PGC Worldwide Lab Call Details

DATE: Friday, September 13, 2013

PRESENTERS:

- **Dr. Andrew Brooks, Chief Operating Officer, Rutgers University Cell and DNA Repository (RUCDR), Director, Bionomics Research and Technology Center (BRTC),**
- **Dr. Michael Sheldon, RUCDR Director, Stem Cell Laboratory**
- **Dr. Jennifer Moore, RUCDR Associate Director, Stem Cell Laboratory**

TITLE: Dr. Brooks: *"RUCDR Infinite Biologics: A Resource for the Investigation of Neuropsychiatric Disorders*"

Drs. Sheldon and Moore: , *""The RUCDR Stem Cell Lab: A Resource for the Investigation of Neuropsychiatric Disorders""*

START: We will begin promptly on the hour.

1000 EDT - US East Coast
0700 PDT - US West Coast
1500 BST - UK
1600 CET - Central Europe
0000 AEDT – Australia (Saturday, June 22nd, 2013)

DURATION: 1 hour

TELEPHONE: **PASSCODE:** 275 694 38

- US Toll free: 1 866 515.2912
- International direct: +1 617 399.5126
- Toll-free number? See http://www.btconferencing.com/btmeetme_v3/index.asp?bid=256&dialin=866 931 5634
- Operators will be on standby to assist with technical issues. "*0" will get you assistance.
- This conference line can handle up to 300 participants.

Lines are Muted **NOW**

Lines have been automatically muted by operators as it is possible for just one person to ruin the call for everyone due to background noise, electronic feedback, crying children, wind, typing, etc.

Operators announce callers one at a time during question and answer sessions.

Dial *1 if you would like to ask a question of the presenter. Presenter will respond to calls as time allows.

Dial *0 if you need operator assistance at any time during the duration of the call.

UPCOMING PGC Worldwide Lab

DATE: Friday, October 11, 2013

PRESENTERS:

- **Prof. Barbara Franke**, PhD; Professor of Molecular Psychiatry, Radboud University Medical Centre in Nijmegen, The Netherlands; Co-Founder, ENIGMA Consortium
- **Dr. Paul Thompson ;** Associate Dean for Research, University of Southern California **;** Professor of Neurology & Psychiatry, Imaging Genetics Center / LONI, UCLA School of Medicine; Co-Founder, ENIGMA Consortium

TITLE: ***"****The ENIGMA Consortium – Exploring the Genetic Architecture of Human Brain Structure"*

START: We will begin promptly on the hour.

1000 EDT - US East Coast
0700 PDT - US West Coast
1500 BST - UK
1600 CEST - Central Europe
0000 AEST – Australia (Saturday, August 10th, 2013)

DURATION: 1 hour

TELEPHONE: **PASSCODE:** 275 694 38

- US Toll free: 1 866 515.2912
- International direct: +1 617 399.5126
- Toll-free number? See http://www.btconferencing.com/globalaccess/?bid=75_public
- Operators will be on standby to assist with technical issues. "*0" will get you assistance.
- This conference line can handle up to 300 participants.

RUCDR Infinite Biologics

A Resource for the Investigation of Neuropsychiatric Disorders

Dr. Andrew Brooks

Chief Operating Officer, RUCDR

RUCDR INFINITE BIOLOGICS

September 13, 2013

Mission

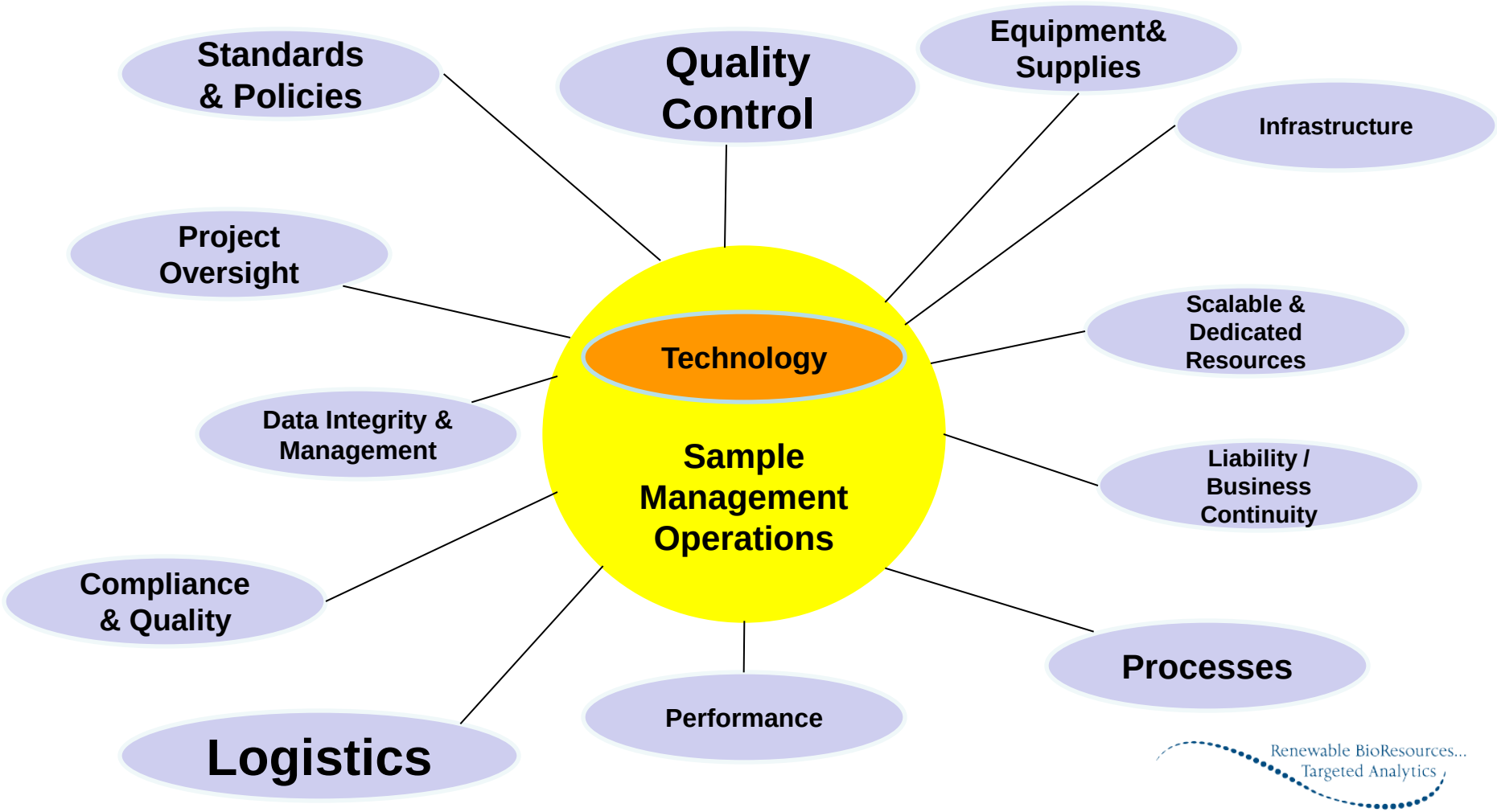
RUCDR Infinite Biologics enables sharing programs (DNA, RNA, cell lines, tissue and clinical data) for NIH Institutes, research advocacy groups & biotechnology corporations

- Speeding discovery of genes for complex diseases by sharing well annotated, high quality human samples
- >$30M annual grant & contract support

- >120 Technical Staff
- 50,000 sq. ft. laboratory and storage space
- 9M nucleic acid samples & 6.5M cell lines
- Distribute ~ 1M samples for genomic/genetic analyses

Renewable BioResources...
Targeted Analytics

Repository Management Operations: Enterprise Level Integration



Renewable BioResources... Targeted Analytics

RUCDR
INFINITE BIOLOGICS

Research Supported Worldwide

National Institute of Mental Health

United States
National Institute of Diabetes & Digestive & Kidney Diseases
of the National Institutes of Health

harlan®
Helping you do research better

RUTGERS

HBDI
The Human Biological Data Interchange

SFARI SIMONS FOUNDATION AUTISM RESEARCH INITIATIVE

AMDeC | Academy for Medical Development and Collaboration

Pfizer

Memorial Sloan-Kettering Cancer Center

NIDA NATIONAL INSTITUTE ON DRUG ABUSE
The Science of Drug Abuse & Addiction
NATIONAL INSTITUTES OF HEALTH

cure Autism now & AUTISM SPEAKS
Working Together

The Progeria Research Foundation

NIAAA NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM
of the NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases
National Institutes of Health

Immune Tolerance Network

AGRE
Autism Genetic Resource Exchange
A SCIENCE PROGRAM OF AUTISM SPEAKS™

NJCTS New Jersey Center for Tourette Syndrome and Associated Disorders, Inc.

