Beyond Sendai Virus: A New High-Efficiency Approach to PBMC iPSC Reprogramming



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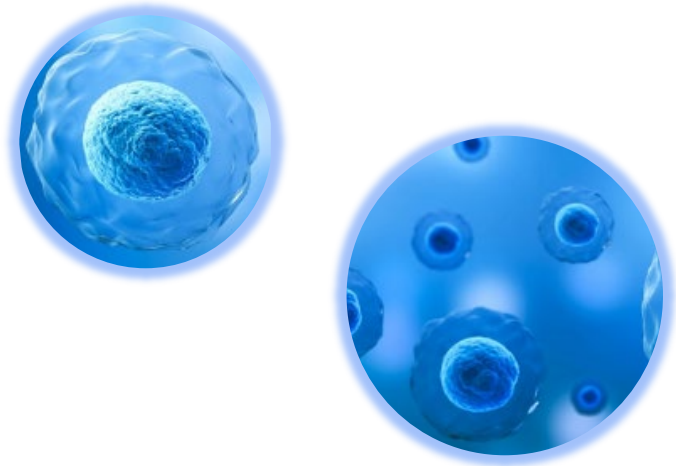


Moderator
Jeff Hung, Ph.D.
VP of Commercial Strategy
uBriGene

Logistics

- You will be put on mute during the webinar
- We welcome you to ask questions using the “Q&A” on the top right corner of the platform
- Your questions will be addressed after the presentation

Agenda



01 uBriGene’s Overview

02 uBriGene’s Reprogramming Cocktail

03 Emory University iPSC Core’s Insights

04 Fireside Chat: The Future of iPSCs

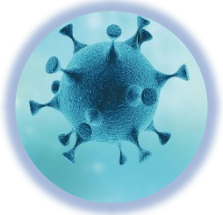
05 Q&A

uBriGene – Cell and Gene Therapy CDMO

Plasmids



Viral Vectors

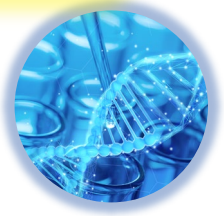


AAV, LVV, Retrovirus,
Oncolytic virus

Non-Viral Platform (RNA-LNP)



mRNA, saRNA,
circRNA



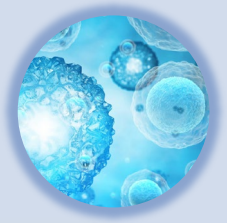
Encapsulation
into LNP

Quality Control



***EX VIVO* CGT**

Cell Therapies



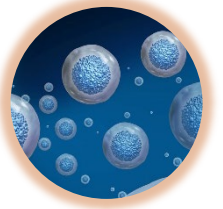
CAR-T/-NK, TIL,
iPSC, MSC

allogeneic

Cell isolation, reinfusion

autologous

Donor



Patient

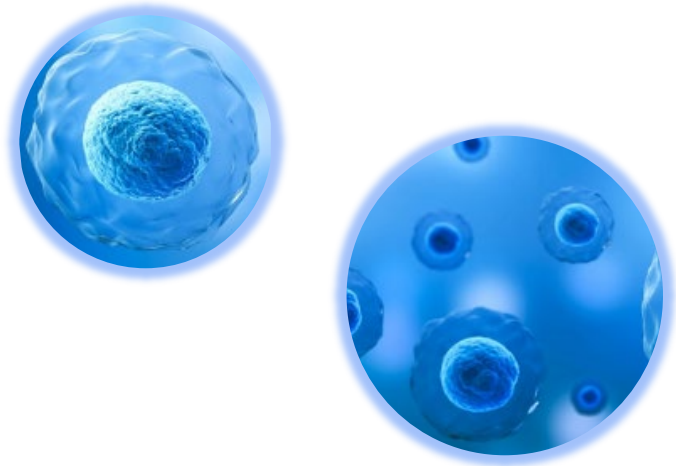


***IN VIVO* CGT**

Direct injection



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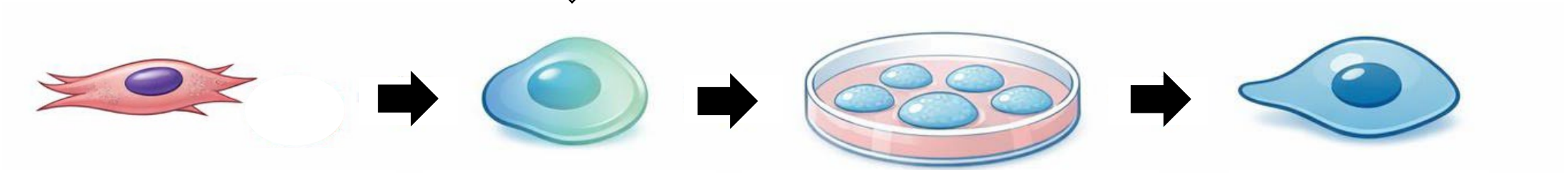
iPSC Workflow Bottlenecks

Bottleneck

1 Lack of non-viral reprogramming tool for PBMC

- Sendai virus
- mRNA, miRNA
- RNA-LNP

4 No clear path to clinic



Somatic Cell Collection | **Reprogramming** | **iPSC Colony Expansion** | **Differentiation**

Day -6 to -1 | Day 0-7 | Day 10-21 | Week 4+

Virus clearing step 3

2 Low reprogramming efficiency

Illustration generated with the assistance of Microsoft Copilot

uBriGene's circRNA-LNP Reprogramming Cocktail

1. Reprogramming cocktail compatible with both fibroblasts and PBMCs
2. High reprogramming efficiency (4-10% on fibroblasts, 0.3% on PBMCs)
3. RNA-based technology, no clearance step needed
4. GMP-grade kit will be released Q3 2026

Best-in-Class PBMC Reprogramming Innovations

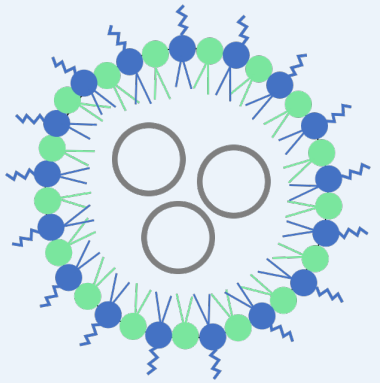
Circular RNAs coding for reprogramming factors for long-lasting expression.

