



A winding road to pluripotency

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CiRA, Kyoto University (Japan)

Gladstone Institutes (USA)



My early days in science

Researches led to iPS cells

Potential of iPS Cells



My early days in science

Unexpected results

Great mentors

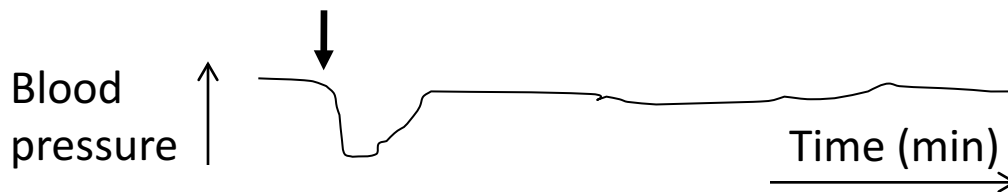
PhD Student: Osaka City University

Dr. Katsuyuki Miura



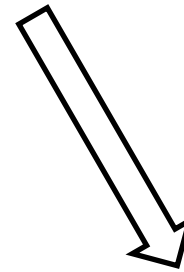
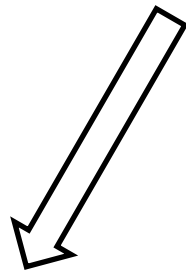
Dr. Miura's Hypothesis

Platelet activating factor
(PAF)



