



# High Efficiency iPSC Reprogramming for Regenerative Medicine: RNA-LNP Complete Kits



**Presenter:**

Scott Pattison, Ph.D.  
Sr. Director of BD



**Moderator:**

Mingjuan Liu, Ph.D.  
Director of Marketing

## 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

Introductions

02

uBriGene's iPSC Portfolio Updates

03

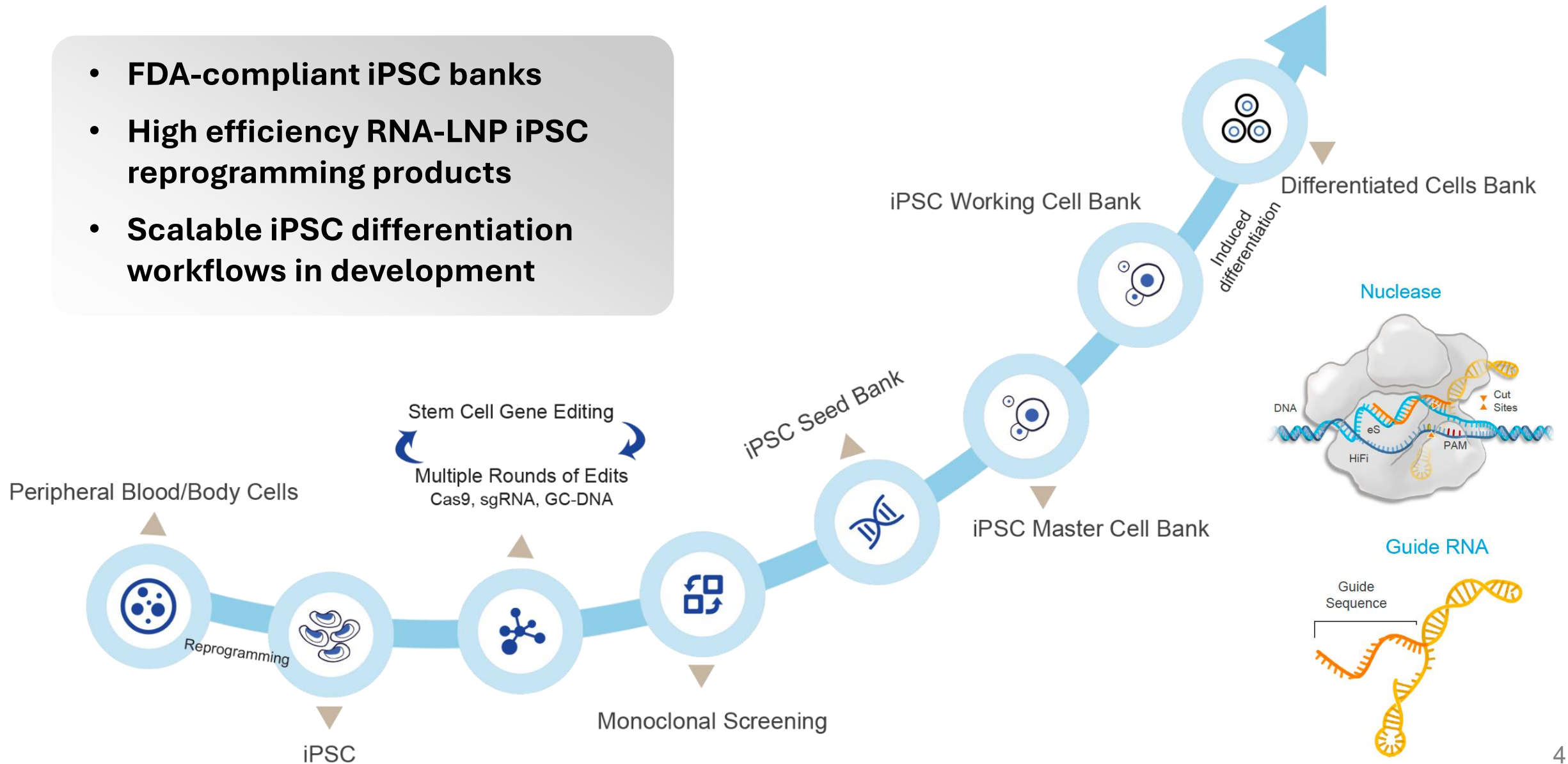
Q & A



**uBriGene iPSC  
Solutions**

# iPSC-Derived Cell Therapy Workflows

- **FDA-compliant iPSC banks**
- **High efficiency RNA-LNP iPSC reprogramming products**
- **Scalable iPSC differentiation workflows in development**



# Clinical Translation of iPSCs: Current Challenges

Bottleneck	Common, but Inadequate Approaches		uBriGene Biosciences' Solution
Donor cell access hurdles	Complex donor cell access & screening logistics		FDA-compliant sourcing & screening infrastructure & <b>off-the shelf GMP iPSC lines</b>
Safety – Genomic Instability	Viral & transfection approaches		RNA-LNP integration-free reprogramming cocktail
Reprogramming inefficiencies	Methods requiring extensive downstream clone screening & characterization		Optimized high efficiency products & protocols <b>including improved v2 kit</b>
iPSC-derived cell type development	Requires deep technical expertise & extended timelines which are challenging to scale		<b>uBriGene is developing differentiation workflows for clinically relevant cell types</b>



Bottleneck

CMC dependencies on multiple products & services partners



uBriGene End-to-End Solution

Reliable One-Stop Shop for scalable RUO & GMP iPSC workflows

## FDA-Compliant Donor Sourcing

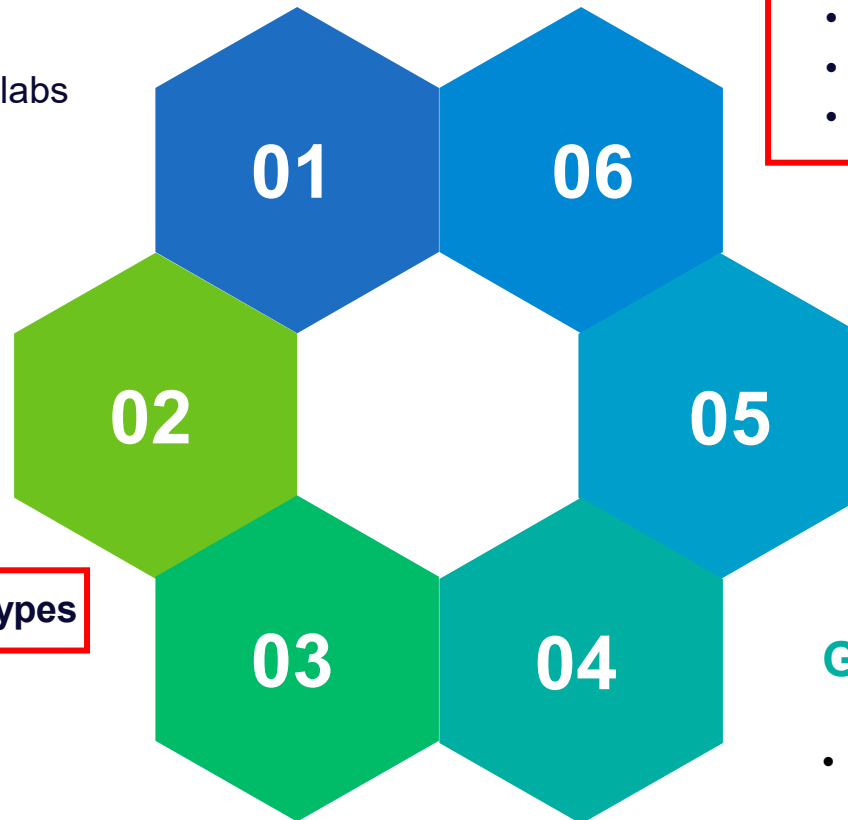
- Medical Centers
- CMS-certified CLIA testing labs
- Courier logistics

## iPSC RNA-LNP Reprogramming Cocktail

- Ready-to-use RNA-LNP product
- No need for viral transduction or transfection
- Non-integrating/footprint-free
- **v2 Kit for tough-to-reprogram cell types**

## iPSC Banking

- Class A production environment - fully isolated production process with zero cross contamination.
- Extensive experience in cell therapy production
- **Catalog GMP iPSC lines**



