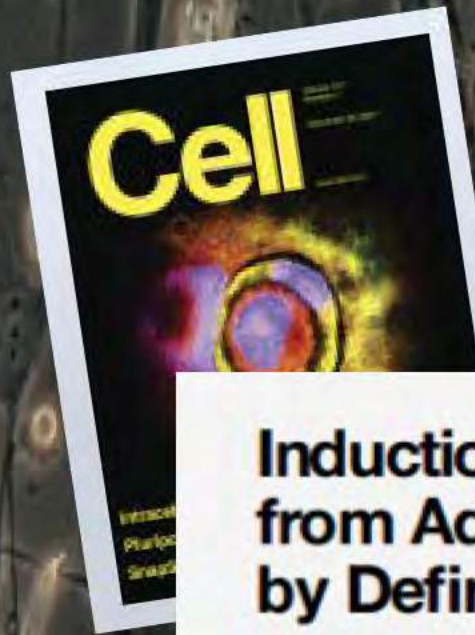


# November 2007



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

Kazutoshi Takahashi,<sup>1</sup> Koji Tanabe,<sup>1</sup> Mari Ohnuki,<sup>1</sup> Megumi Narita,<sup>1,2</sup> and Shinya Yamanaka<sup>1,2,3,4,\*</sup>

<sup>1</sup>Department of Stem Cell Biology, Institute for Frontier Medical Sciences, Kyoto University, Kyoto, Japan  
<sup>2</sup>CREST, Japan Science and Technology Agency, Kawaguchi 332-0012, Japan  
<sup>3</sup>Gladstone Institute of Cardiovascular Disease, San Francisco, CA 94158, USA  
<sup>4</sup>Institute for Integrated Cell-Material Sciences, Kyoto University, Kyoto 606-8501, Japan  
 \*Correspondence: yamanaka@frontier.kyoto-u.ac.jp  
 DOI 10.1016/j.cell.2007.11.019

### SUMMARY

Successful reprogramming of differentiated human somatic cells into a pluripotent state would allow creation of patient- and disease-specific stem cells. We previously reported generation of induced pluripotent stem (iPS) cells, capable of germline transmission, from mouse somatic

issues is to induce pluripotent status in somatic cells by direct reprogramming (Yamanaka, 2007).

We showed that induced pluripotent stem (iPS) cells can be generated from mouse embryonic fibroblasts (MEF) and adult mouse tail-tip fibroblasts by the retrovirus-mediated transfection of four transcription factors, namely Oct3/4, Sox2, c-Myc, and Klf4 (Takahashi and Yamanaka, 2006). Mouse iPS cells are indistinguishable from

## Induced Pluripotent Stem Cell Lines Derived from Human Somatic Cells

Junying Yu,<sup>1,2</sup> Martin A. Bradley,<sup>1</sup> Kim Sangho Cho,<sup>1,2</sup> Jessica Anwarvic-Simpson,<sup>1,2</sup> Jennifer L. Frerking,<sup>1</sup> Blake Nisler,<sup>1</sup> Jeff Wu,<sup>1</sup> Gidon A. Jureidat,<sup>1</sup> Victor Bocharov,<sup>1</sup> and Shoukhrat M. Izpisua-Belmonte<sup>1,2,3,4,5,6</sup>

Somatic cell nuclear transfer allows transposing factors present in the mammalian zygote to reprogram somatic cell nuclei to an undifferentiated state. We show that four factors (SOX2, OCT4, KLF4, and MYC) are sufficient to reprogram human somatic cells to pluripotent stem cells that give rise to all somatic cell types, express pluripotency markers, and maintain pluripotency in culture. These induced pluripotent stem cells are indistinguishable from embryonic stem cells and resemble embryonic stem cells in their ability to be used in the production of mouse chimeras and in the generation of transgenic mice. Our findings indicate that human cell reprogramming can be achieved using a defined set of transcription factors.

