



Pioneering cellular medicines for women's health

6th Annual iPSC Summit || September 2026

Dr Damien Zanker
Head of Clinical Manufacturing

Targeting Ovarian Cancer and Endometriosis

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Cartherics at a Glance

Cartherics is a late pre-clinical stage cell therapy company developing 'off-the-shelf' iPSC-NK treatments for solid cancers and endometriosis



- Based in Melbourne
- Commenced operations Jan 2016
- Currently ~30 staff



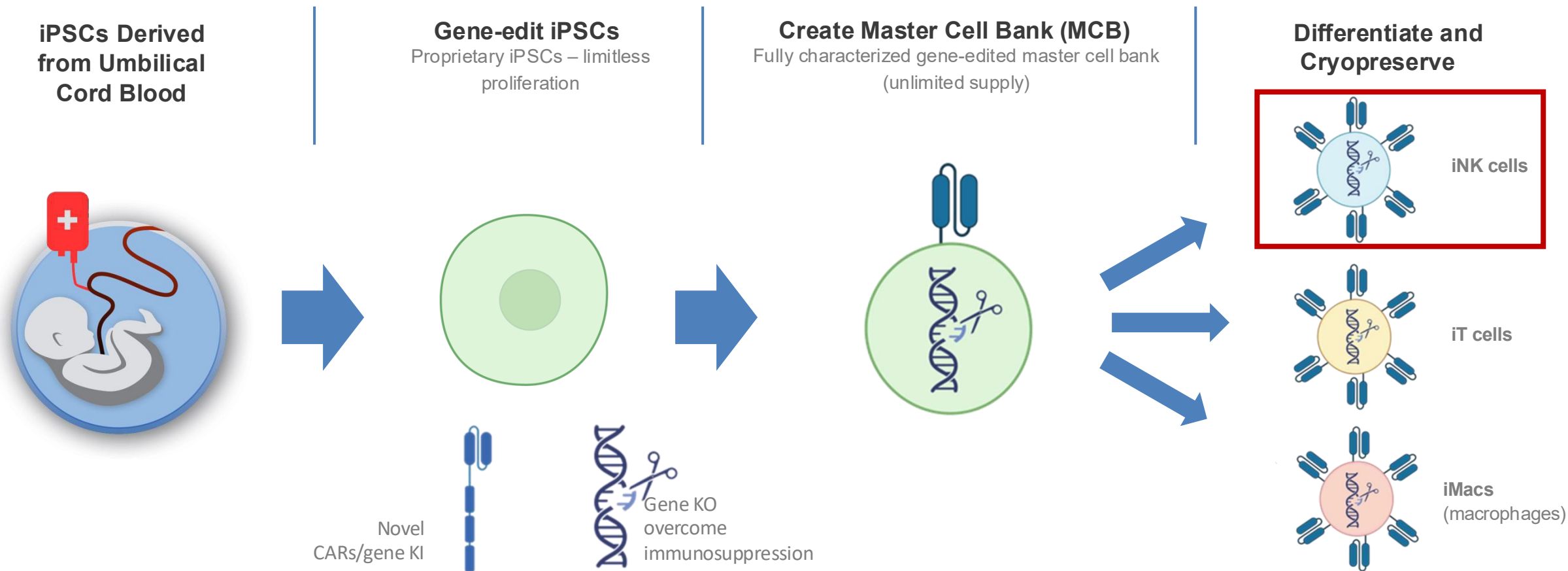
- Operating from a dedicated 1,800m² purpose-built facility
- Recently upgraded cleanrooms



- 'Off-the-shelf' platform, using gene-edited iPSCs to produce immune cells with enhanced function
- 17 issued patents over 6 families

Cartherics Cell Therapy Platform

Enables the rapid development of a diverse range of products and immune cell types



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The Crippling Burden of Neglected Women's Health

A Two-Part Crisis in Women's Health: A Lethal Cancer and a Debilitating Disease

1

Ovarian Cancer: A Lethal Disease of Late Diagnosis

- ~325,000 new cases diagnosed and ~200,000 deaths globally each year.
- Severely limited treatment options.
- >75% of cases diagnosed at a late stage (III/IV).
- 5-year survival rate for stage III is 41% and only 20% for stage IV.

2

Endometriosis: The Widespread and Overlooked Cancer Precursor

- Affects 190 million women globally.
- Cause of debilitating pain, organ damage and infertility.
- Current treatments are inadequate.
- There is no cure.
- Endometriosis is a risk factor for ovarian cancer.

Evidence suggests a strong link between ovarian cancer and endometriosis, and they may have overlapping biology. Cartherics is developing therapies that target specific antigens common to both diseases.

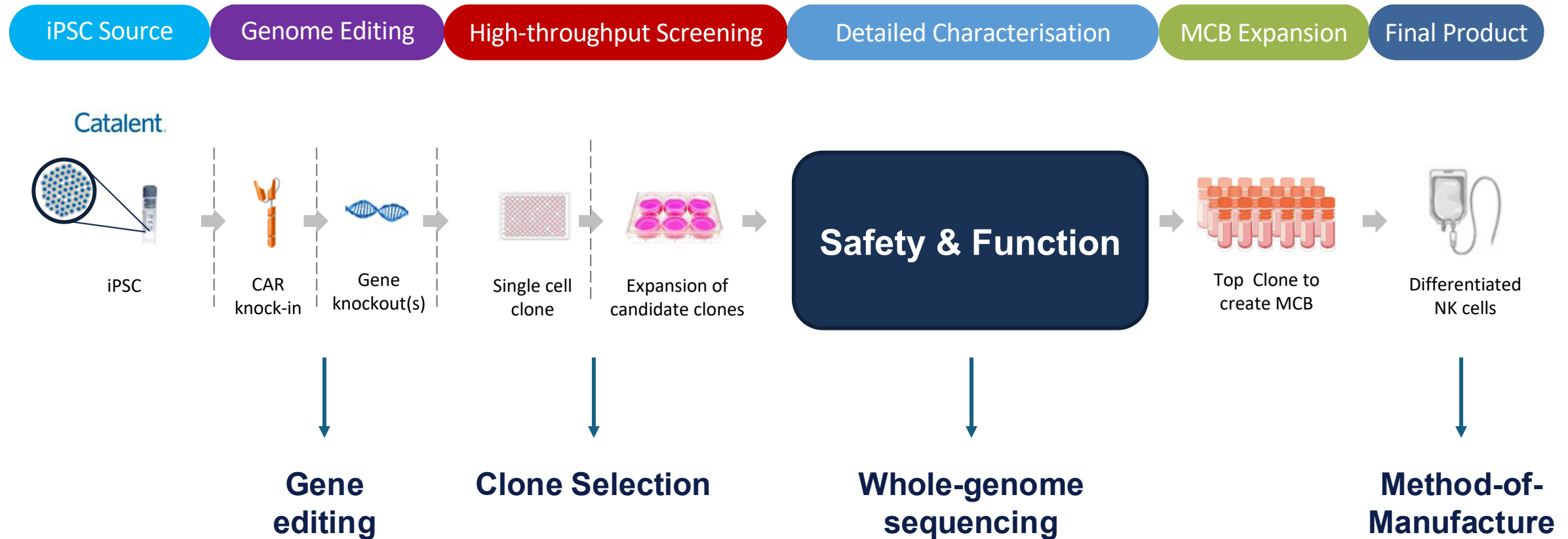


• **Key Takeaway:** Our strategy leverages a de-risked entry in ovarian cancer as a gateway to treating the broader endometriosis crisis.

How do we engineer and screen our clones?

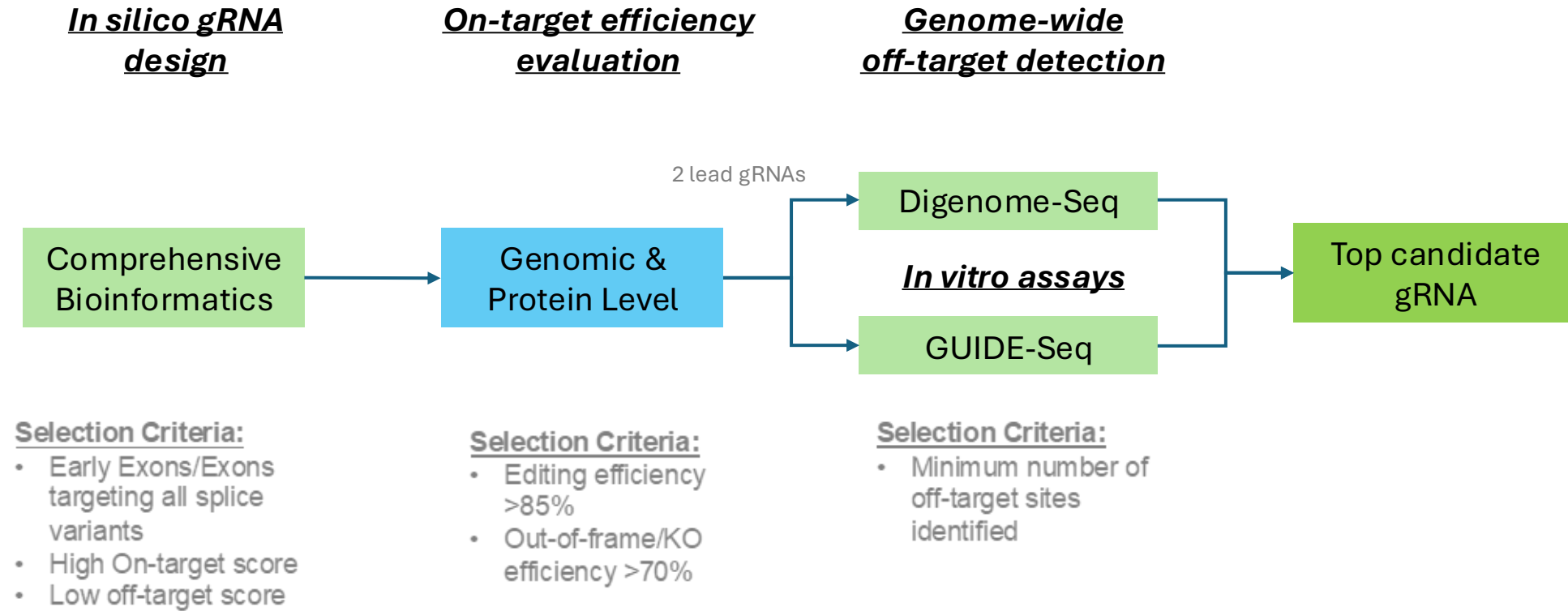
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A Scalable and Robust iPSC-Derived CAR-NK Platform