VASCULAR CURES

The New England Centenarian Study

Renewable BioResources...
Targeted Analytics

5 Major Program Functions

- Sample acquisition
- Processing
- Storage
- Distribution
- Analysis

RUCDR
INFINITE BIOLOGICS

Functional Essentials: Maximizing Biological Resources

- Maximal use of primary samples
  - Undefined application for downstream analyses
- Efficient processing
  - Maximizing extraction technologies to improve yield and quality
- Appropriate storage
  - Defining storage formats and temperatures to maximize storage infrastructure
- Nucleic acid amplification / Cell line establishment
  - Creating renewable resources to preserve primary sample and/or precious collections
- Appropriate distribution guidelines
  - Define needs for specific downstream applications to preserve sample resources

The RUCDR Stem Cell Laboratory

A Resource for the Investigation of Neuropsychiatric Disorders

Michael Sheldon, Ph.D.
RUCDR Director, Stem Cell Laboratories
Associate Professor of Genetics
Rutgers University
sheldon@biology.rutgers.edu
http://www.RUCDR.org

RUCDR
INFINITE BIOLOGICS

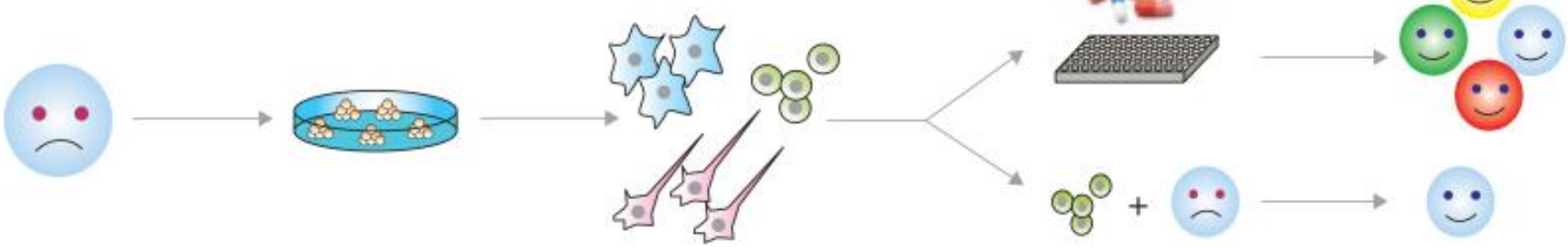
The Promise of iPSCs

✓ Reproduction of disease-specific phenotype
✓ Scalability of assay for drug screens

✓ *In vivo* efficacy
✓ Toxicity in large population

Drug screening
("Disease modelling")

Treatment of multiple patients



Patient

Patient-specific iPSCs

Specialized cells

Cell therapy

Single treated patient

✓ Detection of high-quality iPSCs

✓ Availability of efficient differentiation protocols
✓ Proper preclinical animal models

✓ Successful engraftment
✓ Teratoma risk
✓ Maturation level and functionality of cells

✓ *In vivo* efficacy
✓ Costs associated with patient-specific therapy

Adapted from Wu and Hochedlinger, Nat Cell Biol. 2011 May;13(5):497-505

Why Use iPSC to Study Mental Health Disorders?

- Diseases processes might be manifest only in cells of the brain and central nervous system
- Differentiation provides a developmental paradigm
- Disease onset often occurs later in life making human embryonic stem cells less relevant

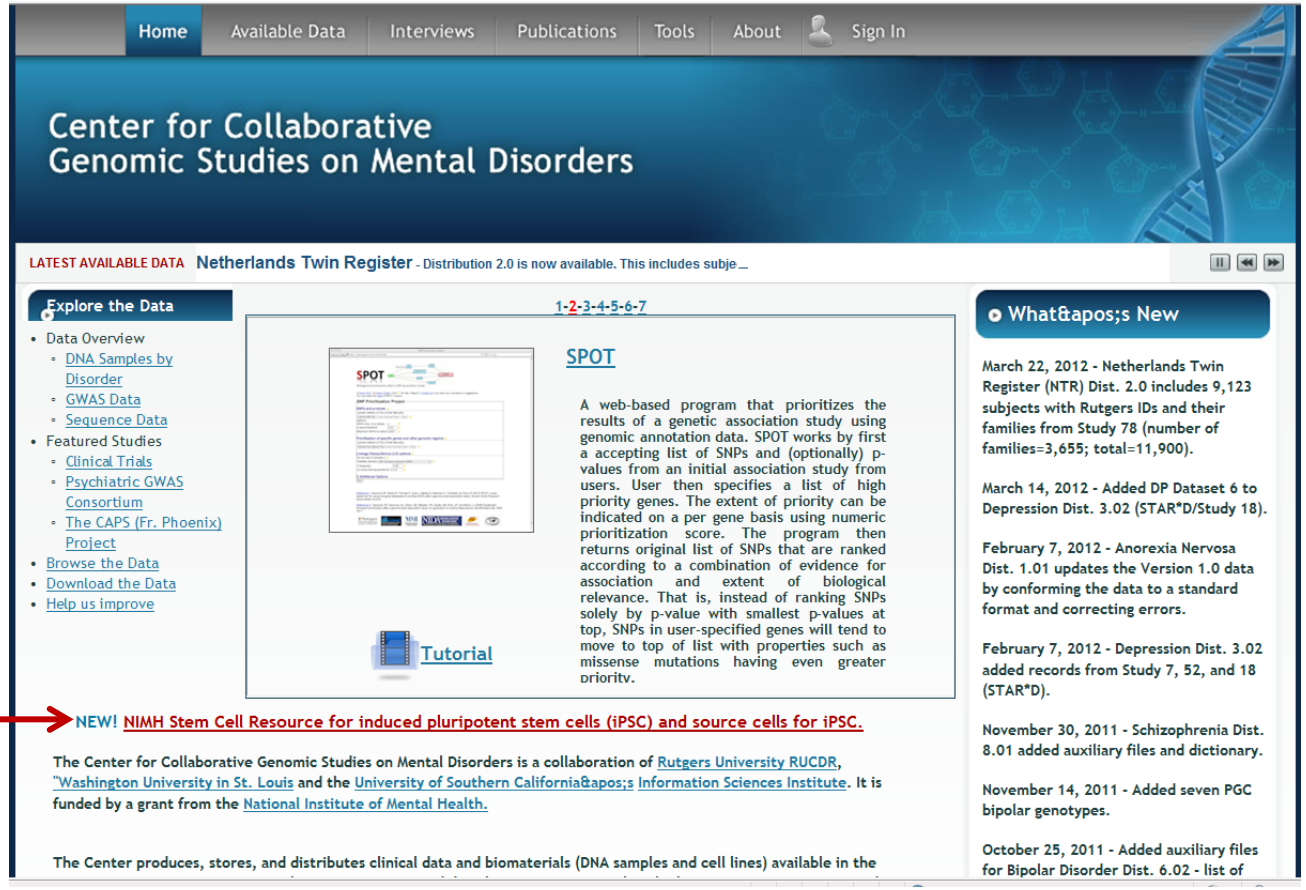
Summary of iPSC lines generated from patients with neurological diseases

Summary of iPSC lines generated from patients with neurological diseases					
Disease	**Genetic mutation**	**Reprogramming method**	**Neural differentiation**	**Relevant phenotype**	**Reference**
PD	Sporadic	Retrovirus; 4 factor	No	No	Park (6)
	Sporadic	Lentivirus; excisable, inducible 3/4 factor	Yes (~5% TH+)	No	Soldner (5)
	LRRK2 (G2019S)	Retrovirus; 3 factor	Yes (3–5% TH)	Yes: Elevated alpha-synuclein expression, increased sensitivity to cellular stressors	Nguyen (8)
	PINK1 (C1366T, T509G)	Retrovirus; 4 factor	Yes (10–15% TH of TUJ1)	Yes: Less recruitment of Parkin to the mitochondria	Seibler (9)
	SNCA (A53T)	Lentivirus; excisable, inducible 4 factor	Yes	No	Soldner (68) (2011)
ALS	SOD1 (L144F)	Retrovirus, 4 factor	Yes (20% HB9)	No	Dimos (13)
	VAPB (C166T)	Retrovirus, 4 factor	Yes (5% HB9)	Yes: Reduced VAPB levels in ALS8 patients	Mitne-Neto (14)
SMA	SMN	Retrovirus, 4 factor	Yes (~10% CHAT of TUJ1)	Yes: Reduced levels of SMN protein and impaired survival of motor neurons	Ebert (3)
FD	IKBKAP	Lentivirus, 4 factor	Yes (defects in neural crest differentiation)	Yes: Tissue-specific mis-splicing incomplete differentiation, reduced motility	Lee (4)
RTT	MeCP2 (1155del32, Q244X, T158M and R306C)	Retrovirus; 4 factor	Yes	Yes: Fewer synapses, reduced spine density, smaller soma size, altered calcium signaling and electrophysiological defects	Marchetto (27)
	MeCP2 (Δ3–4, T158M, R306C)	Retrovirus; 4 factor	Yes	Yes: Smaller soma size	Cheung (24)
FXS	FMR1	Retrovirus; 4 factor	No	No	Urbach (32)
SCZD	DISC1	Episomes; 4 factors	No	No	Chiang (34)
	Sporadic	Tetracycline-inducible lentivirus; 5 factors	Yes	Yes: Decreased neuronal connectivity, neurite number, PSD95-protein levels and glutamate receptor expression	Brennand (35)

ALS, amyotrophic lateral sclerosis; FD, familial dysautonomia; FXS, fragile X; PD, Parkinson's disease; RTT, Rett syndrome; SMA, spinal muscular atrophy; SCZD, schizophrenia.

Adapted from Marchetto et al., Hum Mol Genet. 2011 Oct 15;20(R2):R109-15.