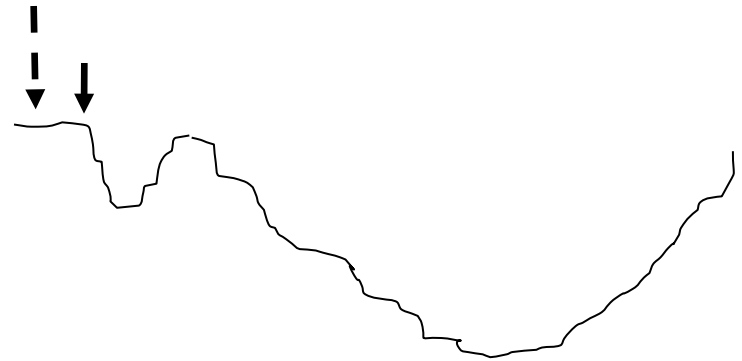
Hypothesis

What happened

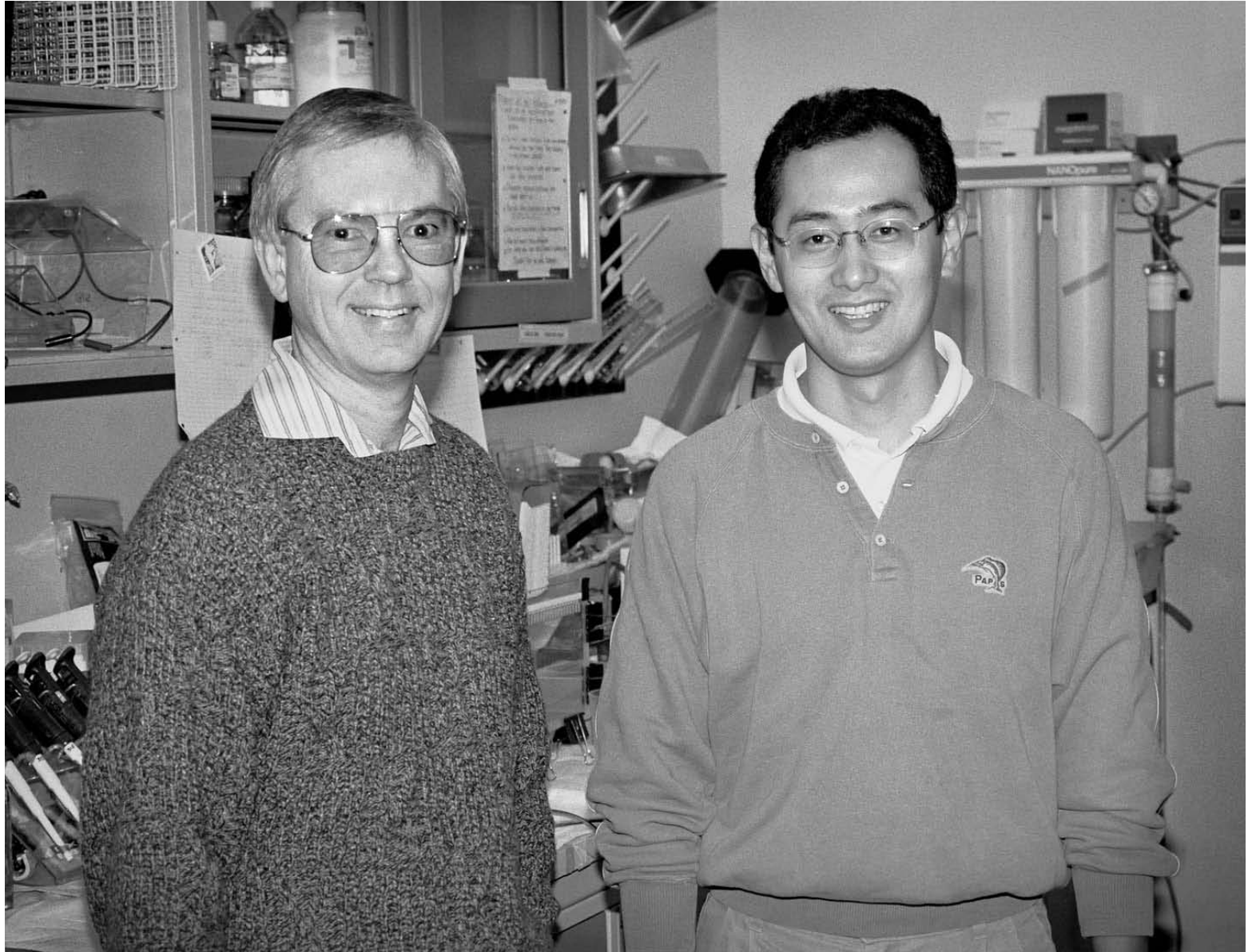


Thromboxane A2
inhibitor

PAF



Postdoctoral Fellow: Gladstone Institute



Dr. Tom Innerarity

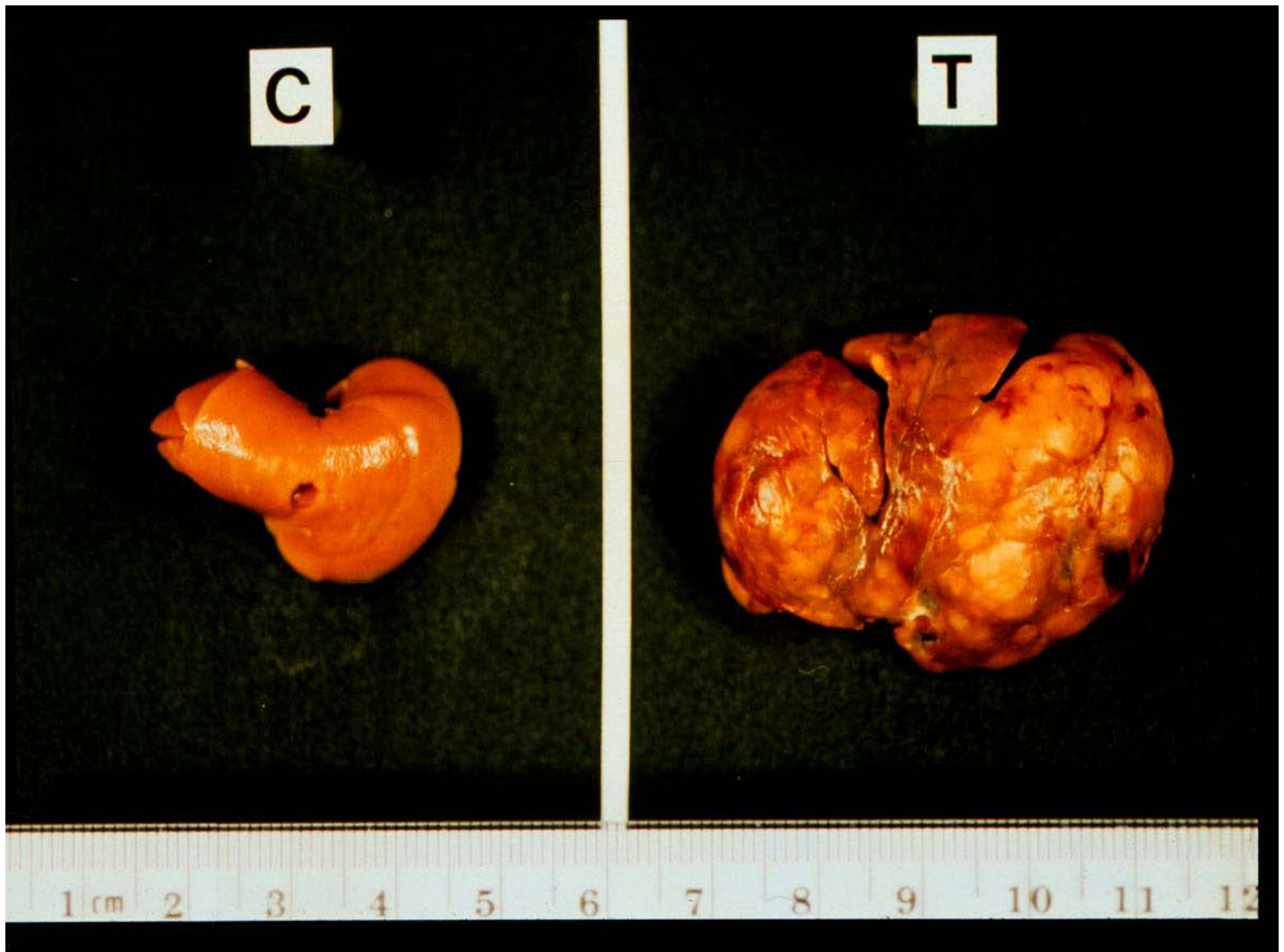


Dr. Innerarity's hypothesis