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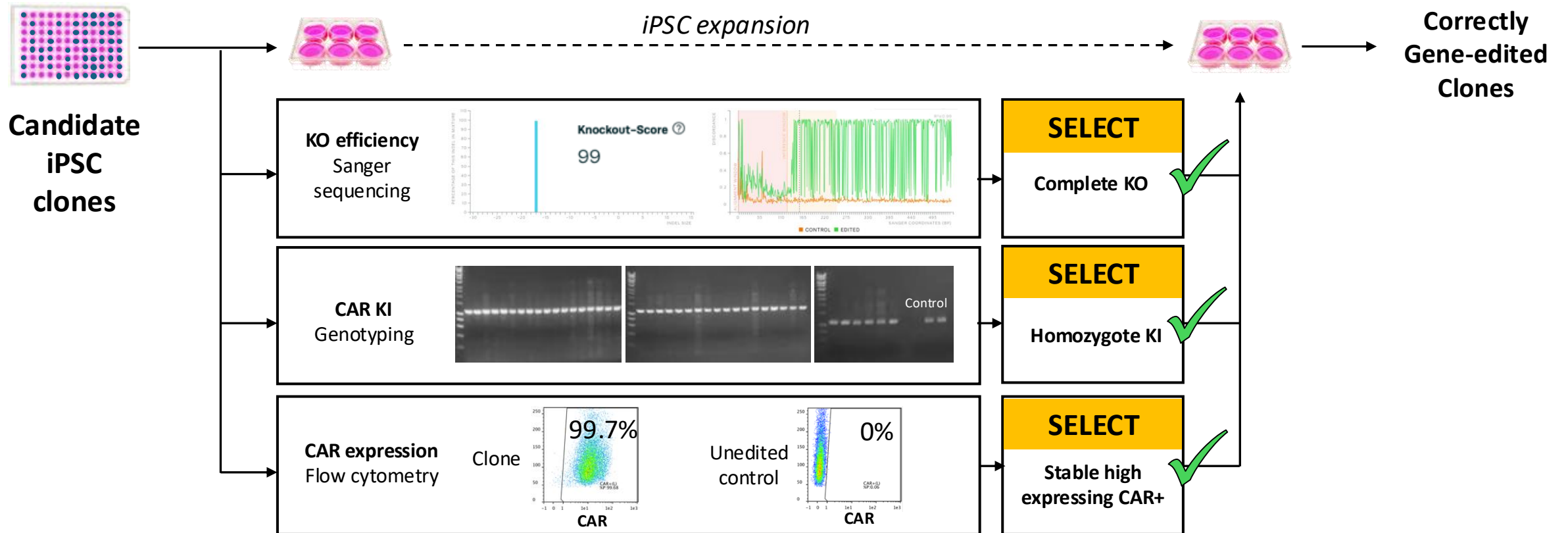
Robust Genome Editing Strategy Using CRISPR/Cas9



- gRNAs selected based on high-editing efficiency and low off-target effects

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High-Throughput Clone Screening for Correct Gene-Edits

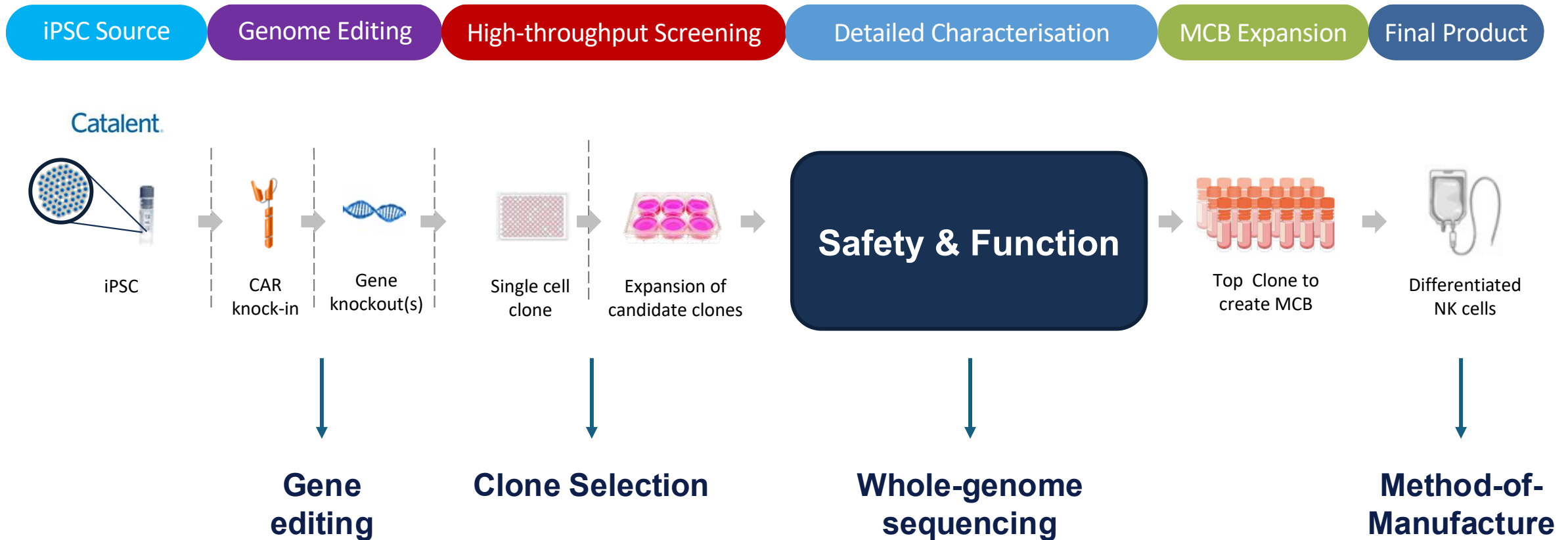


- 30 clones selected based on correct gene editing for further analysis

Walid Azar

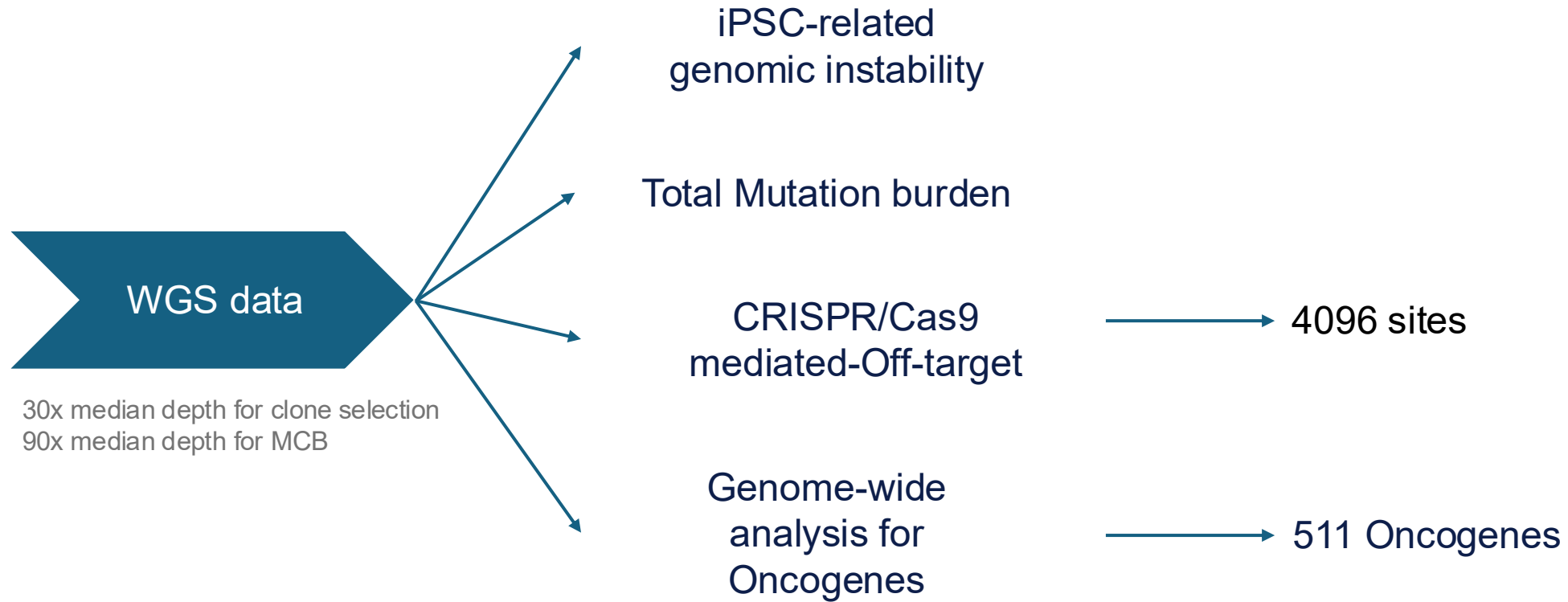
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A Scalable and Robust iPSC-Derived CAR-NK Platform



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Developing a Robust and Comprehensive WGS Pipeline



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Safety Assessment of MCB Candidate Clones

- **Potential sources of safety concerns:**

- CRISPR/Cas9-mediated off-target effects
- DNA structural changes due to cells undergoing single cell cloning and long-term culture
- Oncogenic mutations

- **Strategy:**

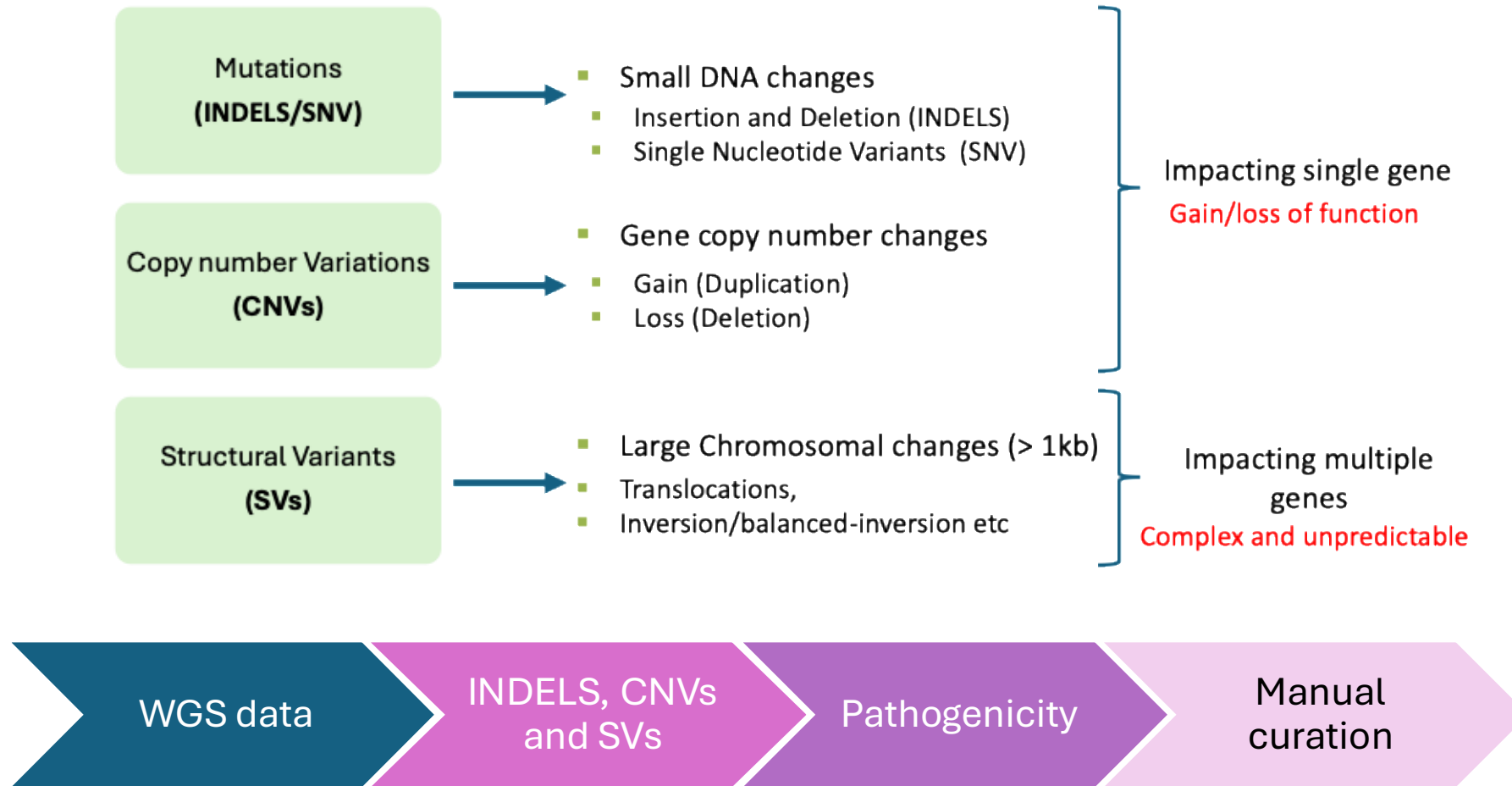
- Karyotyping (SNP analysis)
- **Whole genome sequencing (WGS)**

- **Experimental design:**

- x2 starting/parental cell lines
- x30 gene-edited MCB candidate clones

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What do we look for in the WGS data?

