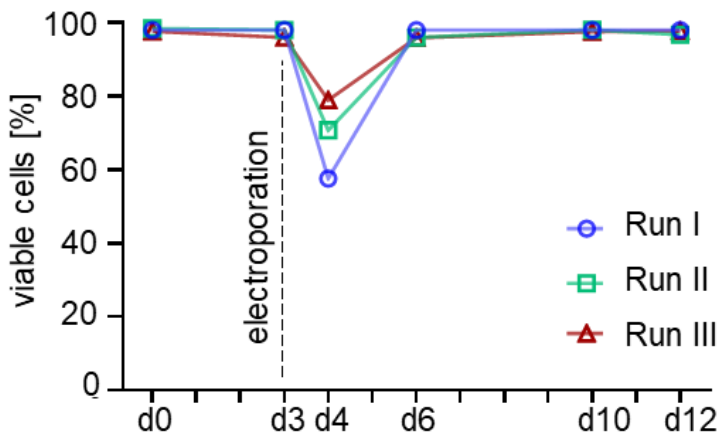
Arbeitspaket 3: Herstellung & Automation. Lead: Fnh-IZI.

→ Verkürzung des Herstellungsprozesses – 7 Tage

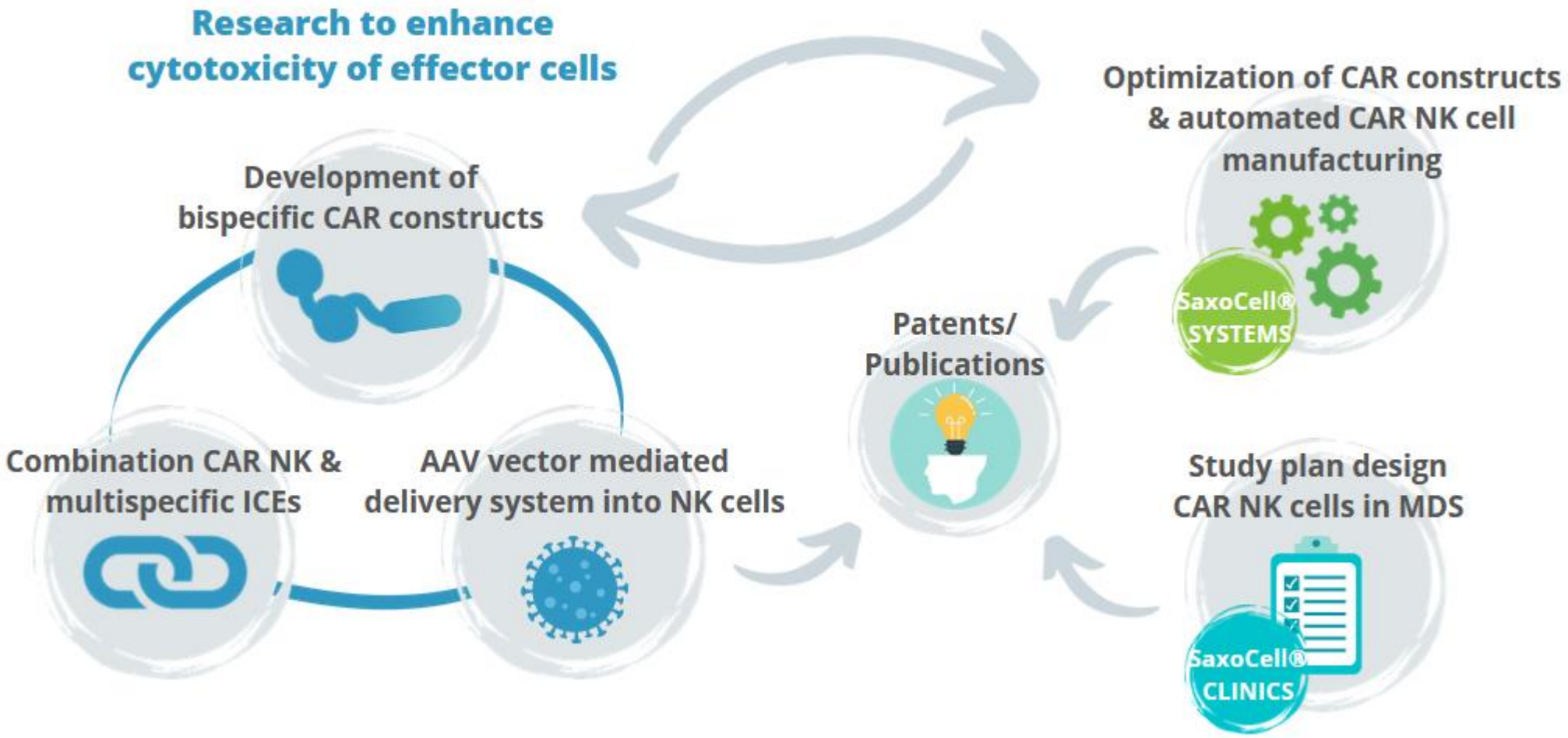
Arbeitspaket 4: Hochauflösende Mikroskopie. Lead: T-CURX.

Arbeitspaket 5: Omics Analytik und Künstliche Intelligenz. Lead: Fh-IZI.



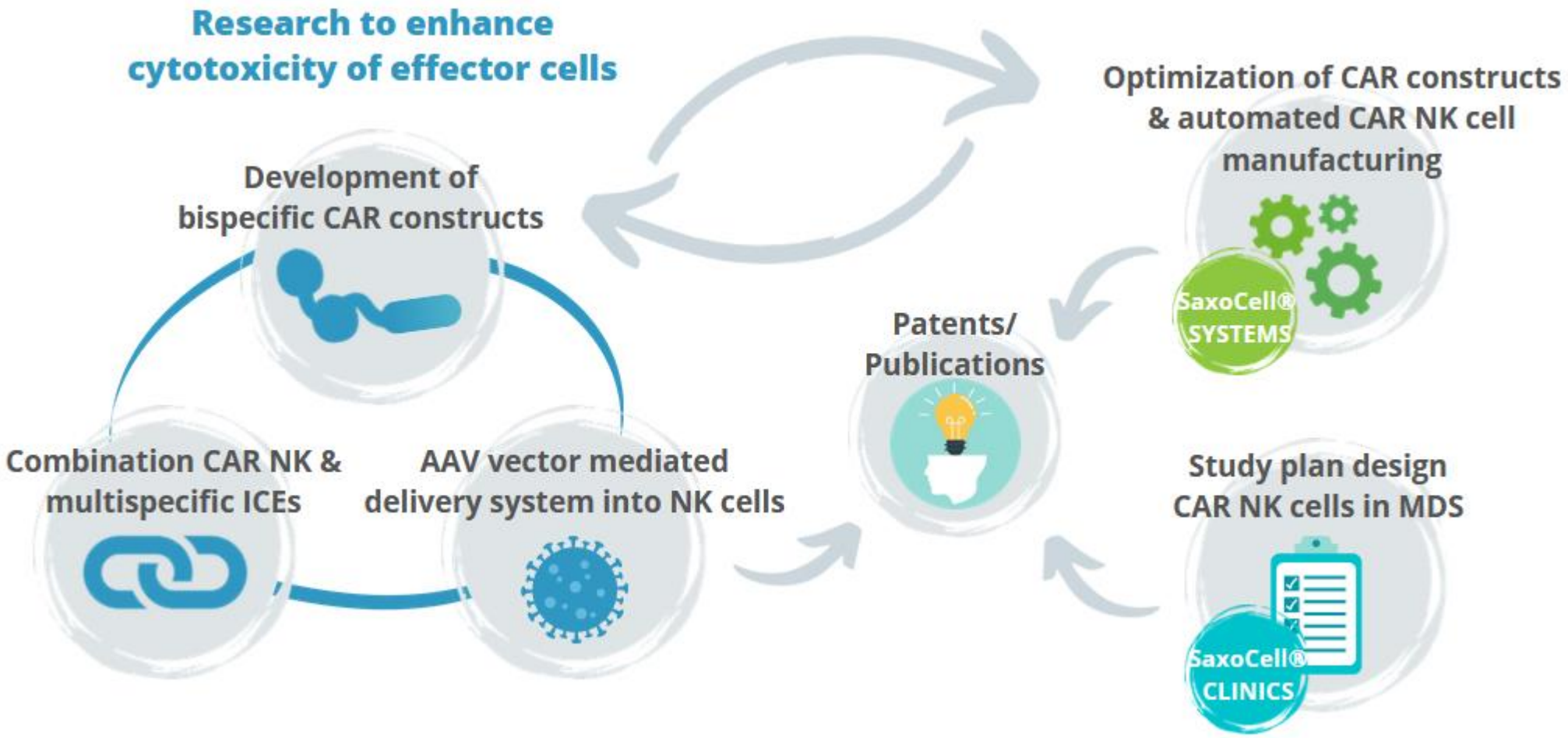


CAR-NK 4.0 – Project Overview



AREA 2 – NK & CAR-NK

CAR-NK 4.0 – Project Overview



AREA 2 – NK & CAR-NK

CAR-NK 4.0 – Results so far

SAXOCELL®

AREA 2 – NK & CAR-NK

AP1

- Continuous improvement and synchronization of NK-protocols, supply of human pNK cells for different WPs (IZI)
- Establishment of an automated process for production of target-specific CAR-NK cells is ongoing (MB)
- RUO protocols for production and testing of CAR NK functionality have been transferred from MB to IZI (MB)

AP2

- Preparation of the study protocol has started (KCh)
- New Proposal (former BMBF-DoNKAR) to ensure the financing of the clinical trial is under development (UKL)

AP3

- Relevant antigen-binding domains have been identified and EMM-specific CAR-domains have been *designed* (IZI)
- Infrastructure to obtain EMM-material has been established (IZI/KCh)
- Common sense on standardized diagnostics (IZI/KCh)
- Recruitments of two project responsibles in Chemnitz, who will guide the scientific transfer to IZI (IZI/KCh)

AP4

- Production of anti-CD19/CD16 ICE®, purity and stability check (AFMD)
- Demonstrating activity in cytotoxicity assays (IZI/AFMD)
- *In vitro* testing of cytotoxic CAR-NKCs via retroviral transduction (IZI)

AP5

- Different AAV-Serotypes and –capsid variants were tested on human pNK cells (IZI)
- Protocol for AAV-vectors has been established with transduction efficiencies in human pNK cells of up to 80% (IZI/UCCL)
- Cloning of CAR-constructs for AAV-vectors started (IZI/UCCL)

AP6

- The works in AP6 will start according to the foreseen timeline in Q3 2022 (MB)

CAR-NK 4.0 – Outlook

SAXOCELL®

AP1

- Finish establishment of the automated process for the production of target-specific CAR NK cells (MB)
- preparation of a data package for *in vitro* analysis of the target-specific CAR NK cells (MB)

AP2

- Continue working on study protocol/ study plan combining forces of KCh and UKL
- Application for new funding for the clinical trial (UKL)

AP3

- Defining methods to analyze EMM-samples for potential CAR-NK-therapie targets (IZI/KCh)
- Improving preparation of EMM-material prior biobanking (IZI/KCh)

AP4

- Affinity assays to check CD19 and CD16 binding of ICE® (AFMD)
- further *in vitro* tests of cytotoxic CAR-NK cells in combination with ICE® (IZI/AFMD)

AP5

- Investigation of the kinetics and the of transgen expression (IZI)
- Transduction of human pNKC with AAV-CAR-Vectors
- Further optimization of transduction efficiency and analysis of intracellular processing and infection biology (UCCL)

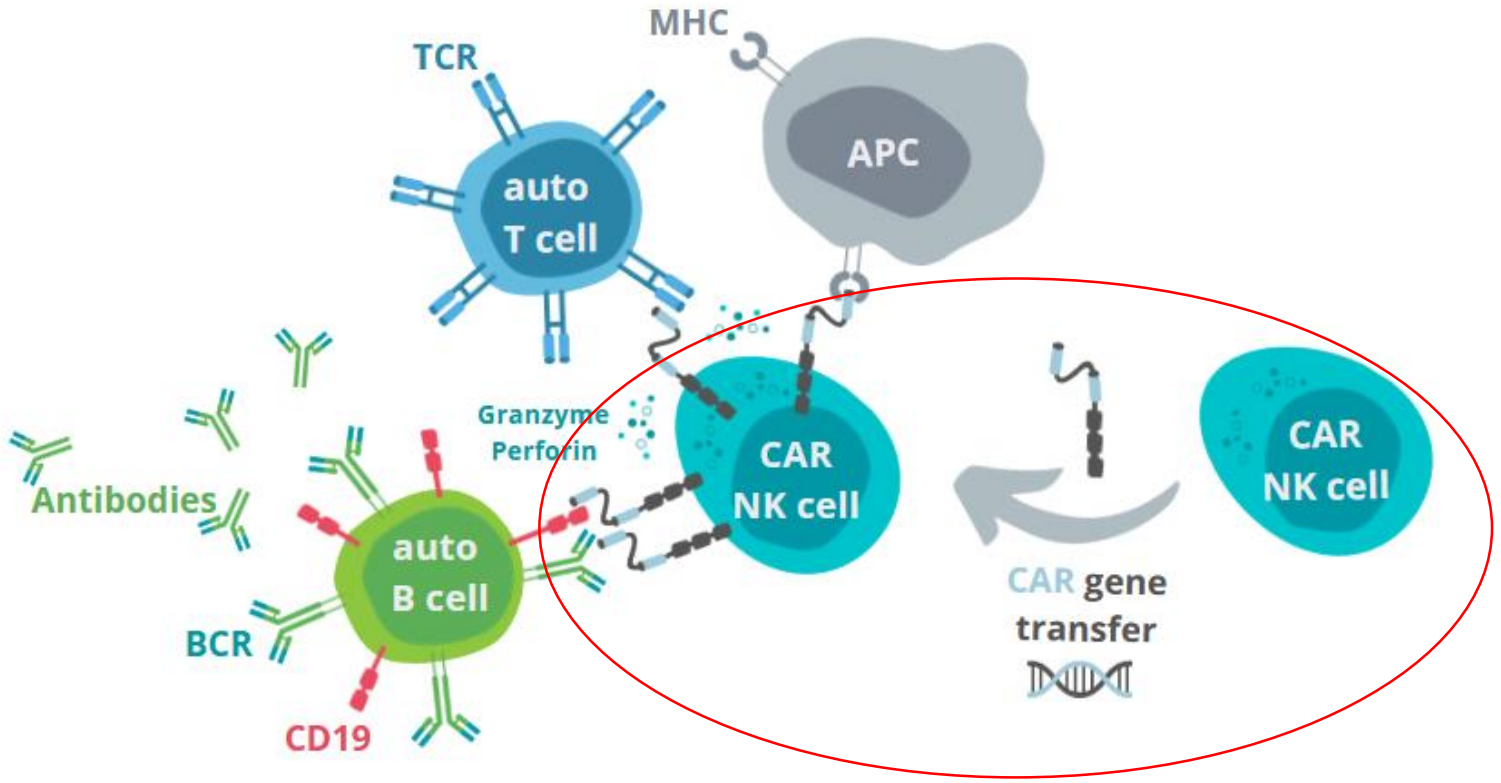
AP6

- Production of optimized target-specific CAR lentiviral vectors in pre-clinical quality (MB)

AREA 2 – NK & CAR-NK

CAReNK-AID – Project Overview

CAR engineered NK cells for the targeting of severe AutoImmune Diseases



AREA 2 – NK & CAR-NK

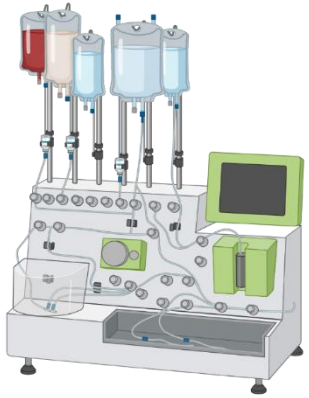
CAReNK-AID – Outlook

WP3
Achim Aigner

MaxCyte® nanoparticles

virus-free gene transfer

WP1
WP2
Torsten Tonn
Achim Temme



GMP/Expansion

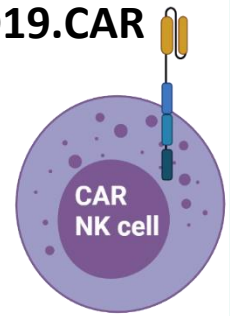
WP5
Stefan Bornstein

autoimmunity model

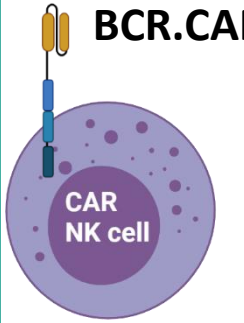
Pan B cell marker

Autoreactive B cell receptors

CD19.CAR

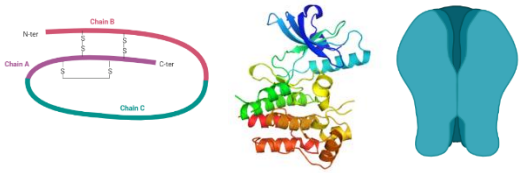


BCR.CAR

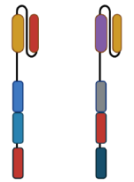


autoimmune targets

WP4
Ezio Bonifacio

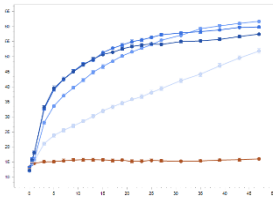


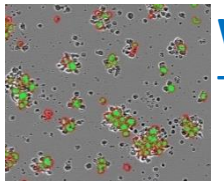
Type I Diabetes, Myasthenia Gravis, Graves disease,…



WP1/WP4
Torsten Tonn
Ezio Bonifacio

CAR generation





WP1
Torsten Tonn

CAR-NK characterisation

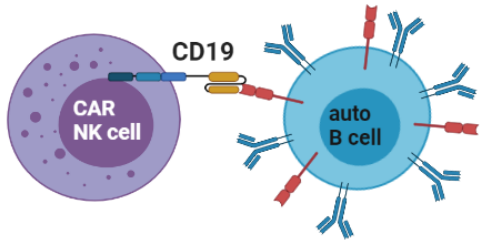
AREA 2 – NK & CAR-NK

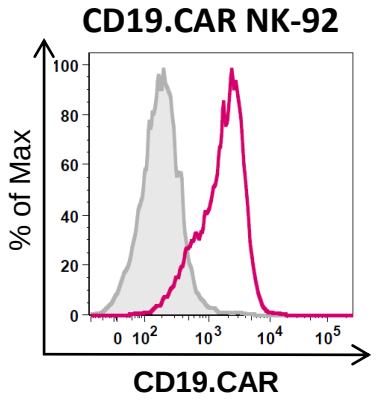
CAReNK-AID – Results so far

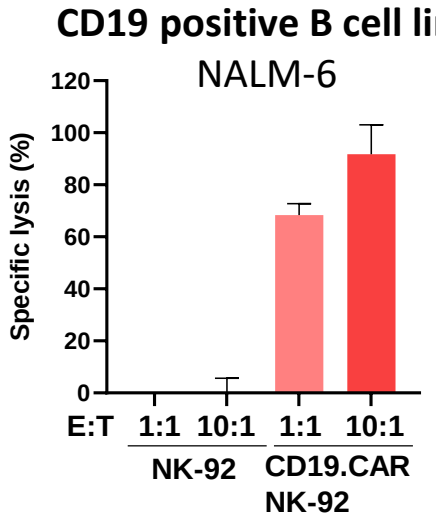
SAXOCELL®

AREA 2 – NK & CAR-NK

CAR NK
Anti-Pan B cells

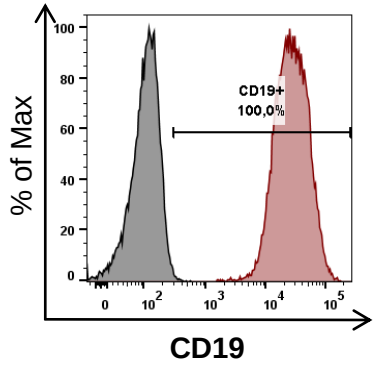




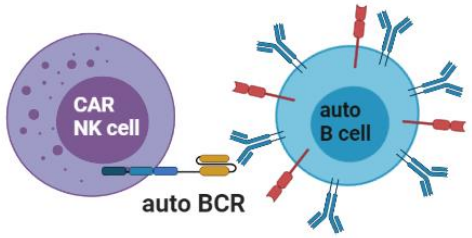


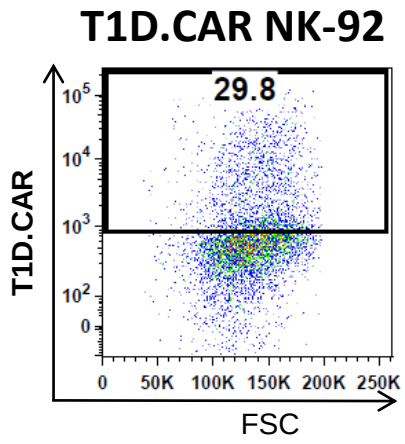
Feeder cells for NK expansion

PC3^{PSCA}-IL2-mIL15d-CD19

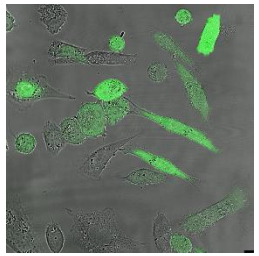


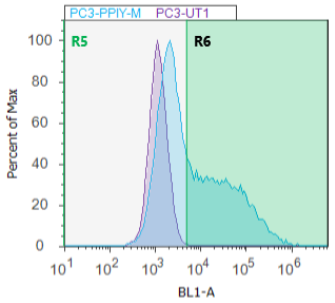
CAR NK
Anti-autoreactive BCR
- Type I Diabetes -



