### Stem Cells

Bioengineering 100 Fall 2016



STEM CELLS



"You want to be a brain cell? You have to study! You goof off - you'll end up in the rectum!"

# 2001 Bush issues executive order restricting stem cell research





### Methods of reprogramming (RP) Nuclear transfer Cell transfusion Somatic cell Oocyst without nucleus Blastcyte ES cell Somatic cell Pluripotent cell (ES cell, iPS cell) Direct RP RP through cell extracts Somatic cell Somatic cell **I**XXXXXXXXX ES cell **1**000000000 Cell Transcriptional factors Susumu Miyazaki et al. Jpn. J∖ Clin. Op∕col. extracts 2012;42:773-779

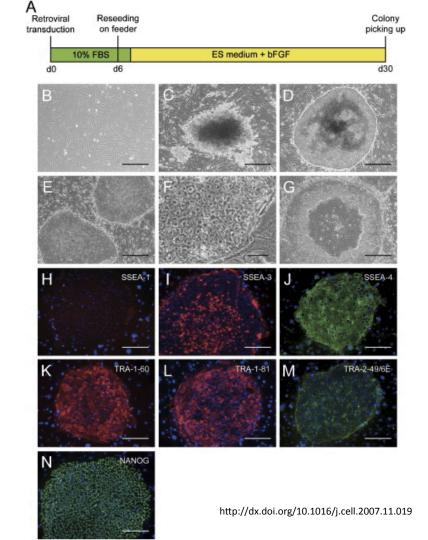
### August 2006: mouse iPS paper



Shinya Yamanaka Kyoto University and The Gladstone Institutes for Cardiovascular Disease, University of California, San Francisco

# Nov 2007: human iPS paper

- (A) Time schedule of iPS cell generation.
- (B) Morphology of HDF.
- (C) Typical image of non-ES cell-like colony.
- (D) Typical image of hES cell-like colony.
- (E) Morphology of established iPS cell line at passage number 6 (clone 201B7).
- (F) Image of iPS cells with high magnification.
- (G) Spontaneously differentiated cells in the center part of human iPS cell colonies.
- (H–N) Immunocytochemistry for SSEA-1 (H), SSEA-3
- (I), SSEA-4 (J), TRA-1-60 (K), TRA-1-81 (L),
- TRA-2-49/6È (M), and Nanog (N). Nuclei were stained with Hoechst 33342 (blue). Bars = 200  $\mu$ m (B–E, G), 20  $\mu$ m (F), and 100  $\mu$ m (H–N).



2009 Obama reverses ban



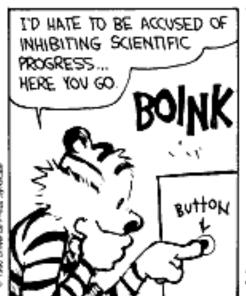
### Stem Cells & Cloning

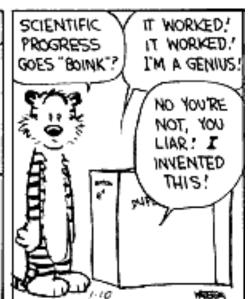
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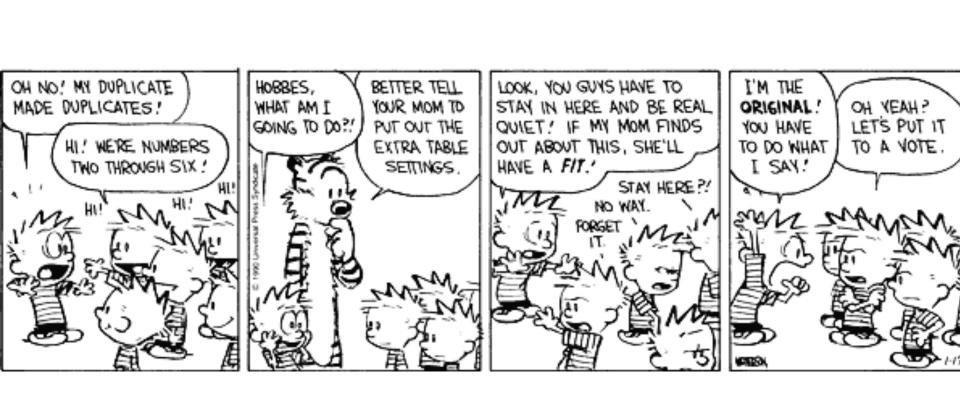