Manufacturing process for circRNAs

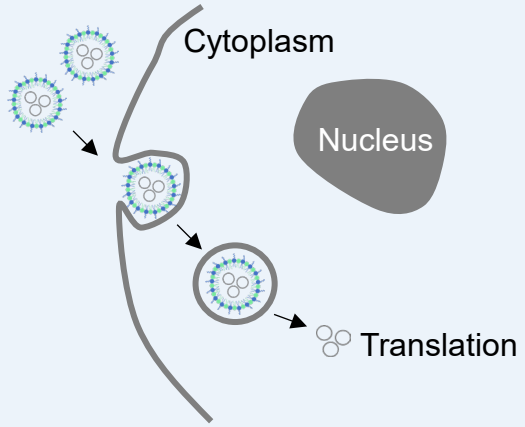
circRNA encapsulated into **LNP**
- Exclusive licensee of lipid
- Proprietary formulation

NO transfection or electroporation needed.

Serum-free Enhancer B to improve the delivery to LNP to the cells.



circRNA-LNP



Endocytosis

Most User-Friendly iPSC Reprogramming Workflow

- Convenient, **ready-to-use LNP formulation** – can be added directly to cells, with no need for transfection reagents or viral vectors
- **System flexibility**: suitable for feeder or feeder-free conditions
- **High iPSC reprogramming efficiencies**

Pipet circRNA-LNP reprogramming cocktail and Enhancer B directly into the cell culture