## Differentiated Cell Types

- **Neuronal cell types**
- Immune cell types
- Muscle cell types

## IVT-gRNA Process

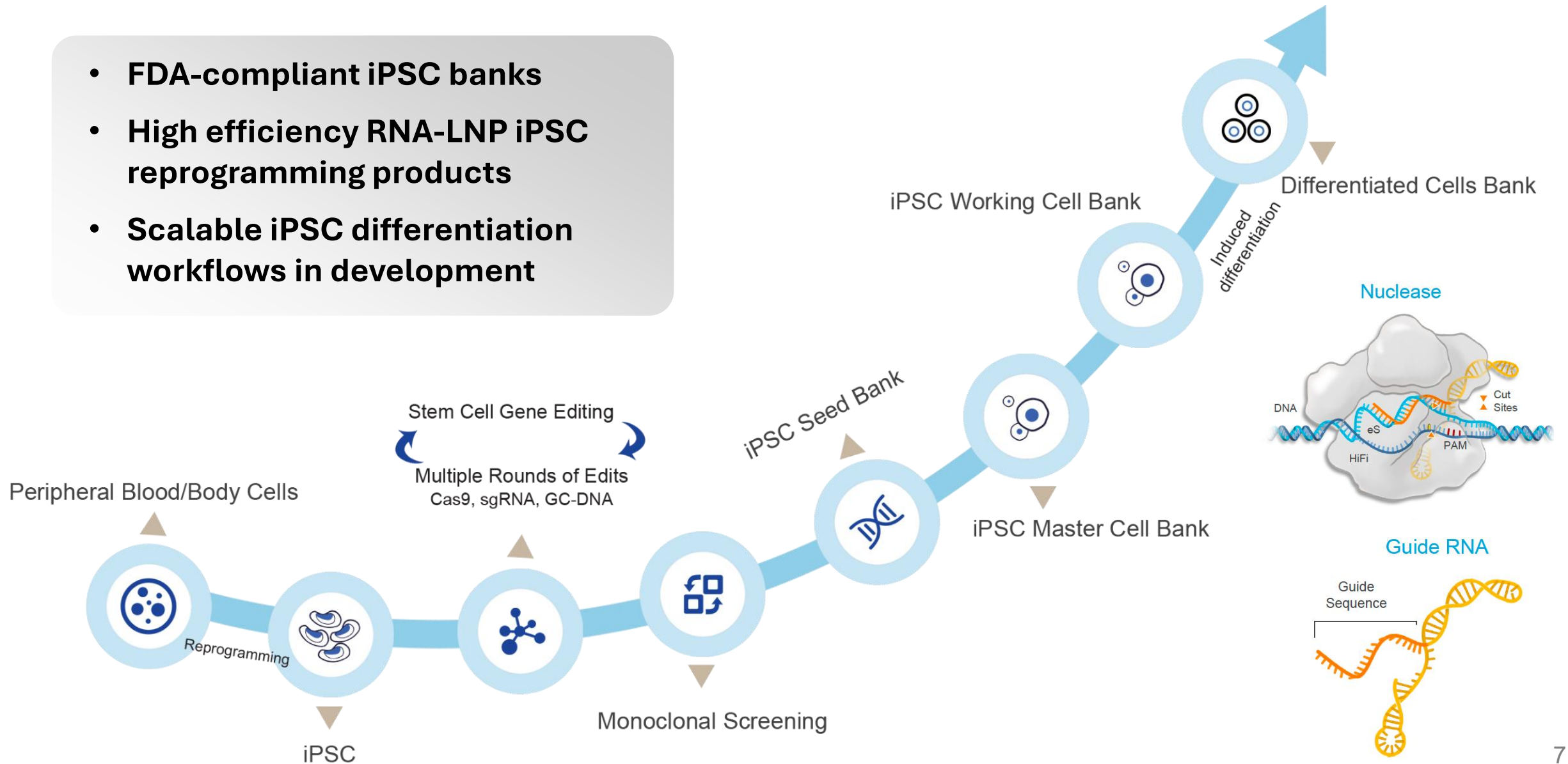
- Simple procedure, high throughput, inexpensive equipment
- No residual organic solvent (compared to the chemical synthesis process)

## Gene Editing Solutions

- **SpCas9 mRNA/SpCas9 protein** (other nucleases available)
- **Nonviral KI template delivery:** linear open- or close-ended DNA templates
- **AAV:** GMP grade AAV packaging, high nucleus entry efficiency and editing efficiency.

# iPSC-Derived Cell Therapy Workflows

- **FDA-compliant iPSC banks**
- **High efficiency RNA-LNP iPSC reprogramming products**
- **Scalable iPSC differentiation workflows in development**



Fully FDA-compliant

**Governing Documentation**  
Trial Master Files



**Qualified Service Partners**



## Medical Clinics

- PI & Staff: Adequate experience and training
- Facility: Certification/Accreditation
- Patient recruitment access
- Investigational Review Board

## CMS Certified Testing Lab with CLIA license

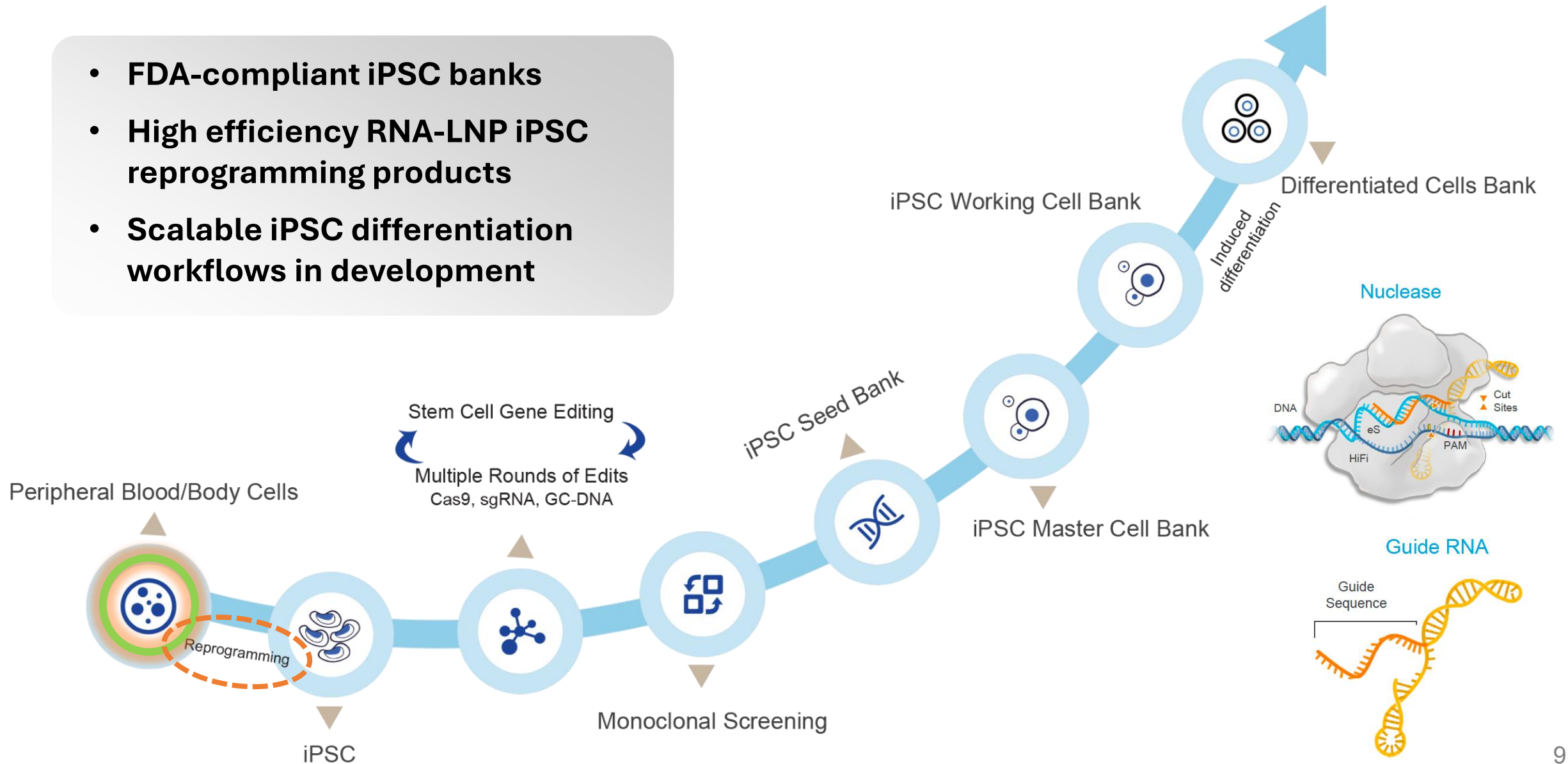
- Accuracy
- Precision
- Reportable range
- Reference intervals/range (normal values) for the laboratory's patient population

## Courier

- Time-critical nature of customized requirement for clinical specimens
- Expert coordination between patients, clinics, and laboratories
- Door-to-door supply chain meets customer demand
- Provide on-demand packaging solutions from small parcels to multi-pallets across all temperature ranges

# iPSC-Derived Cell Therapy Workflows

- **FDA-compliant iPSC banks**
- **High efficiency RNA-LNP iPSC reprogramming products**
- **Scalable iPSC differentiation workflows in development**



## Highly Efficient iPSC Reprogramming RNA-LNP Cocktail



Reprogramming with RNA, no risk of gene integration



Convenient, **Ready-to-use LNP mix**, can be directly added to cells, eliminating the need for transfection reagents or viral manipulation



High iPSC reprogramming efficiencies

- **Fibroblasts: 4-10%**
- **PBMCs: 0.31%**
- **Enables dramatic reduction in clone screening campaign timelines**



System flexibility: suitable for feeder or feeder-free conditions

# uBriGene RNA-LNP Reprogramming Kit Advantages



	uBriGene's RNA-LNP	RNA	Sendai virus	Episomal vector
Reprogramming efficiency on PBMCs	High	Inefficient	High	Inefficient
Number of treatments	4	4 to 10	1	1
Transfection / electroporation	No	Yes	No	Yes
Typical iPSC emergence time (days)	7-14	7-14	7-21	14-30
Integration risk	None	none	None	Small
Residual cleanup	N/A	N/A	Yes	Needs more cell passages
Stability	> 1 year	Short (3 months)	Long (years)	Long (years)