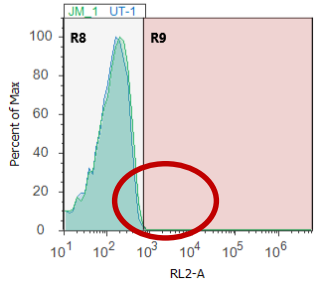


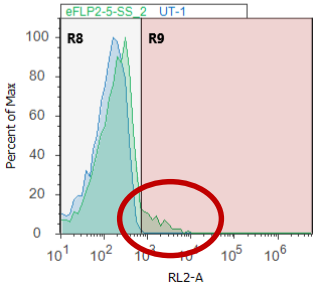
Virus-free NK cell transfection





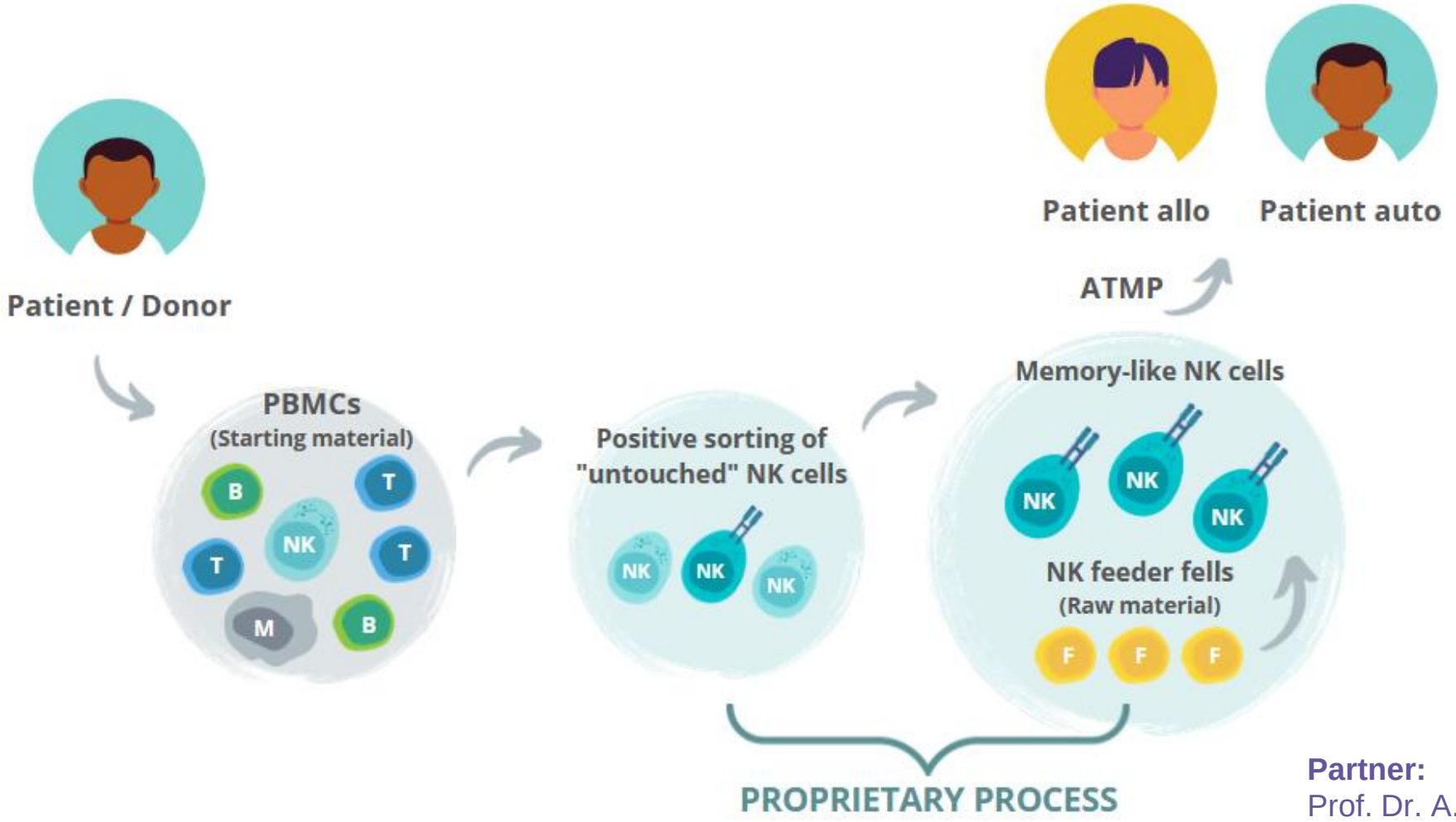
NK-92





NK4Therapy – Project Overview

SAXOCELL®



AREA 2 – NK & CAR-NK

Partner:
Prof. Dr. A. Temme (NCH-FOR, UKD, TUD)
Prof. Dr. T. Tonn (ETM, TUD)
Prof. Dr. M. Bornhäuser (MKI, UKD, TUD)
Cell.Copedia GmbH, Leipzig

NK4Therapy – Workflow/Outlook

SAXOCELL®

WP1 - Feeder cell clones and validation
Temme Group

IMTEK DEPARTMENT OF MICROSYSTEMS ENGINEERING

Cell printing

WP2 - Feeder Cell Master Cell Bank (MCB)
Temme Group

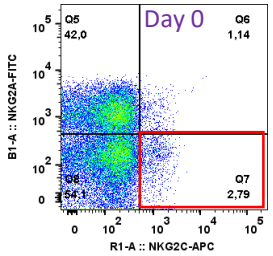
Raw material for production of ATMP

Optimizing production process

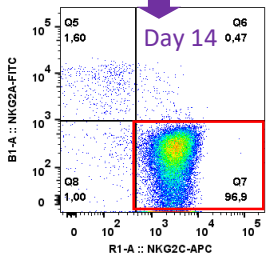
WP3 - Large Scale Expansion of NK cells using feeder cell MCB
Temme Group

ScaleReady.

NK cells from peripheral blood
(raw material)



+ Feeder Cells



NKG2C+
KIR+
CD25+
TIM3+
CD16+
NKG2D+
LAG3-
PD1-

Tumor-reactive NKG2C+ NK cells

Establishing a GMP compliant process for production of NKG2C+ NK cells

WP6 – translation into clinical settings
Temme Group / Tonn Group

WP4 - GMP conformance
Tonn Group
Temme Group

Safety / Identity Tests

WP5
Temme Group
Bornhäuser Group

***in vitro / in vivo* validation of NKG2C+ NK cells**

GMP compliant NK cell isolation

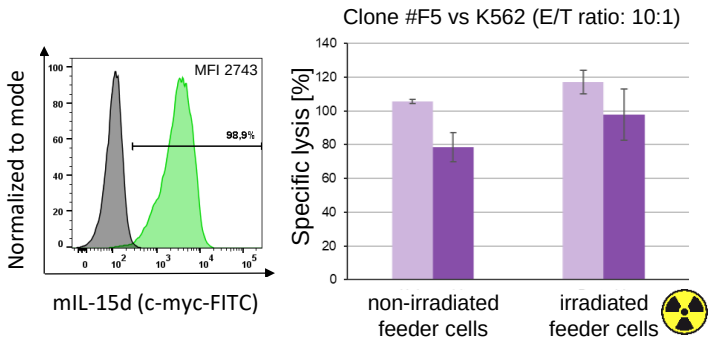
WP7
Cell.Copedia GmbH

CELL COPEDIA
Experience Cell Selection

AREA 2 – NK & CAR-NK

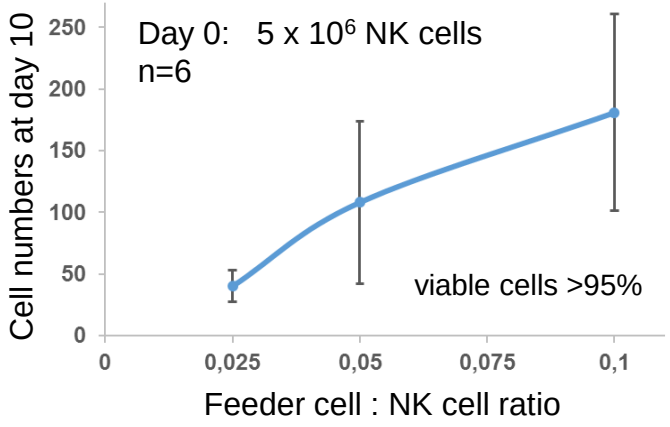
NK4Therapy – Results so far

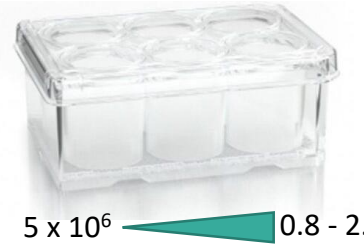
WP1 – Cell clones and validation



- first precursor clones validated ✓

WP3 – Expansion of NKG2C+ NK cells





5 x 10^6 — 0.8 - 2.7 x 10^8

5 x 10^7 — > 10^9 ???

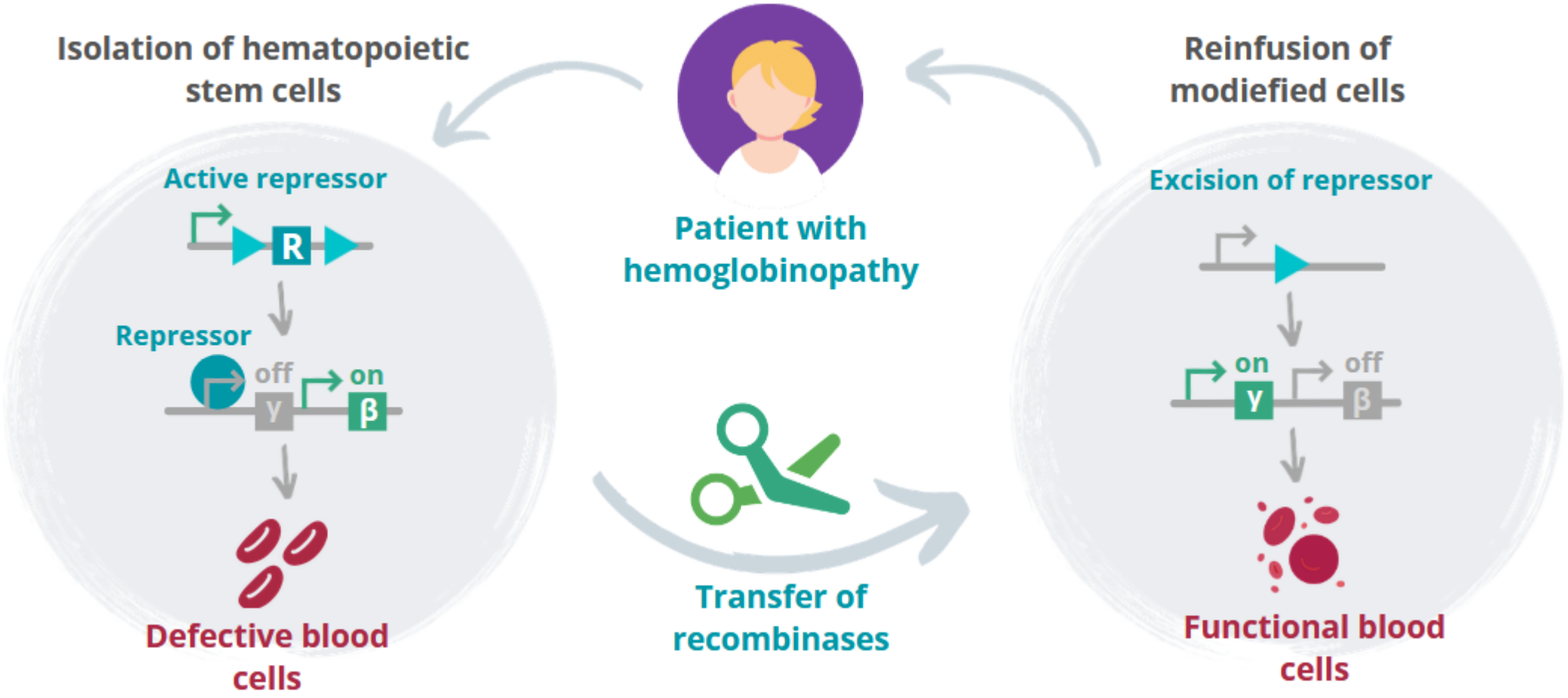
WP4 – Identity Testing

- whole genome seq from 6 clones for establishing locus-specific PCR of transgenes ✓
- ongoing bioinformatic analysis

Soon be started…

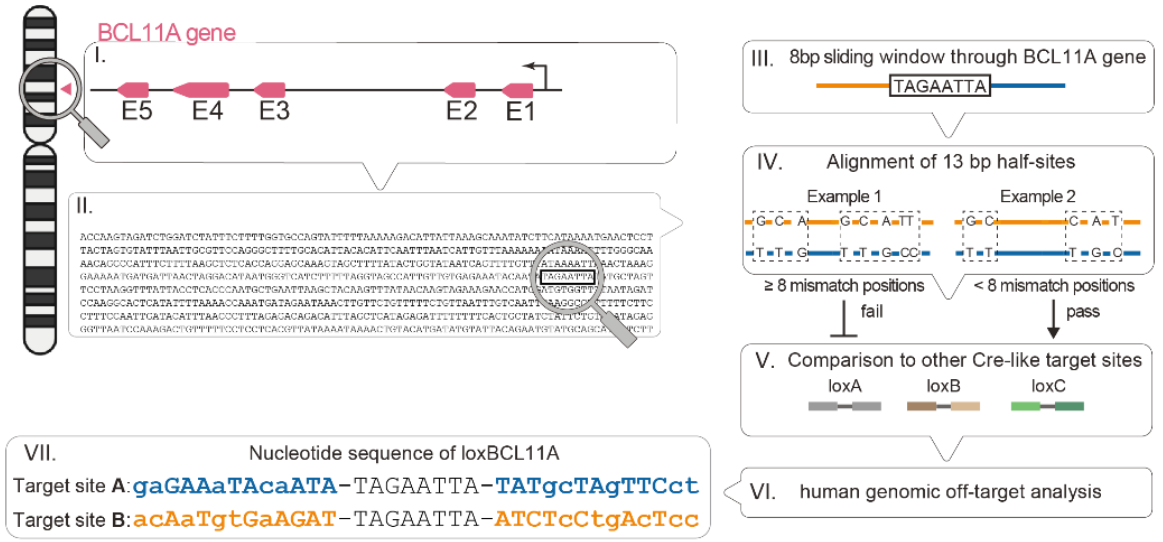
WP2 – Generation of Master Cell Bank (MCB) and End of Production Cell Bank (EoPCB)

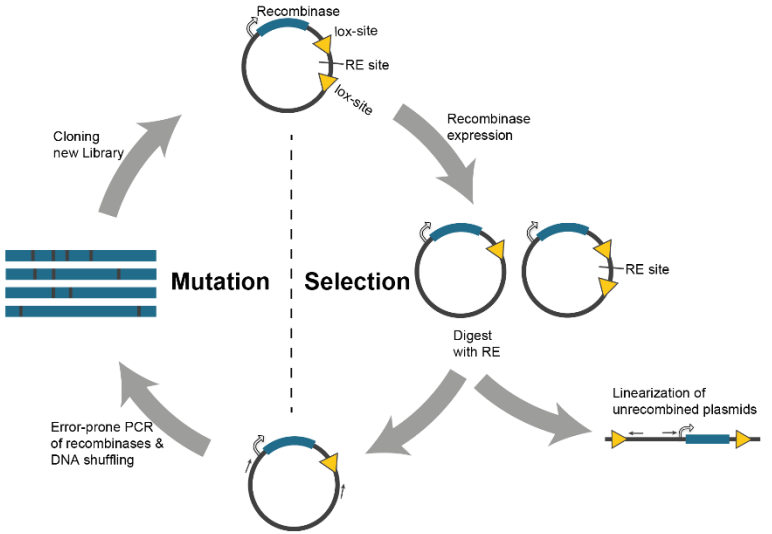
HemRec – Project Overview

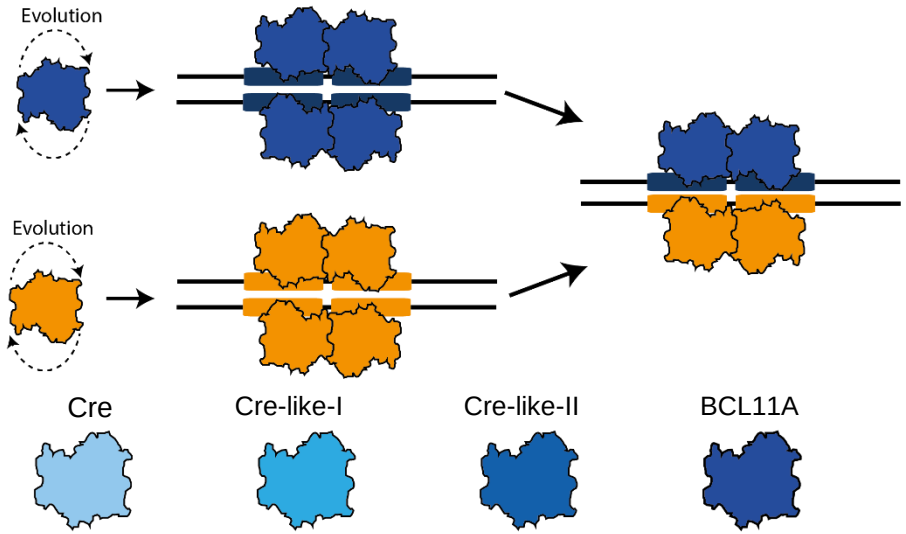


AREA 3 – ATMPs

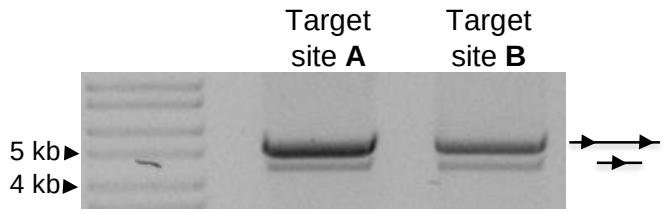
HemRec – Results so far







Recombination test of the BCL11A libraries



AREA 3 – ATMPS

HemRec – Outlook

- Evolving recombinases for final BCL11A target site
- Deep sequencing based screening of the libraries to test efficiency for on-target and potential off-targets in the human genome with support of DKMS
- Analyzing single clones in bacteria
- Testing most promising clones in cell culture in a reporter cell line
- Analysis of the BCL11A deletion at the endogenous locus using adult erythroid cell line
- Analysis of the BCL11A deletion in patient cells with support of DKMS
- BCL11A deletion in patient cells and transplantation of the cells with support of DKMS