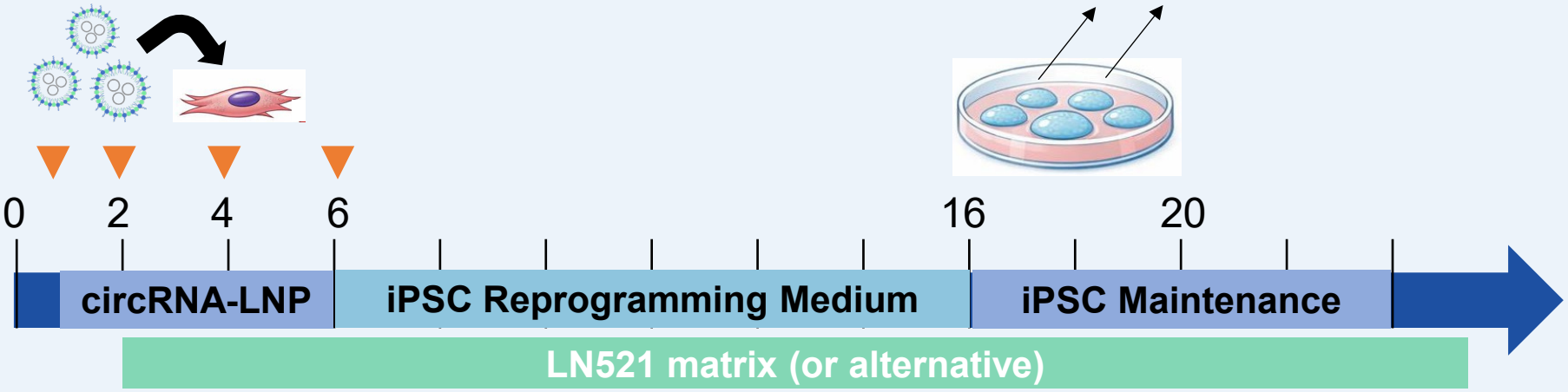
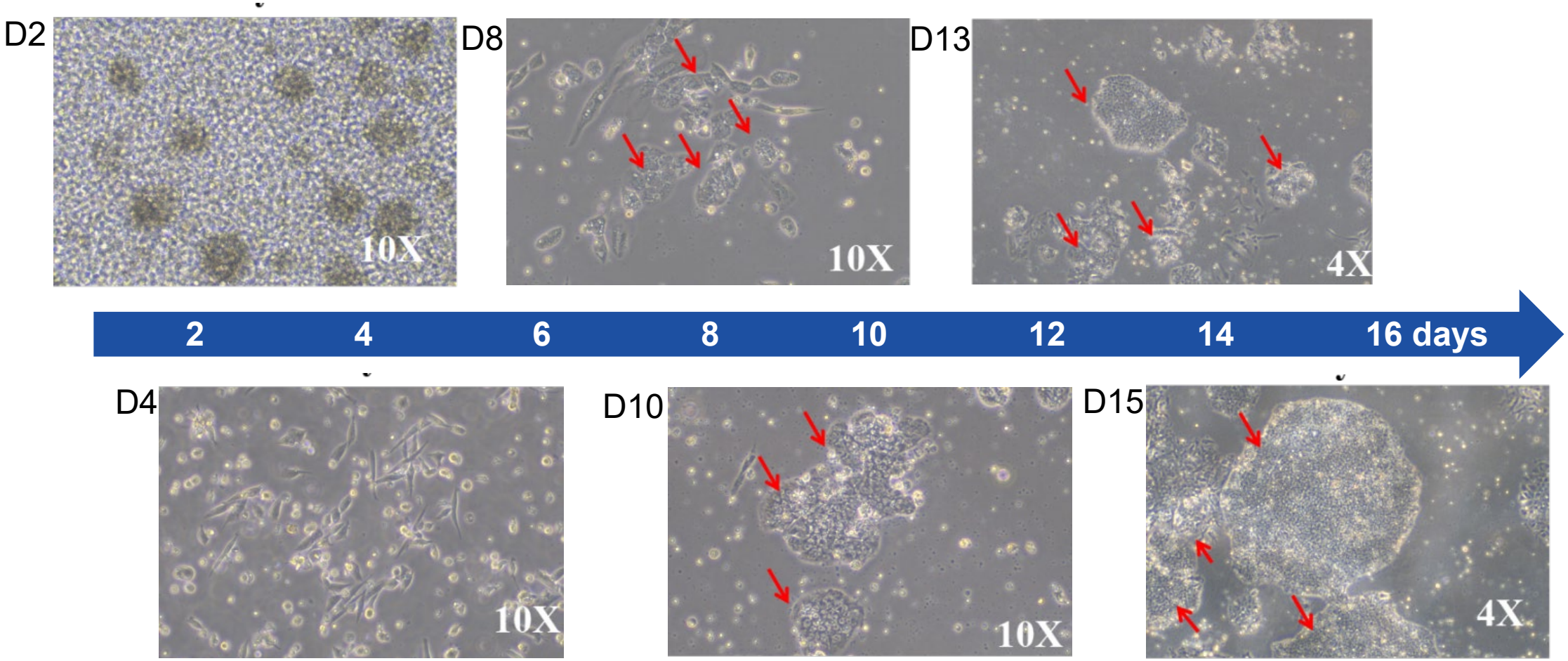
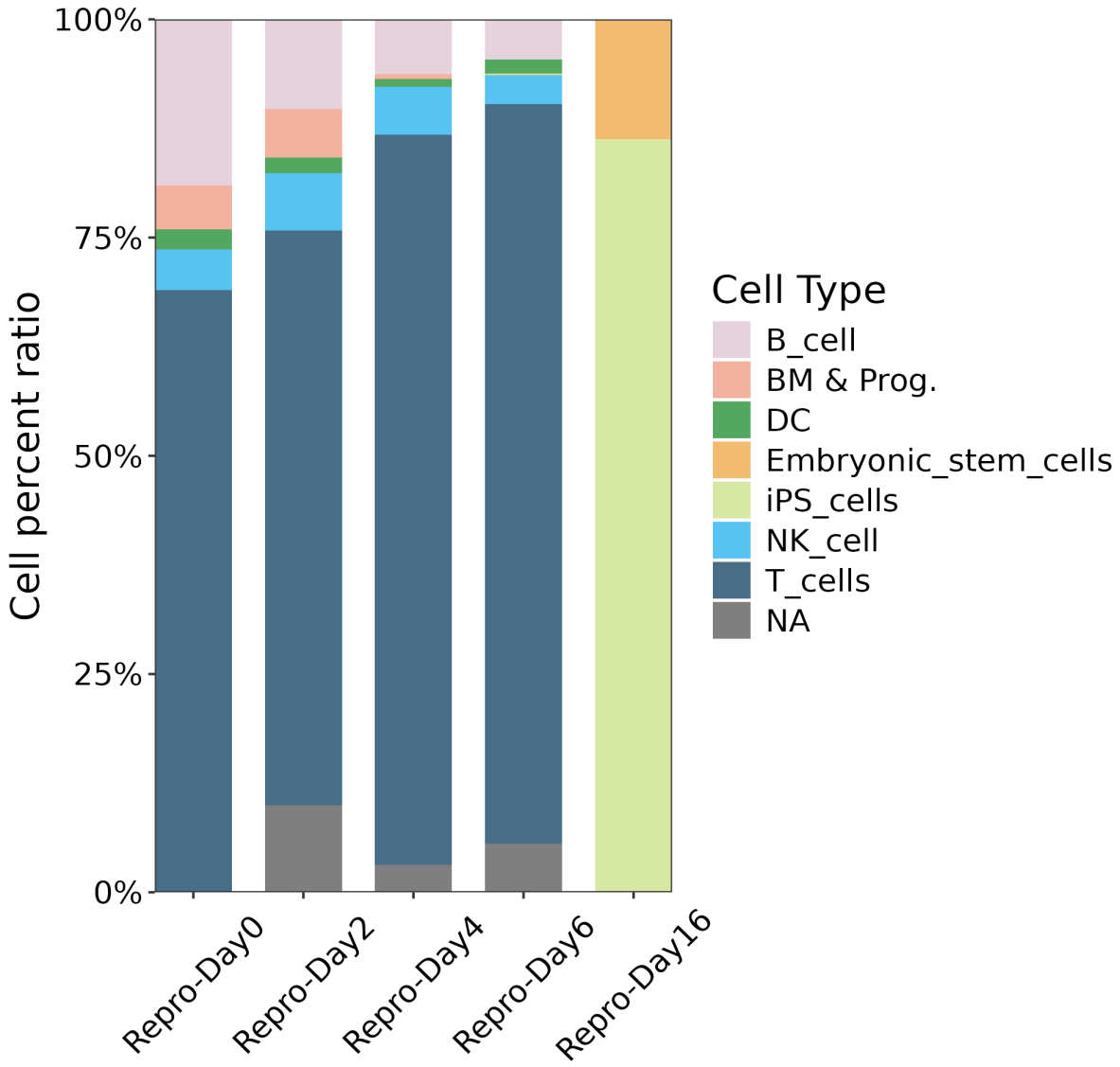


Illustration generated with the assistance of Microsoft Copilot

Colony Formation After Reprogramming PBMCs



Single-cell RNA-Seq Reveals Shifts in Cell Identity During Reprogramming



Day 0 to 6

- T cells, NK cells, Dendritic cells, and B cells are the major cell populations in the PBMC sample prior to reprogramming