✓ RNA optimization for increased stability



✓ LNP reformulation for improved delivery



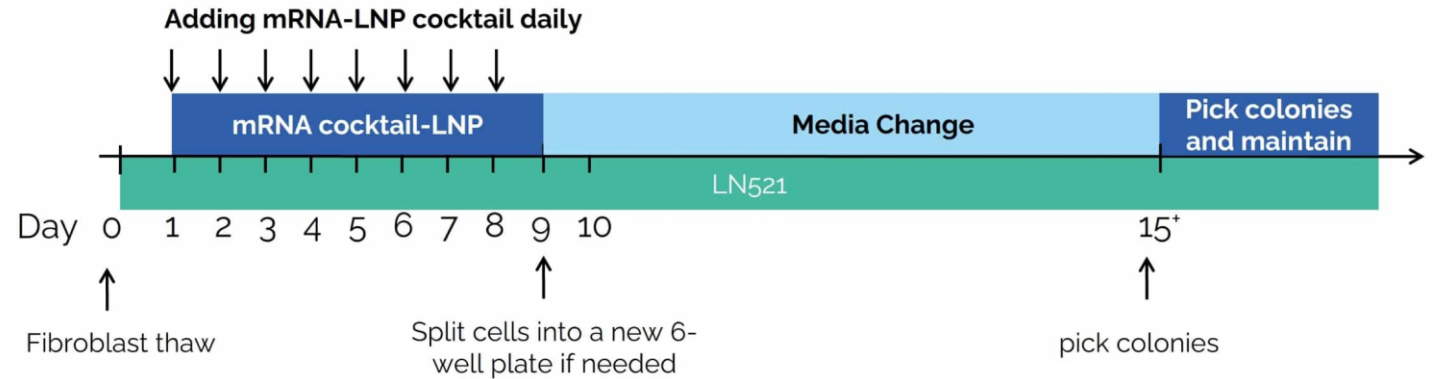
✓ Enhancer B



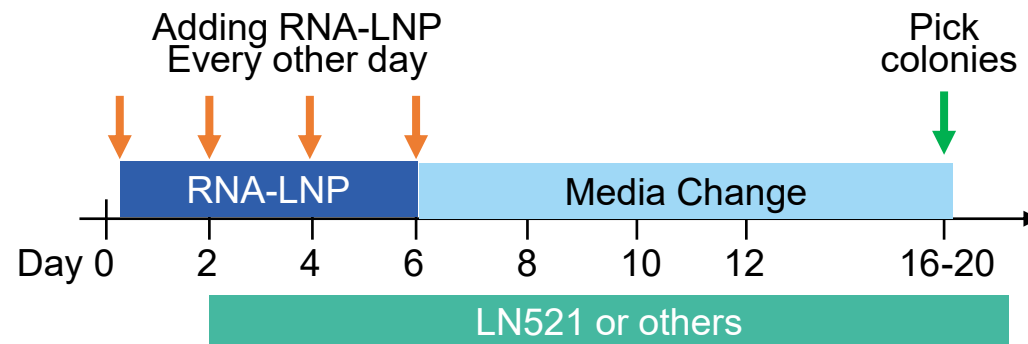
✓ Less frequent treatment and smaller volume of cocktail needed

✓ Improved reprogramming efficiency for PBMC & difficult-to-reprogram cells

Reprogramming kit for fibroblasts:  
**4-10% efficiency**

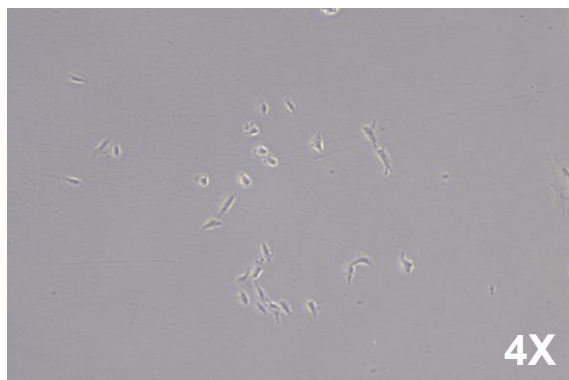


Reprogramming kit for PBMCs and other difficult-to-reprogram cells:  
**0.31% efficiency**  
**(100X higher than competitor products)**

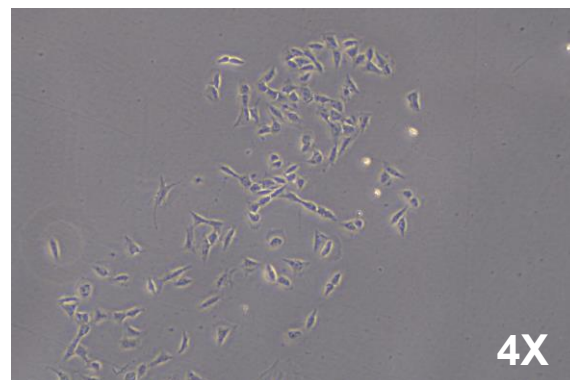


Testing items	Test Methods	RNA-LNP	Release Standard
<b>Appearance</b>	Visual method	translucent, light milky white solution	translucent, light milky white solution
<b>RNA Concentration</b>	Fluorescence-based assay	0.1 mg/mL	≥0.1mg/ml
<b>Encapsulation efficiency</b>	Fluorescence-based assay	95.6%	≥90.0%
<b>Endotoxin Detection</b>	GEL-CLOT Method	< 10EU/ml	< 10EU/ml
<b>Sterility</b>	Culture method	Not detectable	Not detectable
<b>LNP size and polydispersity</b>	Dynamic light scattering (DLS)	Z-Average: 99nm, PDI: 0.1	70nm-160nm, PDI < 0.3
<b>Reprogramming potency</b>	Reprogramming test	Pass	iPSC reprogramming ability from fibroblast