Forced expression of APOBEC1 in liver
lowers plasma cholesterol

Experiment

Liver-specific transgenic mice



Liver cancer



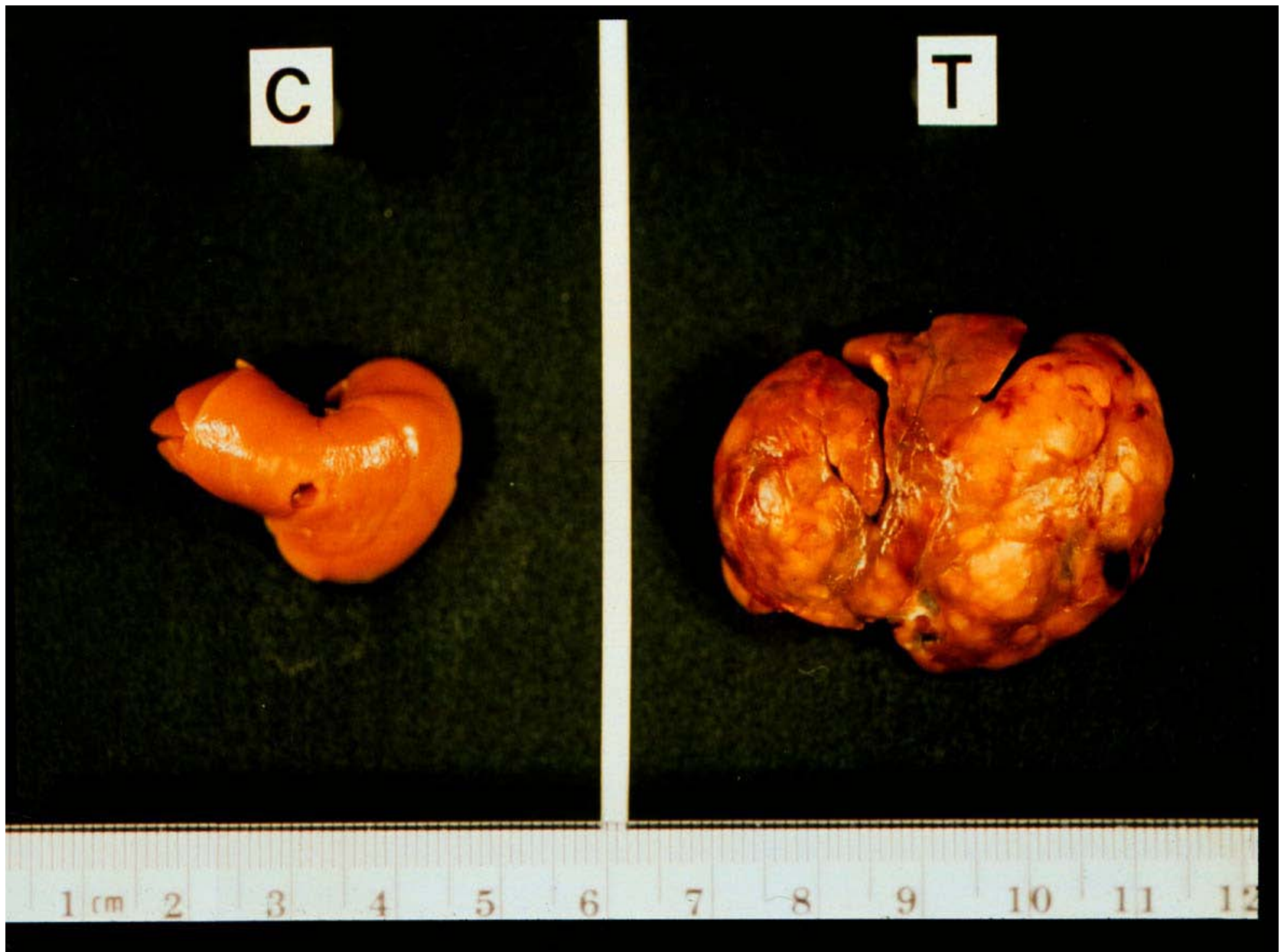
My early days in science

Unexpected results

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Researches that led to iPS cells