Mouse embryonic stem (ES) cell development is initiated by reprogramming of somatic cells. This process is initiated by reprogramming factors that are expressed in the zygote and in the inner cell mass of the blastocyst. The reprogramming factors that are expressed in the inner cell mass are Oct4, Sox2, Klf4, and Myc. These factors are sufficient to reprogram somatic cells to pluripotent stem cells. We show that four factors (SOX2, OCT4, KLF4, and MYC) are sufficient to reprogram human somatic cells to pluripotent stem cells. These induced pluripotent stem cells are indistinguishable from embryonic stem cells and resemble embryonic stem cells in their ability to be used in the production of mouse chimeras and in the generation of transgenic mice. Our findings indicate that human cell reprogramming can be achieved using a defined set of transcription factors.

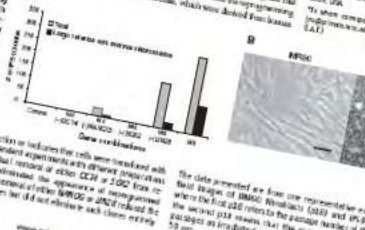


Fig. 2. 100% of somatic cells can be reprogrammed to pluripotent stem cells. (A) Bar graph showing the percentage of iPS cells derived from various somatic cell types. (B) Micrographs showing the morphology of iPS cells derived from different somatic cell types.

REPORTS  
 ES cell derived (EN) human somatic cells (7, 8). ES cell morphology (Fig. 2B) is similar to that of ES cells. These ES cell-derived cell surface markers are indistinguishable from those obtained by using either of the 14 ES cell lines.

ES cell lines derived from 14 ES cell lines, we identified a core set of 4 genes (OCT4, SOX2, KLF4, and MYC) that were common to all ES cell lines. Reexpression of either OCT4 or SOX2 alone in somatic cells was sufficient to initiate reprogramming. Reexpression of both OCT4 and SOX2 showed a synergistic effect in the reprogramming of somatic cells (Fig. 1A).

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# Science Spin: iPS Cell Research in the News

T Caulfield<sup>1</sup> and C Rachul<sup>2</sup>

MADELEINE BRAND and JOE PALCA

GETTY IMAGES



## Embryo cloning should cease

Research should focus on work that doesn't compromise ethics

Calgary Herald

Certain things need to firmly remain taboo in an enlightened society. One of them is performing ghoulish replications of human embryos just for the sake of it, and the other is creating human life, only to kill it for the purposes of science.

Research has come up with a new approach that liberates stem cell work from its moral shadows. It should be embraced for its impeccable ethics.

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...since the discovery of DNA:  
...free way to produce genetically-matched stem cells.

teacher

- King atten
- policeman

# Reality

Published online 13 May 2011 | Nature | doi:10.1038/news.2011.286

News

## Reprogrammed cells trigger immune reactions in mice

Medical applications of induced pluripotent stem cells called into question.

Erika Check Hayden

Cells that have been reprogrammed to grow into different types of tissue might be rejected by the body — even when transplanted into the individual from whom they were made, researchers report in a study published today in Nature.

## Technical challenges in using human cells to model disease

Krishanu Saha<sup>1</sup> and Rudolf Jaenisch<sup>1,2</sup>

Published online 2 February 2011 | Nature 470, 13 (2011) | doi:10.1038/470013a

News

Cell Stem Cell

## Perspective

### Inducing iPSCs to...

Bonnie Barrilleaux<sup>1,2,3</sup> and Paul...

hum  
alter  
chan  
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...ing pairs of

Induced pluripotent stem cells (iPSCs) hold great promise for autologous cell therapies, but significant roadblocks remain to translating iPSCs to the bedside. For

The field of induced pluripotent stem cells has grown up fast. Now it is entering the difficult stage.

BY ERIKA CHECK HAYDEN



# iPS Cells ELSI Challenges

## Gold Standards in the Diamond Age The Commodification of Pluripotency

Douglas Sipp<sup>1,\*</sup>

<sup>1</sup>RIKEN Center for Developmental Biology, 2-2-3 Minatojima Minami-ku, Kobe 650-0047, Japan

\*Correspondence: sipp@cdb.riken.jp

DOI 10.1016/j.stem.2009.09.005

Human embryonic stem cells have been characterized as a rare and precious resource because of the scarcity of the materials used in their derivation and the many restrictions that have been placed on their derivation and use. With the advent of induced pluripotent stem cells, however, pluripotency stands to become a plentiful and unencumbered commodity.