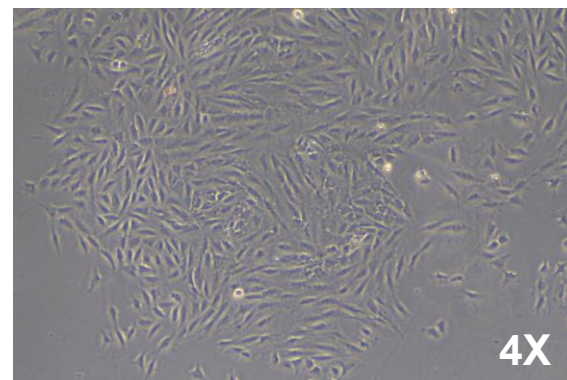
**Day3**



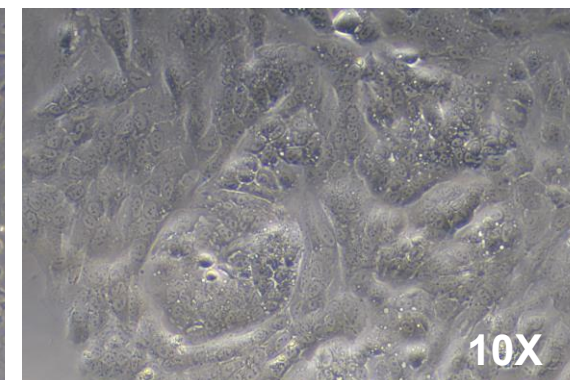
**Day5**



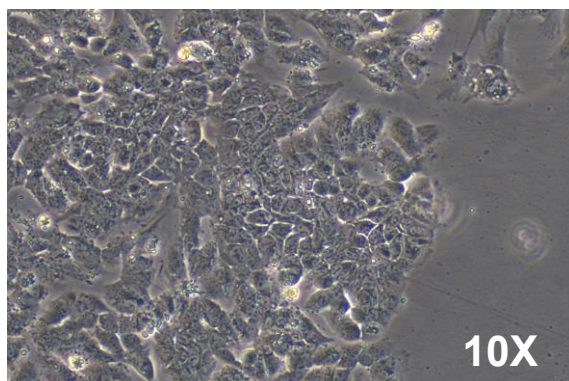
**Day7**



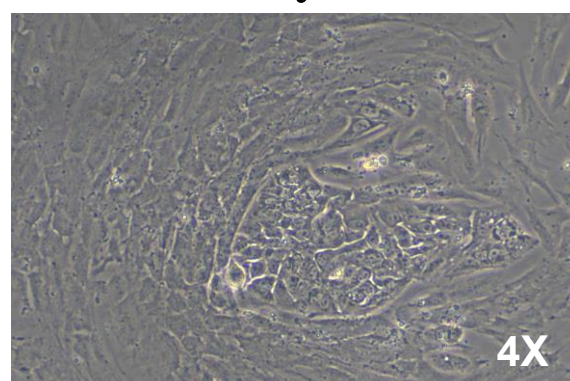
**Day9**



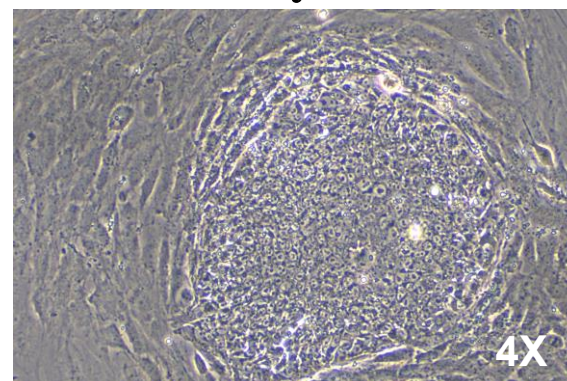
**Day11**



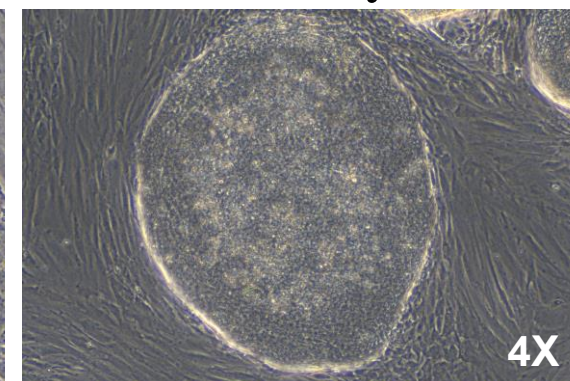
**Day13**



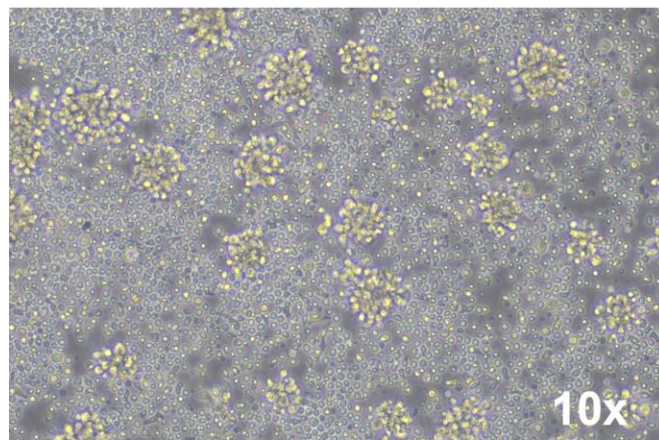
**Day15**



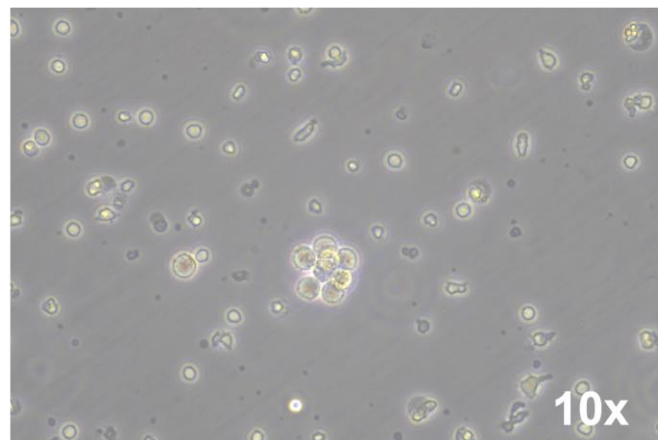
**Day18**



Day 2



Day 4



Day 6



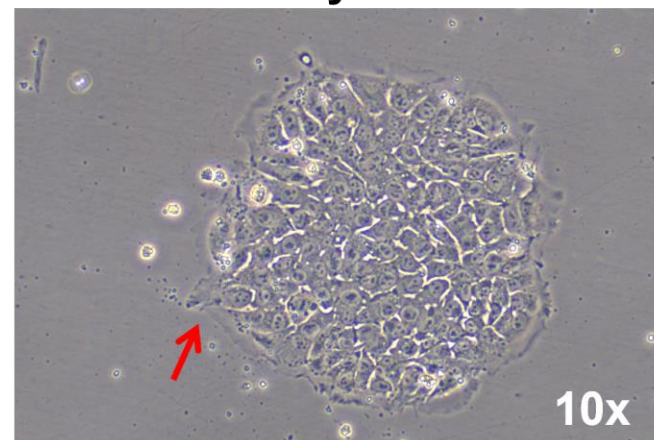
Day 8

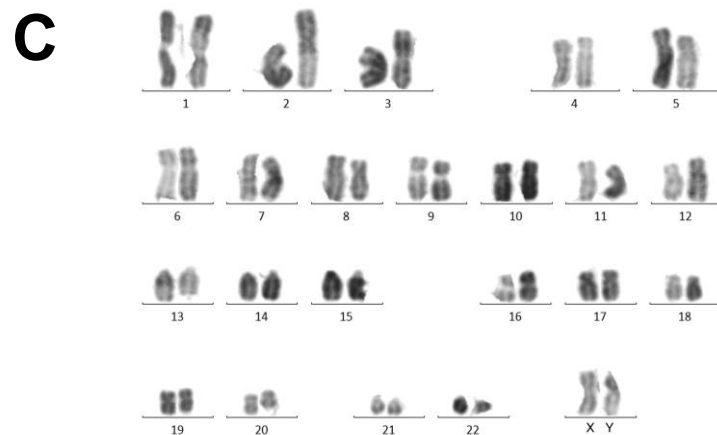
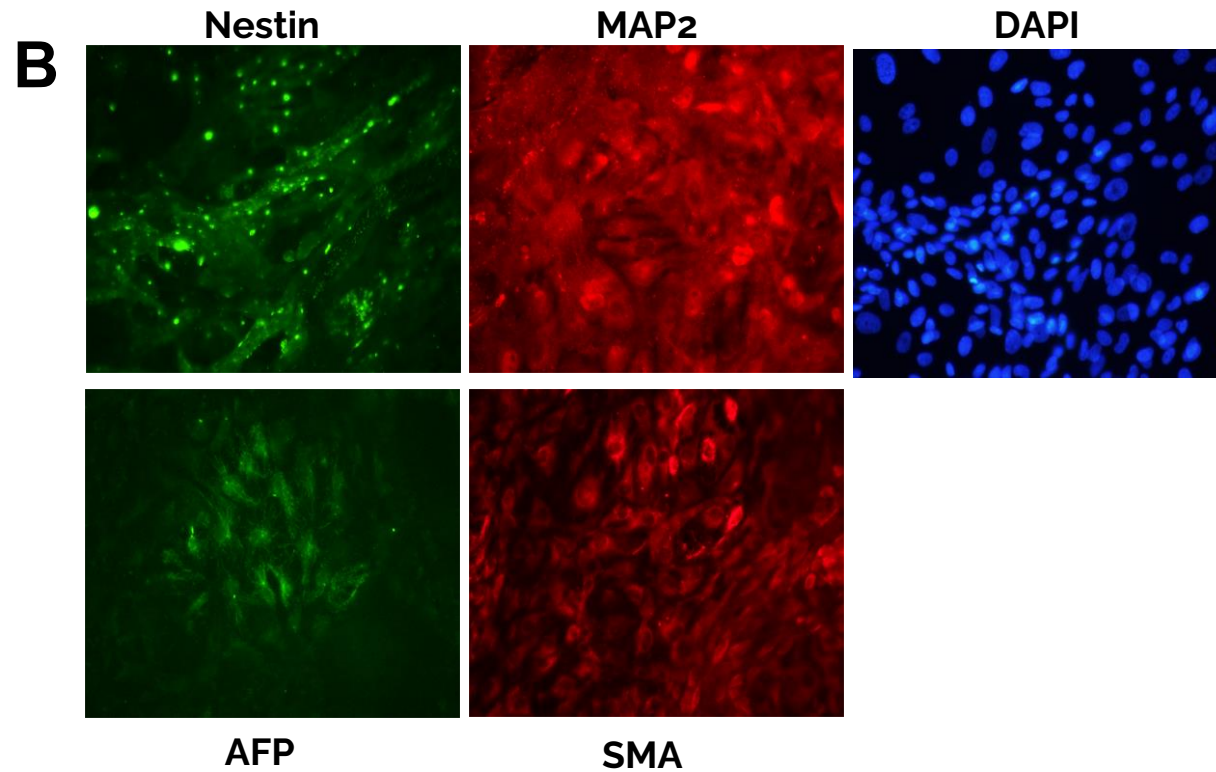
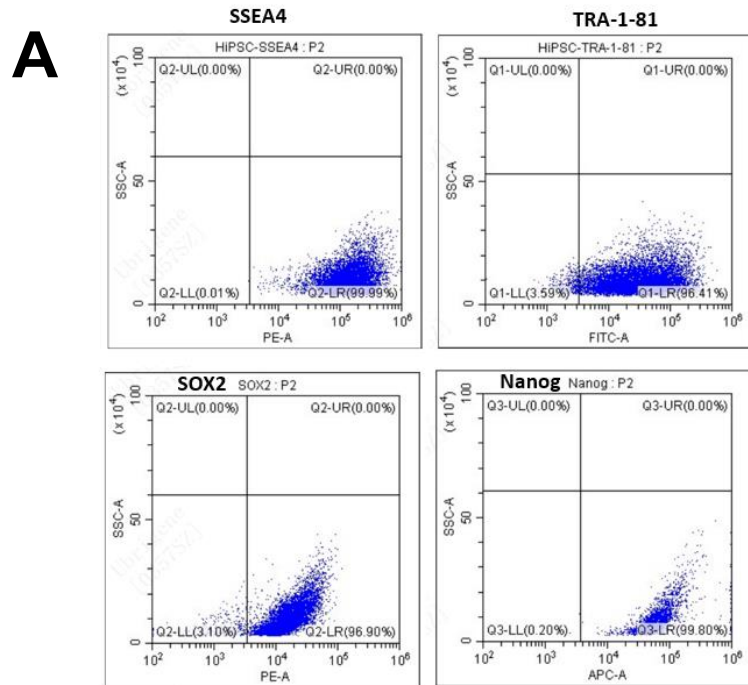