Liver cancer

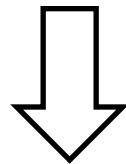


NAT1

(Novel APOBEC1 Target No1)

Identified as a candidate gene responsible for
APOBEC1-mediated tumors

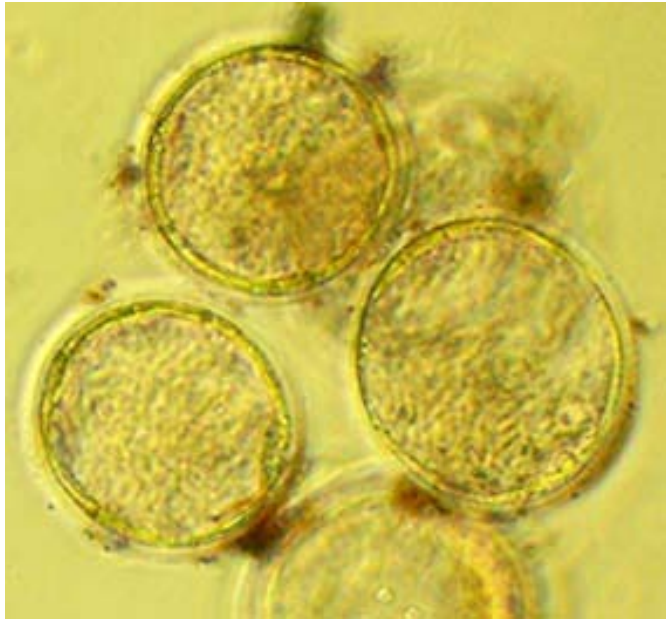
(Yamanaka et al., 1997)