BROTHER! YOU DOUBTING
THOMASES GET IN THE WAY
OF MORE SCIENTIFIC ADVANCES WITH YOUR STUPID
ETHICAL GUESTIONS! THIS
IS A BRILLIANT IDEA! HIT

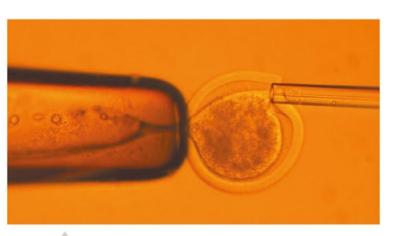








### THE RISE AND FALL AND RISE OF WOO SUK HWANG





Woo Suk Hwang describes the first stem-cell line, NT-1, derived from a cloned human embryo.

### **MAY 2005**

Hwang's group publishes a second paper reporting 11 further human embryonic cell lines.

### **AUGUST 2005**

Hwang's group is the first to clone a dog.



### **NOVEMBER 2005**

US collaborator Gerald Schatten splits with Hwang, citing ethical problems in getting human eggs.



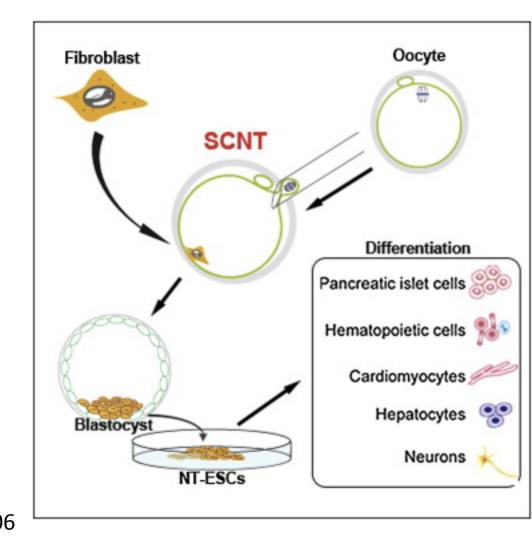
#### **DECEMBER 2005**

Pushed by increasing evidence, Seoul National University (SNU) launches an investigation.

#### **JANUARY 2006**

Hwang's humancloning research is deemed fraudulent by SNU. His dog-cloning claims are upheld.

## Somatic Cell Nuclear Transfer (SCNT)



## Women: Would you donate your eggs?

242 eggs from 16 donors: 30 embryos and 1 cell line (SCNT-hES-1) 2004 Science paper

### Egg donation bioethics

"The donors were anonymous, but one PhD student in the team, Ja Min Koo, initially told Nature that the donors included herself and another woman in the lab. She subsequently called back and said that she had not donated eggs, blaming her poor English for a misunderstanding. But in the initial interview, she named the hospital where her donation was carried out, and explained that she had been happy to donate eggs because she already has two children." 11 new SCNT hES cell lines, x=~17 eggs used per cell line. What changed to increase the efficiency??

2005 Science paper

nature Vol 438|1 December 2005

### **NEWS**

## Clone star admits lies over eggs

After a year and a half of denials, Woo Suk Hwang admitted last Thursday that his stemcell research used eggs from paid donors and junior members of his team. Although planning to continue his research, Hwang said he would quit his other positions.

Despite the confession, which shocked South Korea and the global stem-cell research community many have remained supportive have serious side effects. Paying donors is now illegal in Korea, although it was not at the time of Hwang's study. And receiving donations from subordinates raises a variety of ethical problems, including the spectre of coercion.

Until 24 November, Hwang had denied everything. Then, in a press conference aired live on all three of the country's main television networks he admitted that eggs from his

the eggs. "I don't need any rewards," he says. Hwang has not disclosed his expenditures or budget for the project, saying only that all funds came from private sources.