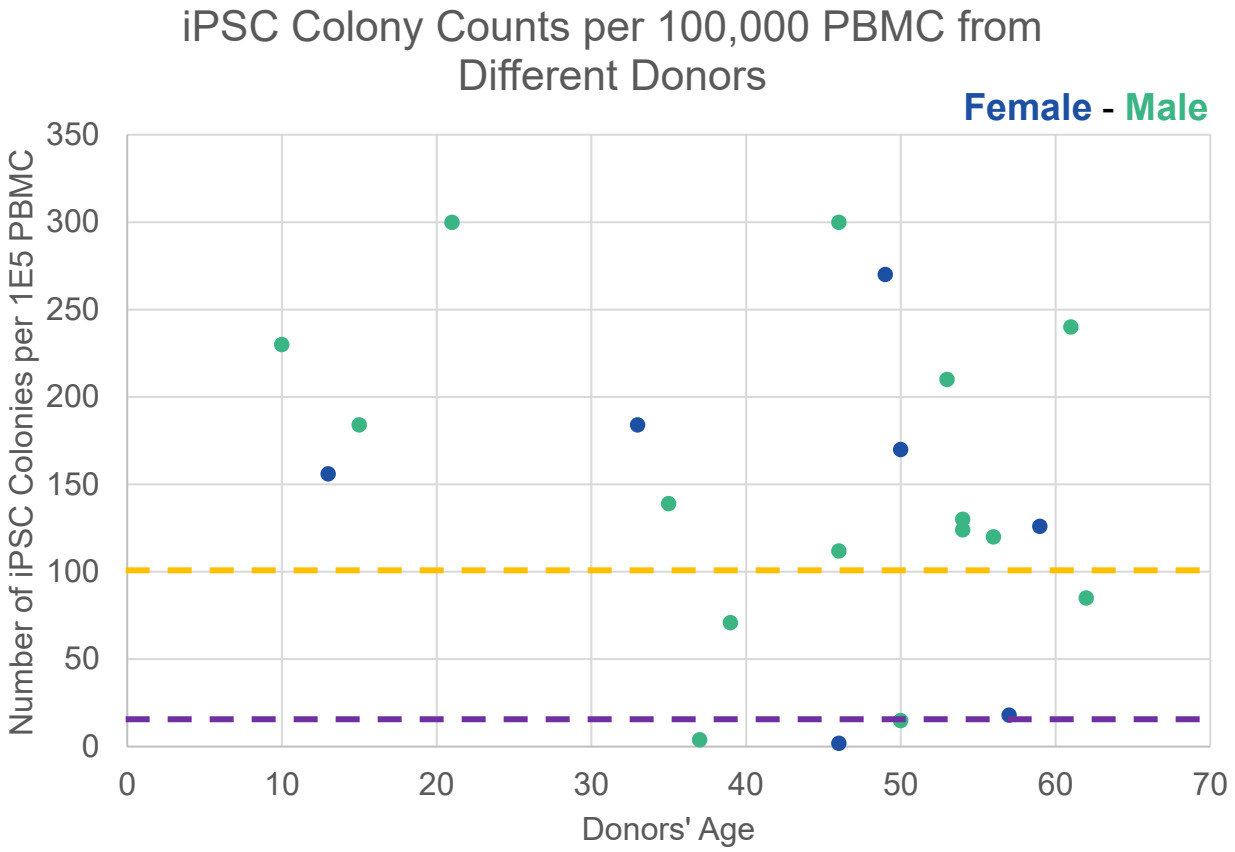
Day 16

- Stem cell signature.

High Reprogramming Efficiency on Samples from Various Donors

Reprogramming kit compatible with:

- PBMC
  (up to 0.3% reprogramming efficiency)
- Fibroblasts
  (up to 10% reprogramming efficiency)
- Cells from aged donors
- Patient-derived cells



Reprogramming efficiencies	0.002% to 0.3%
Number of colonies	2 to 300
Number of samples with >100 colonies	73%
Number of samples with >10 colonies	91%

RNA-LNP *versus* Sendai Virus-Based Reprogramming

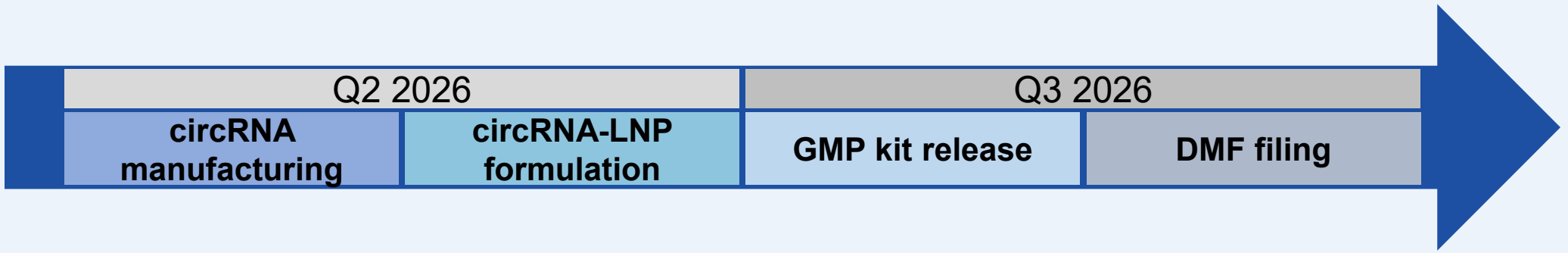
	uBriGene's RNA-LNP	Sendai virus
Reprogramming efficiency on PBMCs	High	High
Typical iPSC emergence time (days)	7-14	7-21
Integration risk	None	None
Residual cleanup	No	Yes
Background	Clean (no spontaneous differentiation)	Some differentiated cells

Stay tuned to hear from Adriana who performed a head-to-head comparison of the two methods!