Raise more debate in Canada, experts say

By [Name] Postmedia News

Stem Cell Rev (2009) 5:135-139  
DOI 10.1007/s12015-009-9059-z

Transla **Product Regulation and the Clinical Translation  
of Stem Cell Research**

Barbara von Tigerstrom

Banned/Regulated?

# Triploid "Clones"

Health care on  msnbc.com

**AR** Don't fear the cloned human stem cells: They're not people

By Arthur Caplan, Ph.D.

The New York Times

## Human Stem Cells After Setbacks in Harvesting Approach Shows Promise

By NICHOLAS WADE

Published: October 5, 2011

...mez, Kathleen Crumm Satriani<sup>3,4</sup>, Robert Prosser<sup>3,4</sup>, Kiboong Oum<sup>3,4</sup>, ...eeby<sup>5,6</sup>, Ellen Greenberg<sup>5,6</sup>, Kun Zhang<sup>2</sup>, Robin Goland<sup>5,6</sup>, Mark V. Sauer<sup>3,4</sup>,

By a lucky accident as part of a control experiment, they left an oocyte's nucleus in place when they implanted an adult nucleus. They noticed that in the presence of the oocyte nucleus, embryos with an inserted adult cell nucleus developed much further than usual. They progressed, in fact, to the blastocyst stage, the point at which embryonic stem cells can be harvested, the researchers report in the Wednesday issue of Nature.

... abnormalities. In contrast, ... added, the resultant triploid cells develop to the blastocyst stage. Stem cell lines derived from these blastocysts differentiate into cell types of all three germ layers, and a pluripotent gene expression program is established on the genome derived from the somatic cell. This result demonstrates the feasibility of reprogramming human cells using oocytes and identifies removal of the oocyte genome as the primary cause of developmental failure after genome exchange.

# Banned by our (hype informed) law?

## Assisted Human Reproduction Act

5. (1) No person shall knowingly

(a) create a human clone by using any technique, or transplant a human clone into a human being or into any non-human life form or artificial device;

(b) create an *in vitro* embryo for any purpose other than creating a human being or improving or providing instruction in assisted reproduction procedures;

"human clone" means an embryo that, as a result of the manipulation of human reproductive material or an *in vitro* embryo, contains a diploid set of chromosomes obtained from a single -- living or deceased -- human being, fetus or embryo.

"embryo" means a human organism during the first 56 days of its development following fertilization or creation, excluding any time during which its development has been suspended, and includes any cell derived from such an organism that is used for the purpose of creating a human being.

# Justifications for the ban?

Leaders  
outraged  
by alleged  
cloning

REASONS FOR JUDGMENT:  
(paras. 1 to 156)

McLachlin C.J. (Binnie, Fish and Charron JJ. concurring)

Anti-abortion  
march focuses  
on stem cell bill

“baby farms”

“dehumanize motherhood”

commodification of reproductive materials

The production of human life in clandestine facilities


Modest (important) research technique



## METH

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**Human bodies:**  
donation for medicine  
and research

NUFFIELD  
COUNCIL ON  
BIOETHICS

Give your eggs to science, get paid, suggests new report - October 10, 2011

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# Science Policy Machine

**Science, Speculation &  
Social Concerns**

*problem?* **Simplify/Crystallize/Distort?**  
hype/political agendas

**Policy/Legal  
recommendations**

*evidence?*

Distracts from real issue, policy responses may not address real issue, deflect policy discussion, polarize debate etc...

# Lessons?

Science moves at a snail's pace...

Is current policy based on  
hyped/distorted portrayals of  
harms/benefits?

If yes, do rationales still have  
relevance? Time to revisit?

Learn from and move beyond  
this era of "hype policy" ....

# Thank you!

Ubaka Ogbogu, Erin Nelson, Amy Zarzeczny, Zubin Master, Robyn Hyde-Lay, Christine Rachul, Nina Hawkins, and the UofA team!



Cancer Stem Cell  
Consortium (CSCC)

Stem Cell  
Network Réseau de  
cellules souches



UNIVERSITY OF ALBERTA  
FACULTY OF LAW  
Health Law and Science Policy Group