Day 11

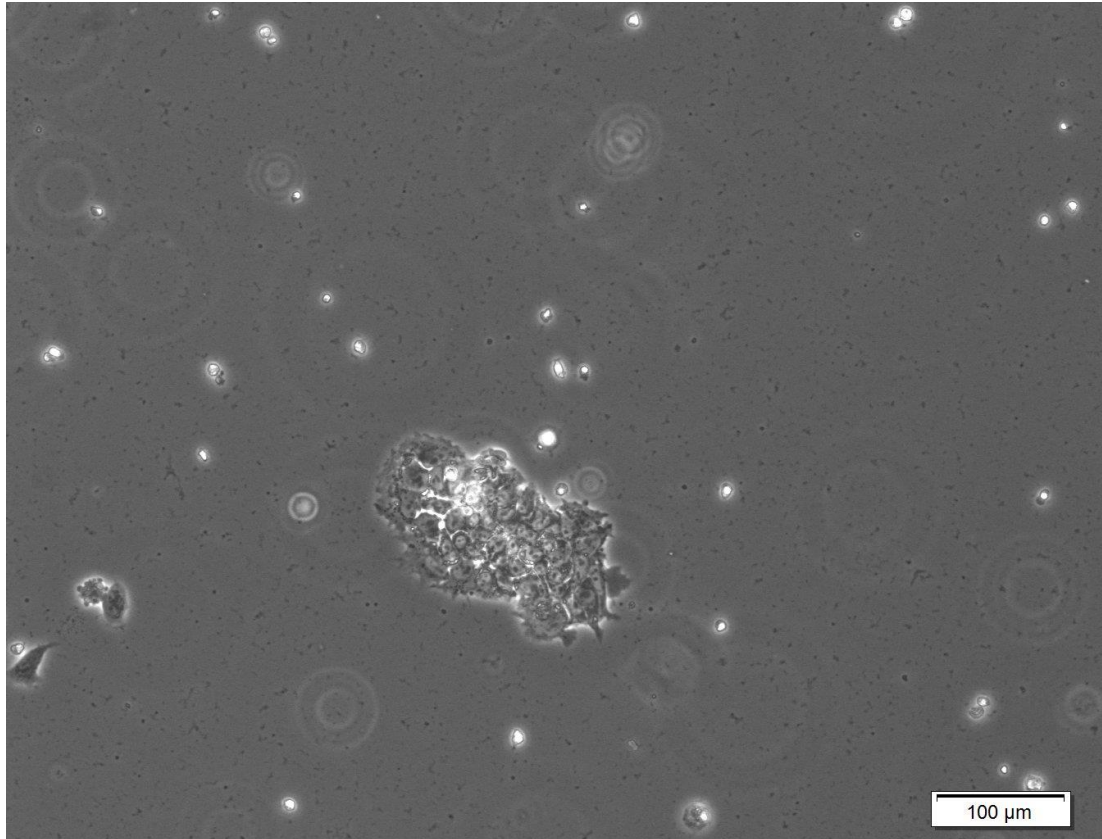


Day 15

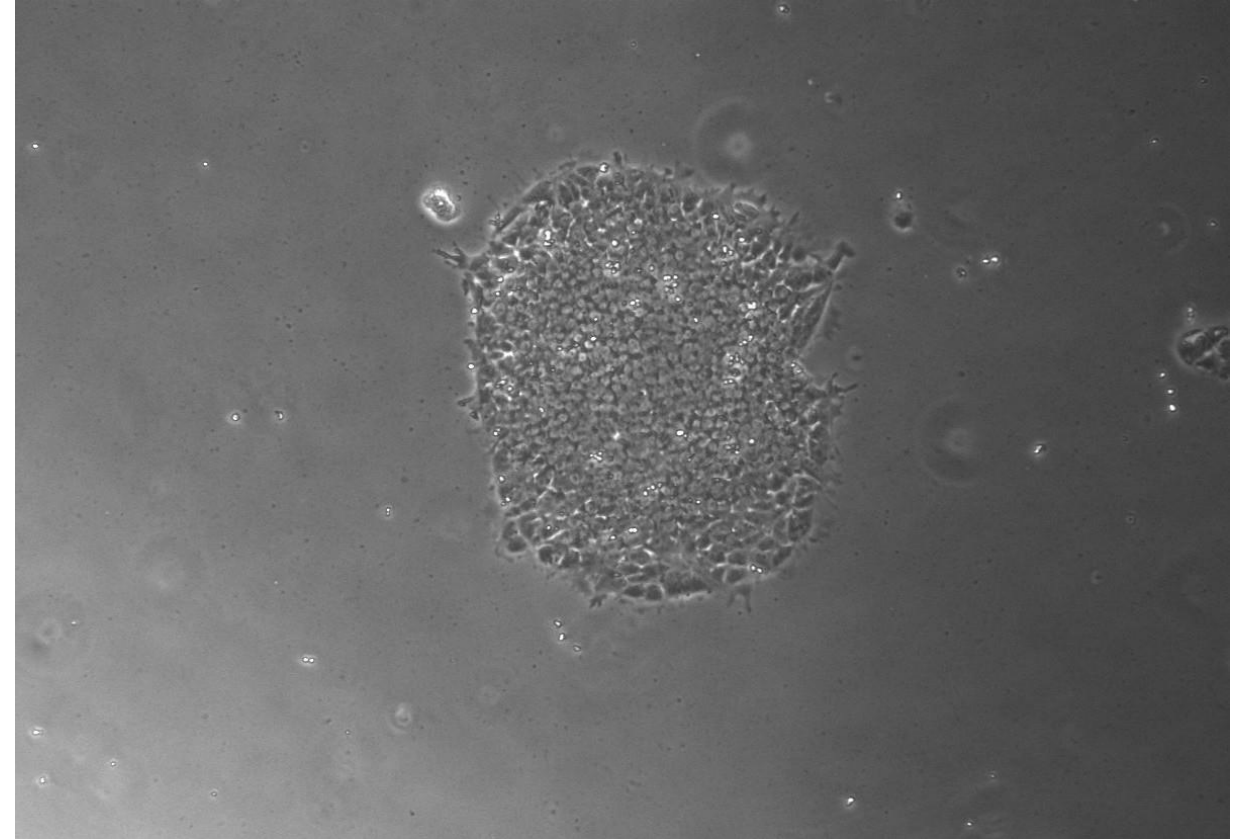




- A. Detection of pluripotency identification markers using flow cytometry.
- B. iPSC cells were differentiated into embryoid bodies to demonstrate their pluripotency
- C. Karyotyping by G-banding to demonstrate genome integrity

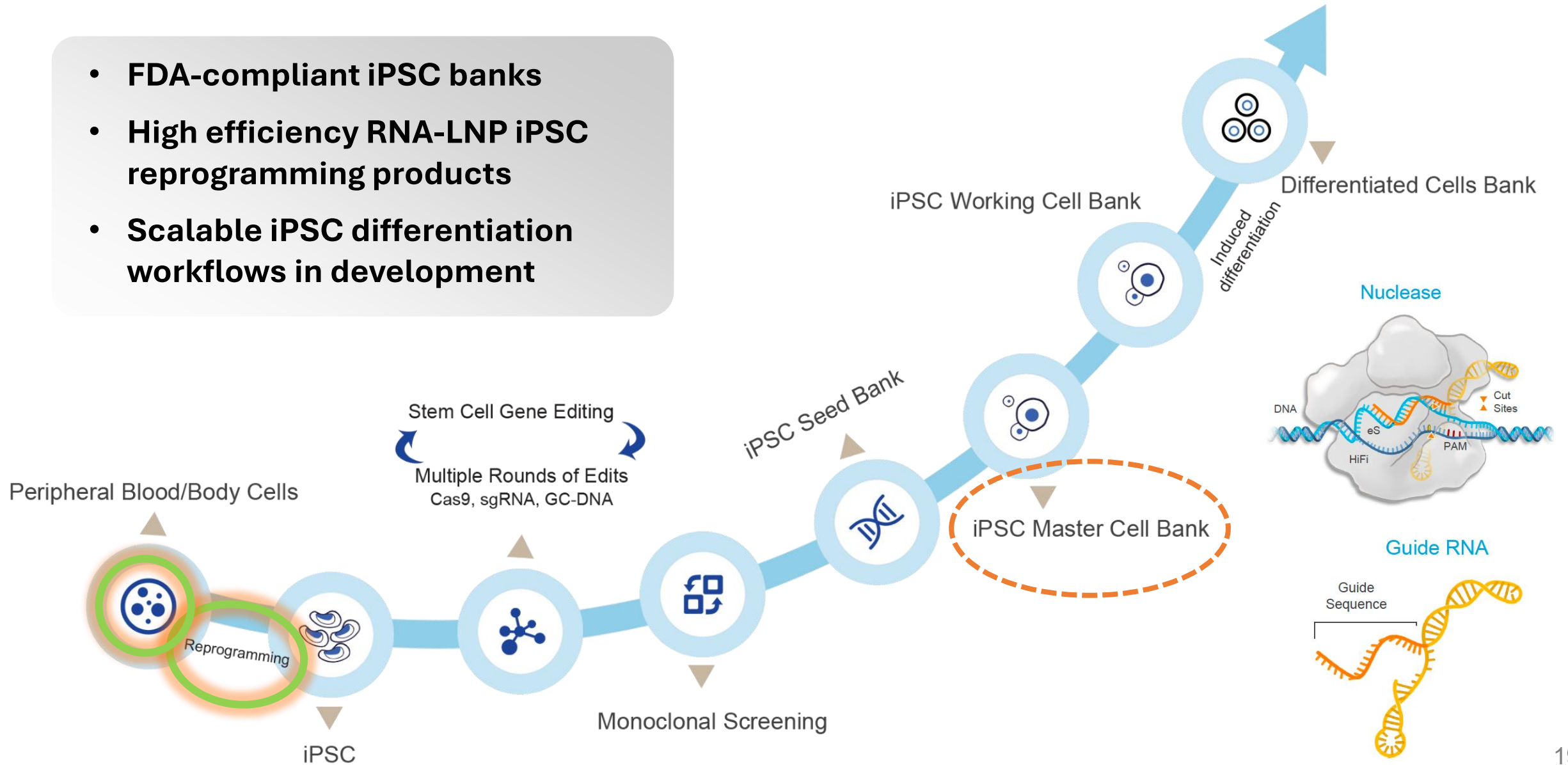


**Day 8  
iPSC Colony**

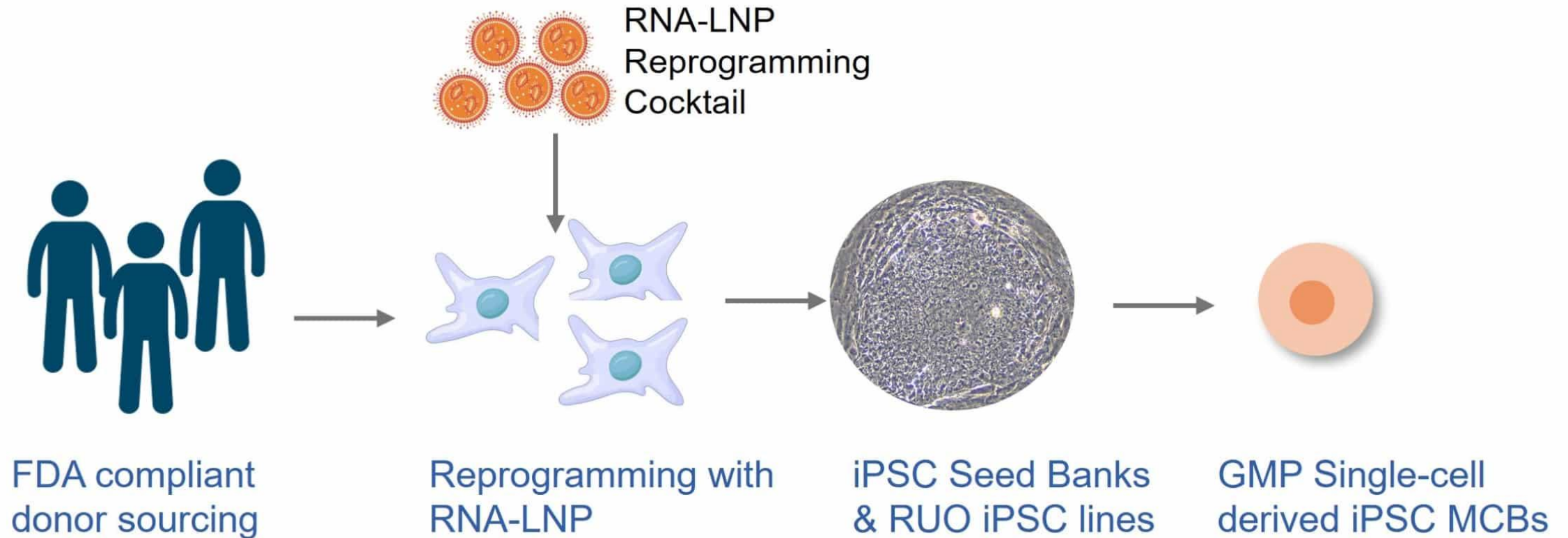


**Day 12  
iPSC Colony**

- **FDA-compliant iPSC banks**
- **High efficiency RNA-LNP iPSC reprogramming products**
- **Scalable iPSC differentiation workflows in development**