Clear Path to Clinic when Using uBriGene's Reprogramming Kit

GMP-grade reprogramming kit will be released in Q3 2026

- Fully traceable materials and manufacturing
- Drug Master File (DMF with FDA)
- Residual QC assay available (qPCR)



uBriGene's Ready-to-Use iPSC Banks

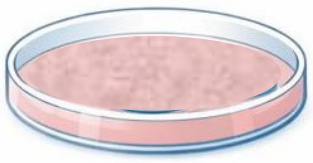
FDA compliant donor sourcing of fibroblasts

Clonal and single cell-derived banks

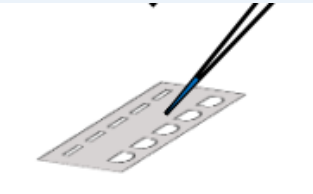
Date Collected: 03/07/2024

Donor Screening Panel 132

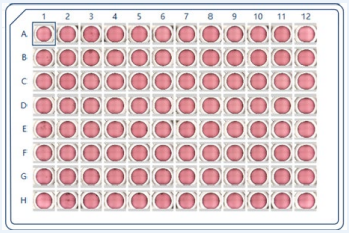
Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
Hepatitis B Surface Antigen [01]	Negative Test performed with Abbott Alinity s HBsAg kit.			Negative
Hepatitis B Core Total Ab [01]	Negative Test performed with Abbott Alinity s HBcore kit.			Negative
Hepatitis C Virus Antibody [01]	Negative Test performed with Abbott Alinity s HCV kit.			Negative
DONOR Syphilis (T pallidum) [01]	Non Reactive Test performed with Beckman Coulter PK TP kit.			Non Reactive
Cytomegalovirus CMV Total Ab [01]	**Reactive** **Abnormal** Test performed with Immucor Capture-CMV IgG and IgM kit.			Non Reactive
HIV-1/HIV-2 Ab, HIV-1 p24 Ag [01]	Negative Test performed with Abbott Alinity s HIV Ag/Ab kit. The HIV Ag/Ab Combo Kit can detect: HIV-1 (groups M and O)/HIV-2 Ab, HIV-1 p24 Ag			Negative
DONOR HIV/HCV/HBV NAT Test [01]	Non-Reactive for HIV RNA Non-Reactive for HCV RNA Non-Reactive for HBV DNA Test performed with Procleix Ultrio Elite Assay Kit.			Non Reactive
HTLV-I/II Antibodies, Qual [01]	Negative Test performed with Abbott Alinity s HTLV I/II kit.			Negative
DONOR WNV NAT Assay [01]	Non Reactive Test performed with Procleix West Nile Virus Assay Kit.			Non Reactive



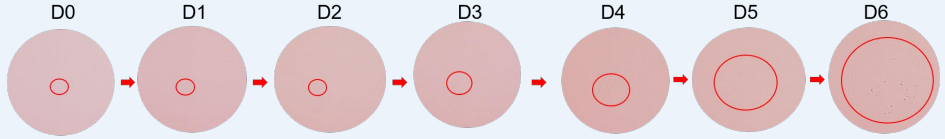
Expansion



Cell count



Transfer to 96-well plate
(0.5cell/well)

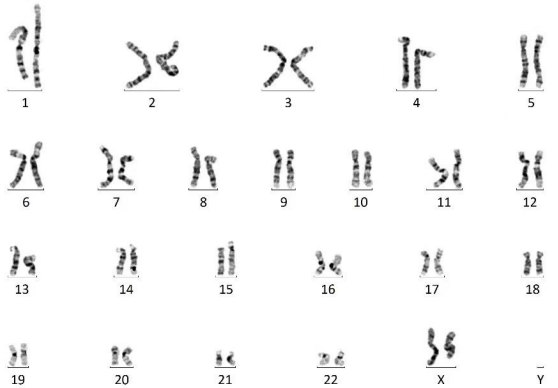


Live imaging from Day 0 to Day N provides a complete traceable monoclonal evidence chain.

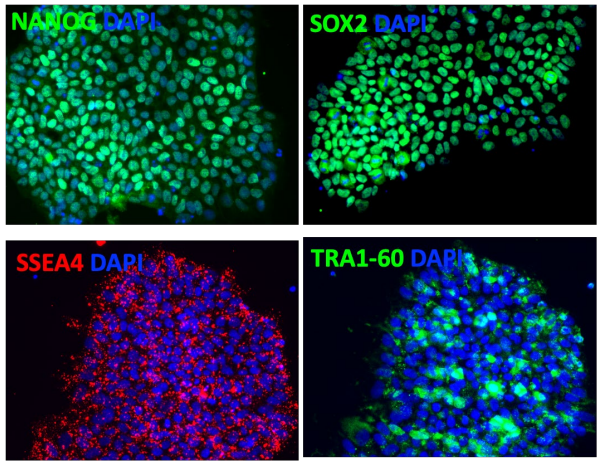
Research or GMP grade iPSC banks from same clone or cell available

Fully Characterized iPSC Banks

Attribute		Testing Method
Appearance		Visual observation
Identity	Cell morphology	microscopic observation
	Karyotype Analysis	G-banding
	STR	STR
Stemness Cell Markers	Intracellular: SOX-2, NANOG, OCT4 Extracellular: SSEA4, TRA1-60-R, TRA1-81	Flow Cytometry
Cell viability		Trypan Blue/AOPI
Differentiation potential *in vitro*	Trilineage Differentiation	Immunofluorescence staining
Differentiation potential *in vivo*	Teratoma formation	Animal inoculation method
Safety	Sterility	Culture Method
	Mycoplasma Testing	Culture Method
	Mycobacterium Testing	Culture Method
	Endotoxin	LAL Method
Safety (viral)	Cell morphology observation and hemadsorption test	Pharmacopoeia method
	In vitro inoculation and culture method with different cell types	
	TEM	
	Porcine virus & PCV	
	Retrovirus examination	
	Inoculation method in animals and chicken embryos	
	Bovine-derived virus detection	
	Human-derived virus detection	