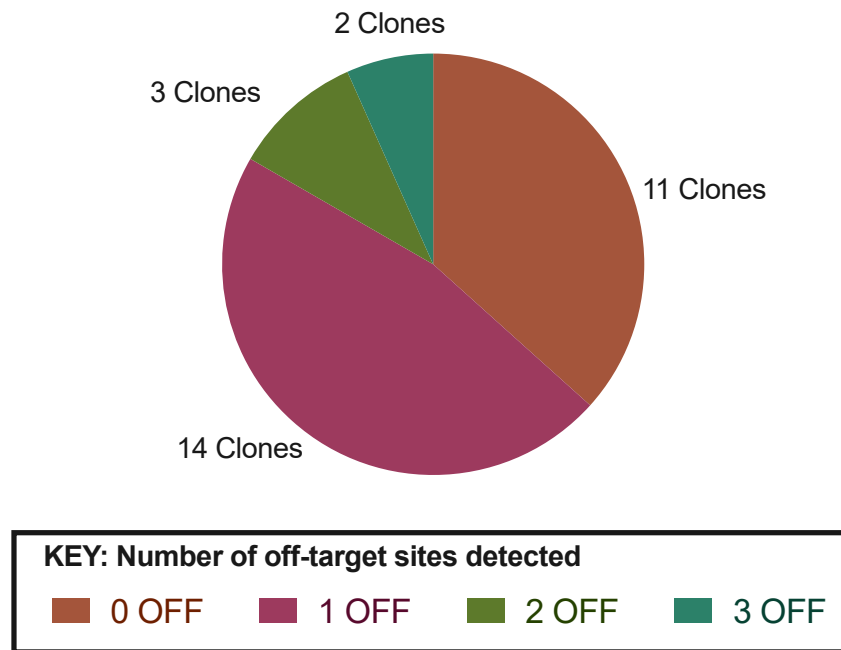


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CRISPR/Cas9-mediated Off-target Effect Analysis by WGS

- **INDEL analysis results:**

- 7 off-target sites detected across the 30 clones



Type of Off-targets

Chr #	Detected by	Locus	Nearest Gene	Region	Location
Chr21	INDEL	-	KCNE1B	Intergenic	NA
ChrY	INDEL	-	-	Intergenic	NA
Chr2	INDEL	-	-	Intergenic	NA
Chr6	INDEL	-	CNR1	Intergenic	NA
Chr8	INDEL	PINX1		Gene	Intron
Chr5	INDEL	ARL15		Gene	Intron
Chr21	INDEL	APP		Gene	Exon

Outcome: All clones were considered safe for further characterisation

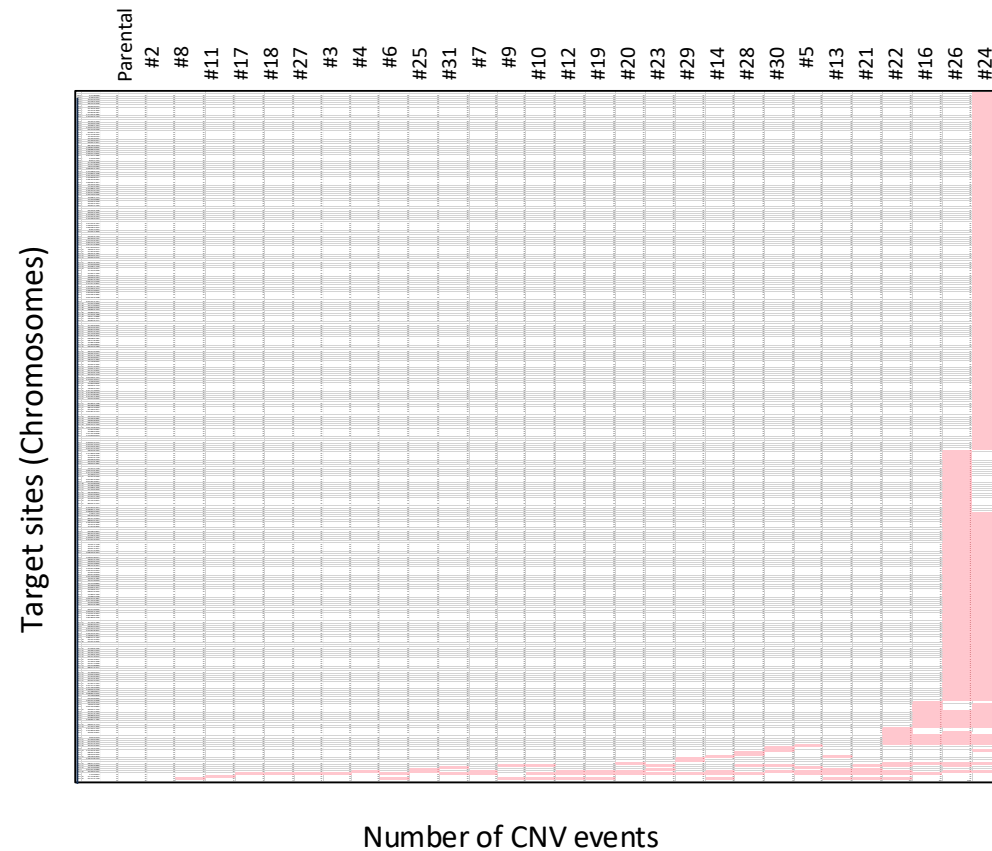
Walid Azar

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CRISPR/Cas9-mediated Off-target Analysis by WGS

CNV analysis results:

- 316 CNV events detected across the 30 clones



Filters

- PASS-1-CNV frequency
 - < 10 events
 - = 10-100 events
 - > 100 events
- PASS-2-Potential consequences
 - Non-Oncogenic

26 clones were
considered safe for
further characterisation

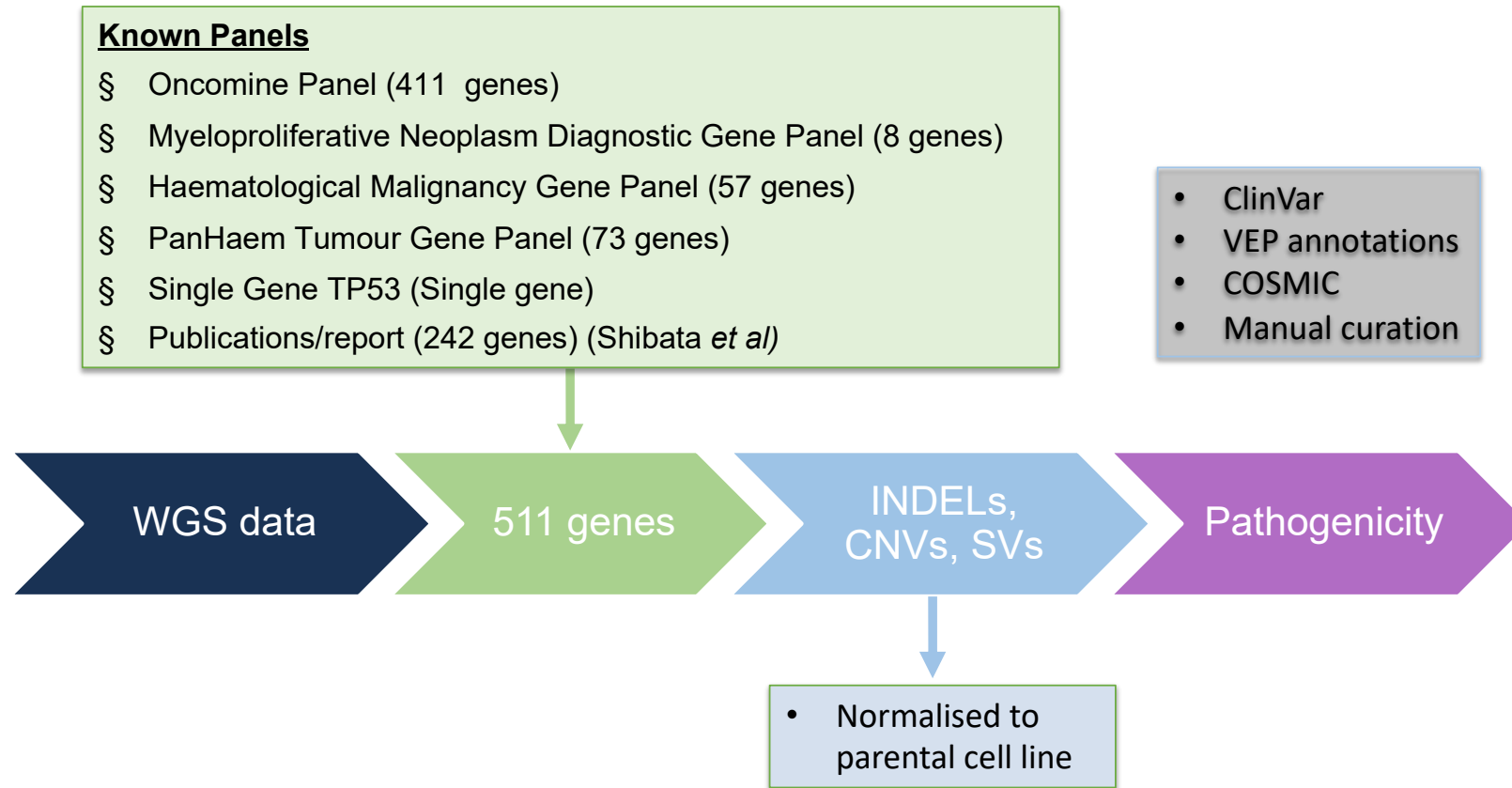
CNV Incidence Summary

Clone #	CNV Frequency
2	1
3	2
4	2
5	5
6	2
7	3
8	1
9	3
10	4
11	2
12	4
13	6
14	5
15	3
16	20
17	2
18	2
19	4
20	4
21	6
22	14
23	4
24	272
25	3
26	134
27	2
28	5
29	4
30	5
31	3

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Detection of Random Oncogenic Mutations by WGS



- **Objective:** To select clone(s) with no mutations in genes associated with cancers

INDEL – Insertion/Deletion; CNV – Copy number variation; SV – Structural Variant; VEP – Variant Effect predictor

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Random Oncogenic Mutation Analysis by WGS

Summary

- 18 clones were analysed for potential oncogenic mutations
 - Clones with pathogenic INDEL(s) or CNV(s) determined by ClinVar were excluded
 - Clones with High Impact SVs determined by VEP annotations were excluded
 - CNVs and SVs which could not be determined by ClinVar/VEP are manually curated
- 5 clones considered genomically stable

* Clone ID	WGS (Oncogenes)			Status
	Pathogenic Mutations	Pathogenic CNV	Pathogenic SVs	
17	0	0	MODIFIER	NO/Minimum safety concerns
9	0	0	MODIFIER	
28	0	0	MODIFIER	
6	0	0	MODIFIER	
7	0	0	MODIFIER	
13	0	?	?	Frurther analysis required (Manual curation)
20	0	?	?	
19	0	?	?	
3	0	?	?	
27	0	?	?	
26	1	1	MODERATE	Significant safety concerns
31	0	1	MODERATE	
24	0	1	MODERATE	
14	0	0	HIGH	
12	0	0	HIGH	
22	0	0	HIGH	
29	0	0	HIGH	
16	0	0	HIGH	

*12 clones were excluded from analysis based on functional data

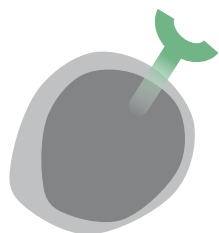
INDEL – Insertion/Deletion; CNV – Copy number variation; SV – Structural Variant; VEP – Variant Effect predictor

Walid Azar

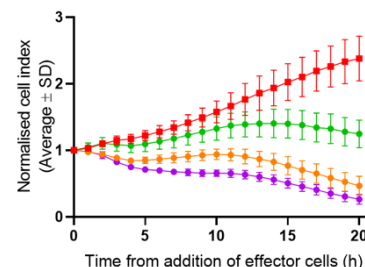
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Robust Functional Characterisation of Top Candidate Clones

Do we have the optimal iNK cell?