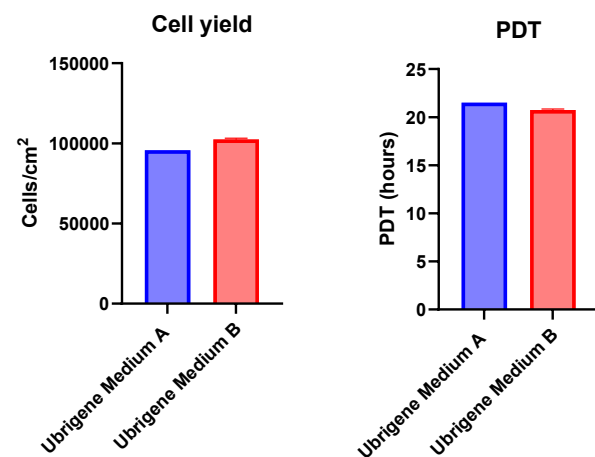
# iPSC Cell Banking Workflow



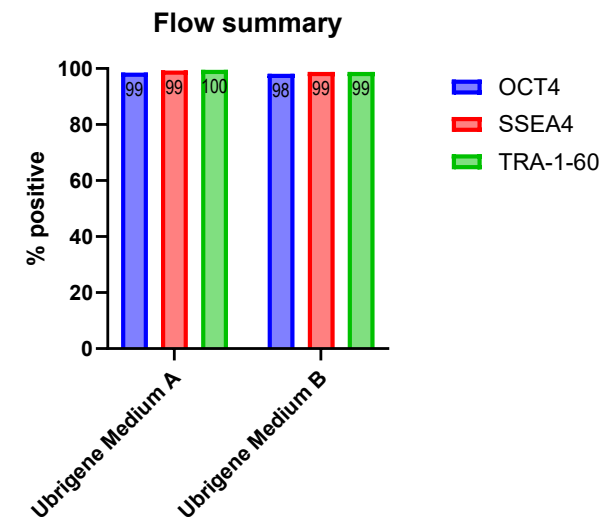
# iPSC Cell Banks QC Items

Objective	Assay	Acceptance Results	Parent cell	iPSC seed	iPSC MCB
<b>Sterility</b>	Immersion Sterility tests(B/F)	No organisms	✓	✓	✓
<b>Mycoplasma Testing</b>	Culture and cell indication assay	Negative	✓	✓	✓
<b>Endotoxin</b>	Kinetic chromogenic LAL	<2EU/ml	✓	✓	✓
<b>Cell Viability</b>	Trypan Blue	>70%	✓	✓	✓
<b>Genotyping*</b>	STR Genotyping		✓	✓	✓
	Karyotype Analysis		✓	✓	✓
<b>Adventitious virus*</b>	In vitro Assay for Adventitious Virus Contaminant	Negative			✓
	Fluorescent Product Enhanced reverse Transcriptase (FPERT) method	Negative			✓
	Transmission Electron Microcopy (TEM)	No viral particles			✓
<b>Multipotency assay</b>	Flow cytometry/ Immunostaining	SEA4 > 70% Tra-1-60 > 70% Tra-1-81 > 70%		✓	✓
		NANOG > 70%; OCT3/4 > 70% SSEA4 > 70%			
		Tra-1-60 > 70%; Tra-1-81 > 70%		✓	✓
	Teratoma formation assay	Three layers			
	Embryoid body formation assay	Detect of at least one marker per germ layer			✓

## Population Doubling Assessments



## Pluripotency Marker Assessments



## Genomic Abnormality Assessments

SUMMARY OF THE DETECTED COPY NUMBER VARIATIONS						
Samples	Cell line	Passage	dsDNA (ng/ $\mu$ L)	dsDNA quantity	CNVs	Sex <sup>**</sup>
Ubrigene Medium A	Ubrigene C17	P4+7	18.8	Good	Not detected	F
Ubrigene Medium B	Ubrigene C17	P4+7	13.2	Good	Not detected	F

The results of this test are for research use only.  
<sup>\*\*</sup> If unknown, sex is deduced from the ChrX and the ChrY copy number.

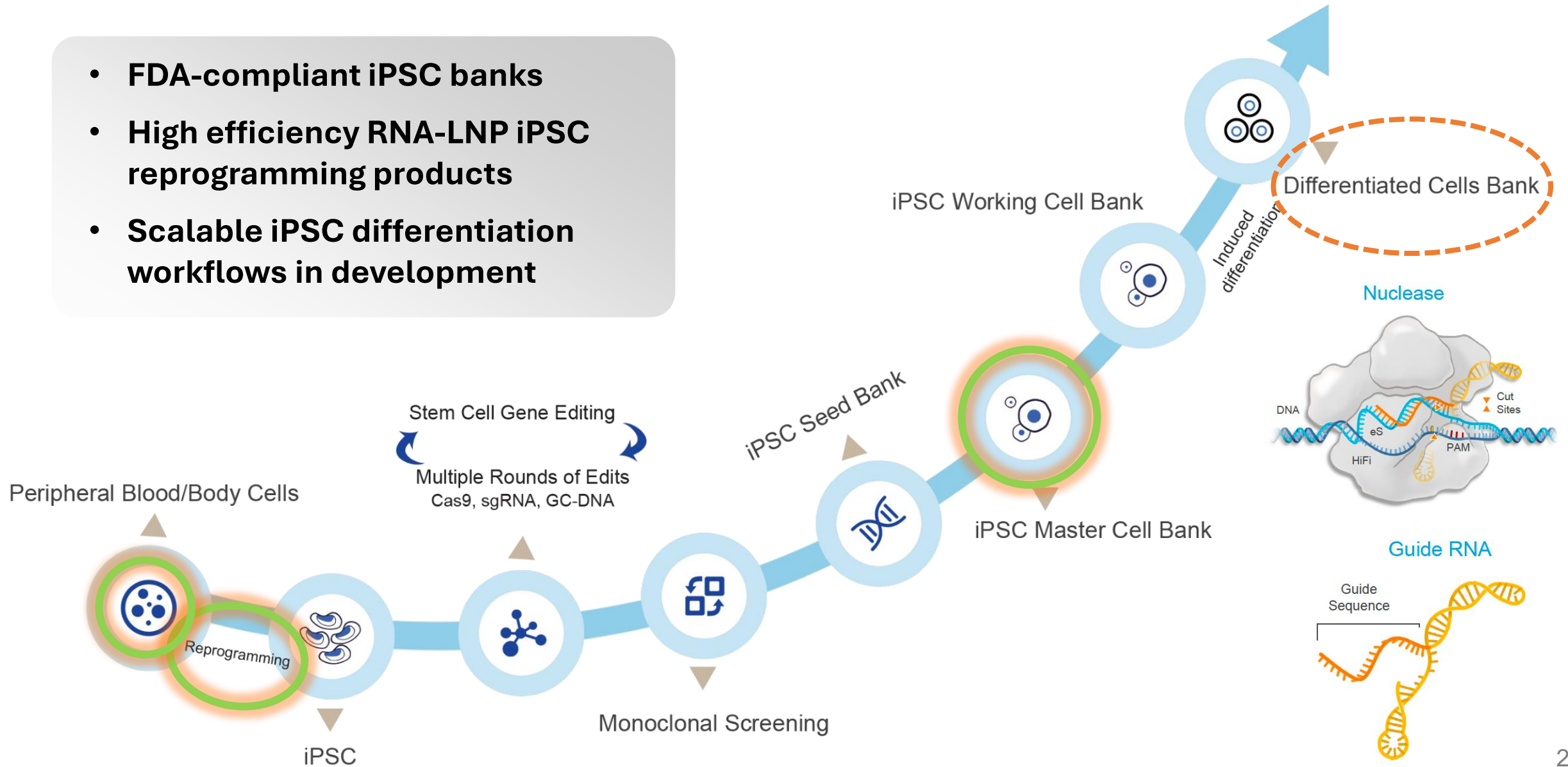
**HOW TO CITE the iCS-digital™ test**

<sup>\*</sup>Genomic stability was assessed by detection of recurrent genetic abnormalities using the iCS-digital™ PSC test, provided as a service by Stem Genomics (<https://www.stemgenomics.com/>), as described previously (Assou et al., 2020).<sup>\*</sup>

- Donor sourced from the USA, **FDA compliant**
- Generated using RNA reprogramming, **no genomic footprint**
- **Fully characterized and rigorously tested**
- Research grade & GMP grade