Karyotyping by G-banding to demonstrate genome integrity



Detection of pluripotency markers by immunostaining

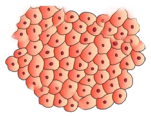
iPSC Differentiation



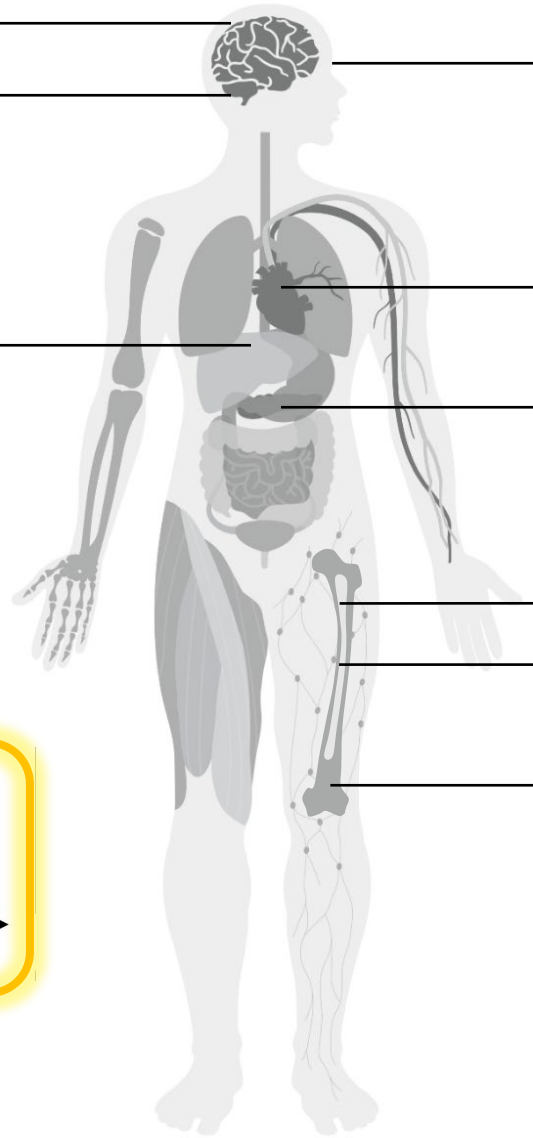
Neuronal cells

Glial cells





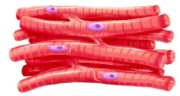
Liver organoids



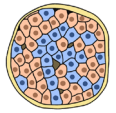
Retinal Pigmented Epithelium (RPE)



Cardiomyocytes



Islets



Stay tuned to hear from Adriana and Ilanit!