AREA 3 – ATMPs

Universitätsklinikum Carl Gustav Carus

DKMS Life Science Lab

Universitätsklinikum Carl Gustav Carus

DKMS Life Science Lab

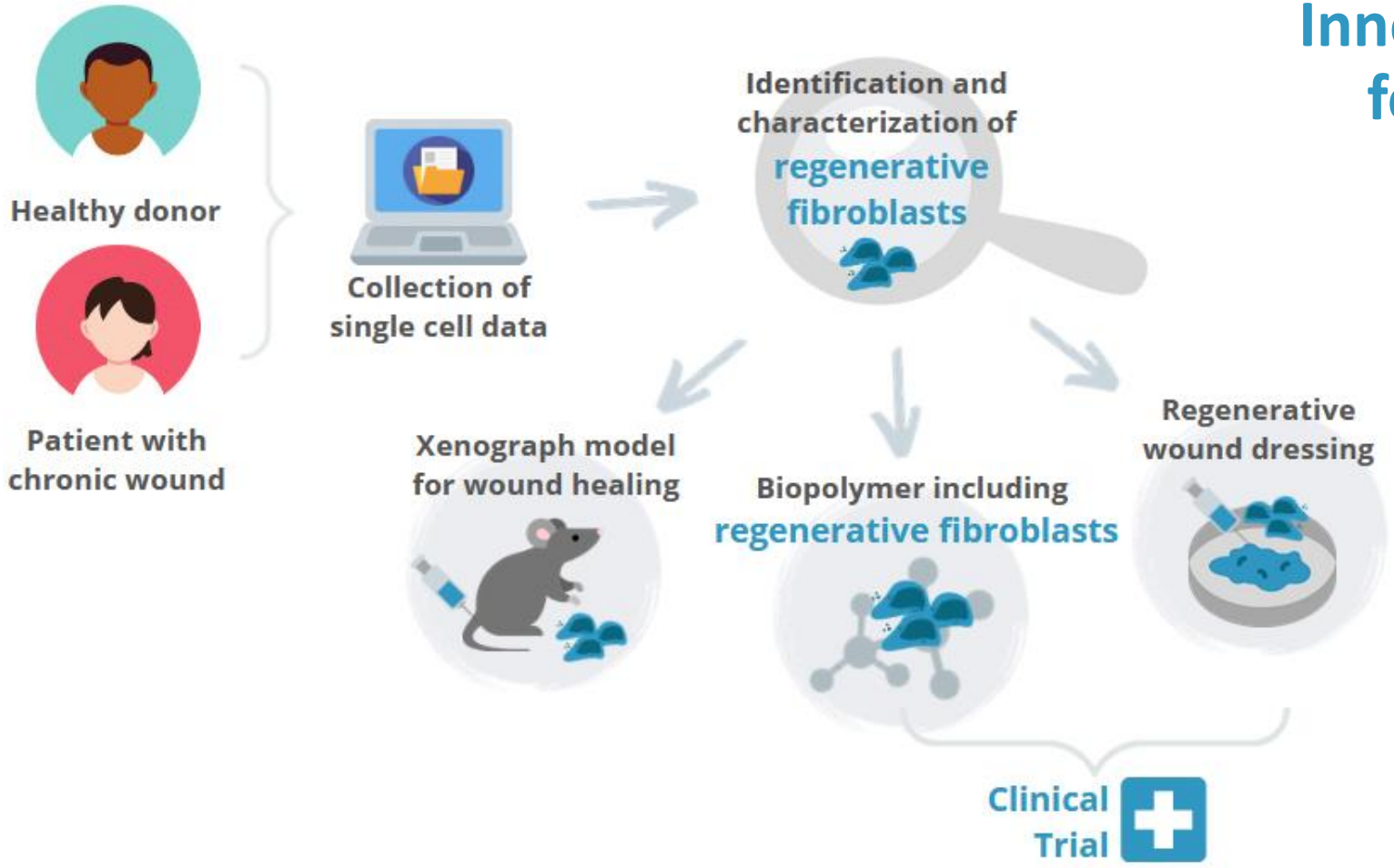
Universitätsklinikum Carl Gustav Carus

DKMS Life Science Lab

Universitätsklinikum Carl Gustav Carus

ZellTWund – Project Overview

SAXOCELL®

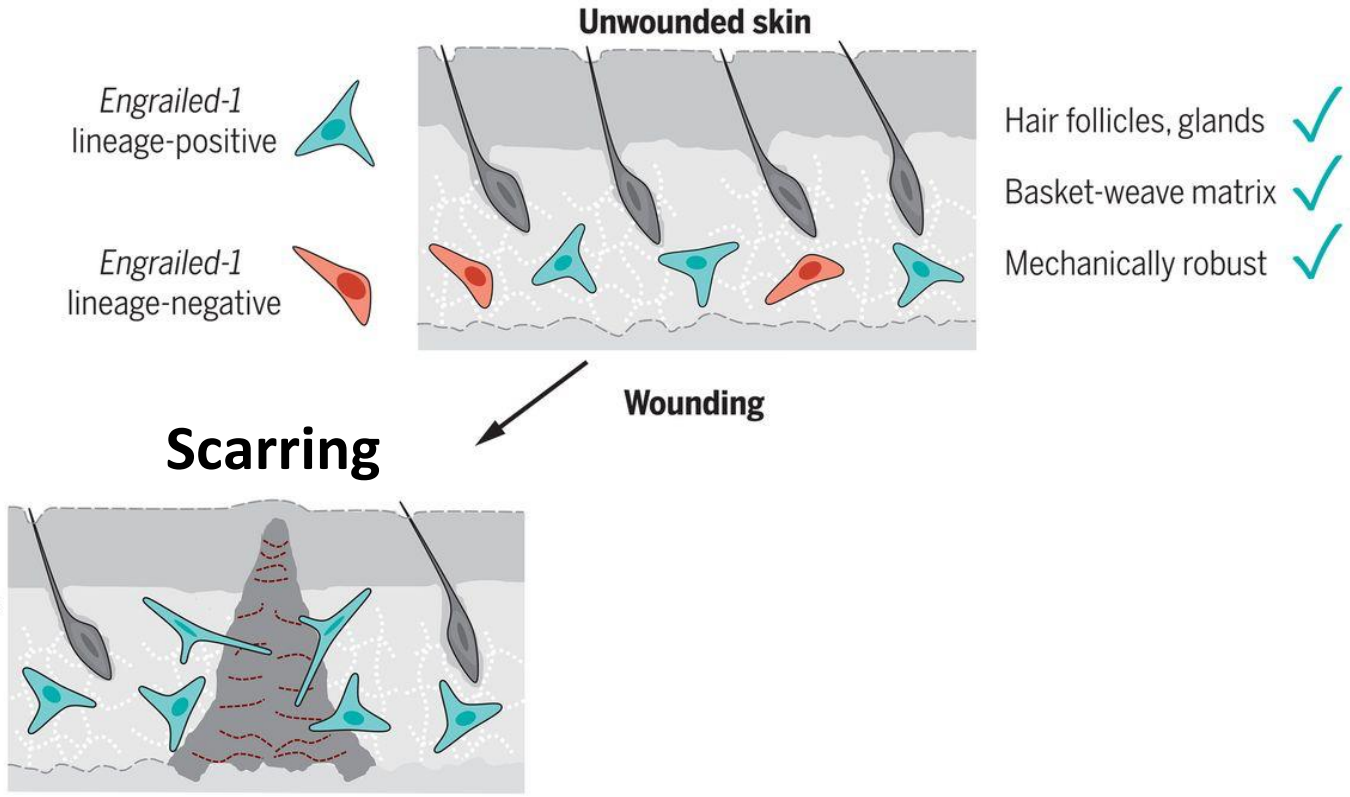


Innovative cell therapy for human wound repair

AREA 3 – ATMPs

Marta Torregrossa, Ravinder Kandi

ZellTWund – Background

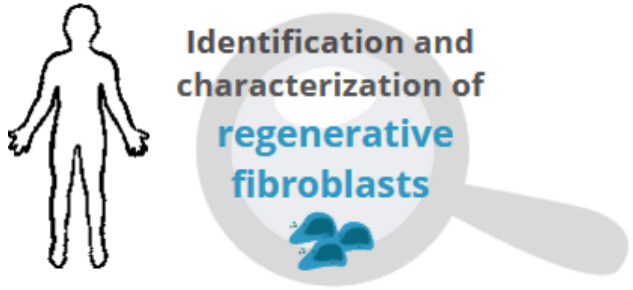


AREA 3 – ATMPs

Marta Torregrossa, Ravinder Kandi

Rinkevich et al., Science, 2015
Correa-Gallegos et al., Nature, 2019
Phan et al., Exp. dermatology, 2020

ZellTWund – Ongoing



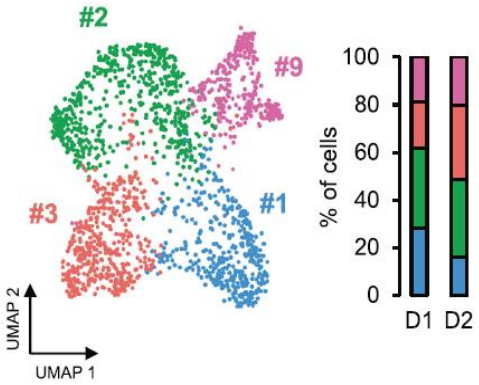
Re-analyse existing single cells analysis human Data

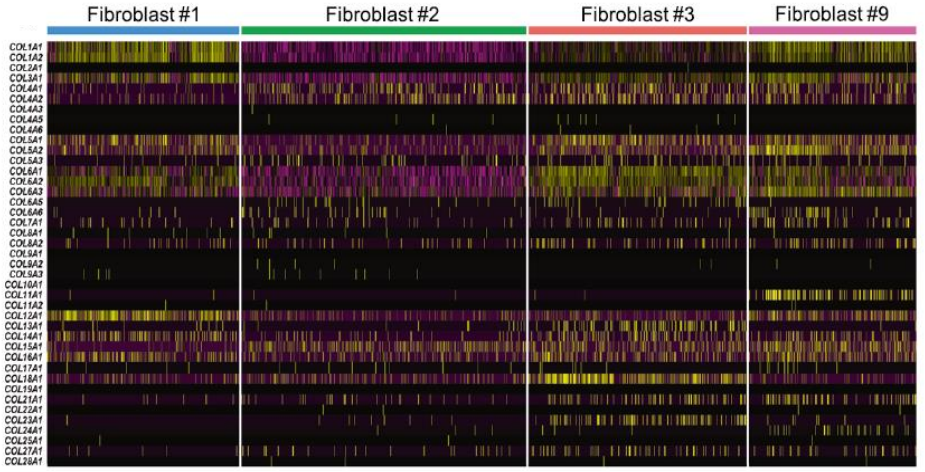
Sole-Boldo et al., Communications biology, 2020
Ascension et al., JID, 2020
Vorstandlechner et al., The faseb Journal, 2019
Tabib et al., JID, 2018

In collaboration with

The Interdisciplinary centre for bioinformatics

University of Leipzig

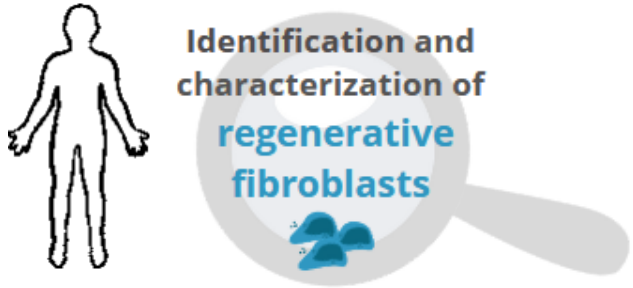




AREA 3 – ATMPS

Marta Torregrossa, Ravinder Kandi

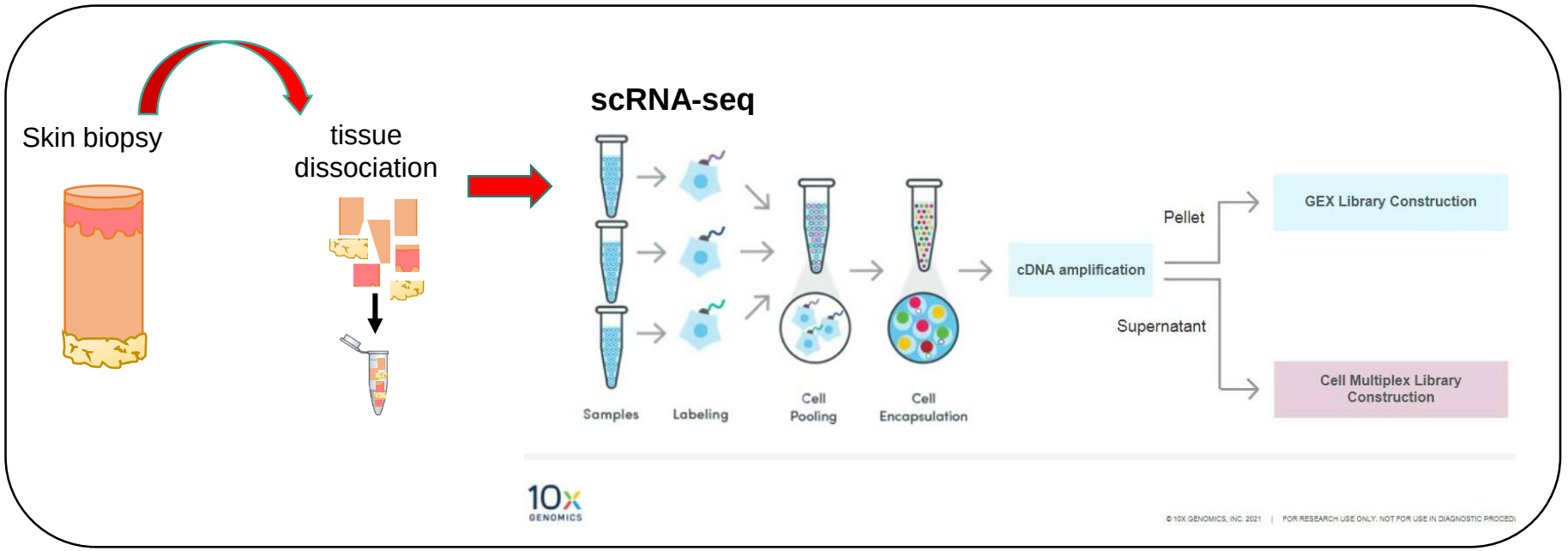
ZellTWund – Ongoing



Samples collection:

- Healthy skin
- Normal healing wounds
- Impaired healing wounds

- Multiple body location
- Wide age range
- Gender (male and female)

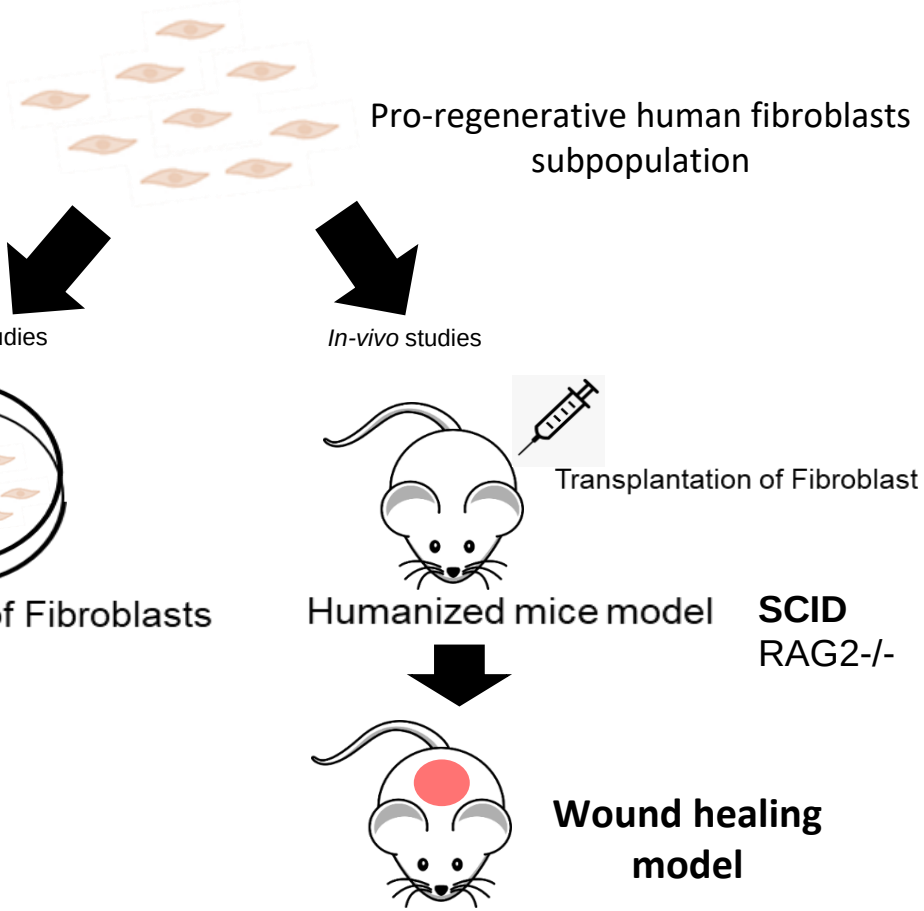


10Xgenomics.com

AREA 3 – ATMPS

Marta Torregrossa, Ravinder Kandi

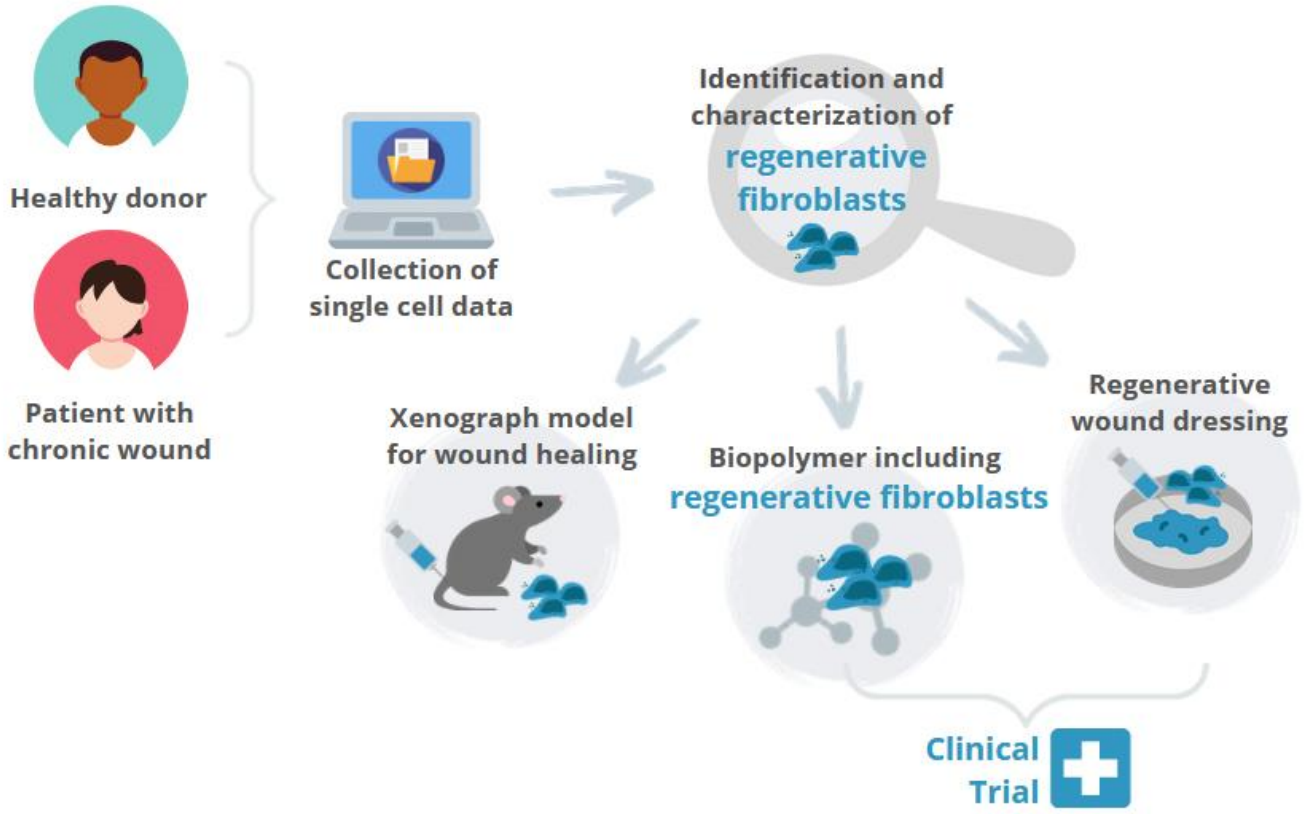
ZellTWund – Outlook



AREA 3 – ATMPs

Marta Torregrossa, Ravinder Kandi

ZellTWund – Thanks for your attention



UNIVERSITÄT LEIPZIG

Universitätsklinikum Leipzig
Medizin ist unsere Berufung.

Marta Torregrossa

Dr. Sandra Franz

Prof. Dr. Jan-Christoph Simon

HELMHOLTZ MUNICH

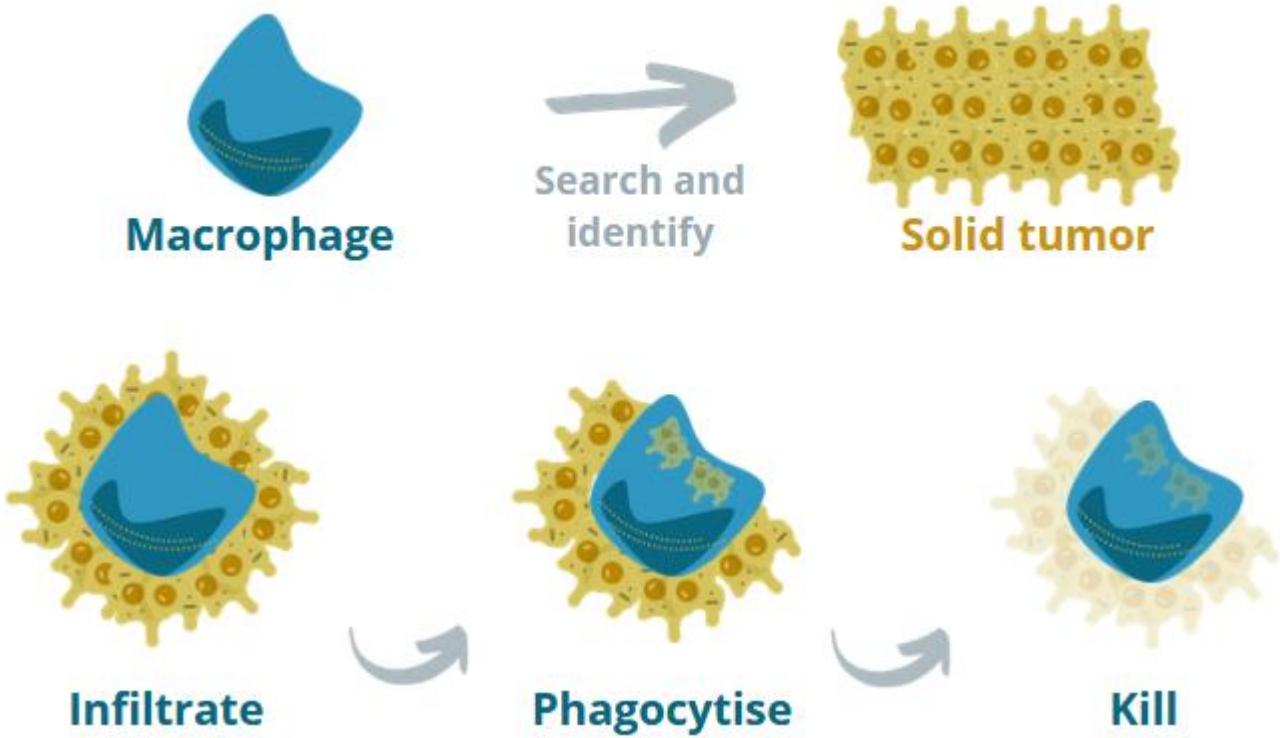
iRBM Institute of Regenerative Biology and Medicine