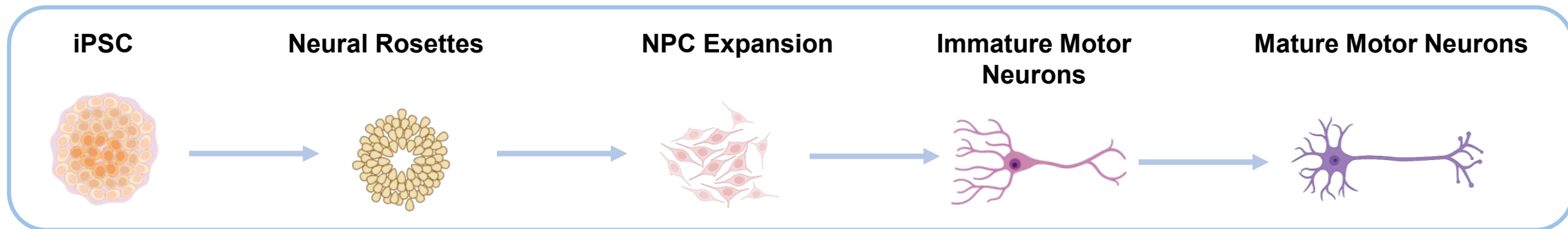


- **FDA-compliant iPSC banks**
- **High efficiency RNA-LNP iPSC reprogramming products**
- **Scalable iPSC differentiation workflows in development**

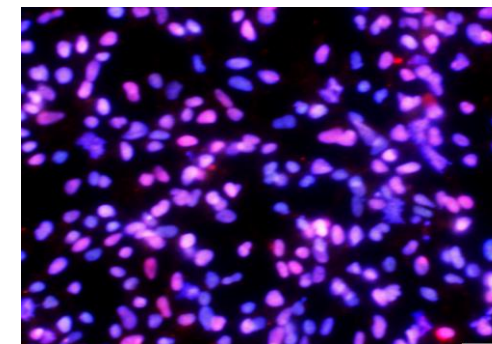
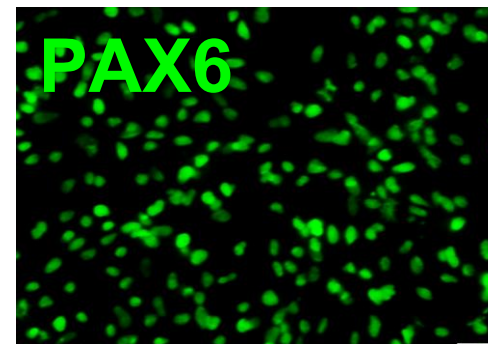
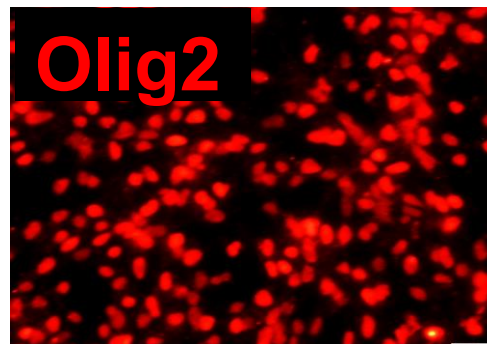
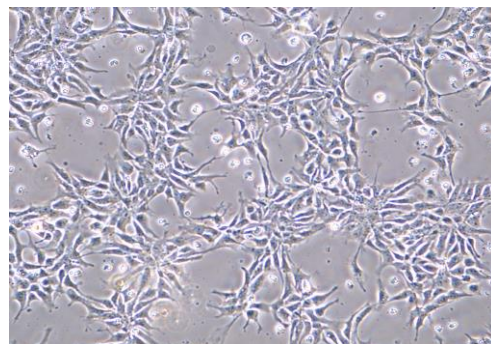


# Launch Polls

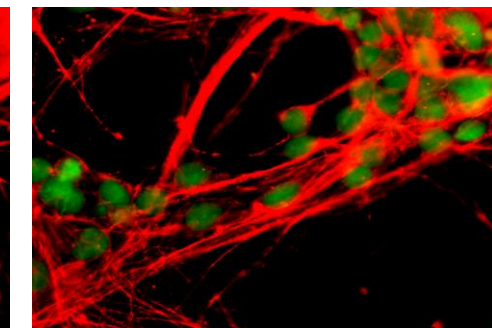
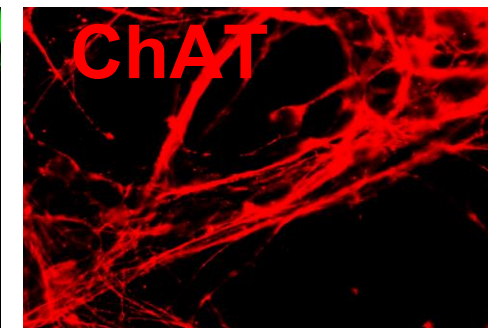
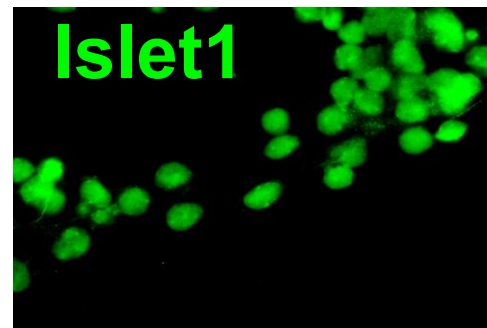
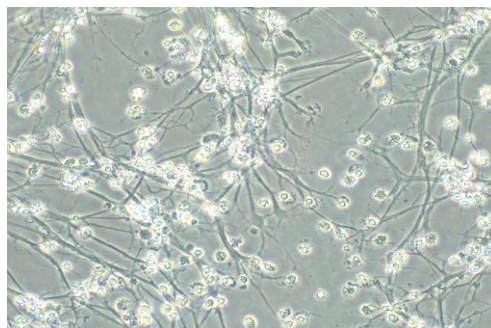
# iPSC Differentiation Workflows: Motor Neurons



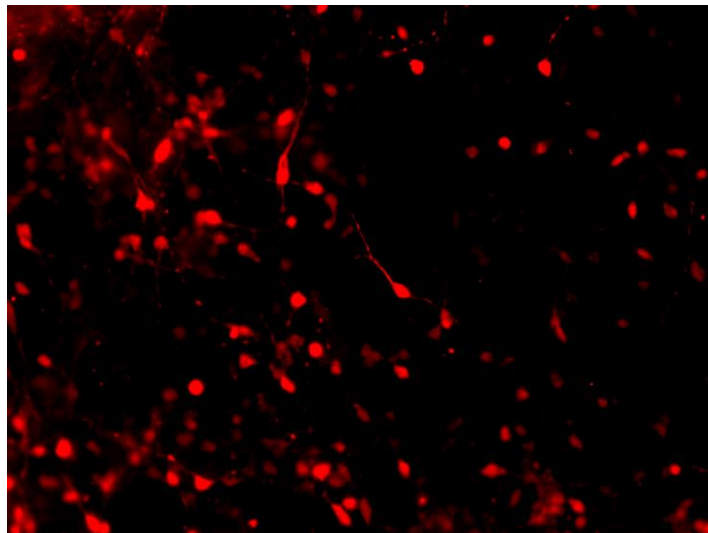
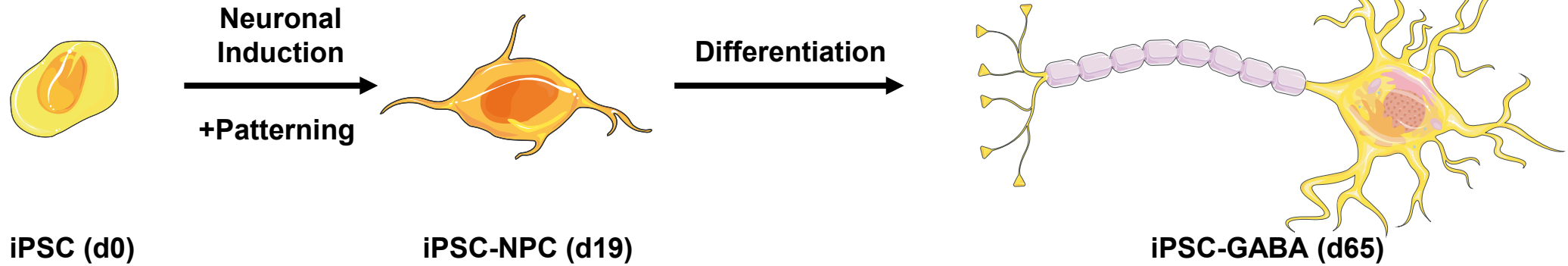
**Motor Neuron Progenitors**



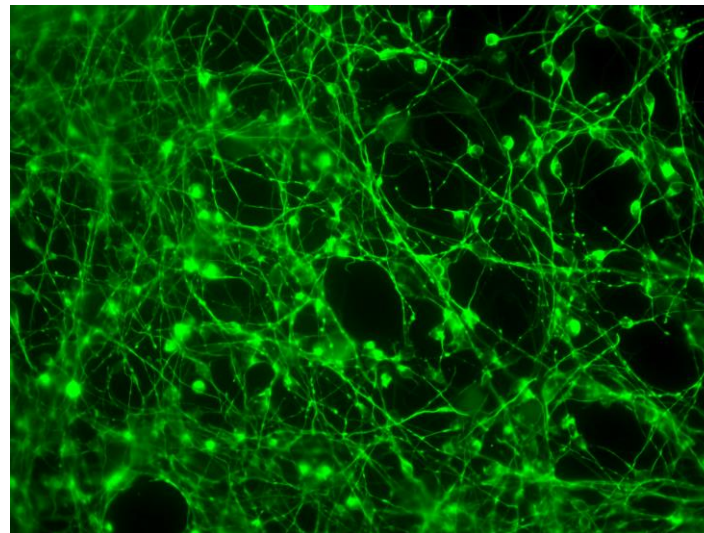
**Mature Motor Neurons**



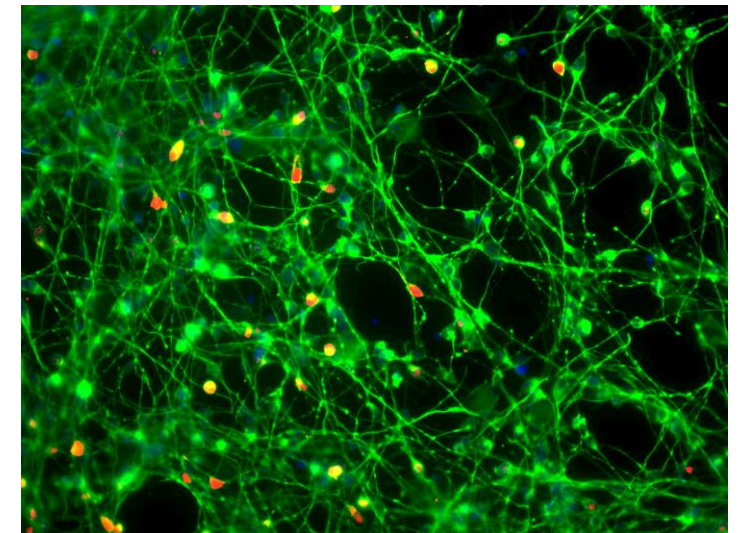
# iPSC Differentiation Workflows: GABA Neurons