Do they kill target cells *in vitro*?



Can they be manufactured at scale?



iNK viability,
purity, phenotype,
CAR expression

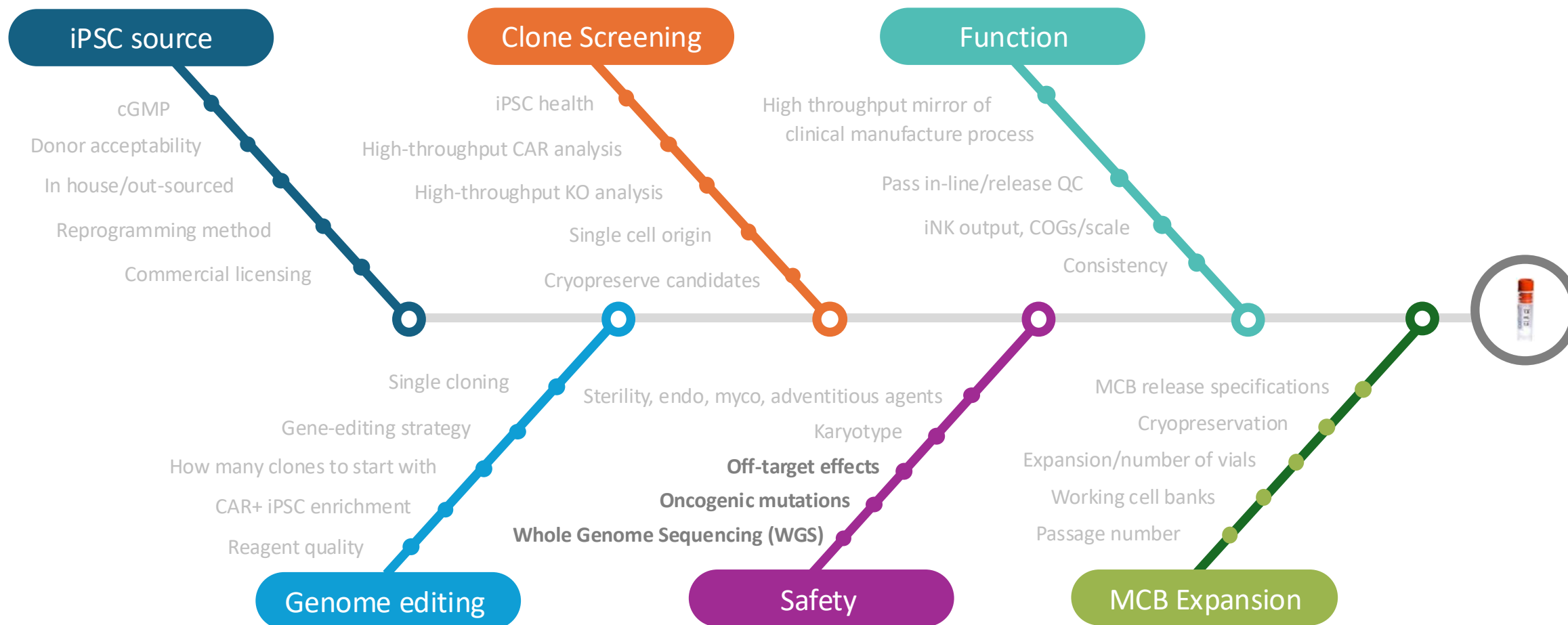
In vitro function

Yield per iPSC and
predicted scale-up

- MCB clone selected based on detailed **safety** and **functional** profile

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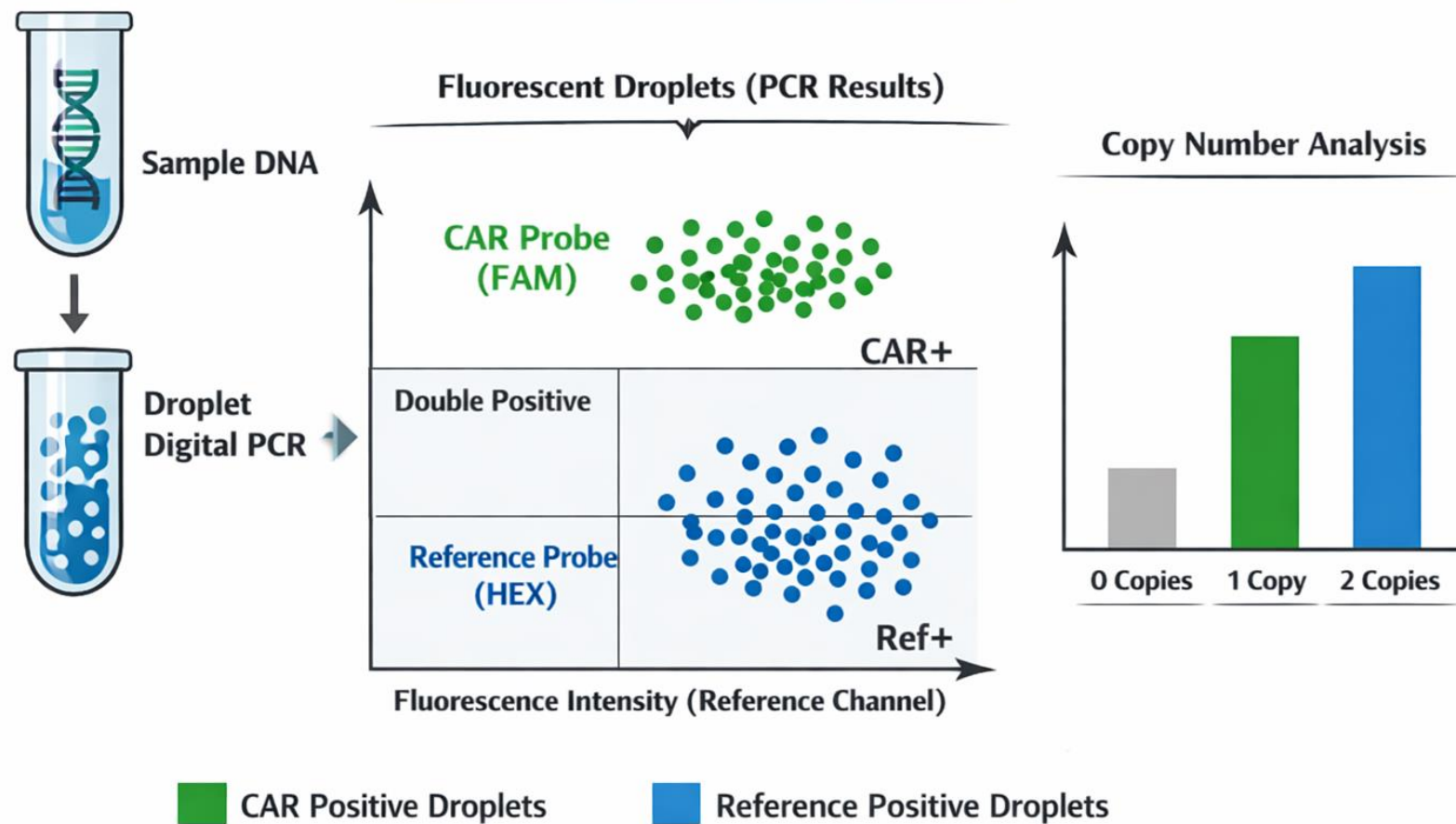
CTH-401 Master-Cell-Bank Development Workflow



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Development of Key Release Assays

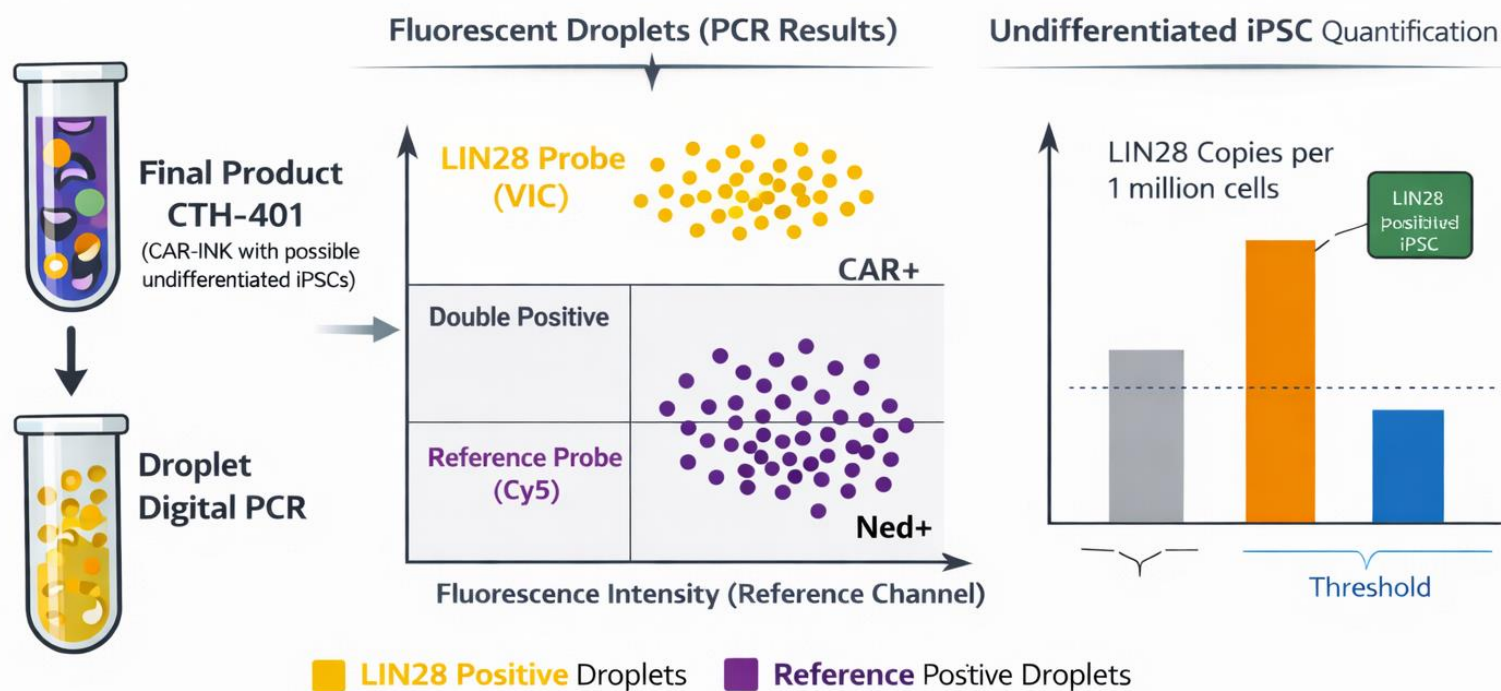
ddPCR CAR Copy Number Analysis



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Development of Key Release Assays