Ravinder Kandi

Dr. Yuval Rinkevich

AREA 3 – ATMPs

xMac – Project Overview

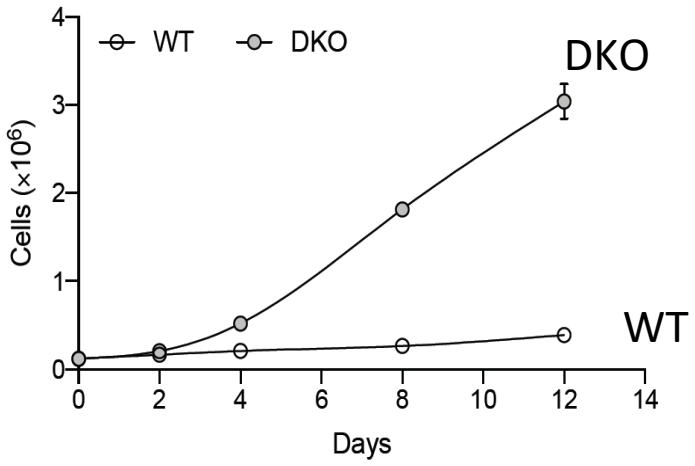


AREA 3 – ATMPs

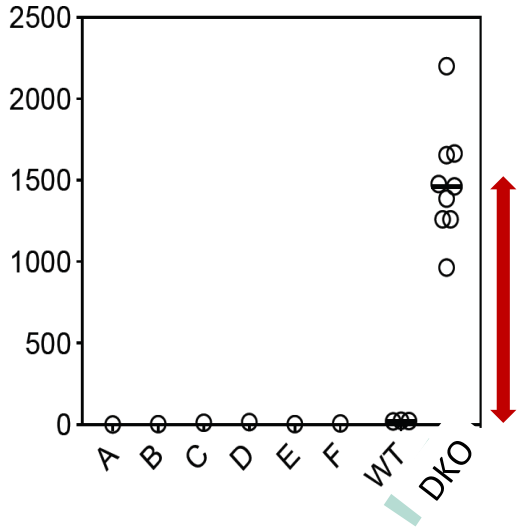
xMac – Results so far

Characterization of human iPSC-derived MAF/MAFB DKO Macrophages: expansion in cell culture

Growth curve after differentiation



Yield comparison

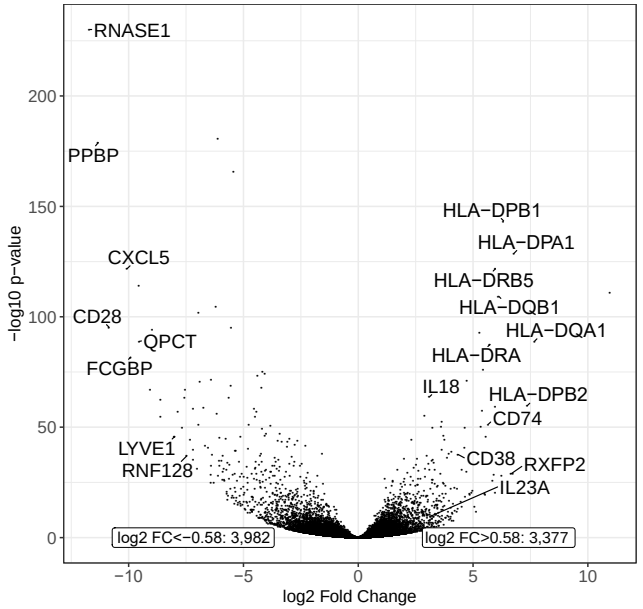


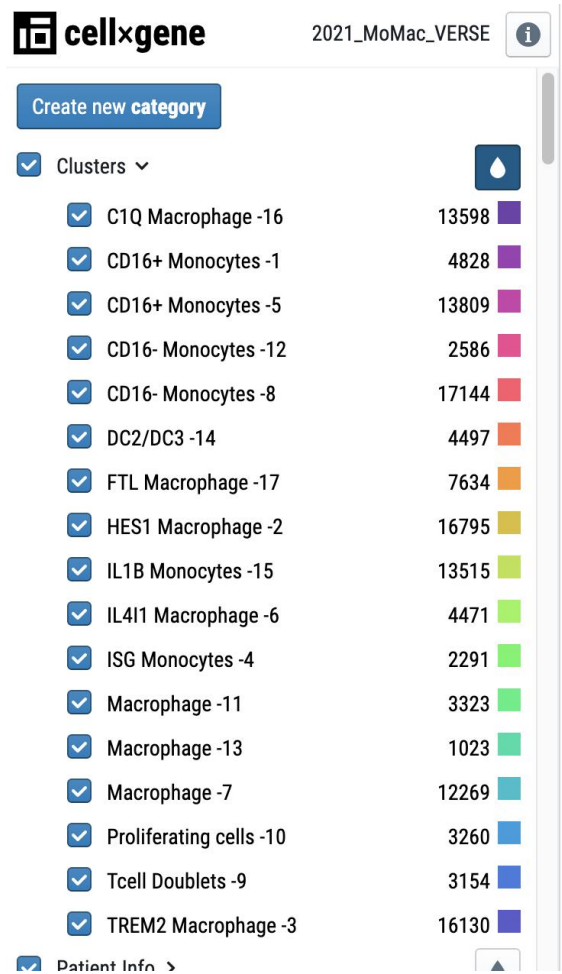
A-F: competitor protocols

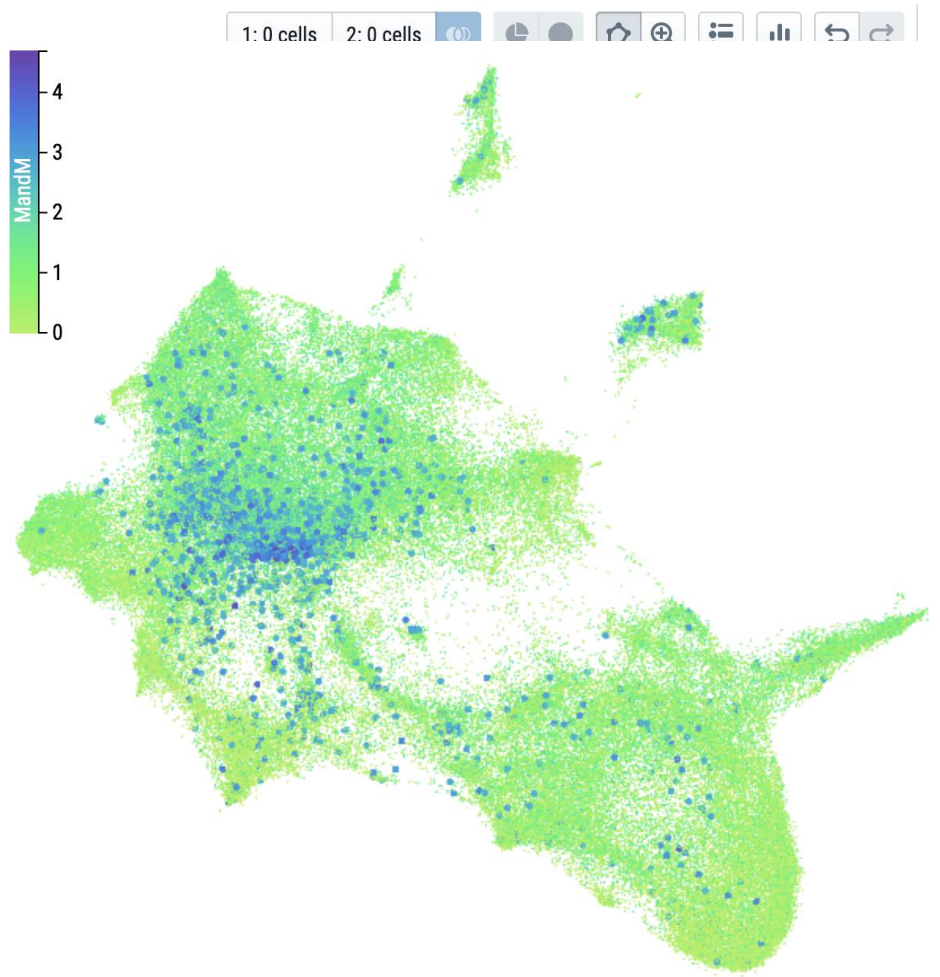
AREA 3 – ATMPs

xMac – Results so far

Characterization of human iPSC-derived MAF/MAFB DKO Macrophages: resistant to M2 polarization







AREA 3 – ATMPS

xMac – Results so far

Scientific advice meeting with PEI on May 4. Road to FIH discussed.

Patent applications filed: the art of abstraction

Patent application 1

- ex vivo proliferating blabla cell

Patent application 2

- human blabla cell with mutations in both alleles of a chromosomal gene
- + its use in the treatment of cancer

AREA 3 – ATMPs

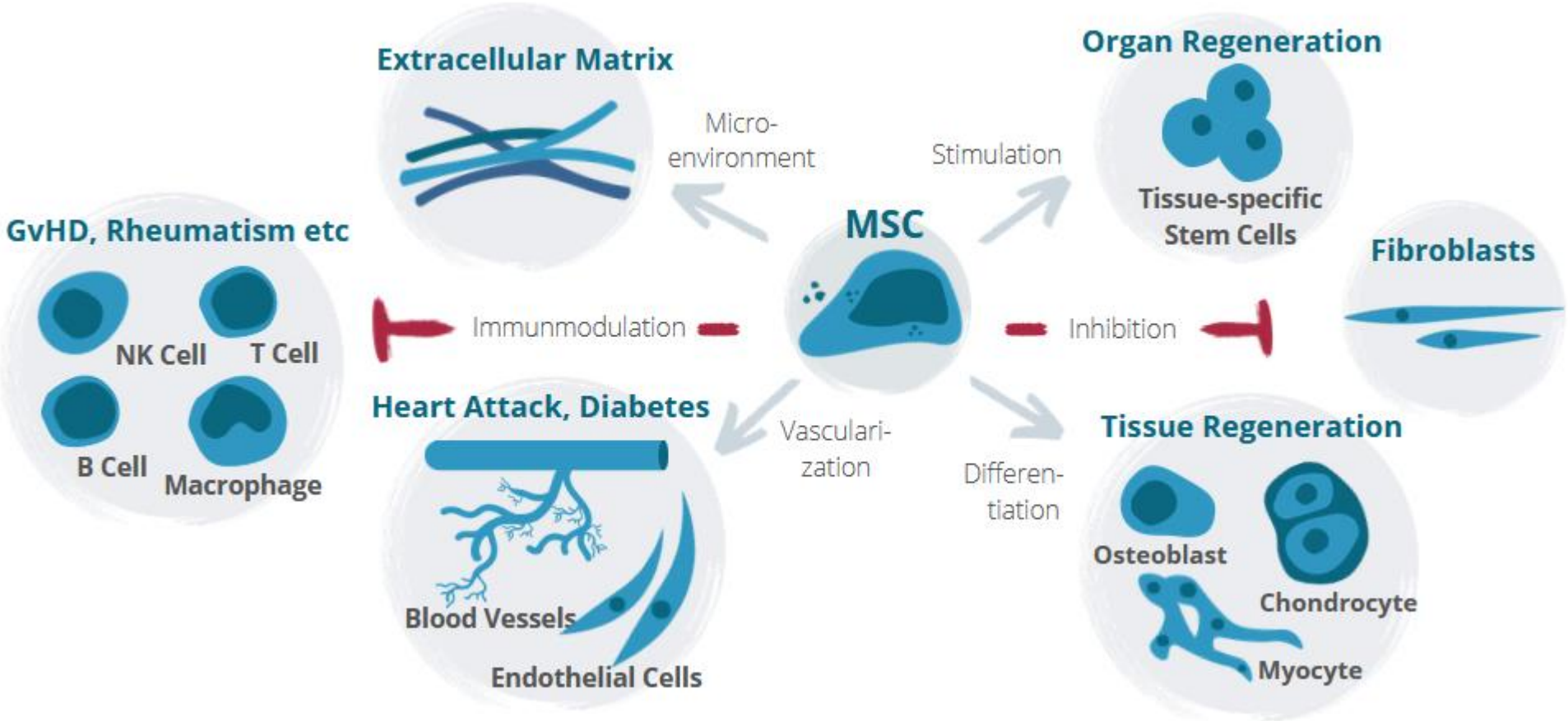
xMac – Outlook

- Functional characterization of DKO Macrophages
- Production under GMP

----------> Phase I trial

- More elegant preparation of DKOs

MSC-Prestige – Project Overview



AREA 3 – ATMPs

MSC-Prestige – Results so far

- ✓ **Project progress on time**
- ✓ **Contracts in place**
- ✓ **AP 1.1: Preparation of the process transfer for MSC (M1-M6) done**
  - ✓ Lastenheft (all specifications and SOPs)
- ✓ **AP 1.2: Process transfer for MSC (M6-M18) ongoing**
- ✓ **AP 3: Characterization ongoing**
  - active profile of Desacell® and of recipients' immune profile

AREA 3 – ATMPs

MSC-Prestige – Outlook

SAXOCELL®

AREA 3 – ATMPs

✓ Target Achievements

1) **Industrial Transfer – high cell amounts**

Manufacturing approach for MSC cell products into an industrial scaling environment

2) **Clinical Translation** progress – **MSC for clinical trials**

Therapy approach for MSC into clinical practice

✓ Work Programme

AP1) **Industrial Value Chain**

AP2) **Process-Ramp for GvHD**

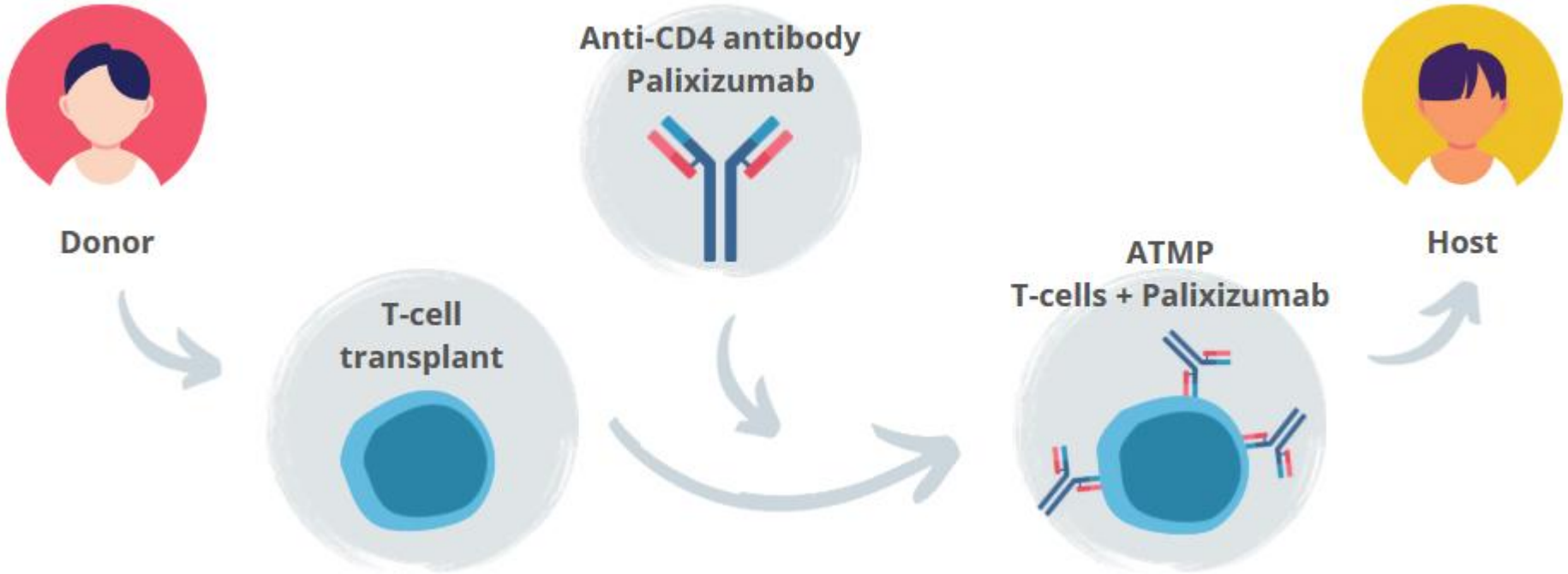
AP3) **Characterization** (active profile of Desacell® and of recipients' immune profile)

AP4) **Internationalization**

✓ Next Projects Phase II

- high scale cell production
- international trials

OPTIX – Project Overview



AREA 4 – CGT

OPTIX – Results so far

SAXOCELL®

AREA 4 – CGT

Tcell Tolerance

Work Package 1 – Optimization of Palixizumab® production

→ Research cell bank transferred to IZI, new master cell bank finished
→ New head of production and new team
→ Postponed for 6 months

Work Package 2 – GMP process transfer of Palintra®

→ Preliminary tests running to define process parameters
→ Delay of 6 months because of delay in WP1

Work Package 3 – Submission of clinical trial documents

Work Package 4 – Sponsor oversight in clinical trials

Fraunhofer IZI

Work Package 1 – Mode of action of Palixizumab®

→ Reduced proliferation due to T cell tolerance induction
→ Tolerance markers identified by RNA seq
→ Verification of markers by qPCR

Work Package 2 – GMP process transfer of Palintra®

→ Preliminary tests running to define process parameters
→ Delay of 6 months because of delay in WP1

Work Package 3 – Quality control transfer of Palintra®

Work Package 4 – Automated data analysis

Work Package 5 – Further applications of Palixizumab®

KLINIKUM CHEMNITZ gGmbH

Work Package 1 – Biobanking of patient material

→ Peripheral blood and bone marrow of patients with hematological cancers after hematopoietic cell transplantation (HCT) for research in WP2 and WP3 is stored (ongoing)

Work Package 2 – T cell fitness after HCT

Work Package 3 – Palixizumab® functionality after HCT

→ Relevant cells were isolated from patient material
→ Assays were established with healthy donors

Work Package 4 – Planning of GvHD prevention study

→ First draft is work in progress

OPTIX – Outlook

SAXOCELL®

AREA 4 – CGT

Tcell Tolerance

Work Package 1 – Optimization of Palixizumab® production

→ First GLP batch produced by 12/22

→ Second batch under GMP-conditions

Work Package 2 – GMP process transfer of Palintra®

→ Process ready to be pre-validated with GLP-antibody

Work Package 3 – Submission of clinical trial documents

→ Preparation of clinical trial

Work Package 4 – Sponsor oversight in clinical trials

→ Clinical trial conduct

Fraunhofer IZI

Work Package 1 – Mode of action of Palixizumab®

→ Finishing of verification of markers by qPCR and publication

Work Package 2 – GMP process transfer of Palintra®

→ Process ready to be pre-validated with GLP-antibody

Work Package 3 – Quality control transfer of Palintra®

Work Package 4 – Automated data analysis

→ Data collection for automated analysis

Work Package 5 – Further applications of Palixizumab®

KLINIKUM CHEMNITZ gGmbH

Work Package 1 – Biobanking of patient material

→ Further collection of biomaterial

Work Package 2 – T cell fitness after HCT

Work Package 3 – Palixizumab® functionality after HCT

→ Application of established assays on patient material of WP1

Work Package 4 – Planning of GvHD prevention study

→ First draft by the end of 2022

OPTIX – Contacts

SAXOCELL®

Tcell Tolerance

Fraunhofer IZI

KLINIKUM CHEMNITZ gGmbH

AREA 4 – CGT

leading level

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ChA PD Dr. Mathias Hänel
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working level

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Dr. Sandy Tretbar
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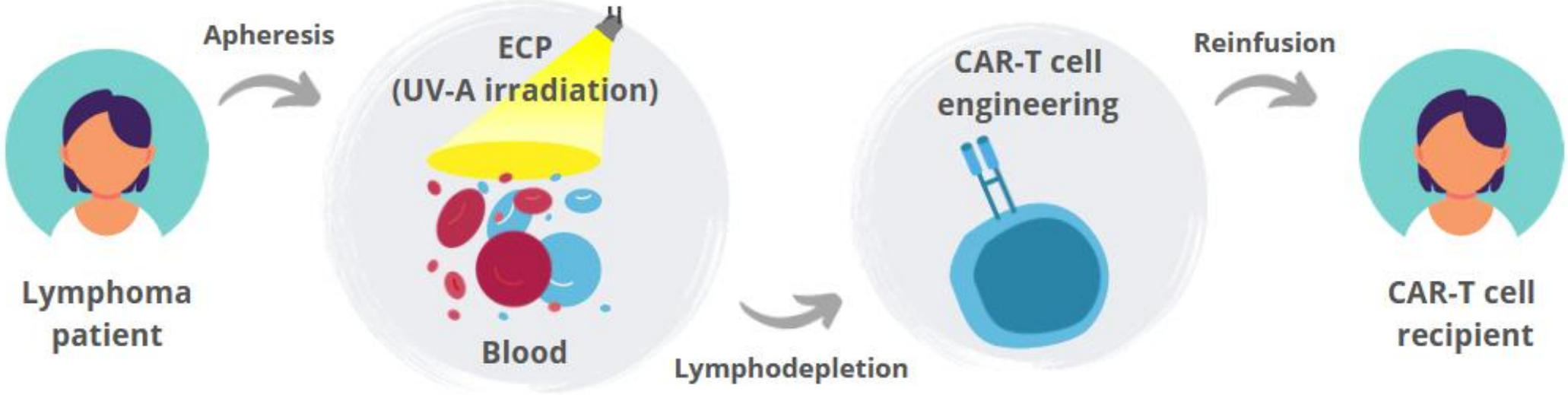
M.Sc. Nadine Heimer
n.heimer@skc.de