The NIMH Center for Collaborative Genomic Studies on Mental Disorders

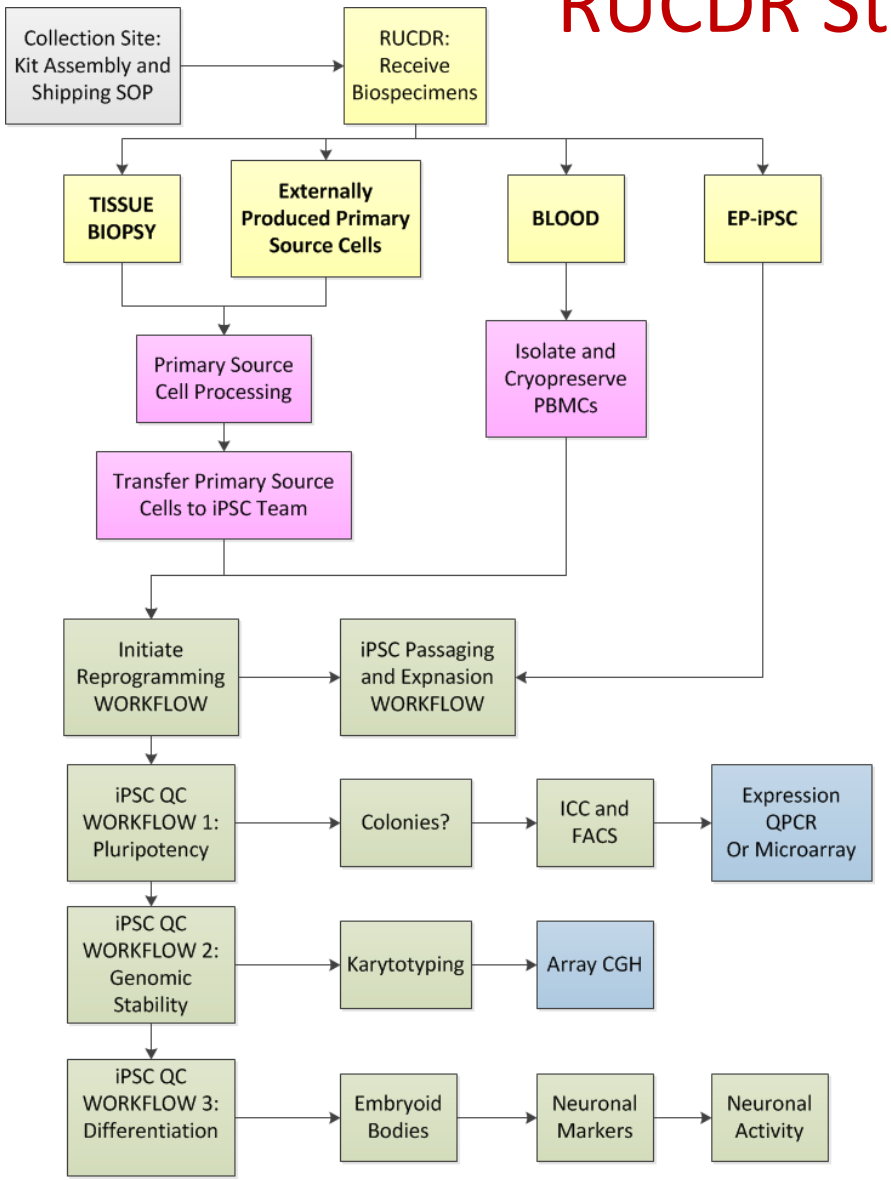


https://www.nimhgenetics.org/

NIMH-Supported Efforts Include:

- **2009-2013 (RFA-MH-09-130, ARRA, etc)**: generation of source cells (e.g., fibroblasts) and reprogrammed cells has occurred through individual competing research project grants rather than a unified derivation effort.
- **2011 (NOT-MH-10-024)**: Central repository to bank, validate & distribute iPSCs and source cells at Rutgers, integrated with NIMH Human Genetics Initiative; http://nimhstemcells.org/.
  - Steering Committee guides Q/C and validation processes.
  - Most lines from schizophrenia, bipolar disorder and autism spectrum disorders; first lines will be available in October 2013.
- **2012 (NOT-MH-13-002)**: Policy statement - NIMH grantees are expected to submit source cells and reprogrammed cells to NIMH repository.
  - Consents and sharing plans stipulate centralized banking and wide distribution, including to for-profit entities.

RUCDR Stem Cell Operations



Client

Communications

Primary Cell Team

iPSC Team

Genomics Team

RUCDR
INFINITE BIOLOGICS

nimhstemcells.org

nimh stem cell center a service of the rucdr

home | resources | catalog | crm | archive | contact us

mission

The purpose of the NIMH Stem Cell Center is to provide a resource for postnatal-to-adult human control and patient-derived cells and their reprogrammed derivatives; this repository will support stem cell research relevant to mental disorders. This includes but is not limited to anxiety disorders, attention deficit hyperactivity disorder, autism spectrum disorders, bipolar disorder, borderline personality disorder, depression, eating disorders, obsessive-compulsive disorder, panic disorder, post-traumatic stress disorder, and schizophrenia. The capabilities of the repository will range from derivation and banking of primary source cells from postnatal through adult human subject tissue to more comprehensive banking and validation of iPSCs or similar reprogrammed/de-differentiated cells.

nimh center for collaborative studies of mental disorders at rucdr

RUCDR is the National Institute of Mental Health (NIMH) Center for Collaborative Studies of Mental Disorders. We have established cell lines and DNA for this initiative since 1998. The NIMH collection now contains a vast array of samples from families with schizophrenia, bipolar disorder, Alzheimer's disease, autism, obsessive-compulsive disorder, depression, and ADHD. Many important discoveries have been made by investigators accessing these collections. There is a catalog listing cells available under the NIMH program.

The Center for Collaborative Genomic Studies on Mental Disorders is a collaboration of Rutgers University RUCDR, Washington University in St. Louis and the University of Southern California's Information Sciences Institute. It is funded by a grant from the National Institute of Mental Health.

nih center for regenerative medicine

RUCDR is the host for a collection of iPSC created by the NIH Center for Regenerative Medicine (CRM). There is a catalog of available lines.

rucdr

Rutgers University Cell and DNA Repository (RUCDR) plays a key role in research aimed at understanding the genetic causes of common, complex diseases. RUCDR activities will enable gene discovery leading to diagnoses, treatments and, eventually, cures for these diseases. RUCDR assists researchers throughout the world by providing the highest quality biomaterials, technical consultation, and logistical support.

news updates

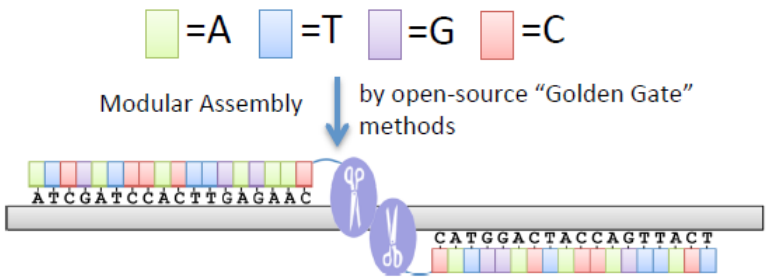
2013 World Congress on Psychiatric Genetics (WCPG). We have organized a symposium entitled "Induced Pluripotent Stem Cells: Tools for the Investigation of Neuropsychiatric Disorders" to be presented at the 2013 World Congress on Psychiatric Genetics on October Boston, MA. October 17-21, 2013.

We have been invited to participate in the International Coordination for Large Scale iPSCs Initiatives retreat being held at the

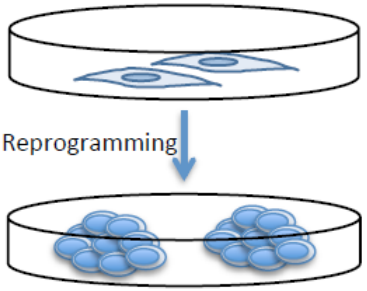
Disease-Specific iPSC Lines at RSCL

Catalog of induced Pluripotent Stem Cell (iPSC) and Source Cells available for distribution through the NIMH Stem Cell Resource						
Updated August 12, 2013						
Disorder	**Study #**	**Abstract**	**# of iPSC Lines**	**# of Fibroblast Lines**	**# of Olfactory Epithelium Lines**	**Projected Release Date**
Schizophrenia (22q11 Deletion)	125	R33MH087840	9	Approx.16		8/1/2013
Autism	116	R01MH089176	23	19		9/1/2013
Phelan McDermid	115	R33MH087898	--	35		10/1/2013
Autism (22q11.2 Deletion)	115	R33MH087898	60	Approx. 60		10/1/2013
Bipolar Disorder	130	R21MH093958	24	50		1/1/2014
Fragile X (Autism)	117	R33MH087925	8	--	--	2/1/2014
Schizophrenia & Bipolar Disorder	131	R01MH091115	Approx. 20	Approx. 20	--	6/1/2014
Bipolar Disorder	101	U01MH092758	--	Approx. 100		6/6/2015
Schizophrenia	92	RC2MH089973	--	35	--	To Be Announced
Schizophrenia	92	RC2MH089973	--	58	--	To Be Announced
Schizophrenia	127	--	--	8	9	To Be Announced
Schizophrenia (Childhood Onset)	132	ZIAMH002581	--	181	--	To Be Announced