The extent to which a junior member of his laboratory might have felt pressure to donate is also under debate. The student spoken to by *Nature* last April showed no signs of having been correct by Hwang During a 28-minute

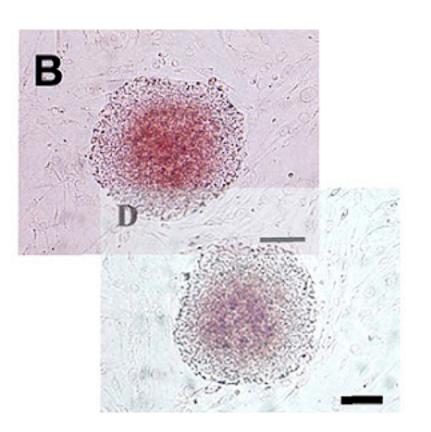
2005: Hwang admits to using eggs from paid donors and junior members of his research team; resigns

## 2006 Seoul National University Final Report

- NT-hES-1 from 2004 paper data fabricated
- All 11 lines from 2005 paper data fabricated

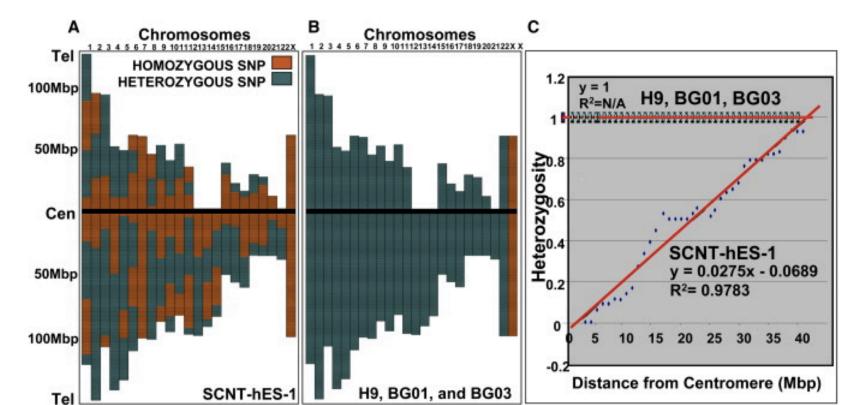
"does not possess patient-specific stem cell lines or any scientific basis for claiming to have created one."

### Example



- 'B' from 2004 paper
- 'D' from a totally different paper that was not related to NThES cell lines

# 2007: NT-hES-1 most likely a parthenogenic line



http://dx.doi.org/10.1016/j.stem.2007.07.001

#### **JULY 2006**

Sooam Foundation starts up, with US\$3.5 million from Hwang's supporters.

#### 2007

The Korean health ministry grants
Sooam the right to do human-embryo and cloning research.

#### OCTOBER 2009

Hwang is found guilty of embezzlement and bioethics violations. Appeal continues.

#### 2011

Canada grants Hwang a patent for the NT-1 cell line.

#### 2012

Sooam scientists clone a coyote using a dog eggcell donor and surrogate mother.

#### 2013

Court tells the Korean Centers for Disease Control and Prevention to register the NT-1 cell line.





Would you clone a favorite pet?



### Snuppy & Sooam

- First cloned dog (2005)
- Sooam Foundation
   (2006) now clones dogs
   and other animals
- ~\$100,000 USD for a dog clone

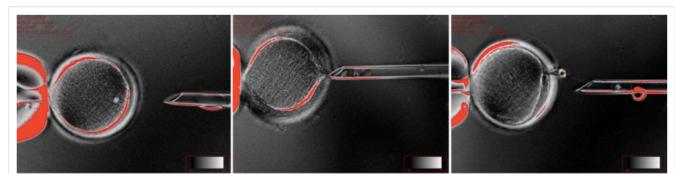
## 2013: SCNT hES cells.. finally!

## Cloning provides human embryonic stem cells with promise for personalized medicine

For the first time, a team of scientists has used SCNT to produce human embryonic stem cells

By Mary Beth O'Leary Posted on 15 May 2013





**Nuclear extraction of a donor egg.** The first image shows the egg cell (the large circular object being held in place by a pipette to the left.) Later shots show the egg nucleus being extracted from the egg cell (by a different pipette) — all in preparation for its fusion with a skin cell to kick off the cloning process. Click to enlarge. (Photos courtesy of Oregon Health & Science University)