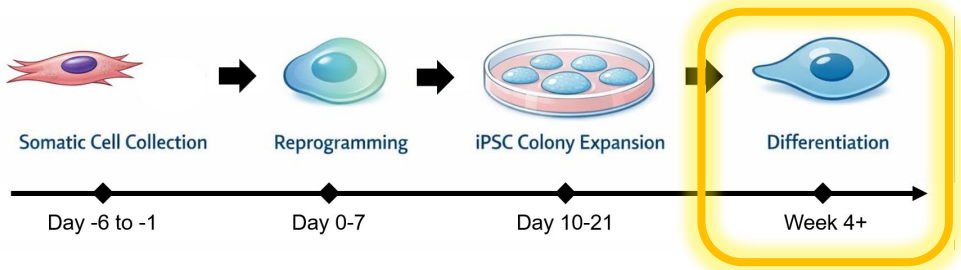
iHSC



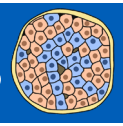
iMSC



Chondrocytes

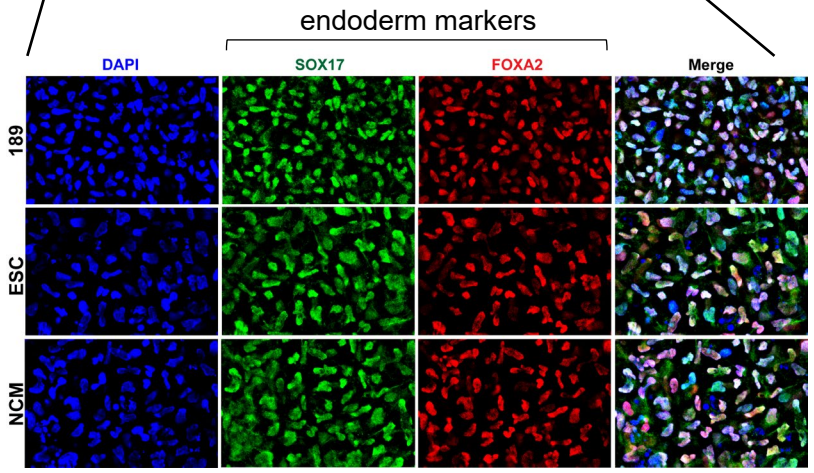


iPSC Differentiation into Islets

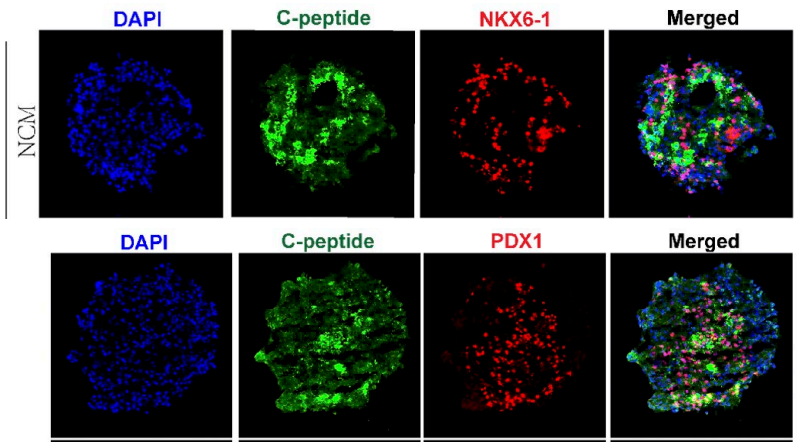


brigene

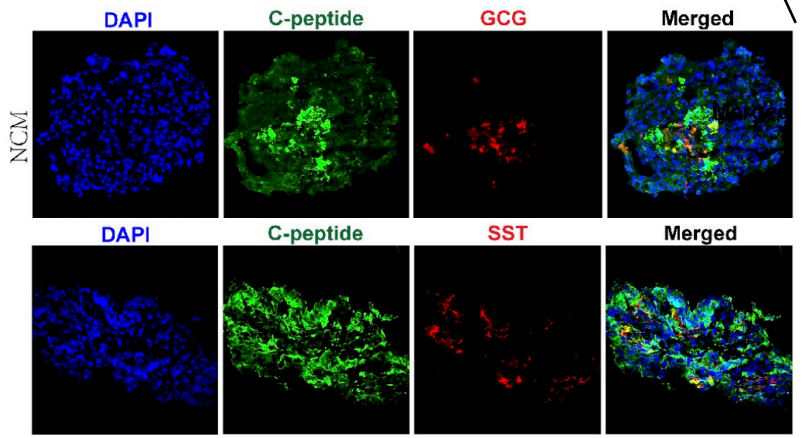
Definitive endoderm	Primitive gut tube	Posterior foregut	Pancreatic progenitors	Pancreatic endocrine progenitors	hCiPSC-islets
Stage 1	Stage 2	Stage 3	Stage 4	Stage 5	Stage 6
D 0-D 4	D 5-D 6	D 7-D 10	D 11-D16	D 17-D 22	D 23-D 24/26