LIN28 ddPCR to Determine Level of Undifferentiated iPSCs Final Product CTH-401



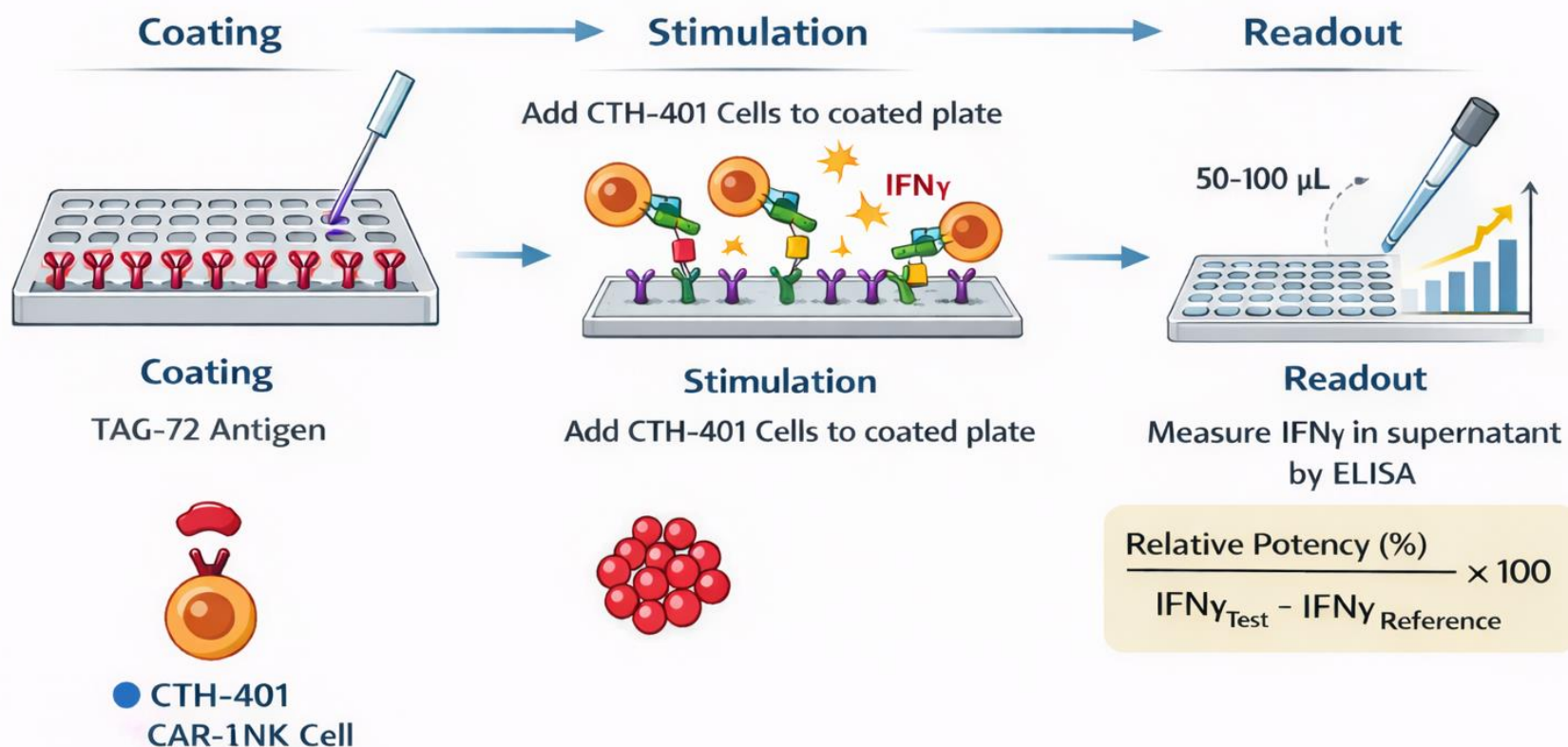
$$\text{PSC} = (\text{LIN28}_{\text{PSC}} + \text{LIN28}_{1 \cdot 0 \cdot 2} \times 100$$

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Development of Key Release Assays

Plate-Bound TAG-72 CAR-iNK Potency Assay

Measuring IFN γ Release as Surrogate Marker of Potency



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How are we using this pipeline?

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Our Pipeline: A Phased Approach to Clinical Strength

A Deliberate Strategy: Validate the Platform, Then Unleash its Full Potential.

1

Program 1: CTH-401, Platform Validation – Lead Program

- **Indication:** Relapsed/refractory ovarian cancer, with expansion potential into earlier-stage ovarian cancer, other TAG-72+ solid tumours and endometriosis.
- **Strategic Goal:** Achieve **first-in-human data** to validate the safety and activity of our core iPSC-NK platform. This is our top priority.



2

Program 2: CTH-501, Next-Generation Target

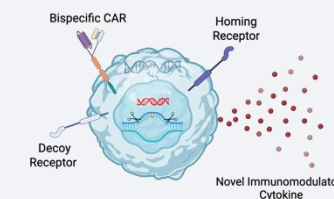
- **Indications:** Endometriosis.
- **Strategic Goal:** Rapidly expand our pipeline with additional product candidates.



3

Program 3: CTH-502, Tumor Microenvironment ("TME")-Resistant "Armoured" Cells

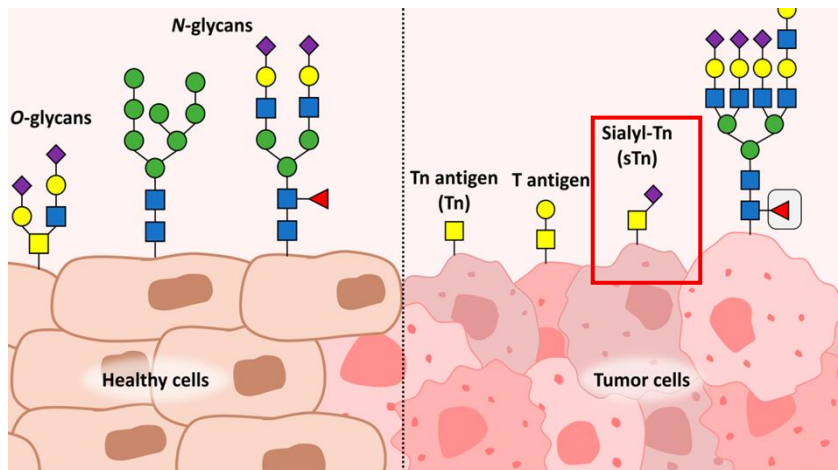
- **Indications:** Ovarian cancer, triple negative breast cancer, other solid tumours expressing TAG-72 or TF.
- **Strategic Goal:** Create a "best-in-class" product with maximal efficacy, designed to overcome the toughest solid tumour microenvironment challenges.



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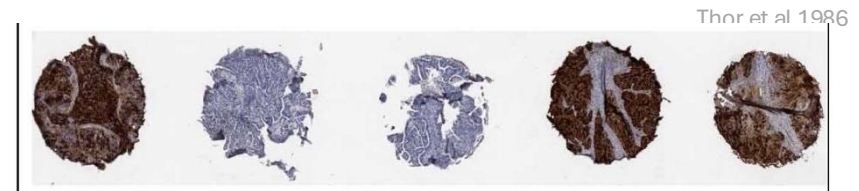
Overview: TAG-72 as a therapeutic target

TAG-72 is not a simple single-gene antigen. It is a large mucin-like glycoprotein carrying the Sialyl-Tn (STn/CD175s) glycan epitope.



TAG-72 antigen expression reported across epithelial-derived cancers

Ovarian	100%
Colorectal	94%
Breast	84%
NSCLC	96%



Ovarian cancer biopsy TMAs with 45 cases of clear cell cancer and 22 cases of Serous cancer confirmed TAG-72 staining (against negative control tissues) in 85% of Clear Cell carcinomas and 95.4% of Serous carcinomas.

TAG-72/STn marks tumour cells and is associated with features of aggressive, immune-evasive disease.

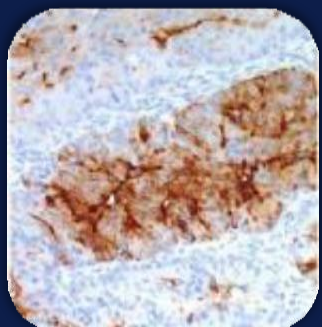
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CTH-401: Lead Product Candidate

First TAG-72 CAR-NK cell therapy

iPSCs gene-edited using CRISPR/Cas9

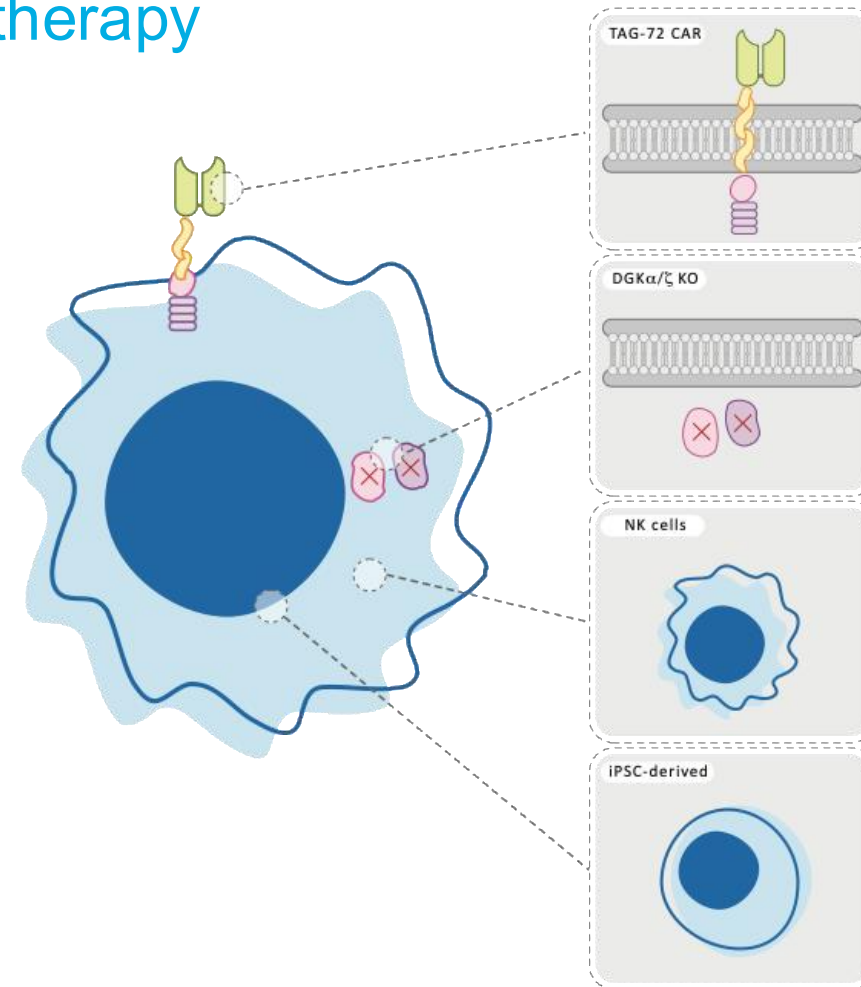
- **TAG-72 CAR knock-in**
 - Complements normal NK cell killing functions
- **DGK α ζ gene knock-outs**
 - Enhance anti-tumoral efficacy



Tumour-associated glycoprotein-72 (TAG-72)