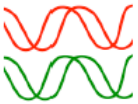
Genome Engineering in Human Stem Cells



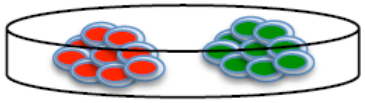
Sequence-specific Designer Nuclease



Self-renewing Human Stem Cells

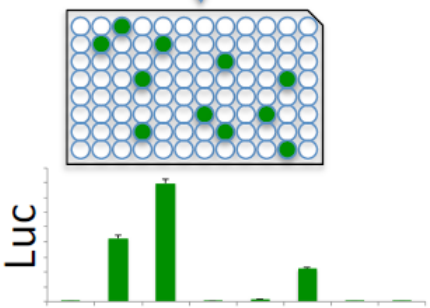


(+ Donor DNA)

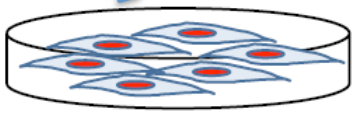


Select and expand **Engineered** stem cell lines

Isogenic Lines for Disease Modeling



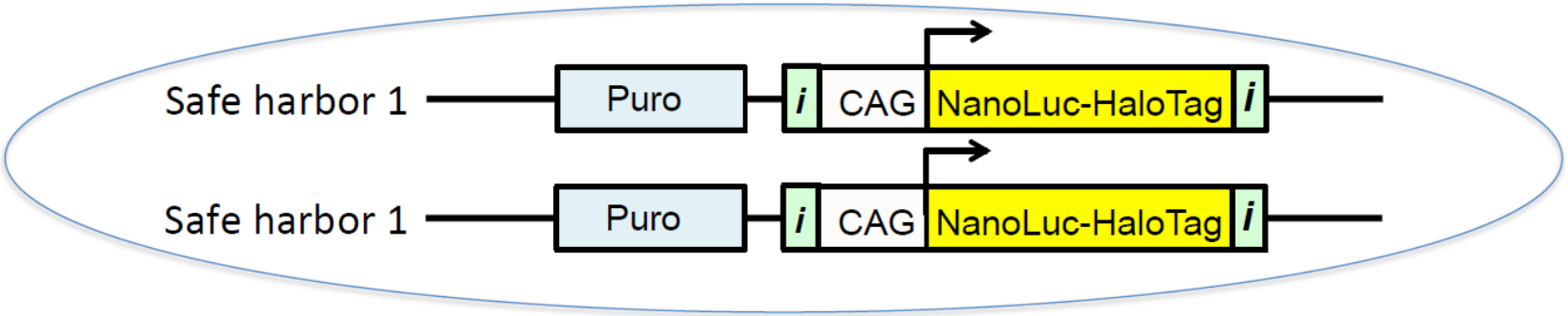
Reporter Lines for Drug Screening



cGMP Differentiation for Gene & Cell Therapy

Engineered Safe Harbor Reporter Lines

- Quantitative and Sensitive
- Stable Expression
- Useful for drug screening



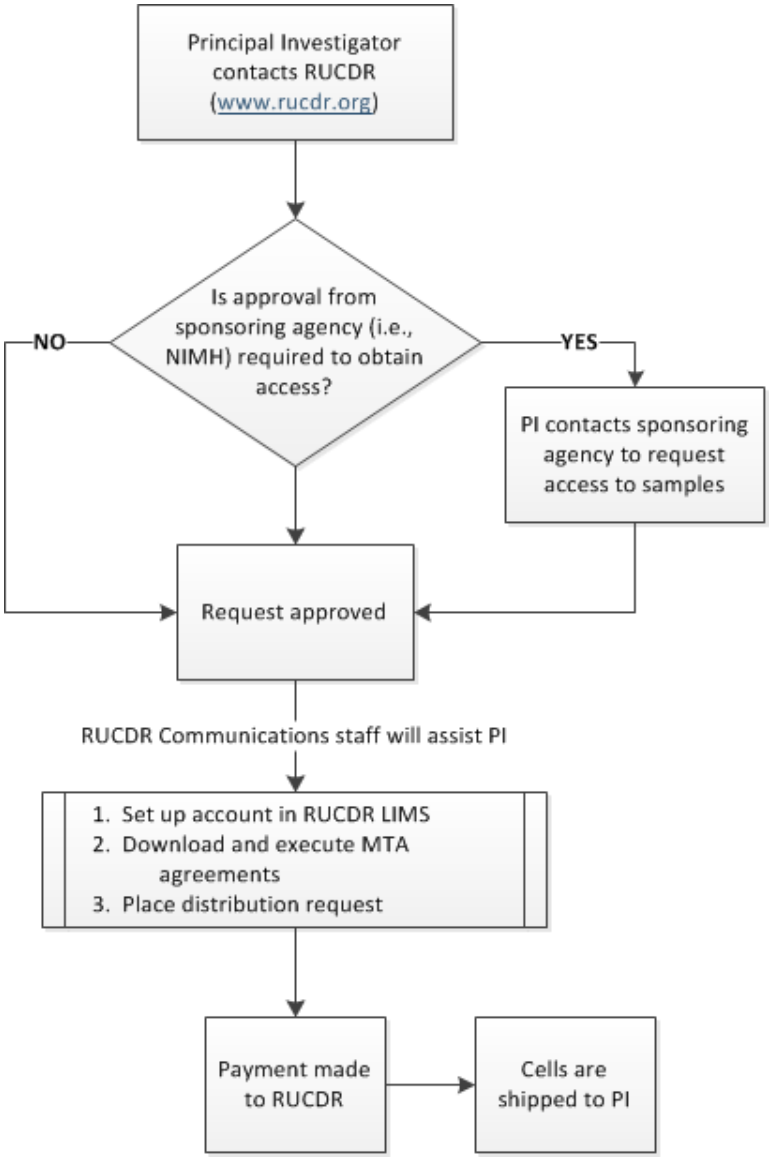
3 Lines available from RSCL later in 2013:

- copGFP with RMCE in C19 locus
- NanoLuc and Halotag in C13 locus
- NanoLuc and Halotag in C19 locus