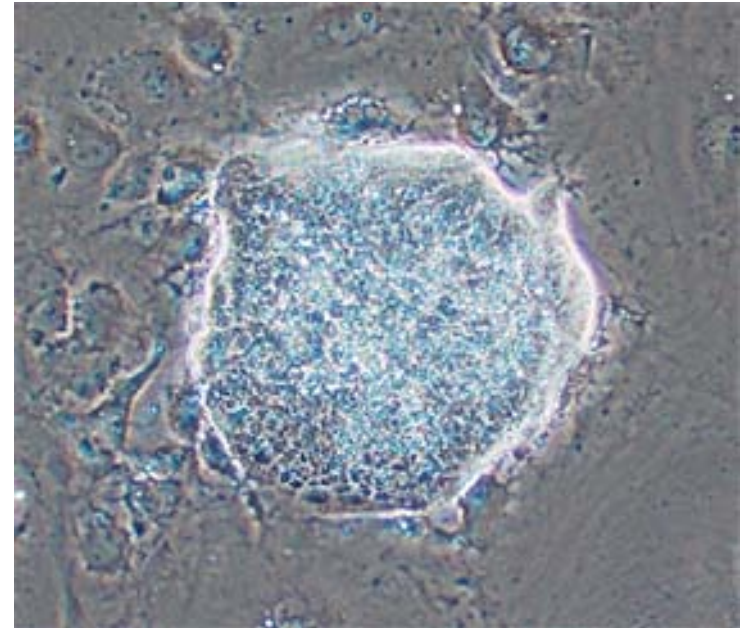
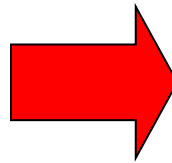
Essential for pluripotency of ES cells

(Yamanaka et al., 2000)