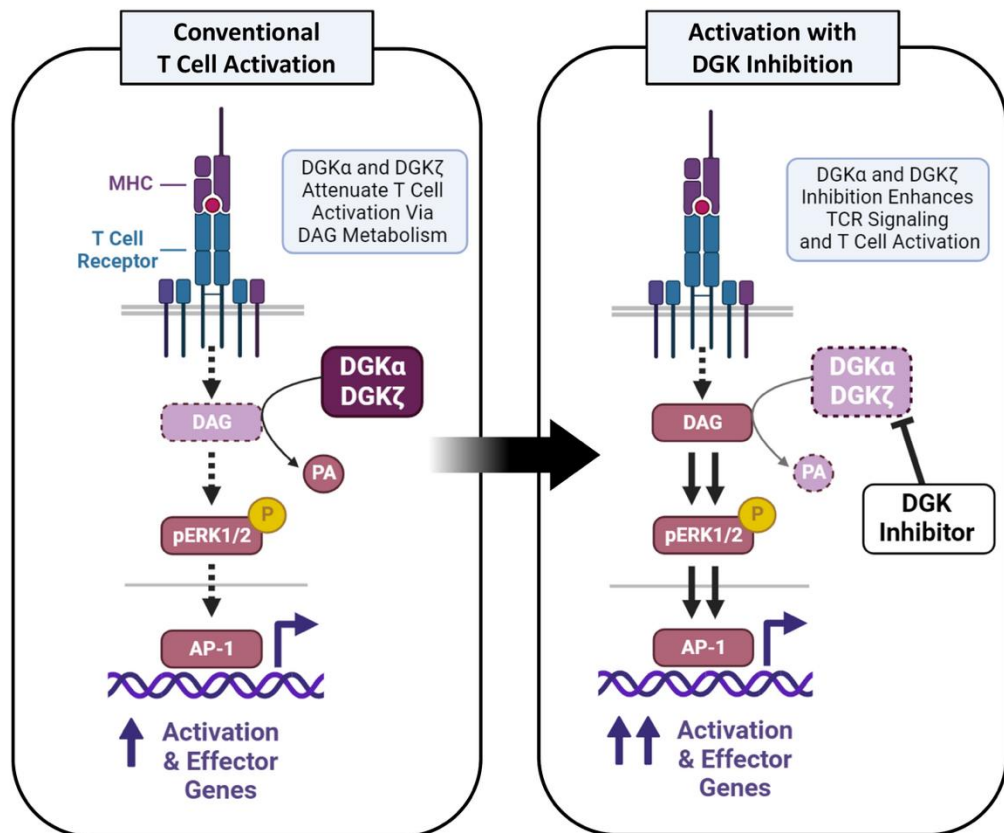
- Well-validated tumour target
- Found on many cancers including ovarian, gastric, colorectal, pancreatic cancers

Image: Ovarian cancer biopsy with TAG-72 staining (brown) by immunohistochemistry (Ponnusamy et al 2007)



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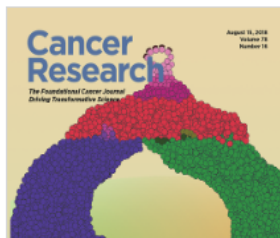
Genetic disruption of DGK signalling strengthens human T cell and CAR-T function



Frontiers in Cell and
Developmental Biology
Signaling

5.3 impact factor 9.9 citescore

Volume 78, Issue 16
15 August 2018



Front. Cell Dev. Biol., 17 October 2016
Sec. Signaling
Volume 4 - 2016 | <https://doi.org/10.3389/fcell.2016.00108>

Diacylglycerol Kinases (DGKs): Novel Targets for Improving T Cell Activity in Cancer

Matthew J. Riese ^{1,2*} Edmund K. Moon ³ Bryon D. Johnson ⁴
Steven M. Albelda ^{3*}

TUMOR BIOLOGY AND IMMUNOLOGY | AUGUST 14 2018

CRISPR/Cas9-Mediated Knockout of DGK Improves Antitumor Activities of Human T Cells **FREE**

In-Young Jung; Yoon-Young Kim; Ho-Sung Yu; Myoungsoo Lee; Seokjoong Kim; Jungmin Lee ✉

Check for updates

+ Author & Article Information

Cancer Res (2018) 78 (16): 4692–4703.

<https://doi.org/10.1158/0008-5472.CAN-18-0030> Article history

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Dual DGKαζ KO delivered durable tumor control in TAG-72 CAR-T cells

ORIGINAL ARTICLE · Volume 33, Issue 2, 200962, June 18, 2025 · Open Access [Download Full Issue](#)

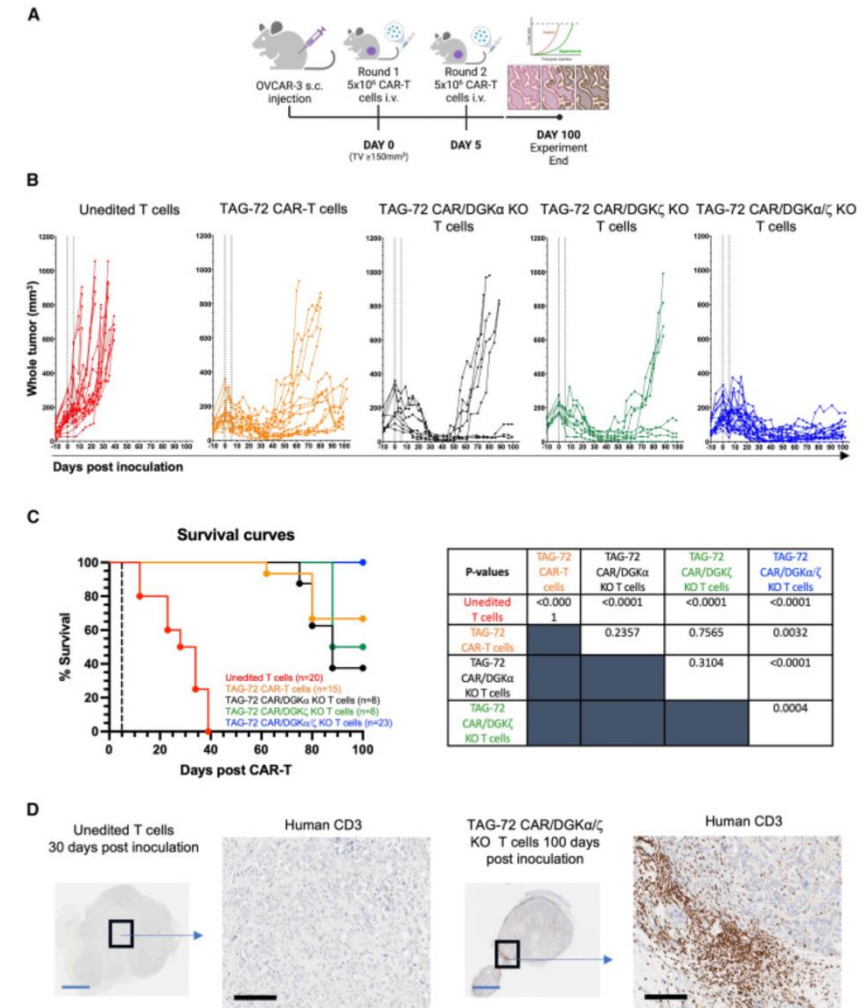
CRISPR-Cas9 knockout of DGKαζ improves the anti-tumor activities of TAG-72 CAR-T cells in ovarian cancer

Vera J. Evtimov^{1,2,5} · Nhu-Y N. Nguyen^{1,2,5} · Maree V. Hammett^{1,2,5} · ... · Alan O. Trounson^{1,2} · Richard L. Boyd^{1,2} · Runzhe Shu^{1,4} ... Show more



- TAG-72 CAR-T cells were evaluated against established OVCAR-3 tumours.
- Unedited TAG-72 CAR-T cells initially controlled tumour growth, but relapse occurred at approximately day 40.
- Dual DGKαζ KO CAR-T cells ablated established tumours for up to 100 days without compromising cell viability or phenotype.

Durable control to Day 100



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Combined evidence supports DGKαζ dual KO in NK cells



DGK-α: A Checkpoint in Cancer-Mediated Immuno-Inhibition and Target for Immunotherapy

Elfriede Noessner*

Immunoanalytics Core Facility and Research Group Tissue Control of Immunocytes, Helmholtz Zentrum München, München, Germany

Volume 21, Issue 22

15 November 2015



MOLECULAR PATHWAYS | NOVEMBER 12 2015

Molecular Pathways: Targeting Diacylglycerol Kinase Alpha in Cancer **FREE**

Benjamin Purow ✉



+ Author & Article Information

Clin Cancer Res (2015) 21 (22): 5008–5012.

<https://doi.org/10.1158/1078-0432.CCR-15-0413> **Article history** ⓘ



Tumor Immunology

NK-cell dysfunction in human renal carcinoma reveals diacylglycerol kinase as key regulator and target for therapeutic intervention

Petra U. Prinz, Anna N. Mendler, Dorothee Brech, Ilias Masouris, Ralph Oberneder, Elfriede Noessner ✉

First published: 11 March 2014 | <https://doi.org/10.1002/ijc.28837> | **VIEW METRICS**



Volume 135, Issue 8

15 October 2014

Pages 1832-1841



References

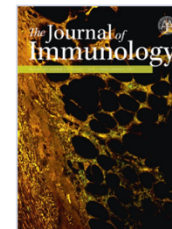


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Volume 197, Issue 3

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JOURNAL ARTICLE

Diacylglycerol Kinase ζ Is a Target To Enhance NK Cell Function **Get access** >

Enjun Yang, Brenal K Singh, Amanda M Schmidt Paustian, Taku Kambayashi ✉

The Journal of Immunology, Volume 197, Issue 3, August 2016, Pages 934–941,

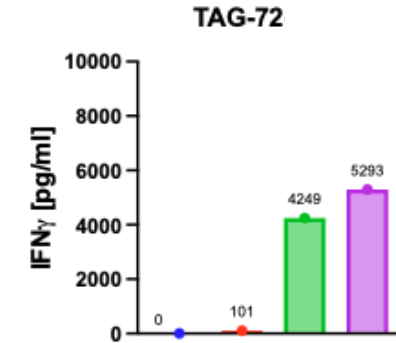
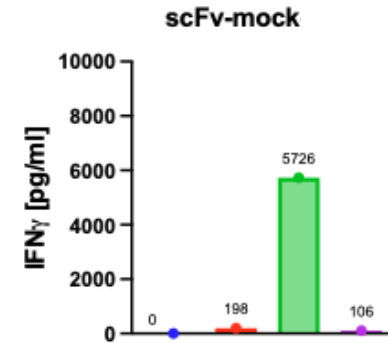
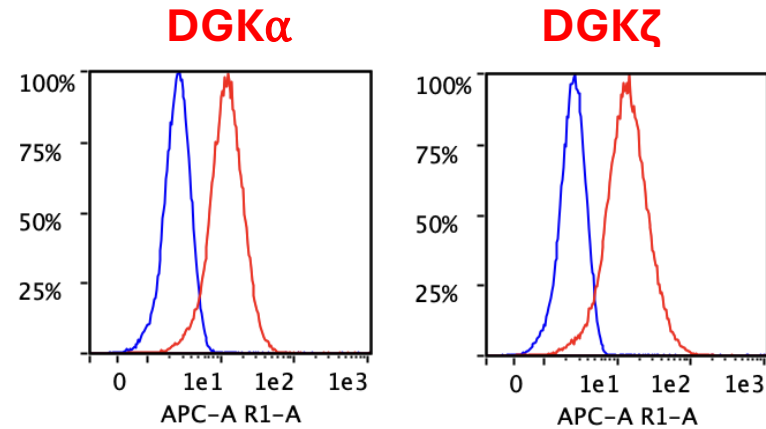
<https://doi.org/10.4049/jimmunol.1600581>

Published: 01 August 2016 **Article history** ▼

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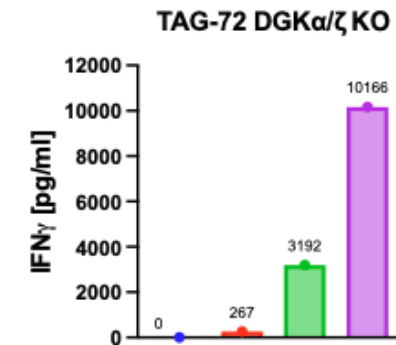
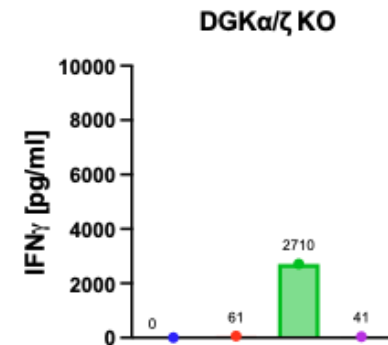
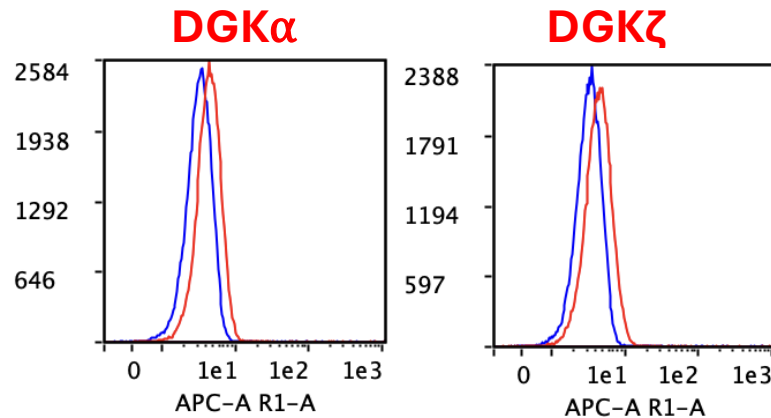
Can inhibition of DGK enhance NK function?