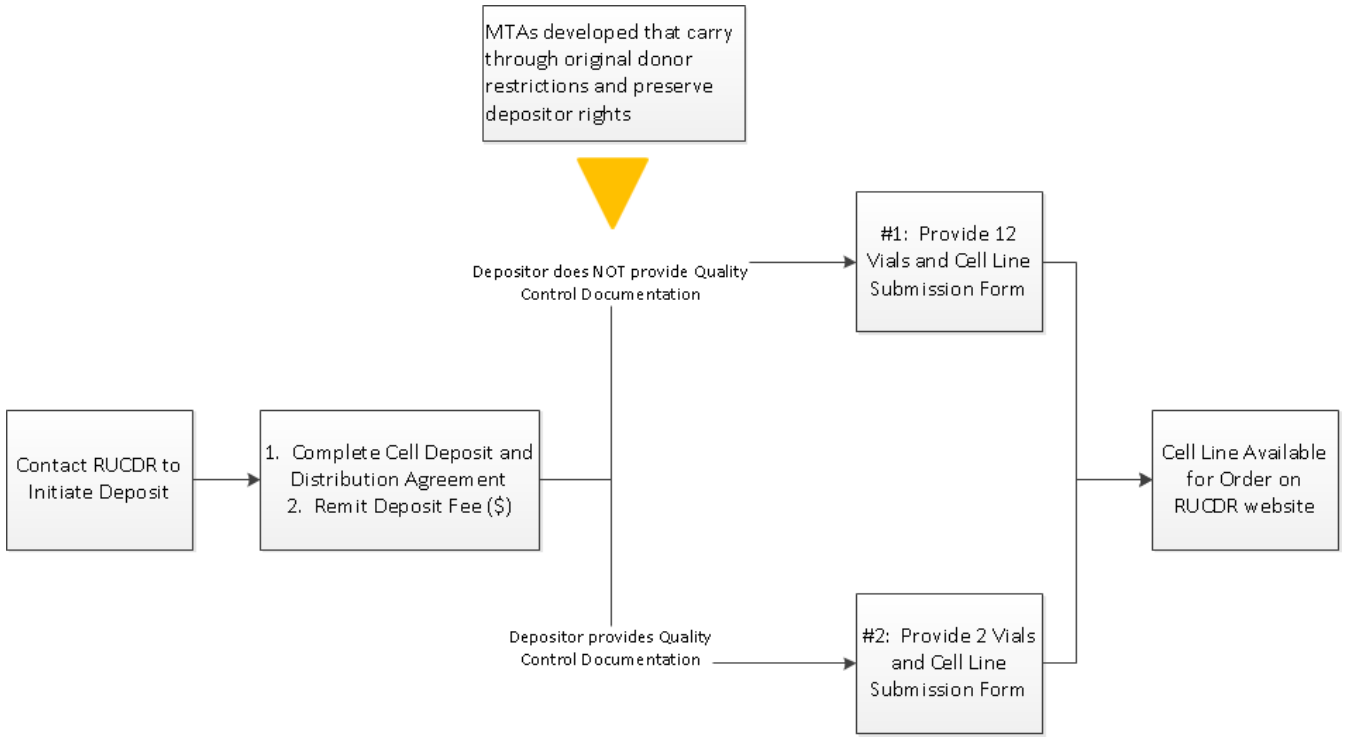
Control NIH-CRM iPSC Lines at RSCL

NIH Center for Regenerative Medicine iPSC Lines currently in distribution at RUCDR Infinite Biologics: August 2013					
Name or Designation	**Description**	**iPSC Reprogramming Method**	**Starting Material**	**Source**	**Currently Available ?**
NCRM-1	iPSC Control	Episomal Plasmid	CD 34+ Cord Blood	NIH CRM Lonza Contract	Yes
NCRM-2	iPSC Control	Episomal Plasmid	CD 34+ Cord Blood	NIH CRM Lonza Contract	Yes
NCRM-3	iPSC Control	Episomal Plasmid	CD 34+ Cord Blood	NIH CRM Lonza Contract	Yes
NCRM-4	iPSC Control	Episomal Plasmid	CD 34+ Cord Blood	NIH CRM Lonza Contract	Yes
NCRM-5	iPSC Control	Episomal Plasmid	CD 34+ Cord Blood	NIH CRM Lonza Contract	Yes
NCRM-6	iPSC Control	Episomal Plasmid	CD 34+ Cord Blood	NIH CRM Lonza Contract	Yes
ND1.4	iPSC Control	Episomal Plasmid	Fibroblast (ATCC)	University of Wisconsin	Yes
ND2.0	iPSC Control	Episomal Plasmid	Fibroblast (ATCC)	University of Wisconsin	Yes
CY2	iPSC Control	Episomal Plasmid	Blood	NIH CRM CDI Contract	Yes
NCRM5AS1-iCAGcGFP	iPSC line with copGFP with RMCE in C19 locus	Episomal Plasmid	NCRM5	Dr. Jizhong Zou (NIH CRM)	Coming soon
NCRM5C13-iCLHN	iPSC line with NanoLuc and Halotag in C13 locus	Episomal Plasmid	NCRM5	Dr. Jizhong Zou (NIH CRM)	Coming soon
NCRM5AS1-iCLHN	iPSC line with NanoLuc and Halotag in C19 locus	Episomal Plasmid	NCRM5	Dr. Jizhong Zou (NIH CRM)	Coming soon

Procedure for Obtaining RUCDR Cell Lines



Depositing Cell lines with RUCDR



Advantages and benefits :

- RUCDR rebanks as needed to assure continued availability
- Quality assurance
- Global distribution
- Save time and effort with MTA management done by RUCDR
- Customized terms of distribution (ie. only to academia) and timed release (ie. after publication)

The RUCDR Stem Cell Laboratory

Operational Overview

Jennifer Moore, Ph.D.
Associate Director, Stem Cell Laboratory, RUCDR
Assistant Professor of Genetics
Rutgers University
moore@biology.rutgers.edu
http://www.RUCDR.org

RUCDR
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Services Offered to the Stem Cell Community by RUCDR

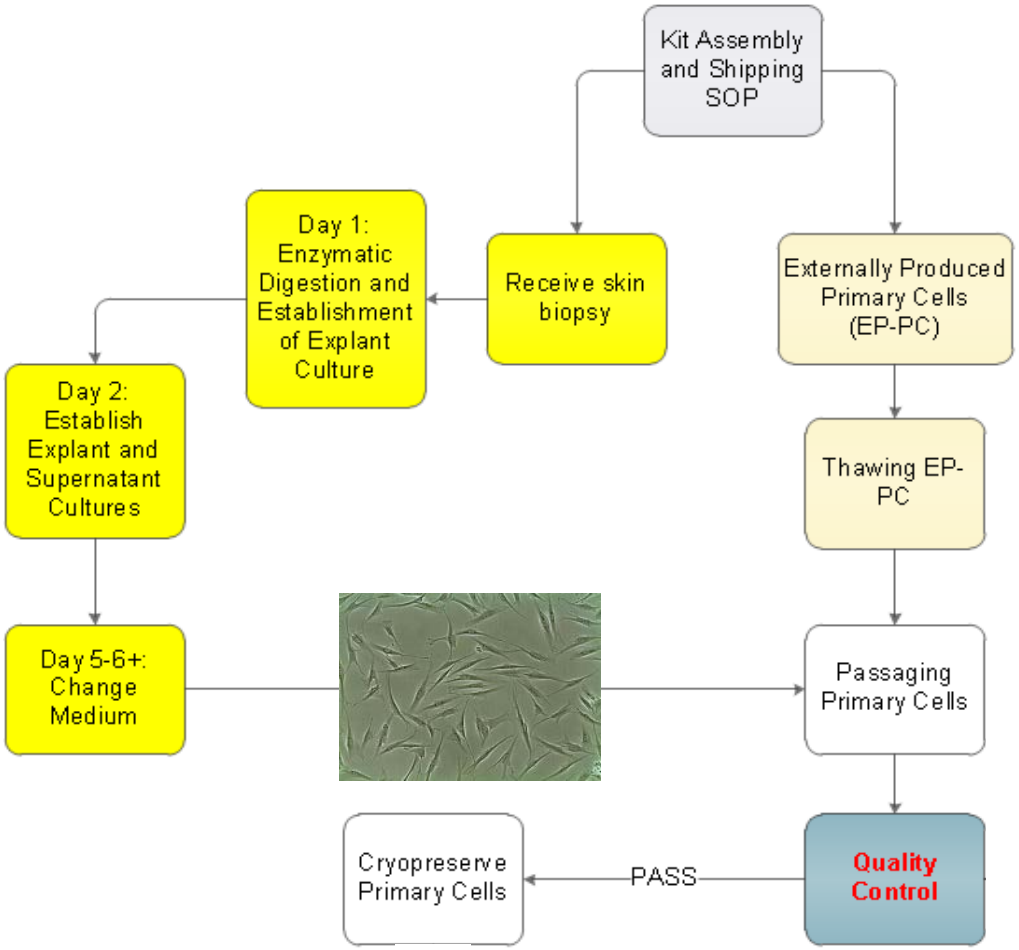
1. Cryopreserve and Distribute the highest quality primary and iPS cells.

2. Culturing primary source cells from tissue biopsies or frozen stocks submitted for banking. Assist clients in tissue collection and shipment as needed.

3. Provide a resource for reprogramming primary cells to iPSC and/or propagating iPSC submitted by clients.

4. Establish a rigorous Quality Control workflow for all cell types.

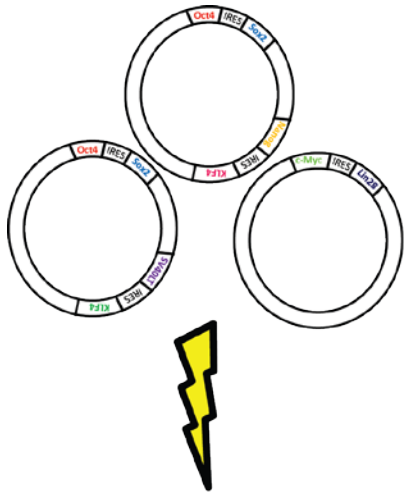
Biopsy and Fibroblast Workflow

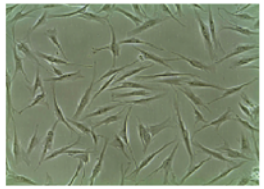


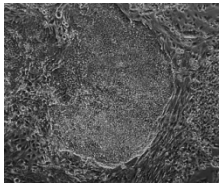
Source Cell Reprogramming

Fibroblasts	Cryopreserved Lymphocytes	Lymphoblastoid Cell Lines	Olfactory Epithelium
Episomal Vectors	Sendai Viral Vectors	Episomal Vectors	Episomal Vectors
Renewable Resource	Semi-Renewable Resource	Renewable Resource	Renewable Resource
>50	>150	>25	N/A