Endocrine stem / Progenitor cells



Beta cells

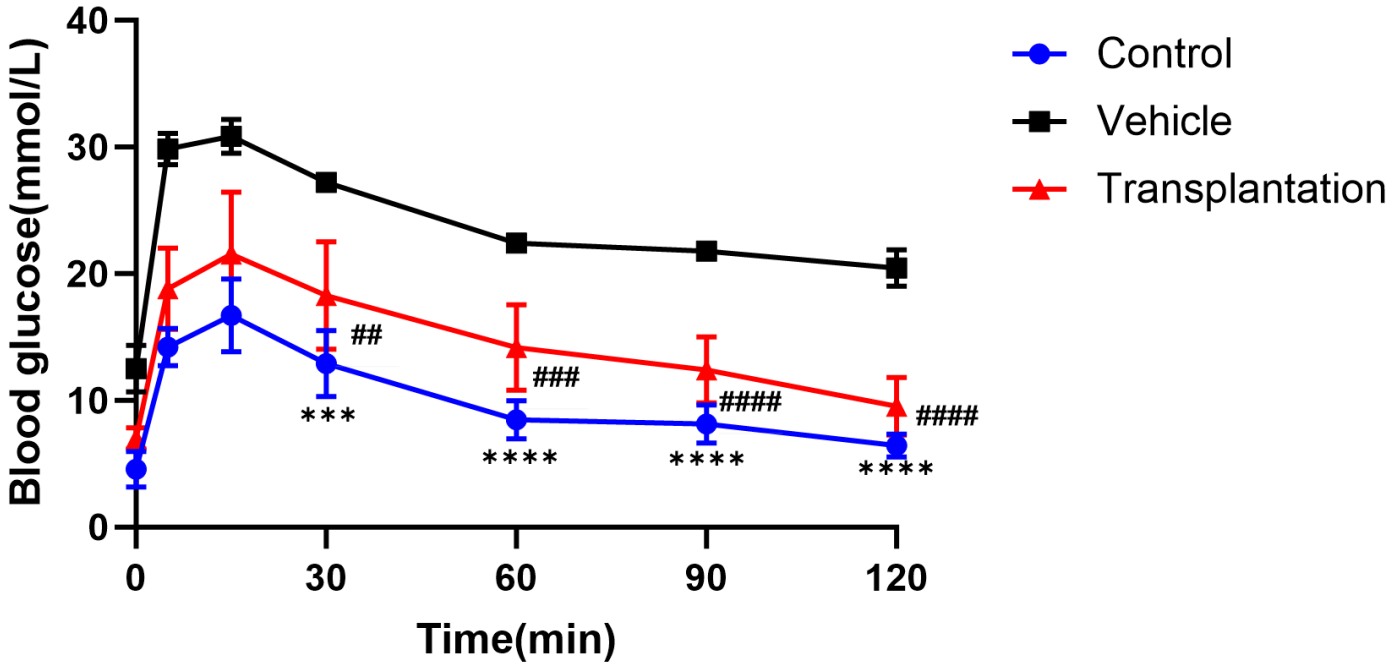


Alpha cells

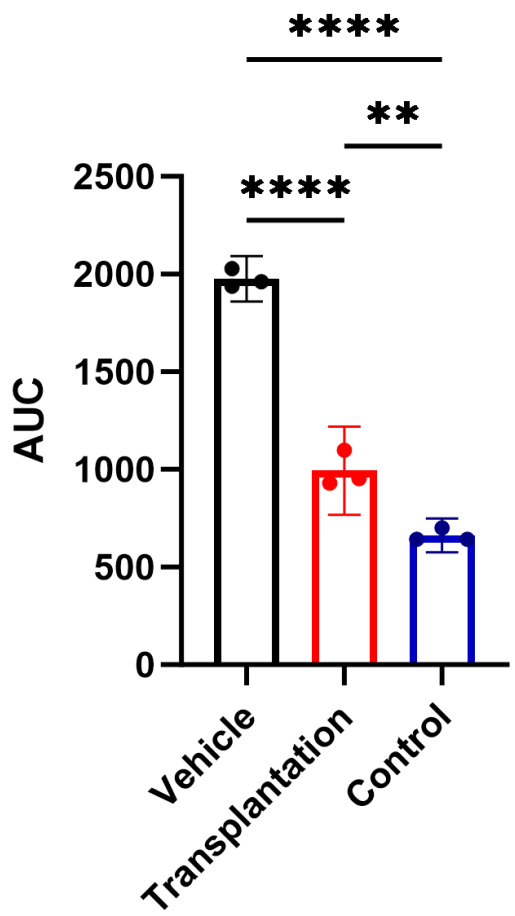
Delta cells

iPSC Differentiation into Islets – Functional Testing *in vivo*

Glucose Tolerance Test (GTT)



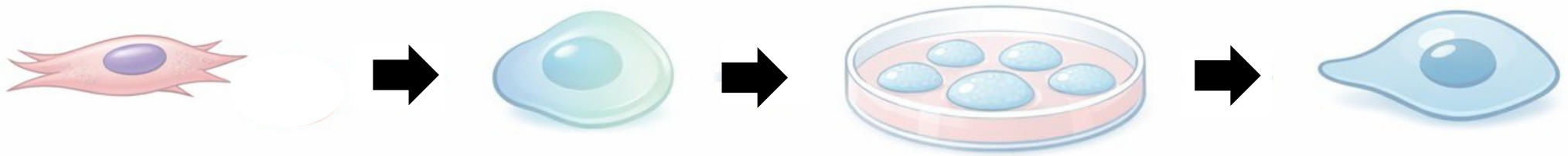
Area Under the Curve at 120min



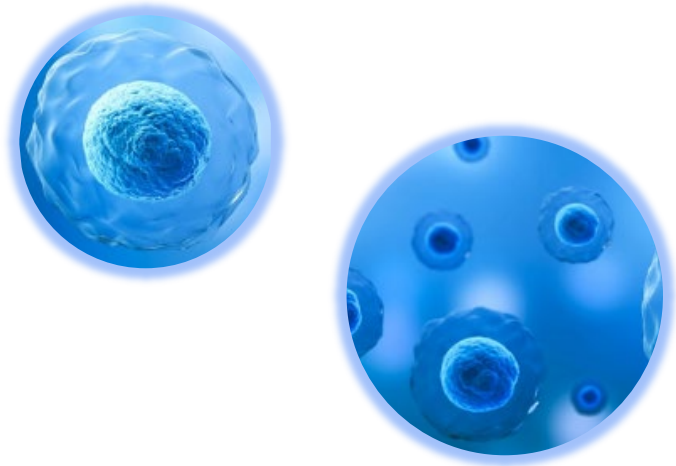
- Mouse model for T1D (ablation of β cells) transplanted with either PBS (vehicle) or iPSC-derived islets
- Mice receiving iPSC-derived islets showed a reduction in glycemia, suggesting that the islets (specifically β cells) are capable of sensing glucose and secreting insulin.

uBriGene's iPSC Reprogramming Solution

Client's Challenges		uBriGene's iPSC Reprogramming Solution
Lack of non-viral reprogramming tool for PBMC	1	**uBriGene's circRNA-LNP reprogramming kit** is **compatible with both fibroblasts** and **PBMC**
Low reprogramming efficiency	2	**High reprogramming efficiencies** on fibroblasts and PBMCs
Virus clearing step	3	**RNA-based technology eliminates the need for clearance step** to save time and reagent cost
No clear path to clinic	4	uBriGene's circRNA-LNP reprogramming kit's **GMP version** will be released in Q3 2026 with a **DMF**



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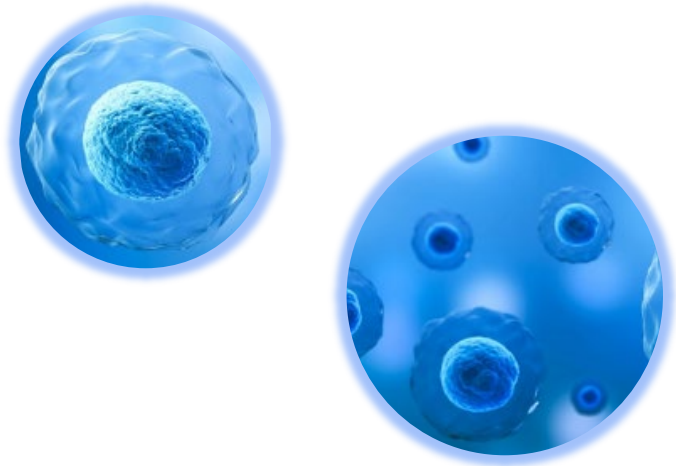
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Cardiovascular Disease Modeling PI
Ilanit Itzhaki, Ph.D.
Assistant Professor
Emory University



Moderator
Jeff Hung, Ph.D.
VP of Commercial Strategy
uBriGene

Logistics

- You will be put on mute during the webinar
- We welcome you to ask questions using the “Q&A” on the top right corner of the platform
- Your questions will be addressed after the presentation



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