Mock CAR iNK



- Media alone
- Untreated
- PMA/Ionomycin
- TAG-72

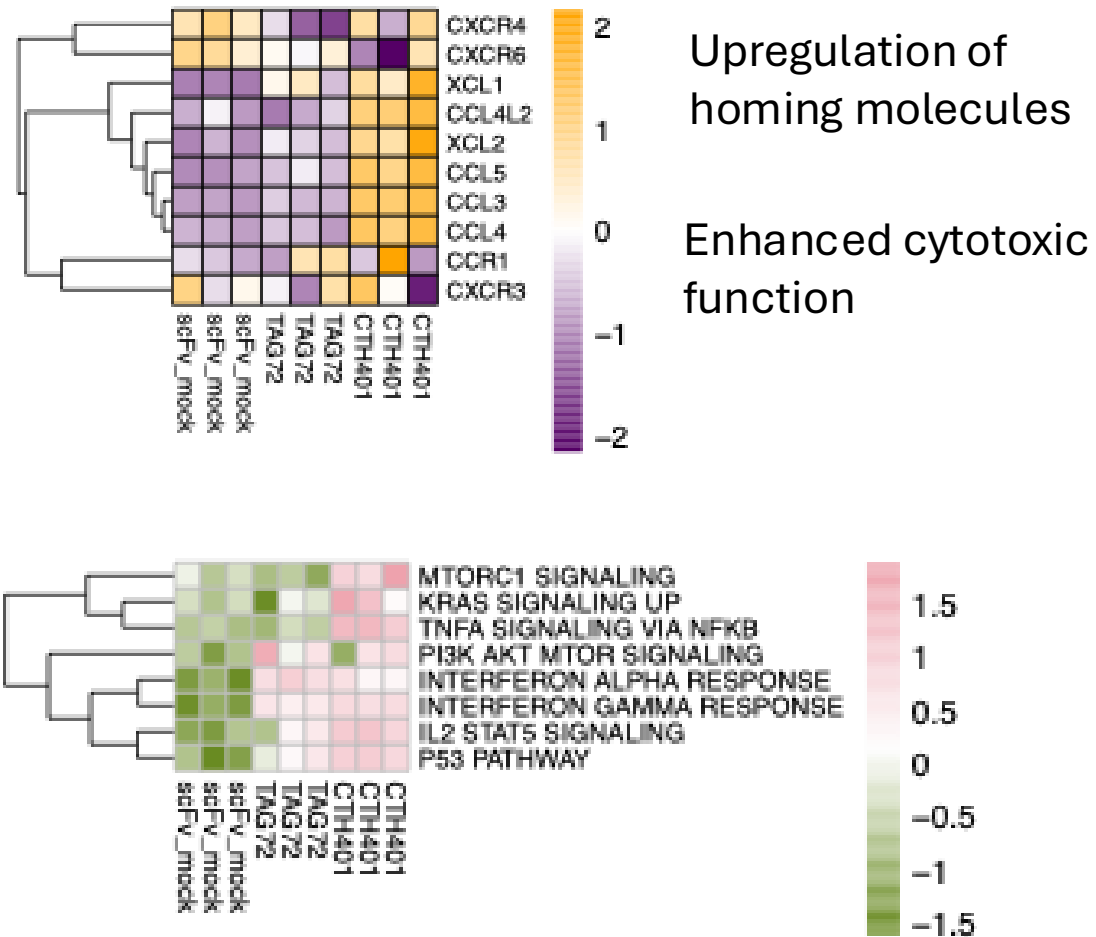
CTH-401



Aleta Pupovac

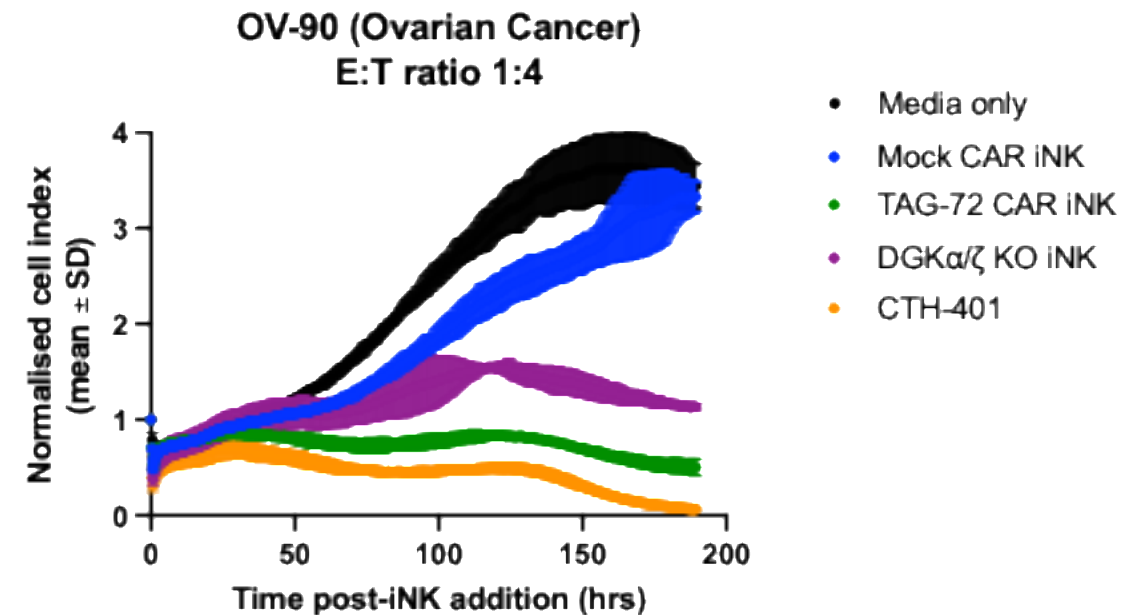
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RNA seq analysis



Keziah Ting

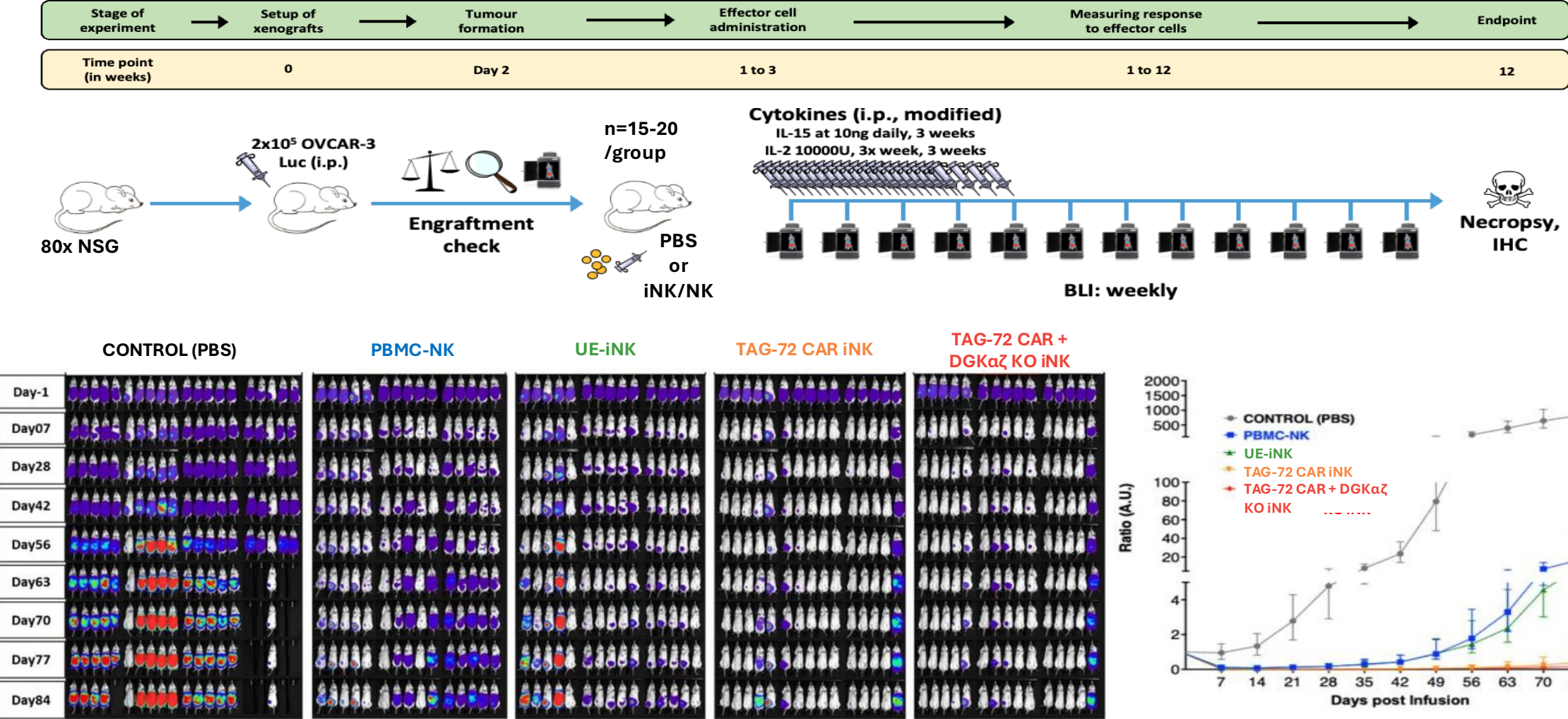
In vitro cytotoxicity



Brittany Doran & Laila Karra Khalil

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TAG-72 CAR + DGKαζ KO iNK show antitumour activity in an ovarian cancer mouse model



Nhu-Y Nguyen

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IND-enabling studies

- 4-week toxicity study ✓
- 9-month tumorigenicity safety study ✓

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Transitioning to clinical manufacture