Reprogramming with Episomes







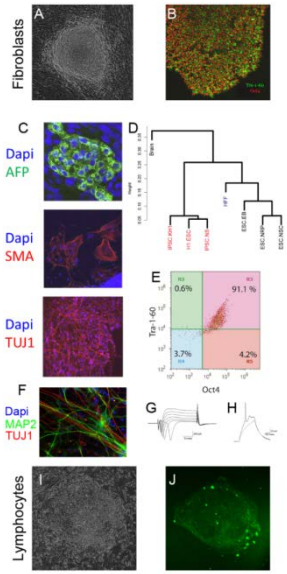


Plate on MG in RM medium

24 hours in suspension in RPMI

~14 days in RM medium

~10-14 days in mTeSR medium

~18 days in RM medium

~12-18 days in RM medium

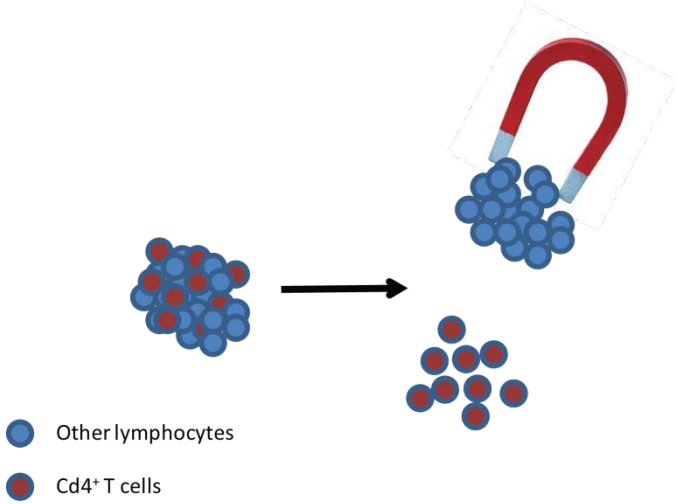
Select Reprogrammed Colonies

mTeSR and MG

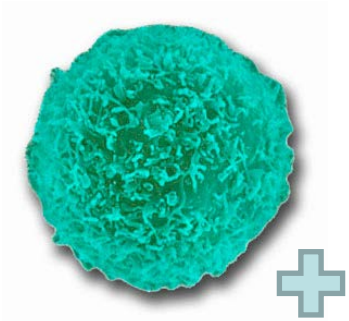
iPSC Characterization

Reprogramming with Sendai Viral Vectors

Lymphocytes

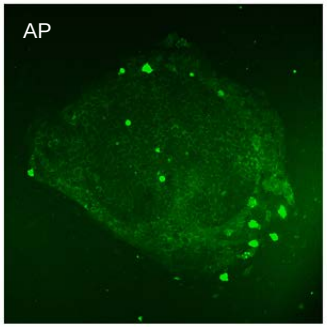


CD4⁺ T cell



Activate
- **CD3**
- **CD28**
- **IL-2**

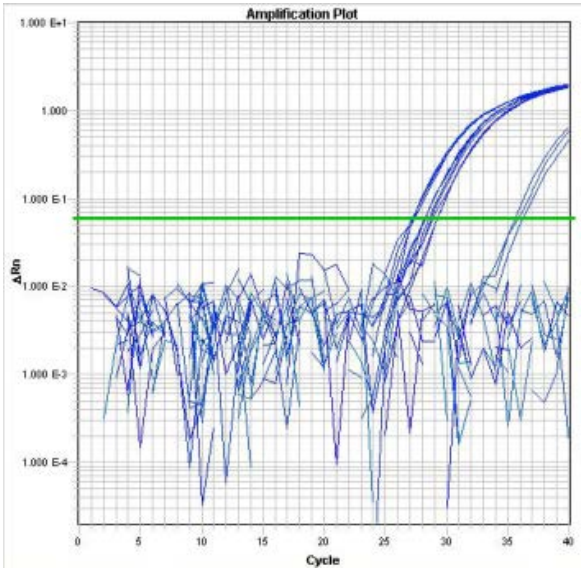
Sendai vectors
- **Oct4**
- **Sox2**
- **Klf4**
- **c-Myc**



Moore, Sheldon & Hart (2012) BioBanking in the era of the stem cell

Quality Control – Standard Panel (Included for all lines generated)

- Mycoplasma
- RUID SNP
- Viability



Quality Control – Standard Panel (Included for all lines generated)

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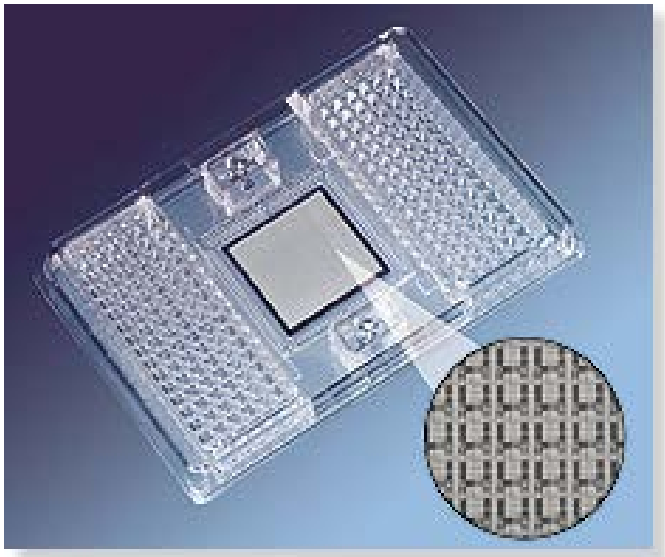
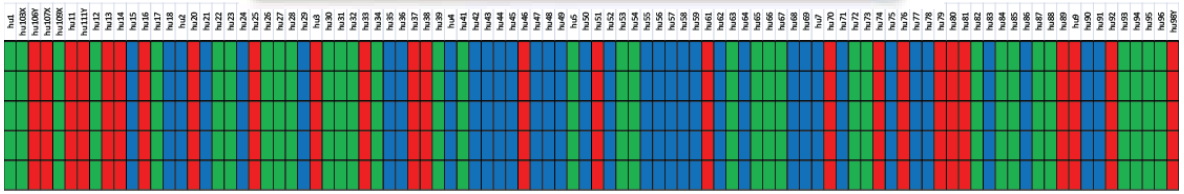
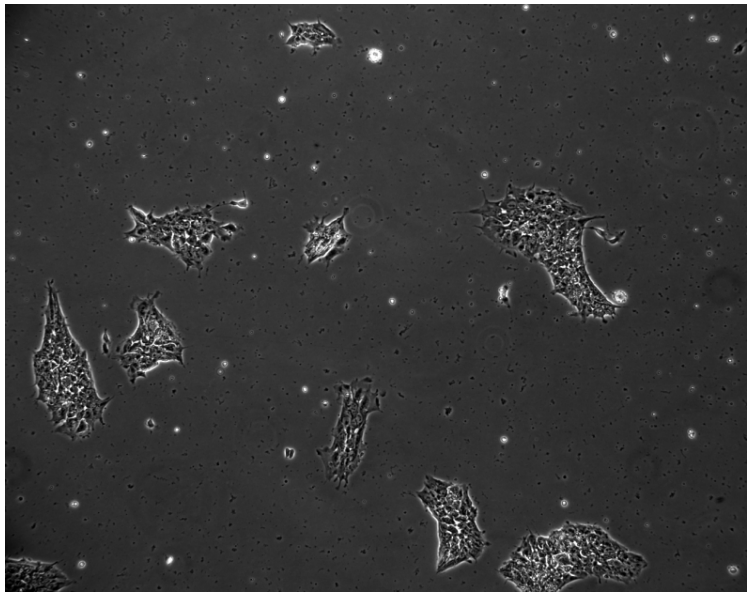
- RUID SNP
- Viability





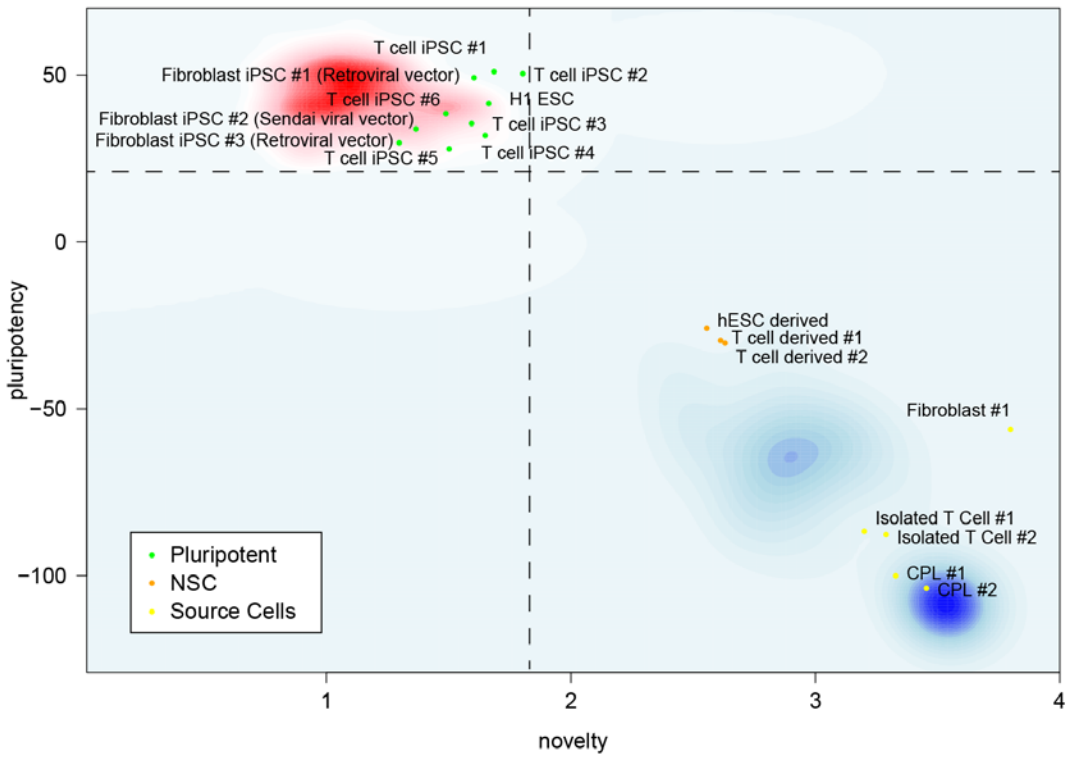
Quality Control – Standard Panel (Included for all lines generated)

