STEM CELL-BASED MEDICINE

MIKE MCCONNELL, Ph.D.

ASSISTANT PROFESSOR
DEPARTMENT OF BIOCHEMISTRY AND MOLECULAR GENETICS
UNIVERSITY OF VIRGINIA
SCHOOL OF MEDICINE

mikemc@virginia.edu
How do human genomes encode human brains?

Human induced Pluripotent Stem Cells

Human Genomes in-a-dish

Human Neurons in-a-dish

Single Cell Genomics

Neurological Disease
Twin Discordance (i.e. individuality)

METHOD OF THE YEAR

"We are just beginning to understand the molecular diversity of cells in the brain," says Thomas Insel, director of the US National Institute of Mental Health. "Single-cell methods will be critical, not only for defining the taxonomy of neurons and glia but for revealing the effects of experience or development on profiles of expression within a brain region."

Mosaic Copy Number Variation in Human Neurons

Duplication

Deletion

McConnell, et al. (2013) Science
Embryonic Stem Cells (hESCs)

- exist only at the earliest stages of embryonic development.

- In humans, these cells no longer exist after about five days of development.

- When grown in a lab dish these hESCs can continue dividing indefinitely.

- James Thomson, a professor of Anatomy at the University of Wisconsin, isolated and first propagated hESCs in 1998.
Restricted Fate Potential during Development

Waddington (1942) “epigenetic landscape”
Induced Pluripotent Stem Cells (iPSCs) Reprogramming Adult Cells

Induction of Pluripotent Stem Cells from Mouse Embryonic and Adult Fibroblast Cultures by Defined Factors

Kazutoshi Takahashi¹ and Shinya Yamanaka¹,²,*
¹ Department of Stem Cell Biology, Institute for Frontier Medical Sciences, Kyoto University, Kyoto 606-8507, Japan
² CREST, Japan Science and Technology Agency, Kawaguchi 332-0012, Japan
* Contact: yamanaka@frontier.kyoto-u.ac.jp
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Candidate Pluripotency factors:

<table>
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<tr>
<th>Ecat1</th>
<th>Sox15</th>
<th>Utf1</th>
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<td>Dppa5</td>
<td>Dppa4</td>
<td>Tel1</td>
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<td>Dppa2</td>
<td>Dppa3</td>
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<td>ERas</td>
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<tr>
<td>Dnmt3l</td>
<td>Oct3/4</td>
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<tr>
<td>Ecat8</td>
<td>Sox2</td>
<td>Stat3</td>
</tr>
<tr>
<td>Gdf3</td>
<td>Rex1</td>
<td>Grb2</td>
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</tbody>
</table>
Induced Pluripotent Stem Cells (iPSCs)

All 24 factors together can reprogram fibroblasts
Induced Pluripotent Stem Cells (iPSCs)

Subtraction Experiments to Find Minimal Combination of Factors
Induced Pluripotent Stem Cells (iPSCs)

Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors

Kazutoshi Takahashi,¹ Koji Tanabe,¹ Mari Ohnuki,¹ Megumi Narita,¹,² Tomoko Ichisaka,¹,² Kiichiro Tomoda,³ and Shinya Yamanaka¹,²,³,⁴,*

¹Department of Stem Cell Biology, Institute for Frontier Medical Sciences, Kyoto University, Kyoto 606-8507, Japan
²CREST, Japan Science and Technology Agency, Kawaguchi 332-0012, Japan
³Gladstone Institute of Cardiovascular Disease, San Francisco, CA 94158, USA
⁴Institute for Integrated Cell-Material Sciences, Kyoto University, Kyoto 606-8507, Japan
*Correspondence: yamanaka@frontier.kyoto-u.ac.jp
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Yamanka four factors (OKSM)
Oct4
Klf4
Sox2
c-Myc
hiPSCs
hiPSCs

TRA-1-60

OCT4

SSEA4

TRA-1-81
hiPSC-derived cardiomyocytes

Cardiomyocytes

In-A-Dish!

Cardiomyocytes

In-A-Dish!

hiPSC-derived cardiomyocytes

hiPSC-derived cardiomyocytes

Cardiomyocytes

In-A-Dish!

hiPSC-derived Neurons
hiPSC-derived MSCs
1) Provide control hiPSCs and CRISPR-derived isogenic lines.

2) Provide hiPSC-derived lineages (NPCs, Neurons, Cardiomyocytes, others).

2) Provide hands-on training in hiPSC culture for students, post-docs, others.

1) Provide project-based support for generation of patient-derived hiPSC lines.

1) Stem Cells and Regeneration Seminar Series.

Director: Araz Toumadje
ph. 434.297.5302
at5kh@virginia.edu
hiPSC-based Medicine

Induced pluripotent stem cells: the new patient?

Milena Bellin¹, Maria C. Marchetto², Fred H. Gage² and Christine L. Mummery¹
Japanese woman is first recipient of next-generation stem cells

Surgeons implanted retinal tissue created after reverting the patient's own cells to 'pluripotent' state.

In a two-hour procedure starting at 14:20 local time today, a team of three eye specialists lead by Yasuo Kurimoto of the Kobe City Medical Center General Hospital, implanted a 1.3 by 3.0 millimetre sheet of retinal pigment epithelium cells into an eye of the Hyogo prefecture resident, who suffers from age-related macular degeneration, a common eye condition that can lead to blindness.
hiPSC-derived Retina

Assawachananont, et al. (2014) Stem Cell Reports
1) Provide control hiPSCs and CRISPR-derived isogenic lines.

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