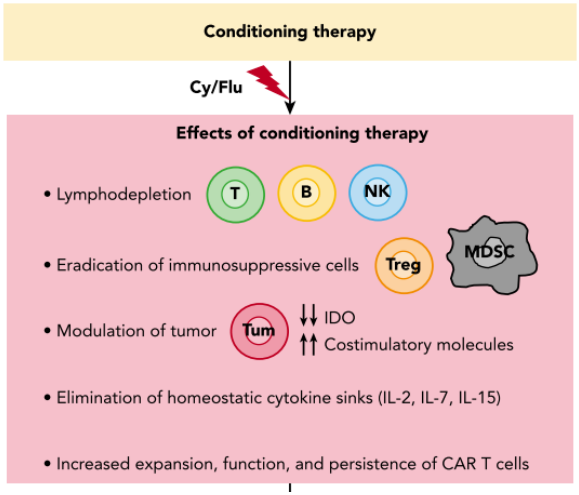
Dr. Paul Warncke
paul.warncke@skc.de

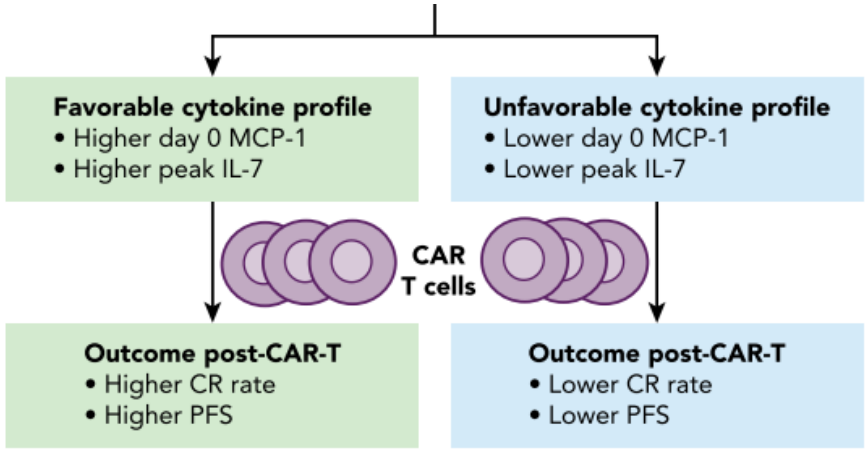
ECP-CAR – Project Overview



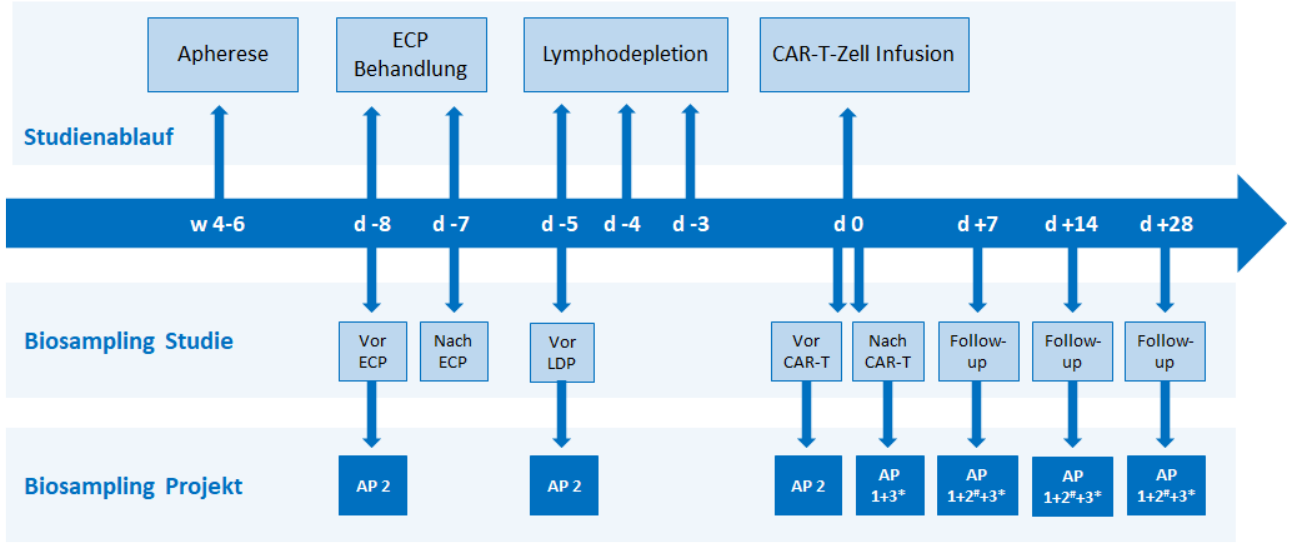
AREA 4 – CGT

ECP-CAR – Project Overview (PhotoCAR clinical trial)





Hirayama, et al. *Blood* (2019)



AREA 4 – CGT

Key inclusion criteria:

- age >=18 years
- ECOG 0-2
- Diagnosis of DLBCL or PMBCL
- indication and planned treatment with licensed CAR T-cell therapies

ECP-CAR – Project Overview

Analyses of:

- patients‘ CAR-T cells (quantitative and qualitative)
- ECP induced modulation of cellular and humoral microenvironment
- dynamics of cytotoxic effector functions and transcriptome-profiles

AREA 4 – CGT

ECP-CAR – Results so far

SAXOCELL®

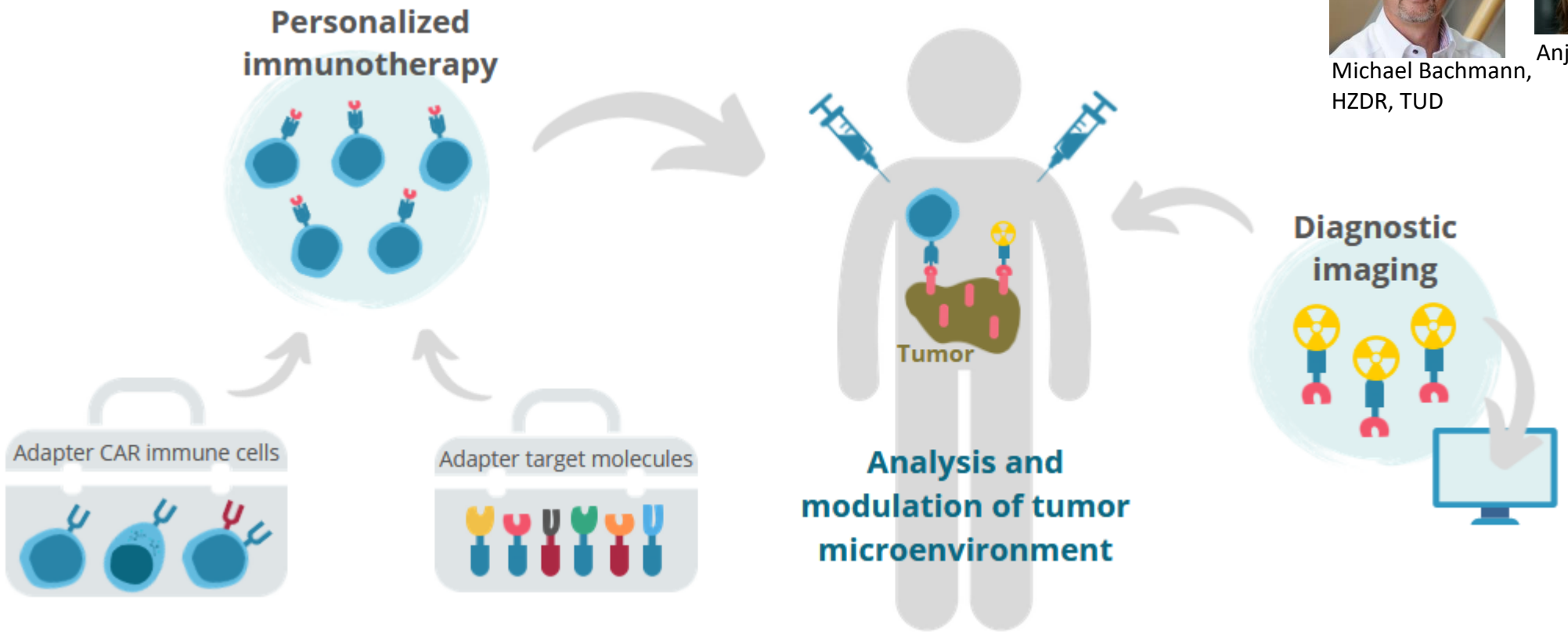
Current Status:

- Lab methodology (immunology) established
- Contract with Malinckrodt (PhotoCAR clinical trial) in discussion
- Manufacturing licence for ECP pending (discussion with local regulations and PEI) – expected Q3 2022

ECP-CAR – Outlook

- Clinical trial start expected Q4 2023

TheraSTAR – Project Overview




Michael Bachmann, HZDR, TUD

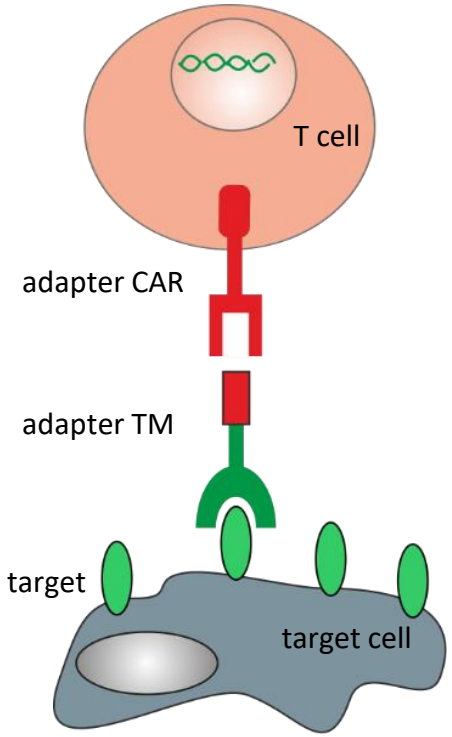

Anja Feldmann, HZDR


Marc Schmitz, TUD

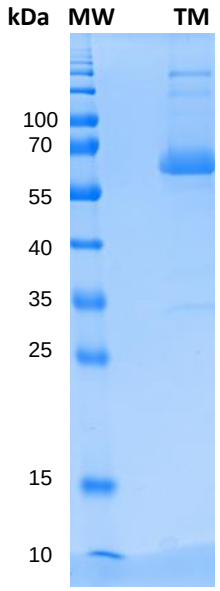
AREA 4 – CGT

TheraSTAR – Results so far

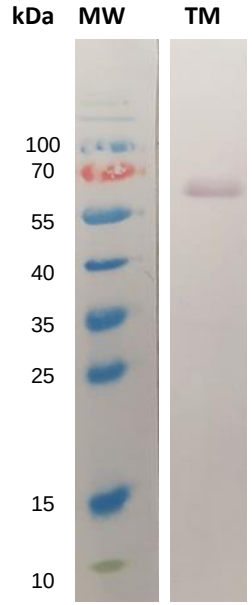
Design and production of novel adapter TM targeting immune checkpoint molecules



Coomassie staining



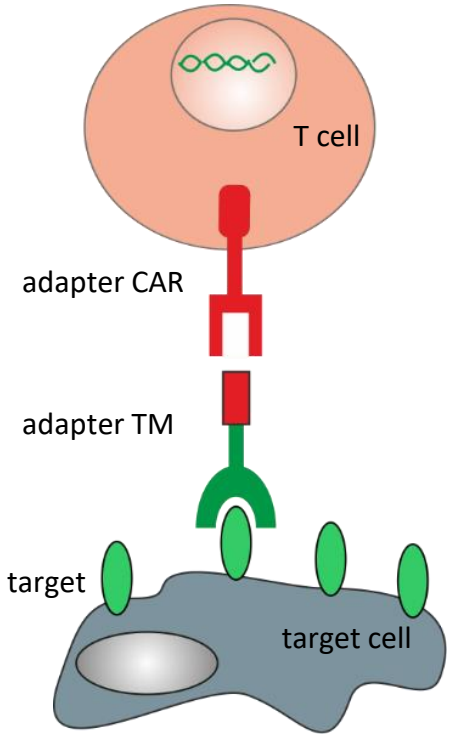
Western Blot anti-His



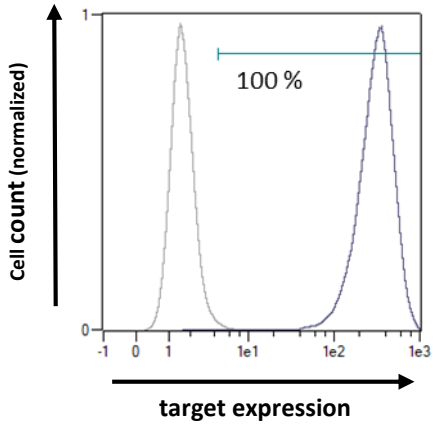
AREA 4 – CGT

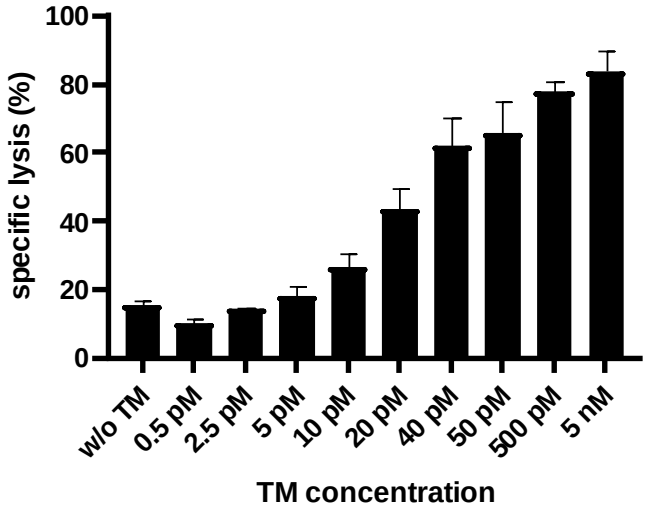
TheraSTAR – Results so far

Redirection of adapter CAR T cells by novel adapter TM to kill target cells

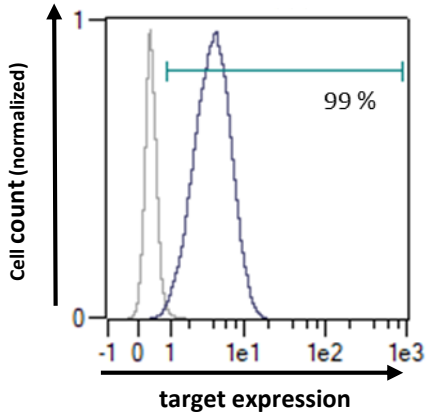


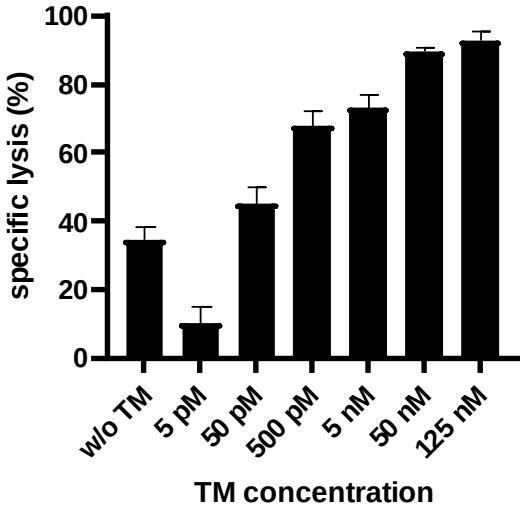
PC3: recombinant target expression





SCP-1: native target expression

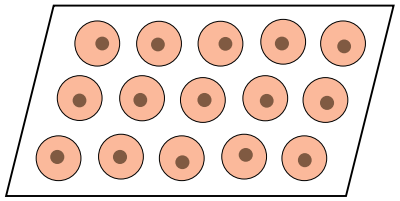




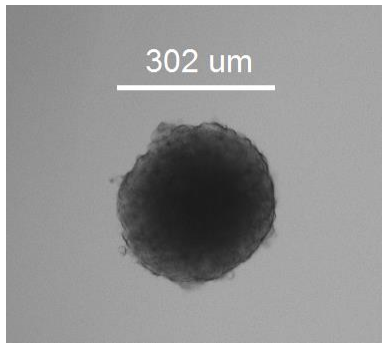
AREA 4 – CGT

TheraSTAR – Results so far

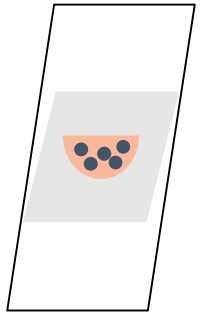
Spheroid formation and immunofluorescence staining