- Mycoplasma
- RUID SNP
- Viability



Quality Control – Pluripotency

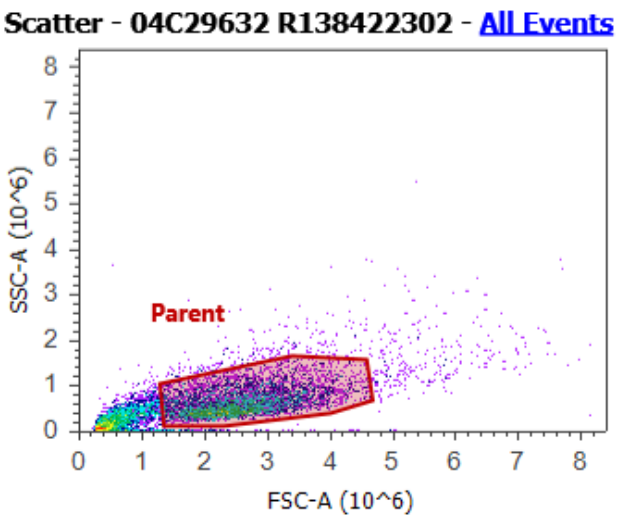
- Pluritest
- FACS
- IHC
- AP Staining

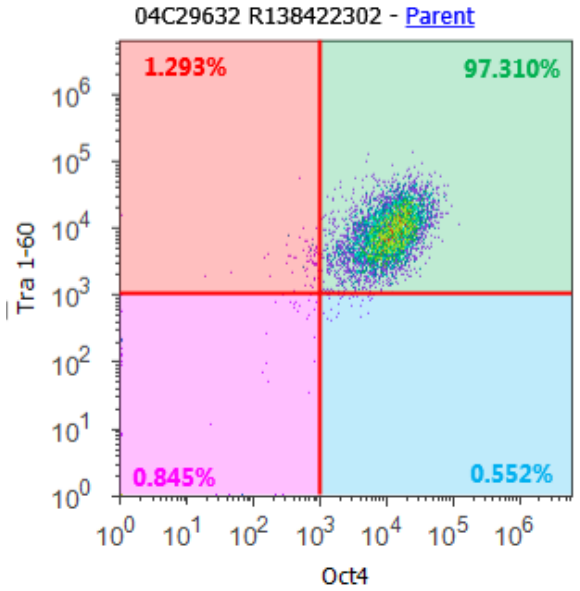


Muller FJ, Schuldt BM, Williams R, Mason D, Altun G, Papapetrou EP, Danner S, Goldmann JE, Herbst A, Schmidt NO, Aldenhoff JB, Laurent LC, Loring JF. A bioinformatic assay for pluripotency in human cells. Nature Methods (8), 315-317. 2011

Quality Control – Pluripotency

- Pluritest
- FACS
- IHC
- AP Staining





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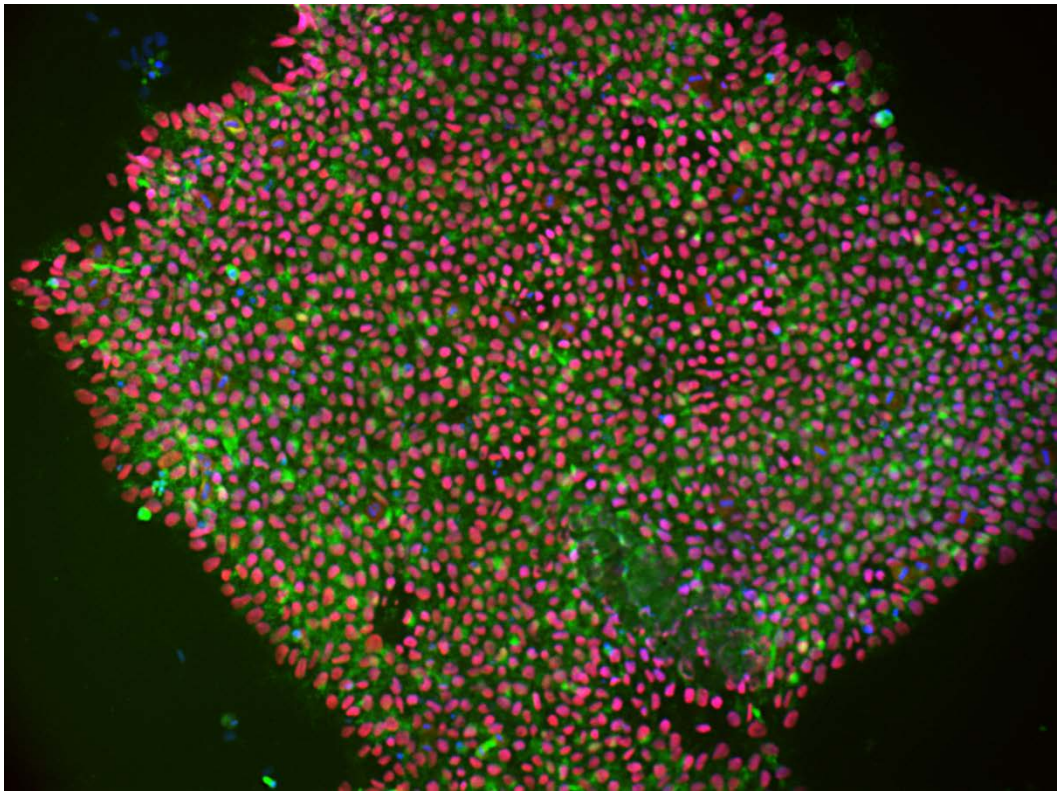
Quality Control – Pluripotency

- Pluritest
- FACS
- IHC
- AP Staining



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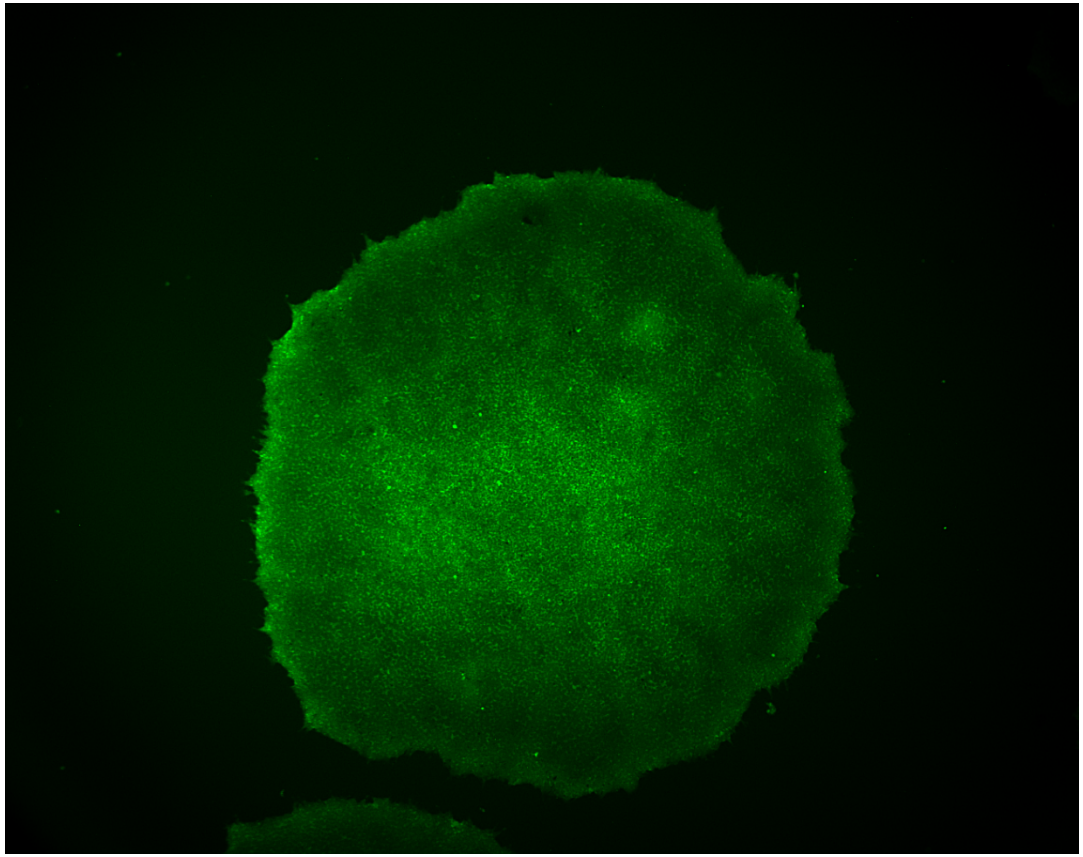
Quality Control – Pluripotency

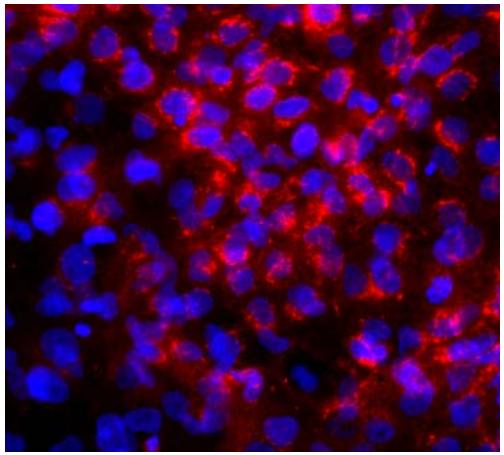
- Pluritest
- FACS
- IHC
- AP Staining



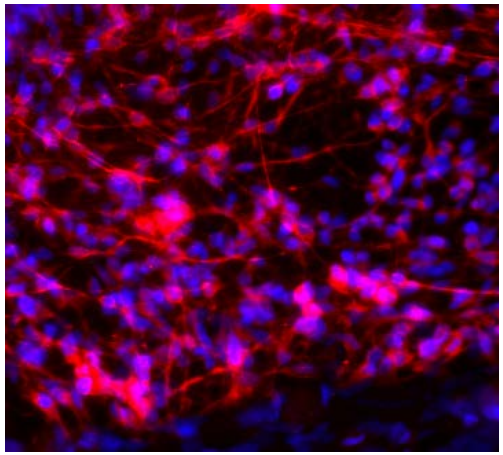
Muller FJ, Schuldt BM, Williams R, Mason D, Altun G, Papapetrou EP, Danner S, Goldmann JE, Herbst A, Schmidt NO, Aldenhoff JB, Laurent LC, Loring JF. A bioinformatic assay for pluripotency in human cells. Nature Methods (8), 315-317. 2011