**GAD67**

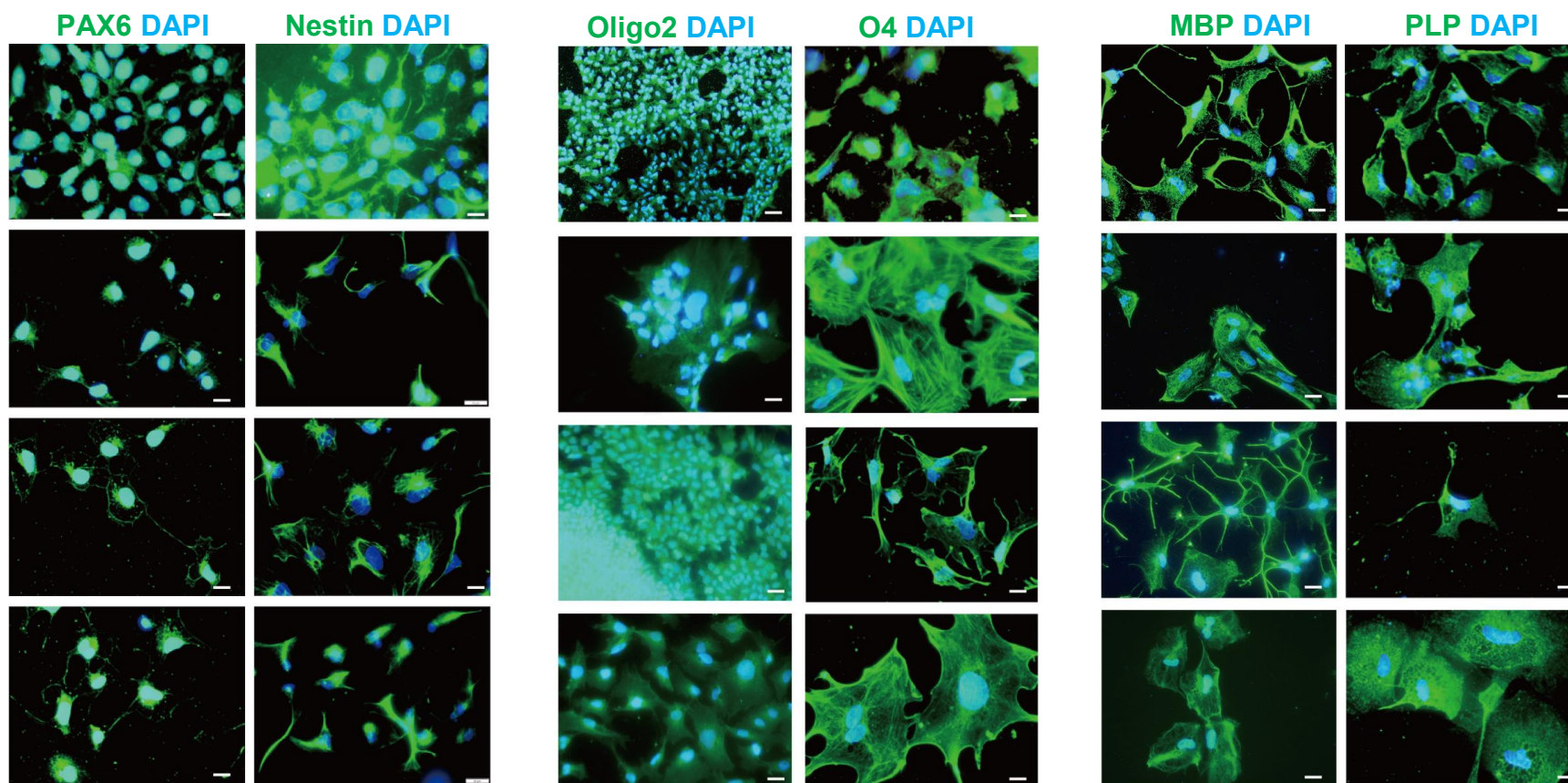
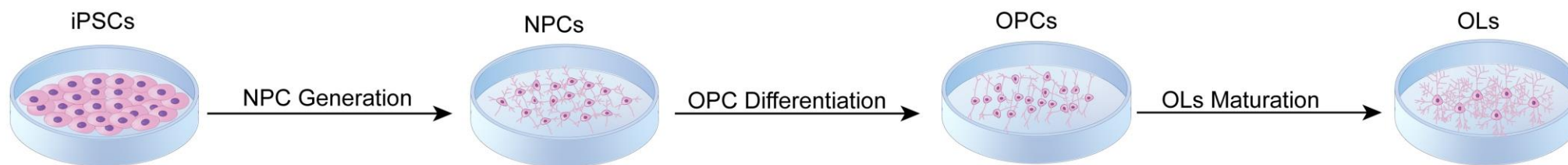


**TUBB3**



**GAD67/TUBB3**

# iPSC Differentiation Workflows: Oligodendrocytes



- **High-efficiency RNA-LNP iPSC reprogramming cocktail kits**
- **Offering off-the-shelf GMP iPSC lines to expedite cell therapy development**
- **Multiple iPSC differentiation workflows are in development**

Cat#	Description	Components / Size	Price
iPSC-RPM-RNA-LNP-V2-S	Efficient iPSC reprogramming RNA-LNP kit for PBMCs, difficult-to-reprogram, and disease-derived cells, can be directly added to cells	Trial size (2 x iPSC reprogramming)	<b>\$497.5</b> \$995
iPSC-RPM-RNA-LNP-V2		Standard size (6 x iPSC reprogramming reactions)	\$2,680

A large white circle with a soft drop shadow, containing the text 'Thank You' in a bold blue font. The background of the slide features a blue molecular structure with glowing nodes and connecting lines.

**Thank You**

**uBriGene (MA) Biosciences, Inc.  
20400 Century Blvd, Suite 125  
Germantown, MD 20874**

**Scott Pattison, PhD  
Sr. Director Bus Dev  
[scott.pattison@ubrigene.com](mailto:scott.pattison@ubrigene.com)  
301-606-8243**

# Appendix

Established in 2015, uBriGene is committed to advancing and implementing cutting-edge CGT technologies and offering comprehensive solutions for the CGT industry.



## CRO Services

- Plasmid
- Lentivirus
- AAV
- iPSC
- Autologous Cell Therapies
- Allogeneic Cell Therapies
- Gene Editing
- mRNA/circRNA

## CDMO Services

- Plasmid
- Lentivirus
- AAV
- iPSC
- Autologous Cell Therapies
- Allogeneic Cell Therapies
- Gene Editing
- mRNA/circRNA
- QC/Release Testing
- Stability Testing

## Chinese IIT Coordination

- Preliminary Communication
- Medical Center & PI recruitment
- Protocol Preparation
- Process Initiation
- Patient Management
- Clinical Process Management
- Data Management
- Work Completion & Reporting

**uBriGene is your one-stop-shop from concept to clinical proof-of-concept**

## QUALITY

### **Customer Support**

Clear, timely, accurate technical support & project management updates

### **GMP excellence**

Team with a track record of GMP success across multiple modalities

### **QMS rigor**

Ensures our personnel, processes, and products exceed client & regulatory expectations

## COLLABORATION

### **CRO & CDMO Services**

One-stop shop of PD, AD & GMP platform solutions for ATMP developers

### **Regulatory Support**

Experienced Reg Affairs team & 10 FDA DMFs in-place to help clients navigate regulatory body engagements

### **Chinese IIT Coordination**

Rapid and cost-effective path to first-in-human clinical data

## INNOVATION

### **Upstream Processes**

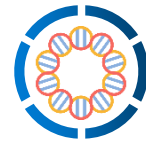
Proprietary vectors, RNA methodologies, cell lines, & cell culture processes

### **Downstream Processes**

Cost & time saving purification processes for cells, viruses, and RNA assets

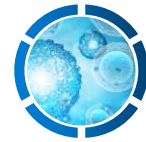
### **Novel Technologies**

Constant commitment to optimizing every unit operation of our GMP manufacturing platforms



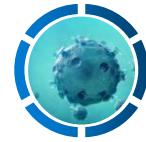
## Plasmids

- ◆ Plasmid construction
- ◆ Strain banking
- ◆ Plasmid PD & manufacturing



## Cell therapy

- ◆ CAR-T, TCR-T
- ◆ CAR-NK
- ◆ MSC, **iPSC banking & differentiation**



## Viral Vectors

- ◆ LVV, RVV
- ◆ AAV
- ◆ Adenovirus
- ◆ OV



## Gene Editing

- ◆ IVT-sgRNA
- ◆ Nuclease
- ◆ RNP PD



## RNA-LNP

- ◆ mRNA
- ◆ circRNA, saRNA
- ◆ IVT-sgRNA



## QC release testing

- ◆ Safety
- ◆ Identity
- ◆ Potency