spheroid formation



target cells e.g. SCP-1



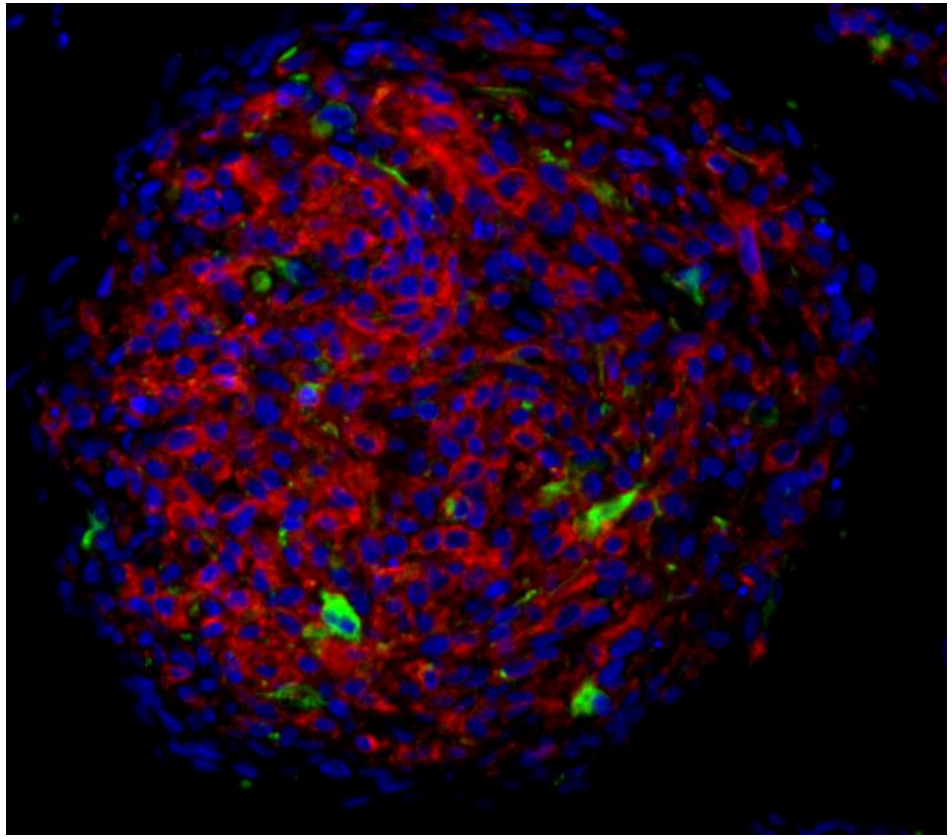
fixation, embedding, cutting

Autostainer Ventana discovery

Vectra automated quantitative imaging system

AREA 4 – CGT

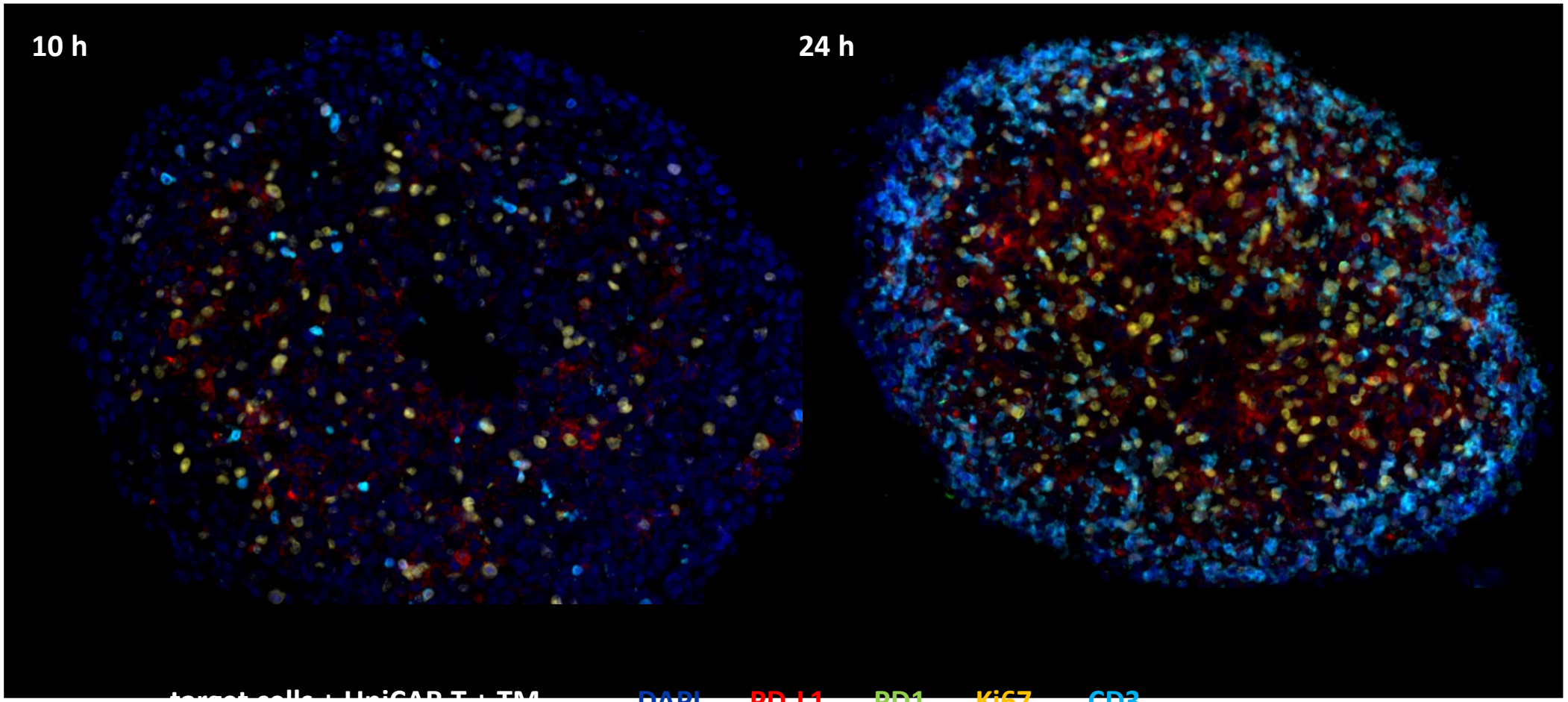
TheraSTAR – Results so far

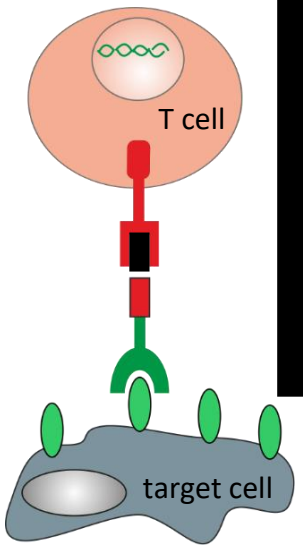


DAPI Target PanCK

AREA 4 – CGT

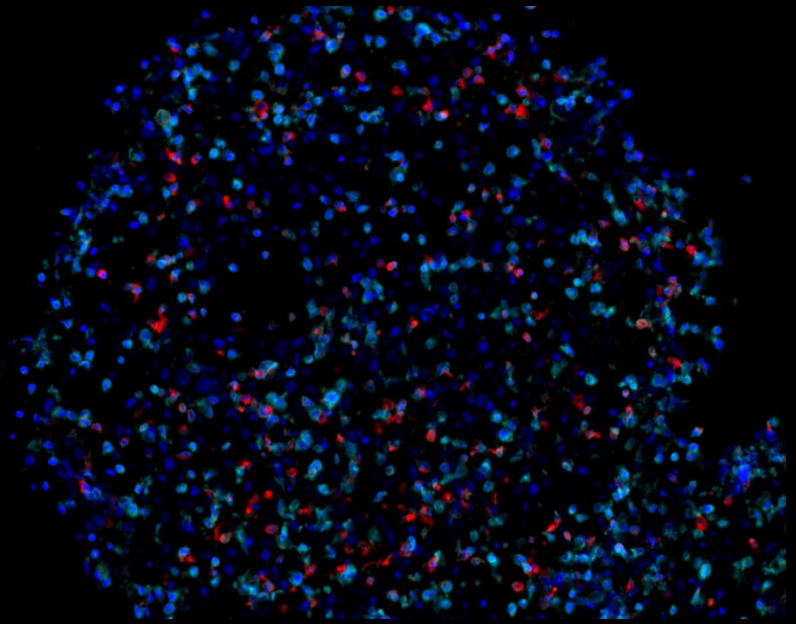
TheraSTAR – Results so far



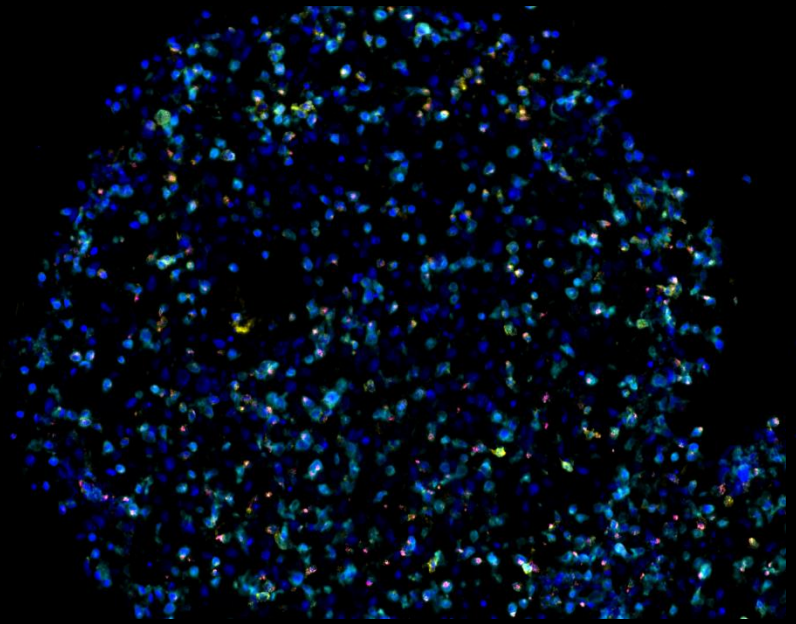


AREA 4 – CGT

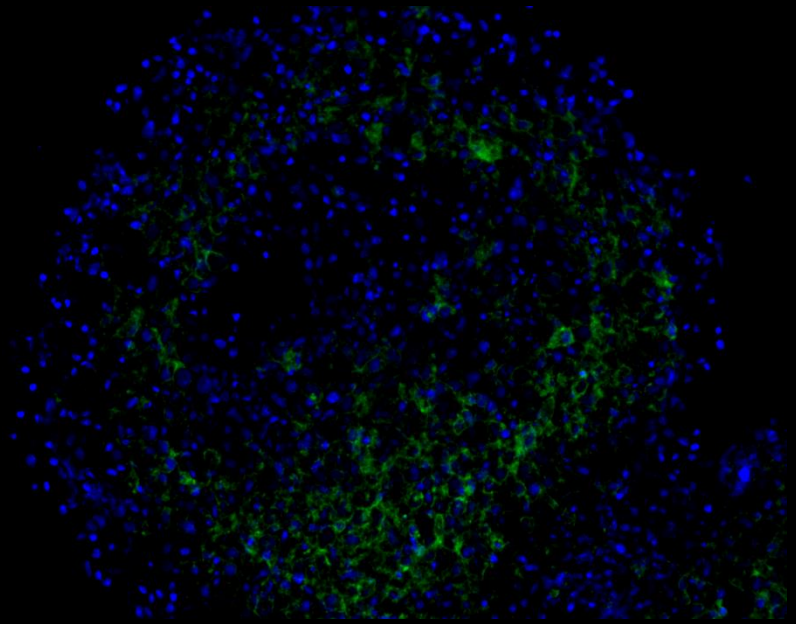
TheraSTAR – Results so far



DAPI CD3 LAG-3



DAPI CD3 PD-1 GrzB

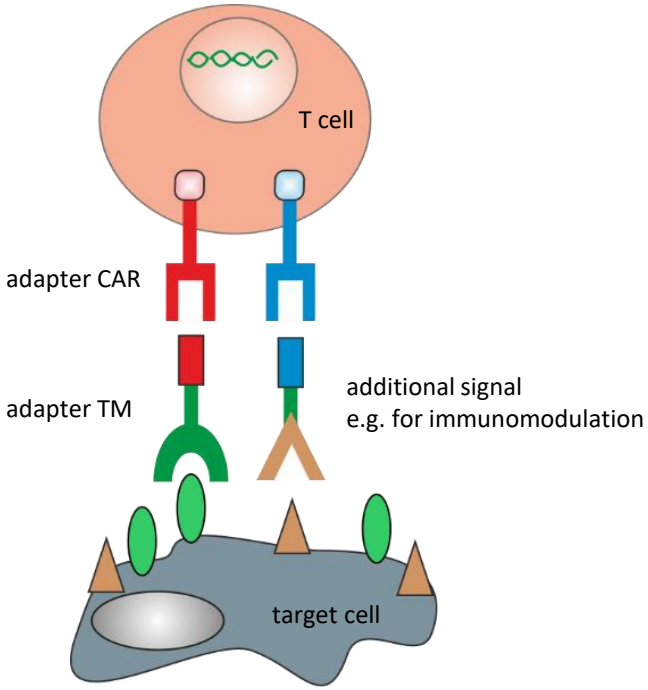


DAPI PD-L1

target cells + UniCAR T + TM

AREA 4 – CGT

TheraSTAR – Outlook



Generation of adapter CAR T cells and TMs for immunotherapy, diagnostic imaging and immunomodulation

Preclinical validation of theranostic platform technology

Novel IP and clinical translation

Analysis of tumor microenvironment

Characterization of tumor cells

Characterization and quantification of tumor infiltrating (adapter CAR) immune cells

AREA 4 – CGT

Lunch Break

Be ready for the SaxoCell group photo

Side activity: Create your own project poster

CLUSTERS 4 FUTURE
Next generation innovation networks

Federal Ministry of Education and Research

PLATFORM – OMICS

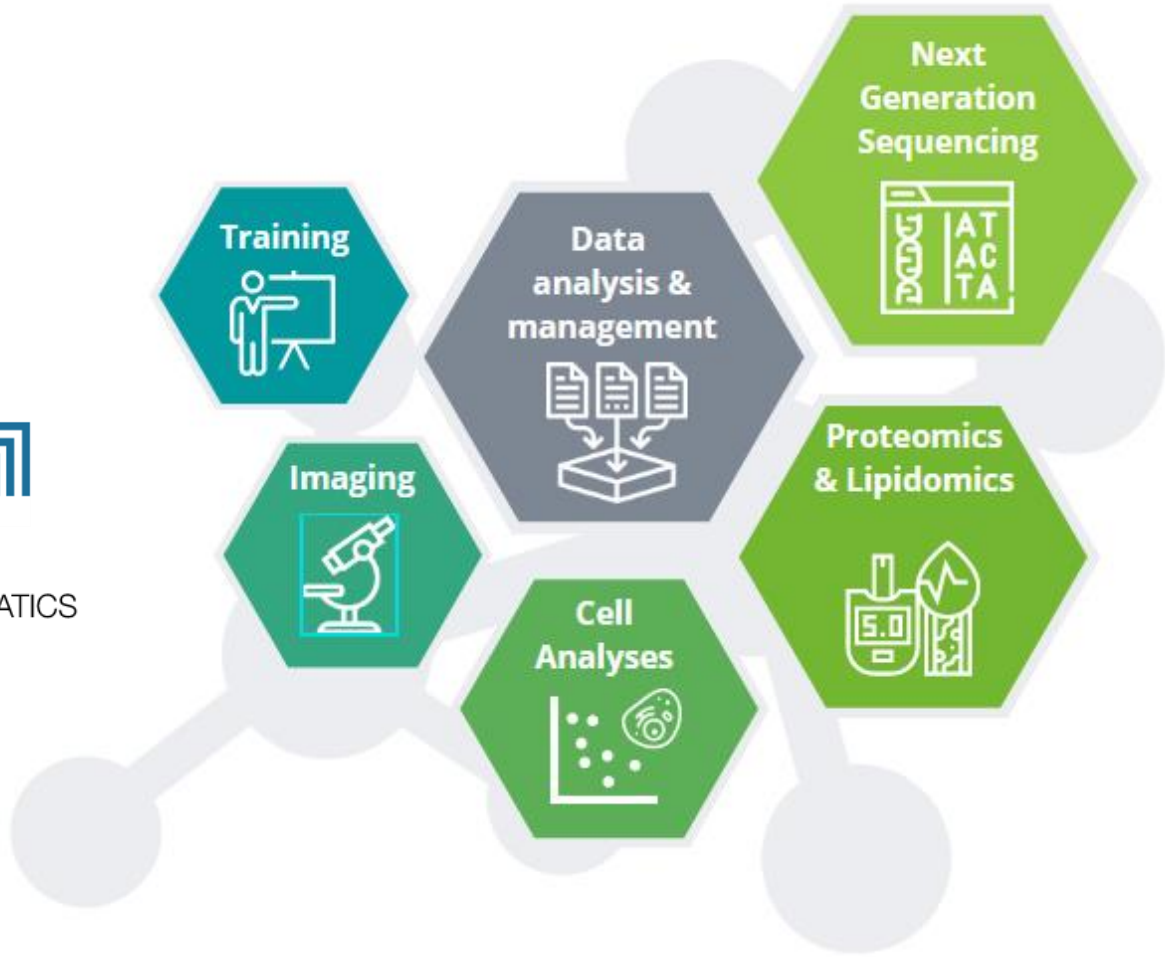
Dr. Kristin Reiche
Fraunhofer IZI / Leipzig University

Prof. Dr. Ezio Bonifacio
CRTD / TU Dresden

Partners:

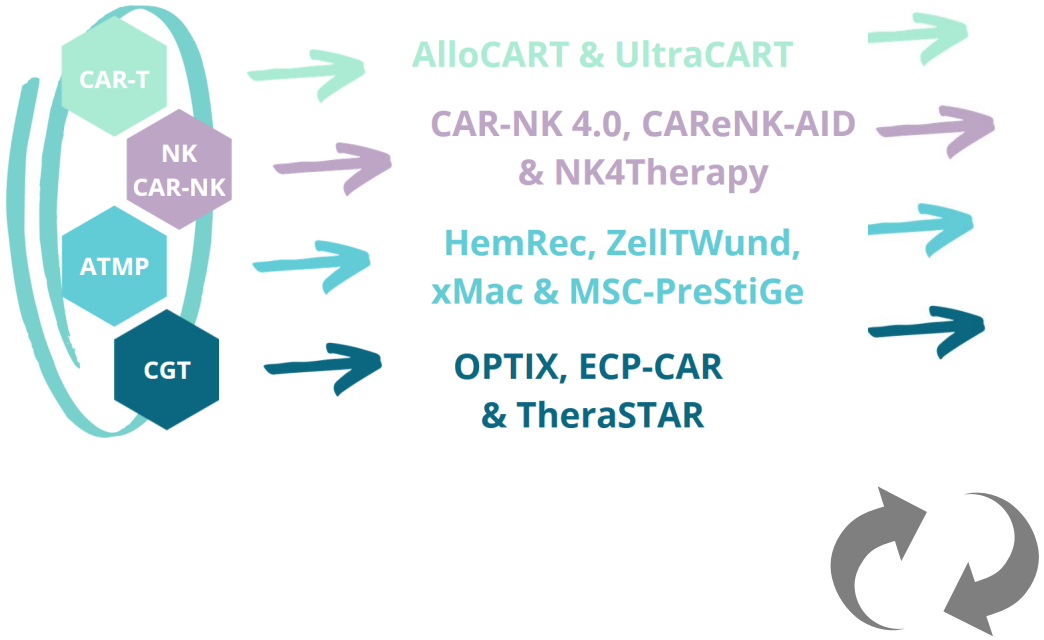
ScaDS.AI DRESDEN LEIPZIG

ECSEQ BIOINFORMATICS



PLATFORM - OMICS

PLATFORM – OMICS



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 (cell) product

SaxoCell Omics

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

PLATFORM - OMICS

PLATFORM – OMICS

SaxoCell PROJECTS

data generation/ ownership

DATA & METADATA (e.g. SHIMMER, DIZs)

SaxoCell OMICS

support infrastructure

TRAININGS, TOOLS & WORKFLOWS

ScaDS/IZI/TUD central server

CONSULTATION & GUIDANCE

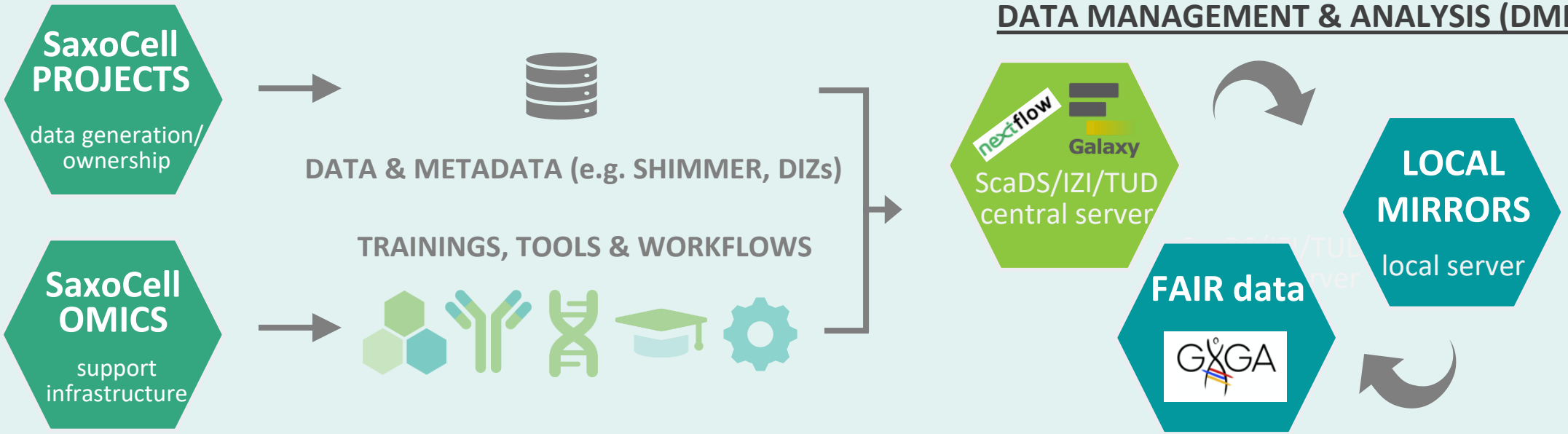
OPERATING PROCEDURES

PROCESS STANDARDIZATION

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

PLATFORM - OMICS

PLATFORM – OMICS



PLATFORM - OMICS

- **Versatile & scalable platform**, with plethora of tools & workflows **for "living drugs"** (**centralized & de-centralized** acc. to the needs of SaxoCell project)
- Data storage and management following **FAIR principles**; full **compliance with ethical and privacy** aspects; **infrastructure** for storage and analyses servers
- **Data analyses tailored to the needs of SaxoCell project:**
  - ❖ GUI-SUPPORTED ANALYSIS through graphical workflow manager for **non-expert users**
  - ❖ SCALABLE COMMAND-LINE bioinformatic pipelines **for advanced users**
  - ❖ DIRECT SUPPORT & COOPERATION (e.g. training of predictive models & algorithm development)

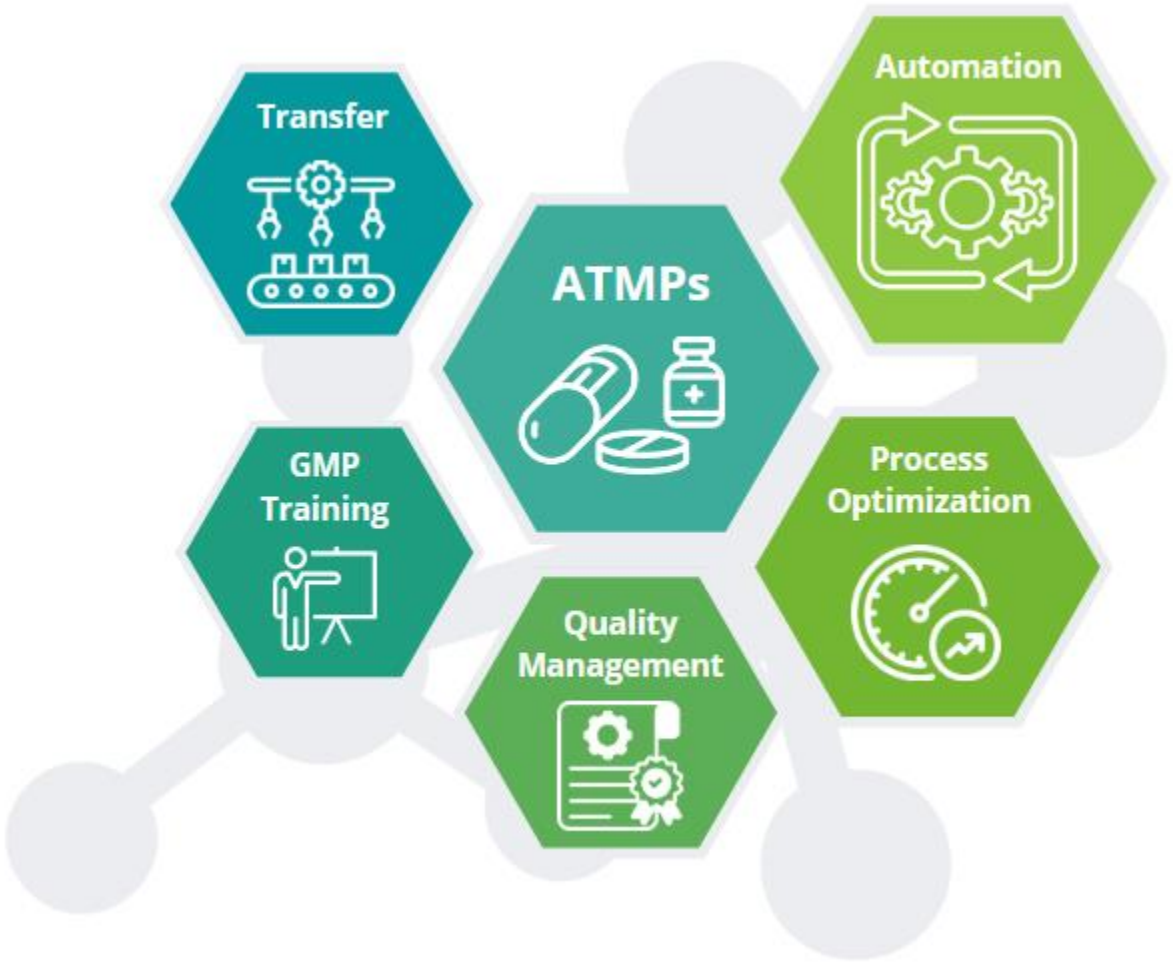
https://galaxyproject.org/
https://www.nextflow.io/
https://www.ghga.de/