Quality Control – Differentiation

AFP



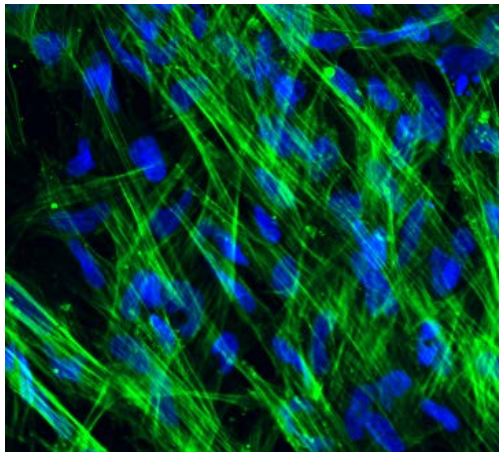
MAP2



Embryoid Bodies

Teratomas

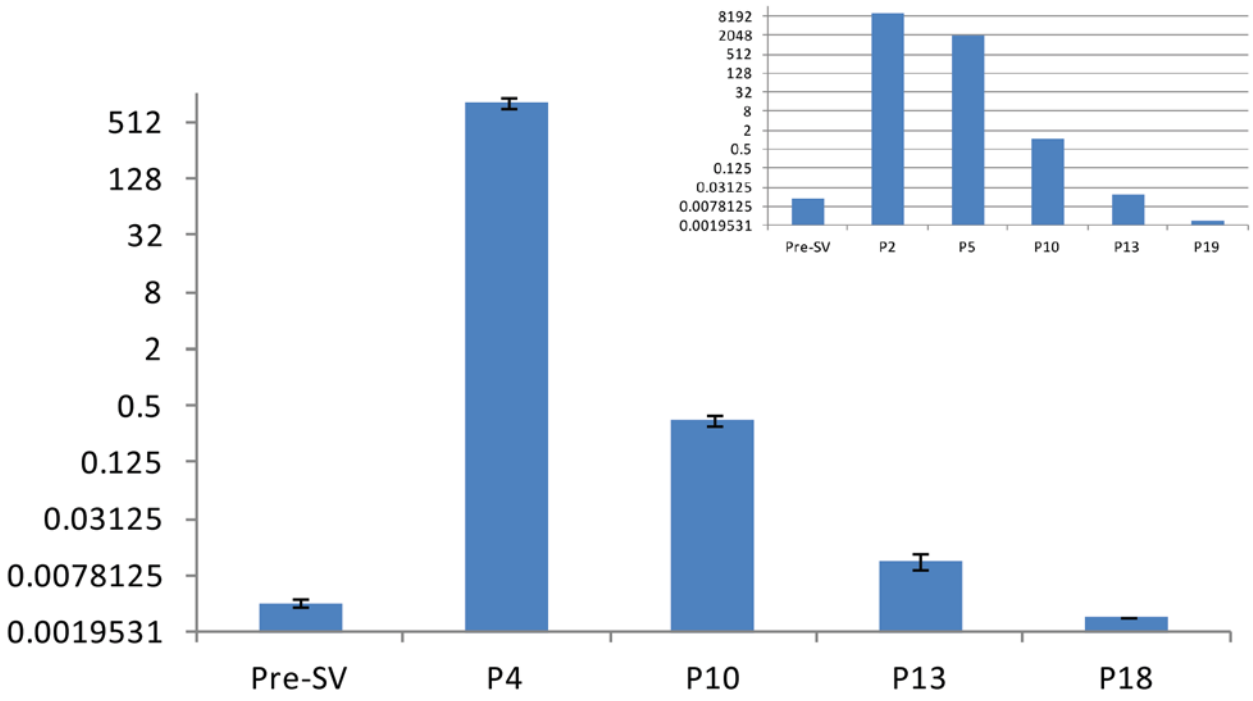
SMA



Quality Control – Loss of Reprogramming Factors

Sendai Persistence Assay

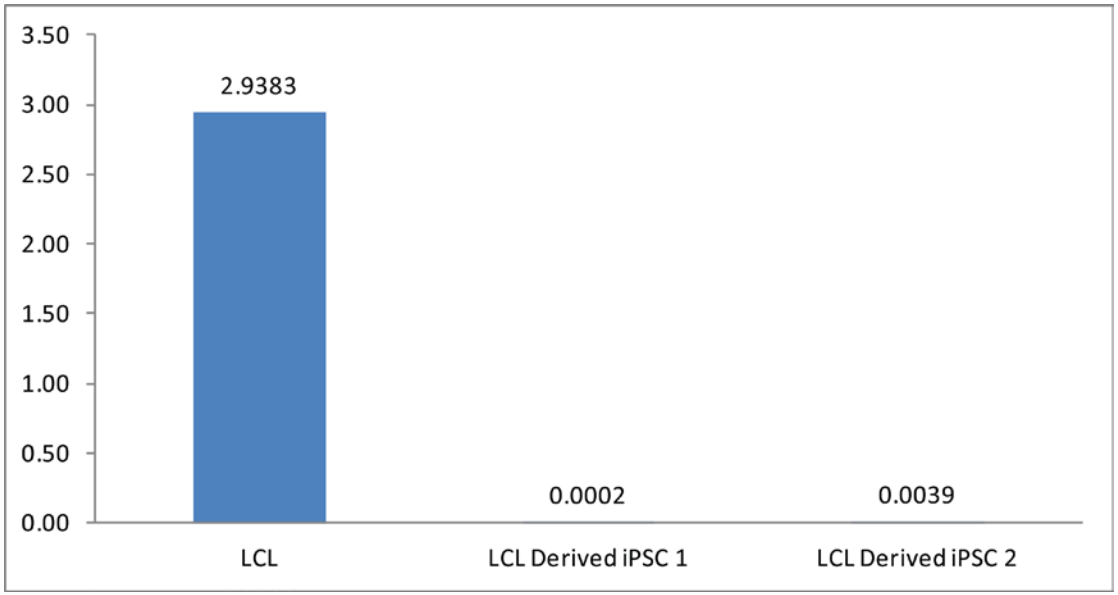
EBV Persistence Assay



Quality Control – Loss of Reprogramming Factors

Sendai Persistence Assay

EBV Persistence Assay



iPSC Produced at Rutgers

>250 iPSC lines completed (~85 subjects)

Episomes/EBV-lymphocyte lines
- •Alcoholism
- •Autism
- •Alzheimer's
  (86-year-old subject;
  Cells frozen 18 years ago)

Episomes/fibroblasts
- •Schizophrenia

Sendai/Lymphocytes
- •Addiction
- •Alcoholism
- •Schizophrenia
- •Tourette's
- •TSC
- •Autism

RUCDR Leadership Team and Collaborators

Andrew Brooks, PhD
Technology Director & COO

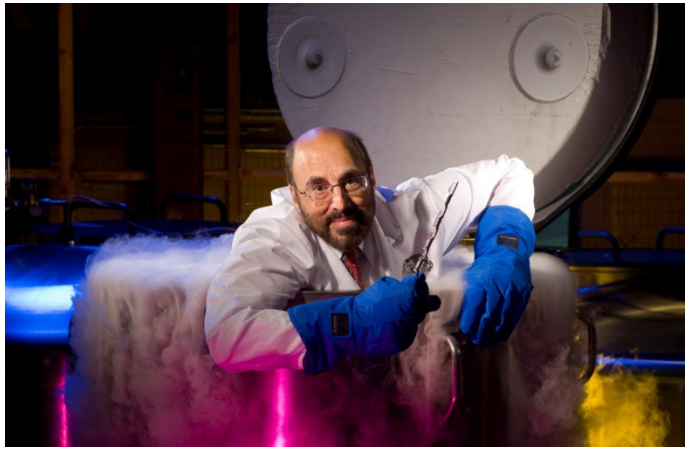
Douglas Fugman, PhD
Lymphocyte Lab Director

Amrik Sahota, PhD, FACMG
Clinical & Regulatory Compliance Director

David Toke, PhD
Biomaterials QA Director

Michael Sheldon, PhD
Stem Cell Lab Director

Linda Brzustowicz, MD
Phenotype Quality Director



Jay Tischfield, PhD, FFACMG
Scientific Director & CEO

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Stem Cell Lab Assoc. Director

Ron Hart, PhD
Rutgers University

Dana Witt
Communications Director

Jack Schrum, AOS, BA
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Sanghamitra Pati, MBA
Finance Director

Janet McKim
Development Director