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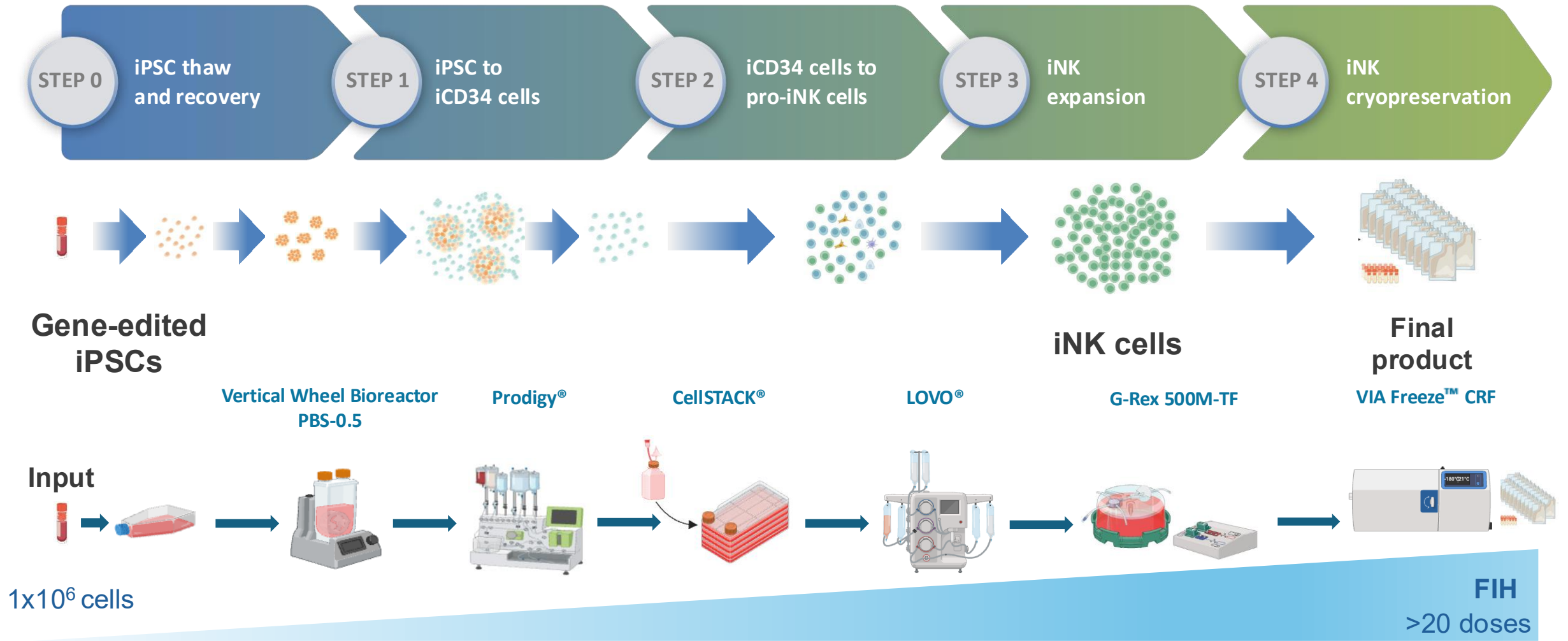
Manufacturing Facilities

- Commissioned Oct 2025
- Two 45m² (500f²) Grade B manufacturing spaces
- In-house QC and EM testing spaces
- Support for closed processing
- Completion of two clinical scale CTH-401 batches



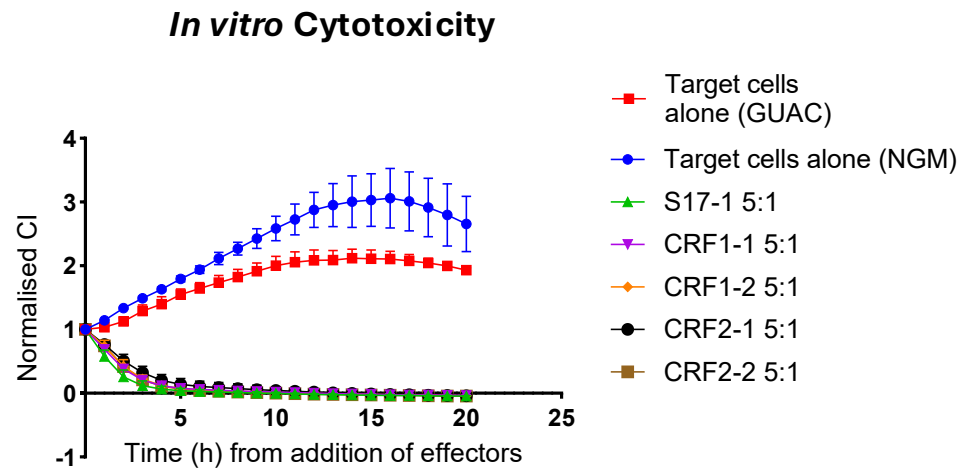
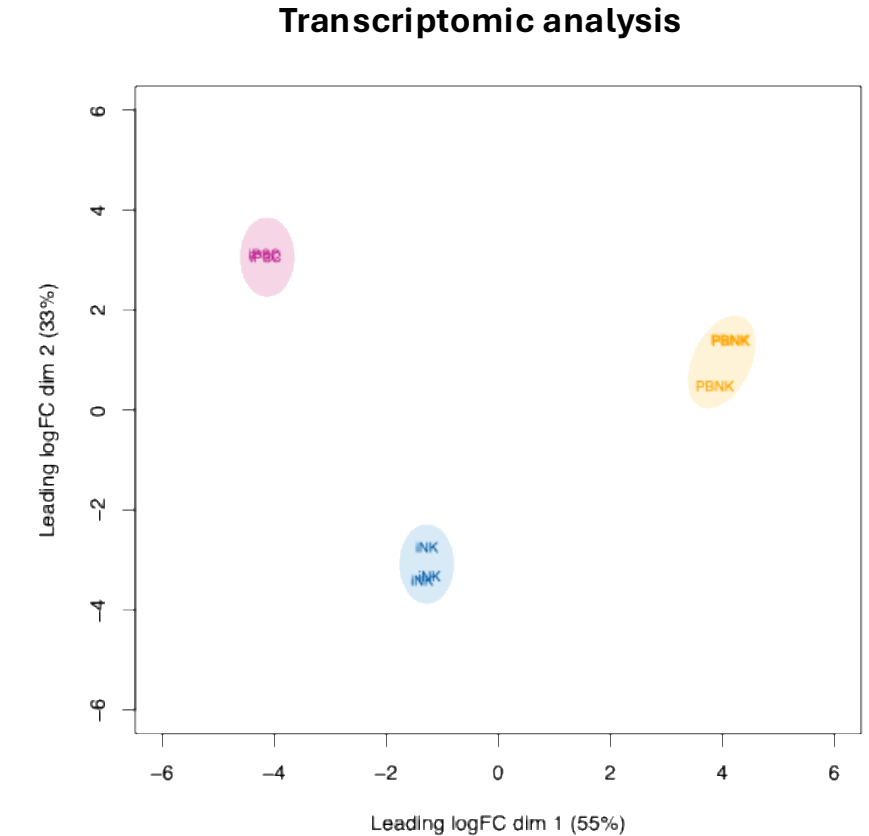
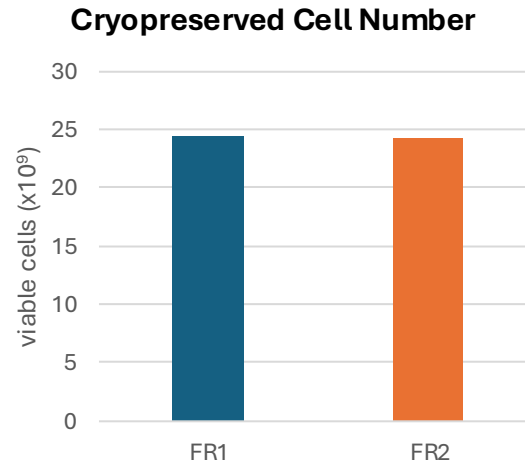
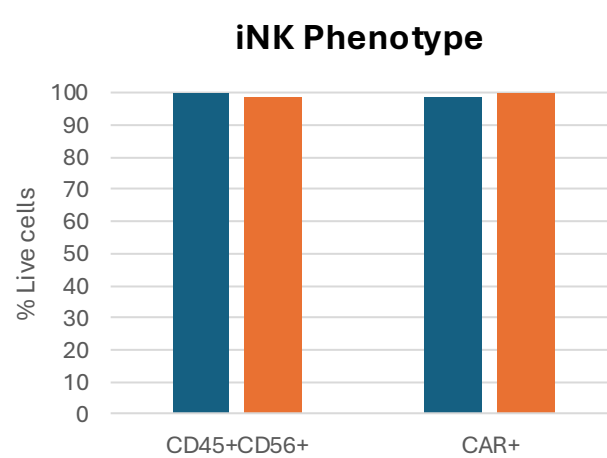
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Clinical scale manufacturing: One vial of iPSC into >20 billion iNK cells



Madeline Cao STRICTLY CONFIDENTIAL AND PROPRIETARY TO CARTHERICS PTY LTD.

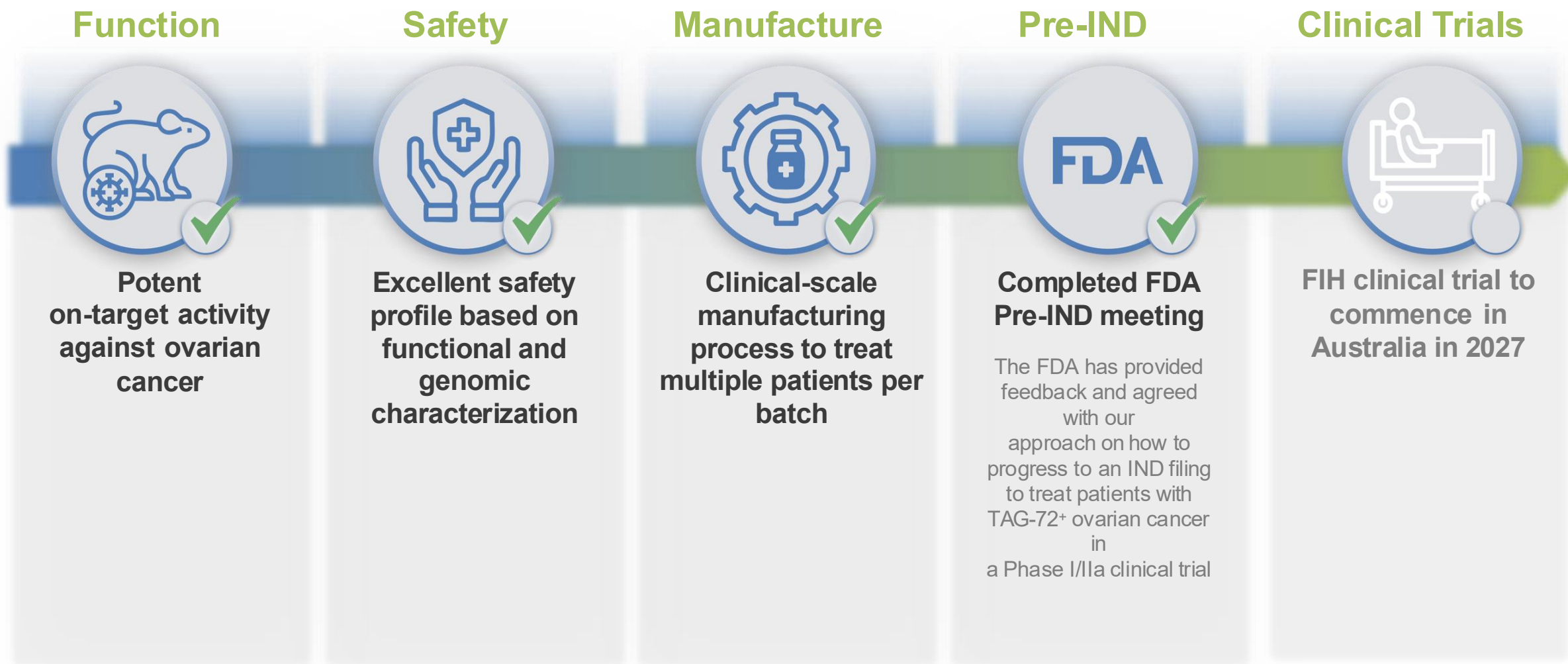
Reproducible production of clinical scale batches



Maree Hammett, Vera Evtimov & Keziah Ting

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Summary: CTH-401- Clear, De-Risked Path to First-in-Human Trials



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