PLATFORM – SYSTEMS

SAXOCELL®

PD Dr. Stephan Fricke
Fraunhofer IZI

Dr. Ulrich Blache
Fraunhofer IZI



PLATFORM – SYSTEMS

SAXOCELL®

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TU Dresden

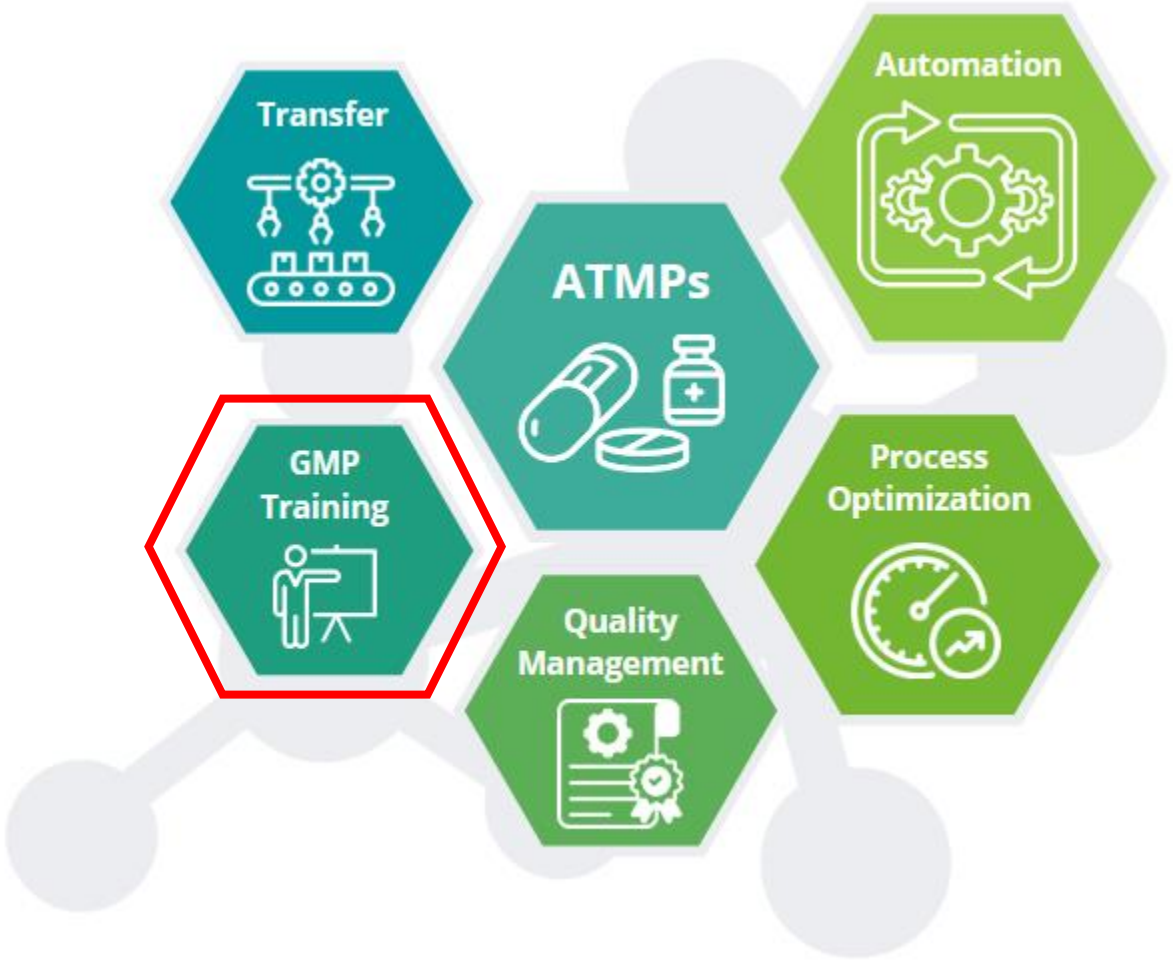
Prof. Dr. Neumuth
Uni Leipzig, ICCAS

Prof. Dr. Rahm
Uni Leipzig, ScaDA.AI

Prof. Dr. Henschler
Uni Leipzig, UKL

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

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



GMP Training: Für ATMPs

SAXOCELL®

Grundkurs Theorie (3 Module)

Grundkurs Praxis (3 Module)
+ Automatisierung und KI

Online Trainingsmodul

PLATFORM - SYSTEMS

Curriculum Theorie

SAXOCELL®

MODUL 1

1. Einführung in Kursinhalte (2h)
2. Vorstellung Fraunhofer Gesellschaft (2h)
3. Grundlagen Zellbiologie (4h)
4. Grundlagen Biotechnologie (4h)
5. Grundlagen Arbeit im Labor (2h)
6. Grundlagen Laboranalytik (2h)

(Insgesamt: 16h)

MODUL 2

1. Einführung in pharmazeutische Produktion (2h)
2. Grundlagen GMP (2h)
3. Grundlagen ATMP (2h)
4. Qualitätsmanagement im GMP-Bereich (2h)
5. Herstellung / Produktion unter GMP (3h)
6. Qualitätskontrolle unter GMP (3h)

(Insgesamt: 14h)

MODUL 3

1. An- und Umkleiden im Reinraum (Gowning) (2h)
2. Verhalten im Reinraum (2h)
3. Mikrobiologisches und Partikel Monitoring (2h)
4. Produktion von Zelltherapeutika (ATMPs) (2h)
5. Arbeitssicherheit und Belehrung S2 (2h)

(Insgesamt: 10h)

PLATFORM - SYSTEMS

Mirko Müller, Dipl.-Biol. u. M.Eng (Fraunhofer IZI)

Curriculum Praxis

SAXOCELL®

MODUL 4

1. An-Um- und Auskleiden für Reinraumtätigkeit (Gowning)
2. Allgemeines Verhalten im Reinraum Produktionsbereich, allgemeine Geräteeinweisung, Waagen, Zentrifugen etc.
3. Aseptisches Arbeiten unter einer Sterilbox
4. Mikrobiologisches und partikuläres Monitoring
5. Mediafill

(Insgesamt: 30h)

MODUL 5

1. Allgemeine Einweisung in den Laborbereich Qualitätskontrolle
2. Einweisung in QK-Geräte
3. Messung exemplarischer Proben an QK-Geräten
4. Ein und Ausschleusen von Material und Inprozesskontrollen

(Insgesamt: 30h)

MODUL 6

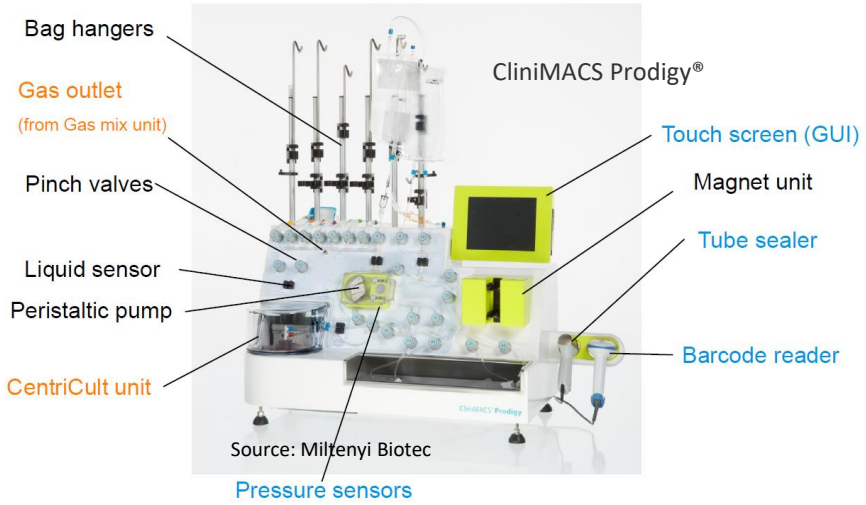
1. Produktion eines exemplarischen Zelltherapeutikums

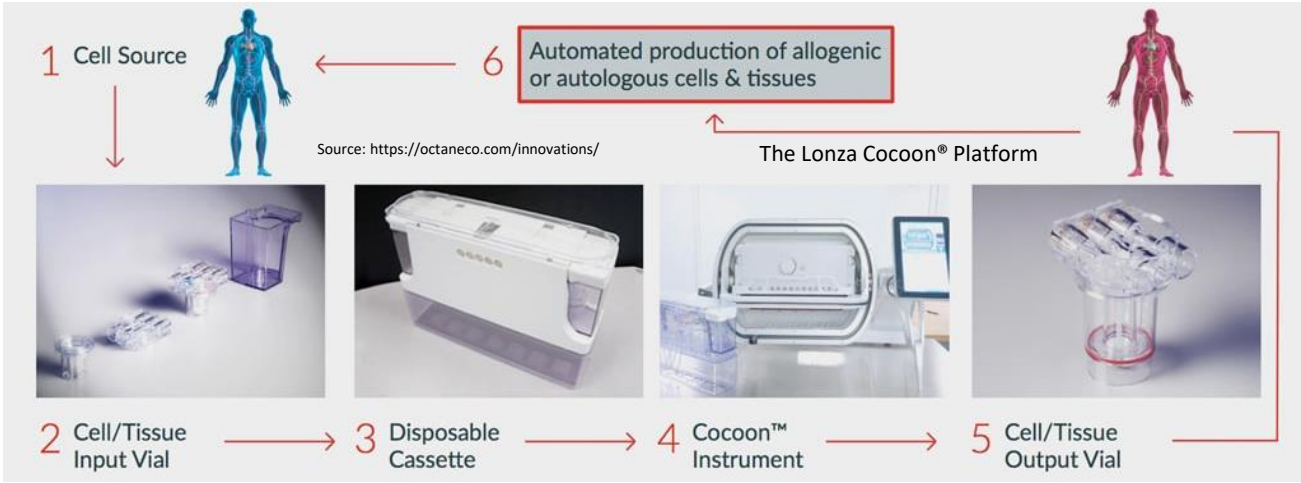
(Insgesamt: 98h)

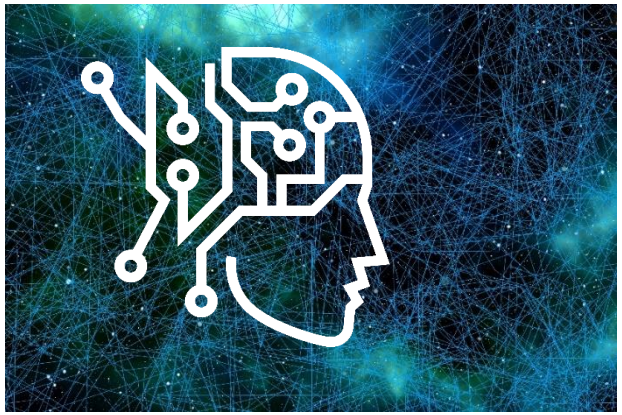
PLATFORM - SYSTEMS

Mirko Müller, Dipl.-Biol. u. M.Eng (Fraunhofer IZI)

Automatisierung & KI







Theoretischer Kurs

- Grundlagen GMP mit Schwerpunkt Automatisierung und künstliche Intelligenz
- GMP gerechter elektronischer Batch Record (eBR)

Praktischer Kurs

- Einführung in die automatisierte Herstellung von Zelltherapeutika
- Arbeit mit dem eBR

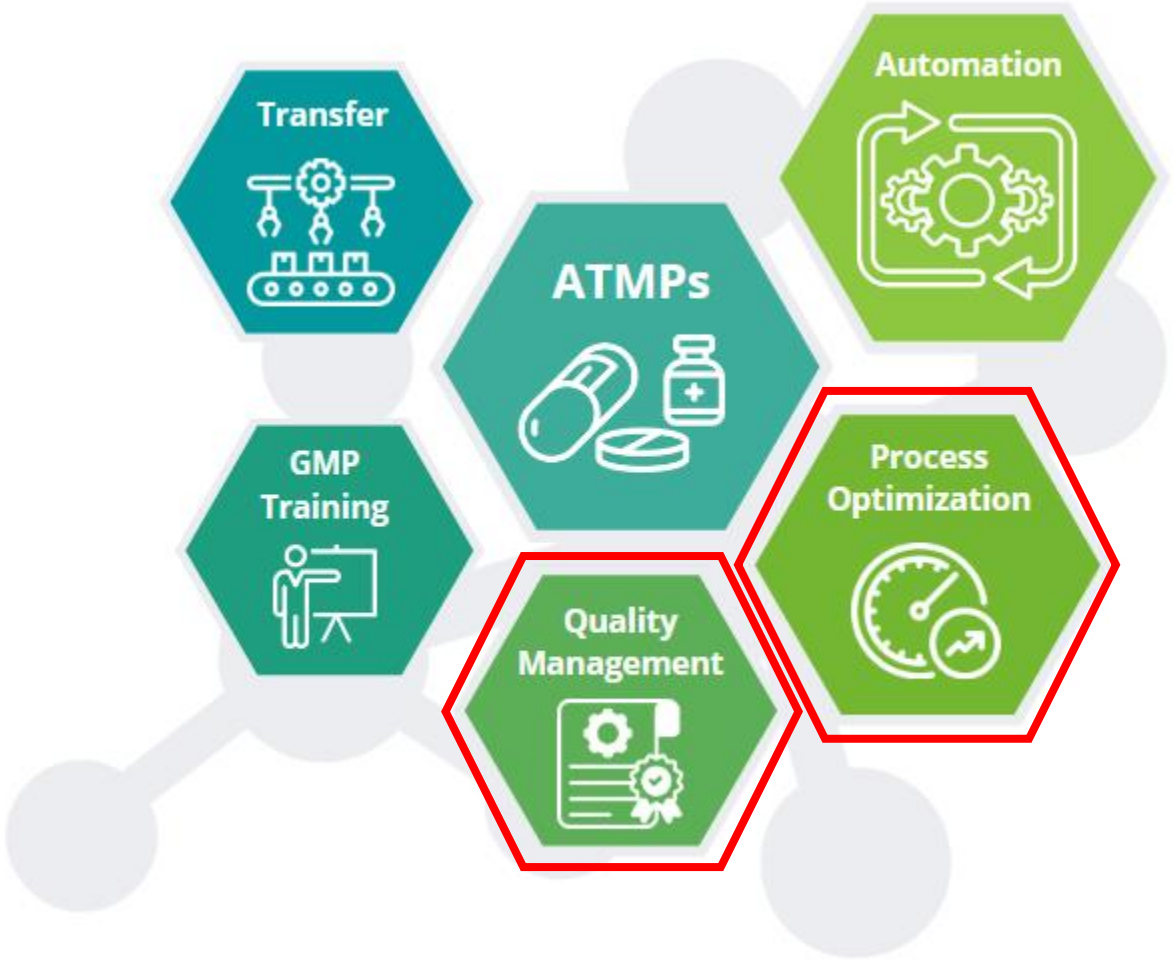
PLATFORM - SYSTEMS

Nächster Impulsvortrag

SAXOCELL®

Plattform-integriertes Monitoring und Evaluation von Zellkulturen und Prozessabläufen mittels KI

(Uni Leipzig, ICCAS und ScaDA.AI)

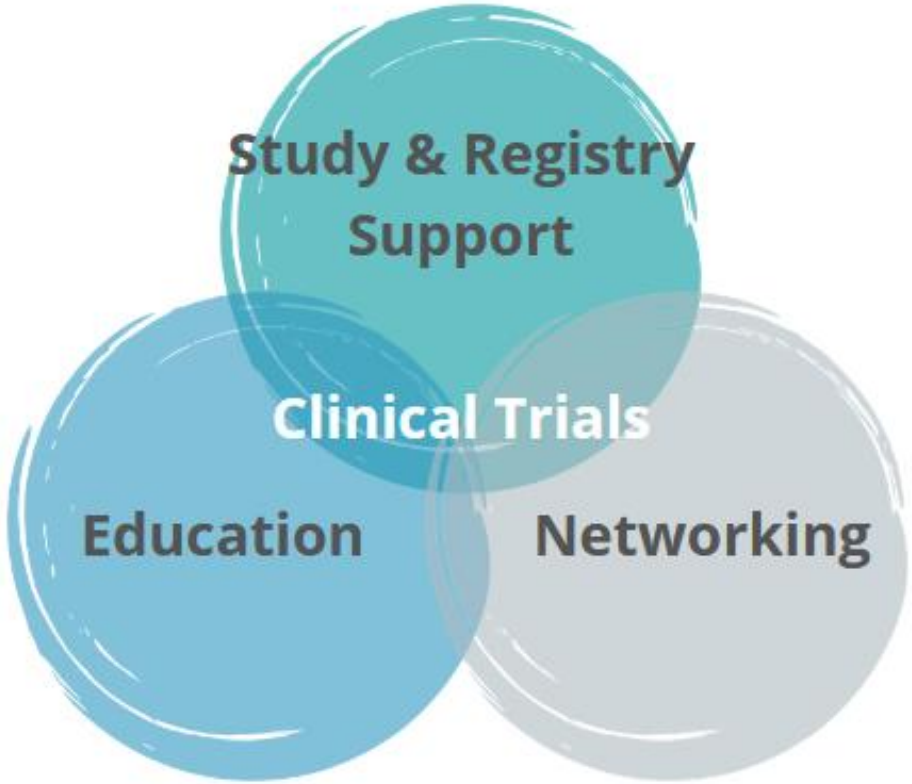


PLATFORM - SYSTEMS

Clinics – Overview

Silke Gloaguen
University Hospital Leipzig

Prof. Dr. Uwe Platzbecker
University Hospital Leipzig



Clinics

- **Current activities**
  - Setting up educational workshop „clinical trials“
    - In collaboration with ZKS Leipzig and HUB
  - Preparational activities and negotiations for PHOTOCAR trial
    - Regulatory challenges
  - New strategy for CAR-NK4.0 / DoNCAR trial → funding
    - Meeting on 21st June with all partners
  - Preparation of newsletter for SHIMMER registry
  - Preparation of Working Paper
    - ATMPs and clinical trials

Clinics

- **Task exemple – PHOTOCAR** (in collaboration with ZKS)

  - General brainstorm/discussion of project/protocol
  - Support in protocol writing
  - Build budget for the trial
  - Support in negotiations with Financier (i.e. in the case of industry financing)
  - Support in discussion with SponsorQM of University of Leipzig
  - Support in discussions/negotiations with local (Landesdirektion) or national (PEI) authorities
  - Link between clinicians and Sponsor/ZKS

Clinics

- **Task exemple – DoNCAR**

  - SaxoCell had accompanied BMBF proposal in 2021
    - Study support unfortunately declined in last round of the call
  - Tasks now → support clinician team in building new strategy for funding acquisition and corresponding adjustment of the project
    - Discussions are ongoing

Hub people

Thomas Tradler
Fraunhofer IZI

Ira Illgen
TU Dresden

Ilka Henze
Fraunhofer IZI

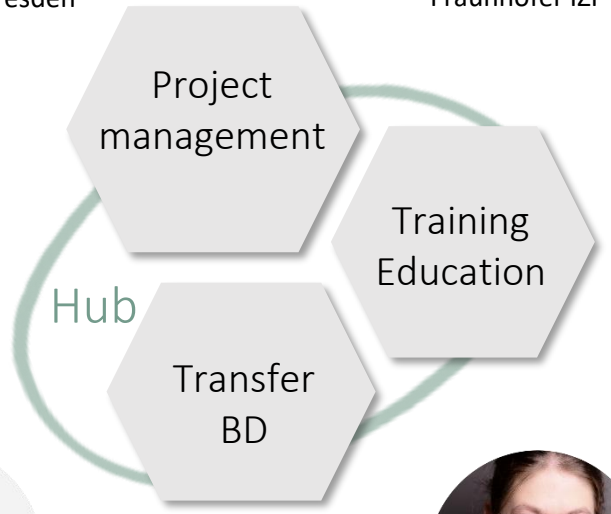
Luisa Brückner
TU Dresden

Maren Henneken
TU Dresden

Nicole Modler
Uni Leipzig

Beatrice Berneck
Uni Leipzig

Sophia Kolbe
Fraunhofer IZI



Andrea Zimmermann
Uni Leipzig

Paul Starz
Fraunhofer IZI

Dorit Teichmann
TU Dresden

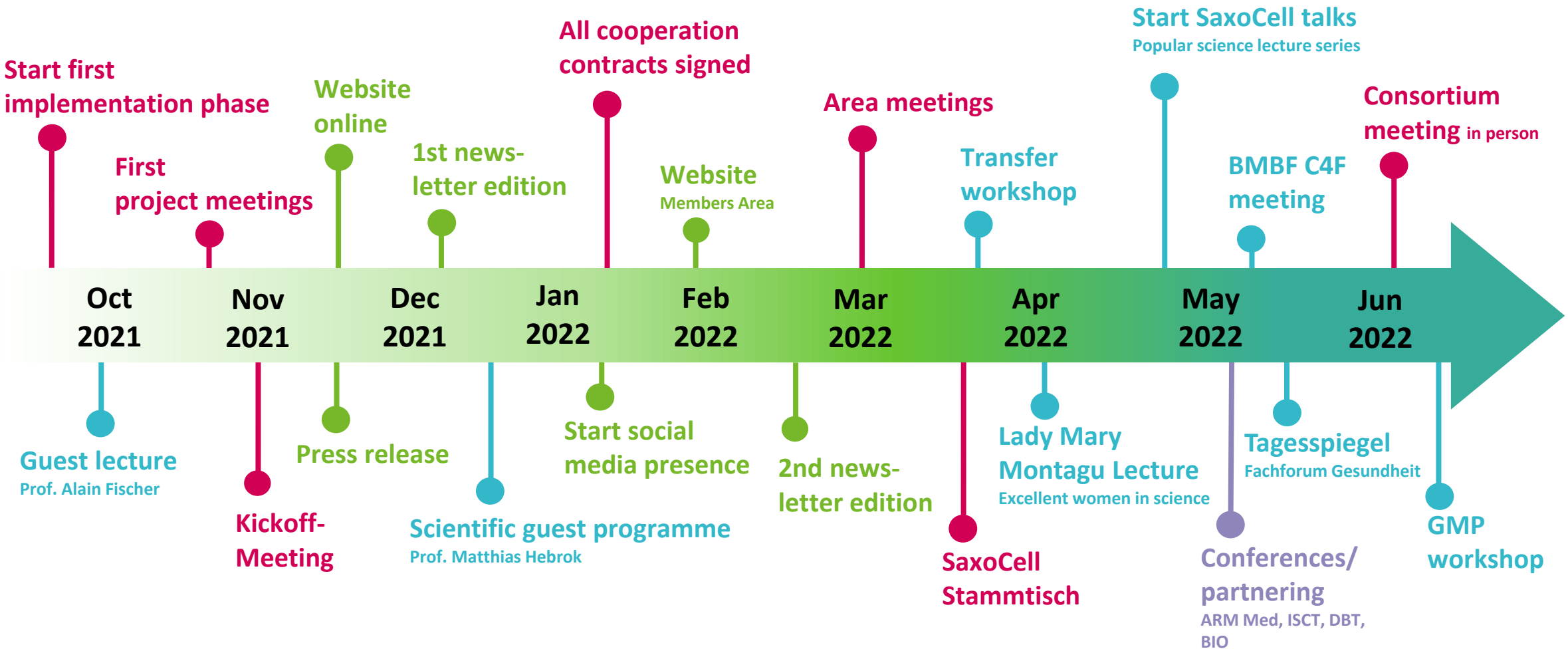
Anette Bartsch
Fraunhofer IZI

Franziska Viebach
TU Dresden

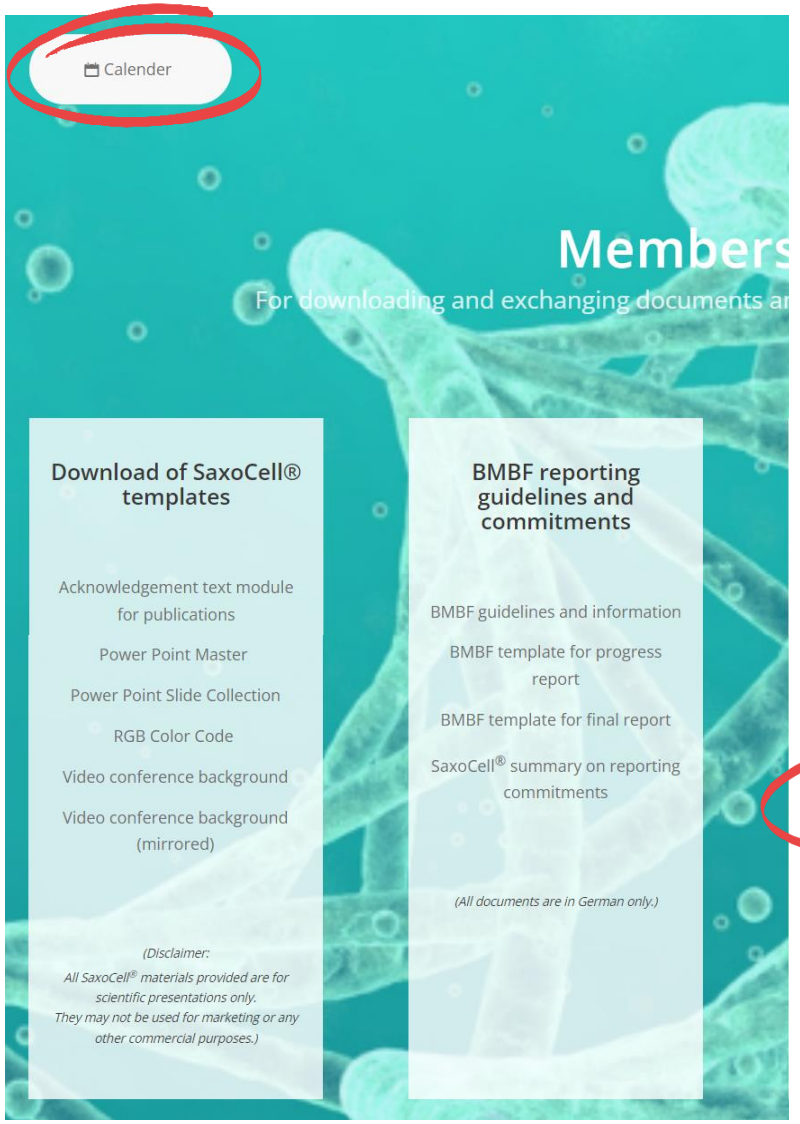
Stefanie Binder
Uni Leipzig

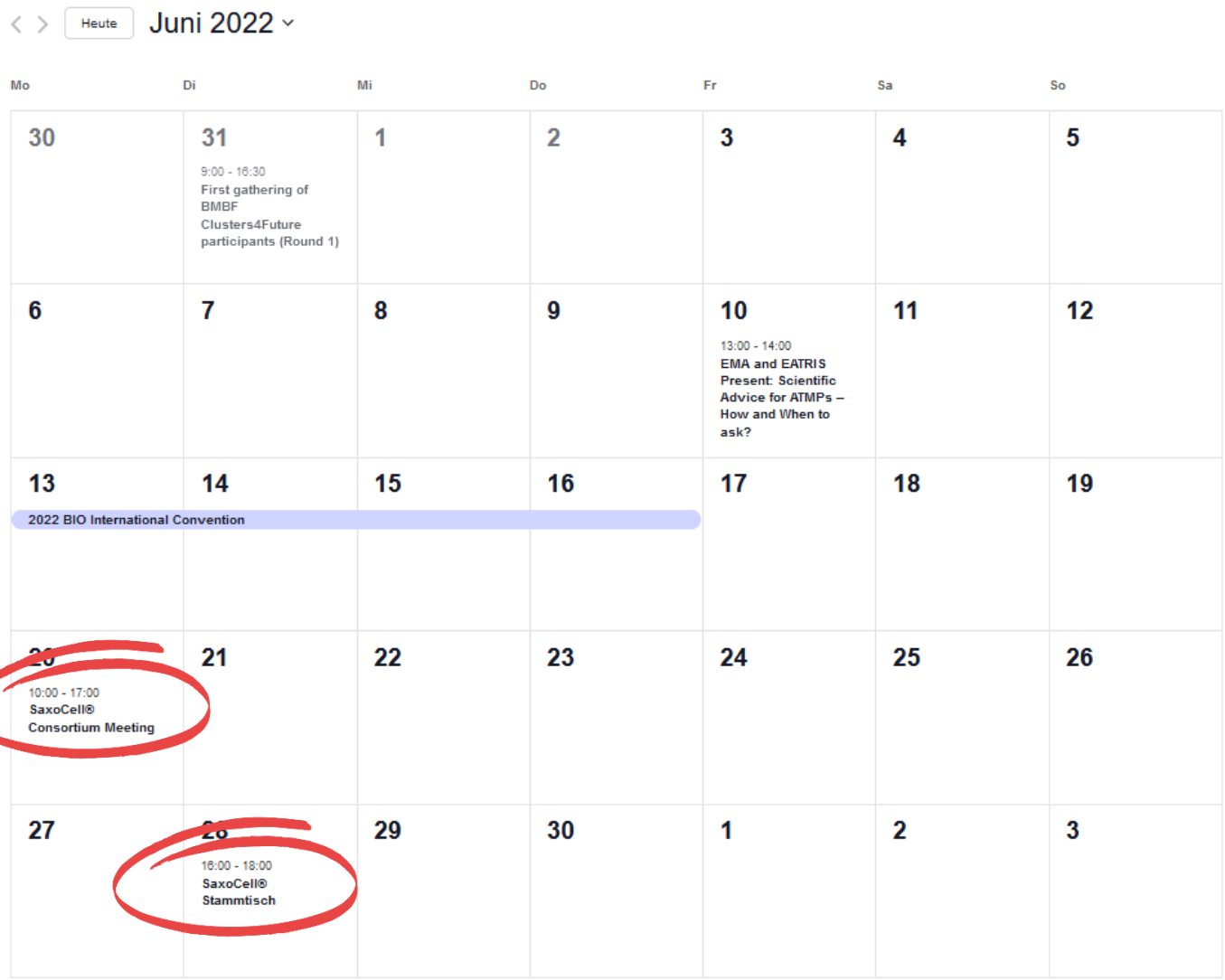
Hub

Hub activities so far



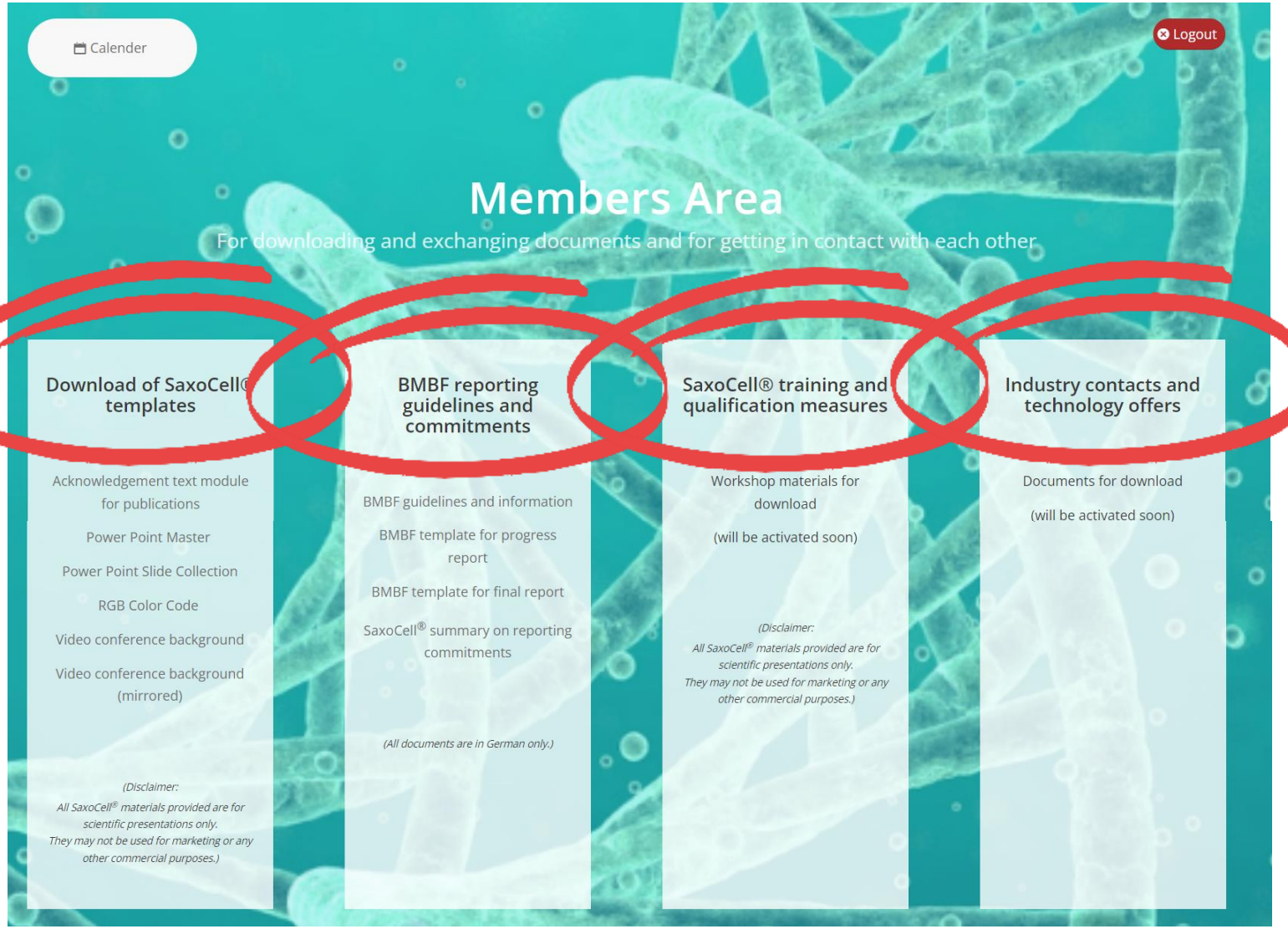
Use the opportunities!





Hub

Use the opportunities!



Additionally included:

- List of current publications
- Newsletter Archive
- Discussion Forum

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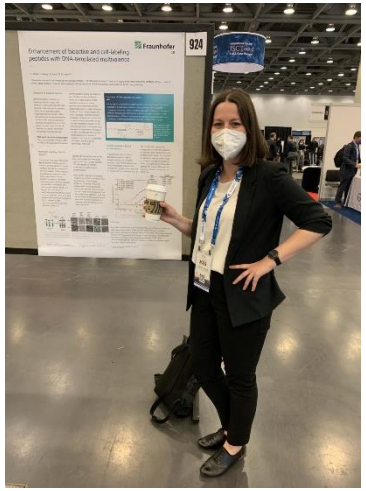
We transfer!



- Deutsche Biotechnologie-tage 2022
- ARM-MED 2022
- ISCT 2022
- BIO 2022

Hub

BIO Europe 2022 in Leipzig!

BIO Europe 2022

Europe's largest life sciences partnering event - will take place in Leipzig
October 24th-26th

Supporting transfer efforts for R&D results of our cluster, SaxoCell will get comprehensively presented at this large conference:

- SaxoCell booth
- SaxoCell partnering
- SaxoCell symposium

Hub

We support you!

Upcoming events!

SaxoCell Training Series

1st GMP basic course with certification

June 30th 2022 / 9:30 – 17:00 / CRTD Dresden

2nd Transfer workshop „How to start-up"

July 6th 2022 / 12:30 – 14:30 / online

SaxoCell Lecture Series

"Immuntherapie bei Blutkrebs - Status und Perspektiven"

By Uwe Platzbecker

July 11th 2022 / 13:00 – 14:00 / University Hospital Leipzig & online

Hub

Stay in touch!

Website + Members Area
https://www.saxocell.de

LinkedIn
https://www.linkedin.com/company/saxocell-cluster/

Twitter
https://twitter.com/SaxoCell

Instagram
https://twitter.com/SaxoCell

Next Newsletter
Mailed this week

Next Stammtisch
28.06.2022
16:00 - 18:00
Online (Wonder.me)

Hub

Area Sessions & Topics

SAXOCELL®

AREA 1
CAR-T-Cells

Mechanisms of T cell transplantation failure

Mechanisms of 'failure' in T cell engraftment & persistence and strategies to overcome them.

AREA 2
NK/CAR-NK-Cells

NK cell therapy and animal models

Important factors for NK cell therapy (tumor entities, target antigens, KIR or HLA genotyping, NK cell cytotoxicity, type of CAR, Uni-CAR, technology platforms, protocols) and determination of suitable animal models.

AREA 3
ATMPs reg. Med.

Delivery Technologies and Industry Collaborations

AREA 4
CGT modulating

Dealing with regulatory authorities

ATMP research in Germany - Biggest obstacles with regulatory authorities and how to overcome them in the future.

Getting ready for Area Sessions

Coffee Break

Time	Topic	Responsible
14:50 – 16:15	Area Meetings	All
16:15 – 16:35	**Coffee Break**	**All**
16:35 – 16:40	Results and Discusson Area 1	Area 1
16:40 – 16:45	Results and Discusson Area 2	Area 2
16:45 – 16:50	Results and Discusson Area 3	Area 3
16:50 – 16:55	Results and Discusson Area 4	Area 4
16:55 – 17:15	Discussion	All
17:15 – 17:30	Wrap up, outlook and Goodbye	All
17:30	**Get together**	**All**

AREA 1 – CAR-T

Topic for Discussion:

Mechanisms of 'failure' for T cell engraftment and persistence (and strategies to overcome them)

AREA 1 – CAR-T – Session Results

T regs

Case study

- Unmodified ex vivo cultured T regs
- PK^{max} at day 1/week 1 post infusion
- TCR repertoire analysis

→ Expect therapeutic window of weeks (>1)

→ Address high risk GvHD patients (GI)

To do‘s / Open questions:

- Optimal source of T regs
- Metronomic activation with adaptor
- Epigenetic profile → Super donors
- PK analyses / Biodistribution (liquid biopsy?)

T effector

Case study

- CD19 CAR-T vs. CLL/lymphoma
- PK correlates with outcome
- Persistence for decade possible

→ Same for BCMA CAR-T vs. Multiple Myeloma?

To do‘s / Open questions:

- T cell subsets
- T cell transcription factors
- Metabolic enigneering
- Vaccination
- Epigenetic engineering

ESH EUROPEAN SCHOOL OF HAEMATOLOGY

MARK YOUR AGENDA

2nd Translational Research Conference
Immune & Cellular Therapies:
Focus on Advanced Gene-Engineered Immune Cells

Berlin, Germany
September 12-14, 2022
#ESHIMMUNE2022

Chairs: Chiara Bonini, Michael Hudecek, Stan Riddell

DEADLINE FOR ABSTRACTS: JULY 10th, 2022

To register and for further information: www.esh.org - info@esh.org

AREA 2 – NK/CAR-NK – Session Results

- Share points: cell lines, protocols, expertise for such protocols, GMP issues (negative controls, ab validation)

-> lists (on membership area)

- NSG mice is convincing PEI
- Questionnaire for ethical votes
- DKMS for HLA/KIR genotyping?
- seminars with area 1 – inviting speaker of area 1 (every 6 weeks)

-> hybrid mode

AREA 3 – ATMPs – results

- *Future Perspectives of the group*
- First in person meeting - Divers topics of joint interest identified
- Meetings quarterly, hybrid
- Further topics to be discussed
  - Future funding options
  - Experiences with PEI
  - Spin-out creation

AREA 4 – CGT – Session Results

ATMP approval

AREA 4 – CGT – Session Results

- Best time point to go to the PEI: preclinical investigations are done, your ATMP works efficiantly

→ ask the „right“ and specific questions:

  - Is this assay sufficient as release assay?

  BE AS PREPARED AS YOU CAN!

- Team is important for Scientic Advice meetings: Clinician, Researcher, a person who can write clinical trials…

  (You can go with as many people as you like)

AREA 4 – CGT – Session Results

- Early SaxoCell platform interaction and communication is important
- → SaxoCell Hub could distribute calls and grant application topics
  - Preclinical
  - Clinical Topics
- List information to each call:
  - What is funded?
  - Funding volume?
  - Etc.

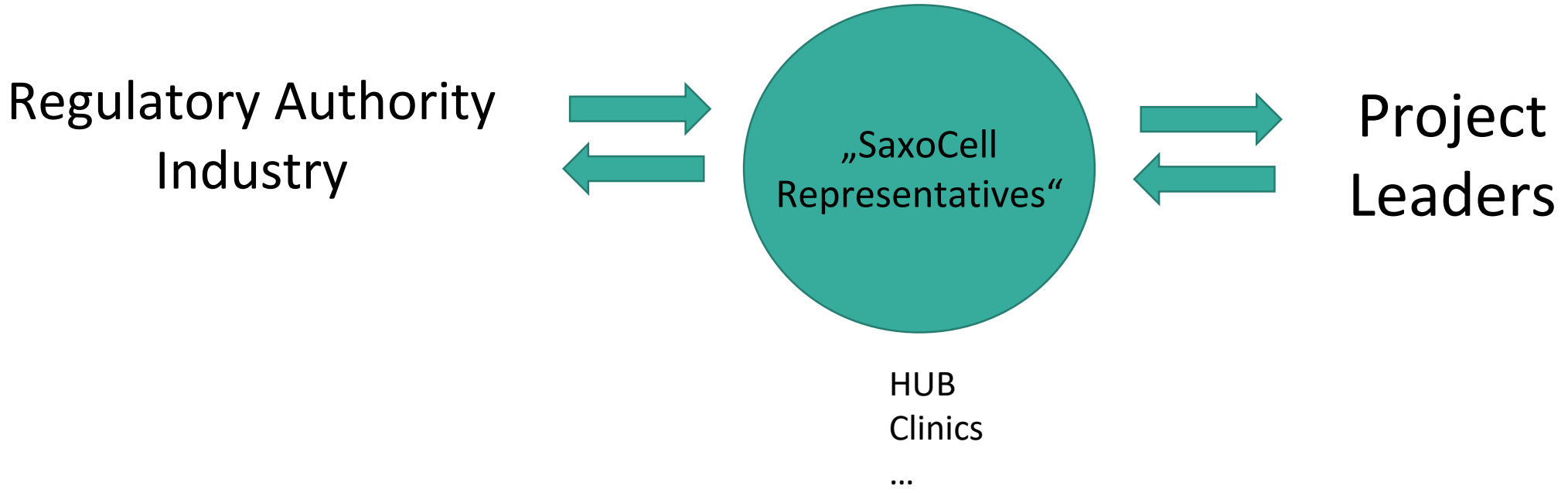
- List all applications and their outcome → Accepted? Rejected? Why?
- How were ATMP studies funded in the past?

AREA 4 – CGT – Session Results

Gather and combine the knowlegde that is already there!

AREA 4 – CGT – Session Results

- SaxoCell Hub and Platform = „Representative“ for SaxoCell at the Regulatory Authority



SAXOCELL®

CLUSTERS 4 FUTURE
Innovationsnetzwerke für unsere Zukunft

GEFÖRDERT VOM
Bundesministerium für Bildung und Forschung

Thank you for your attention!

For questions and further information please contact the Hub team!

saxocell@tu-dresden.de

Visit us on

TECHNISCHE UNIVERSITÄT DRESDEN

UNIVERSITÄT LEIPZIG

Fraunhofer IZI

KLINIKUM CHEMNITZ gGmbH