Embryonic Stem (ES) cells



Embryos

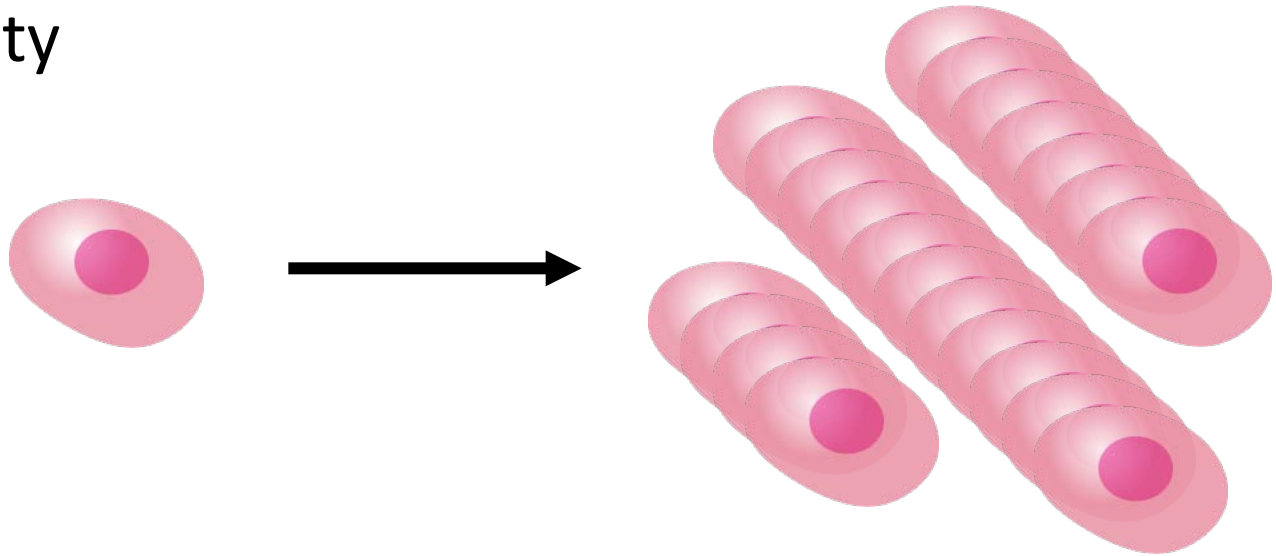


ES cells

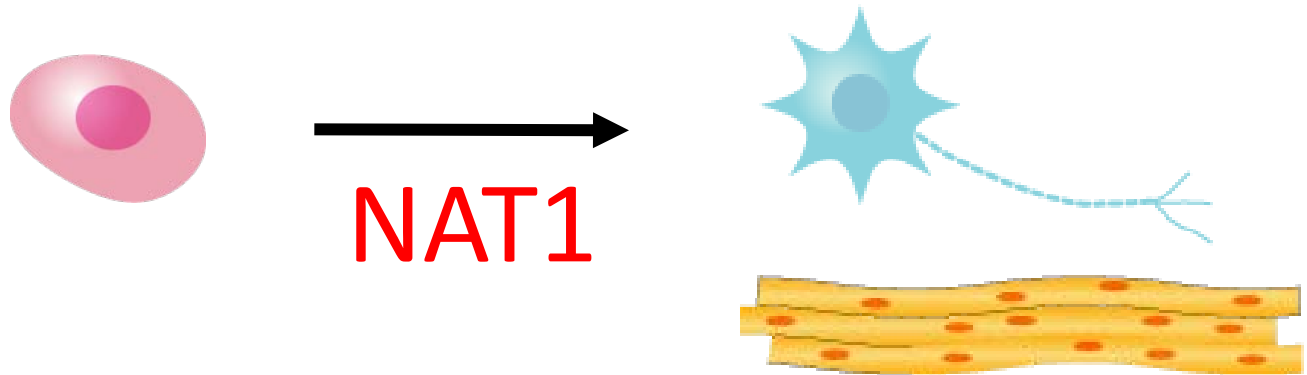
Established in mice in 1981

Properties of ES cells

Immortality



Pluripotency



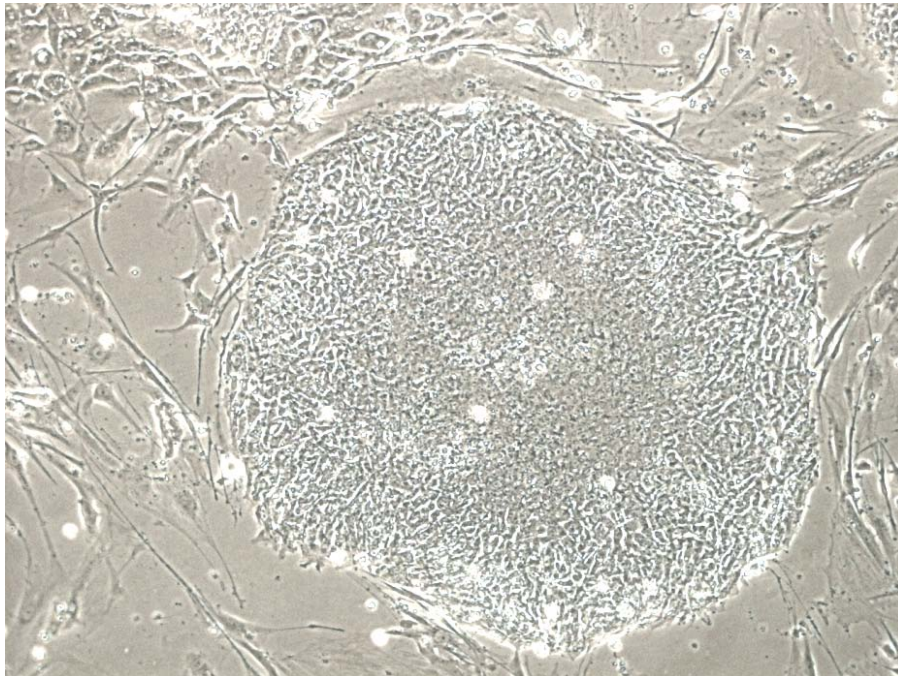


PAD

Post America Depression

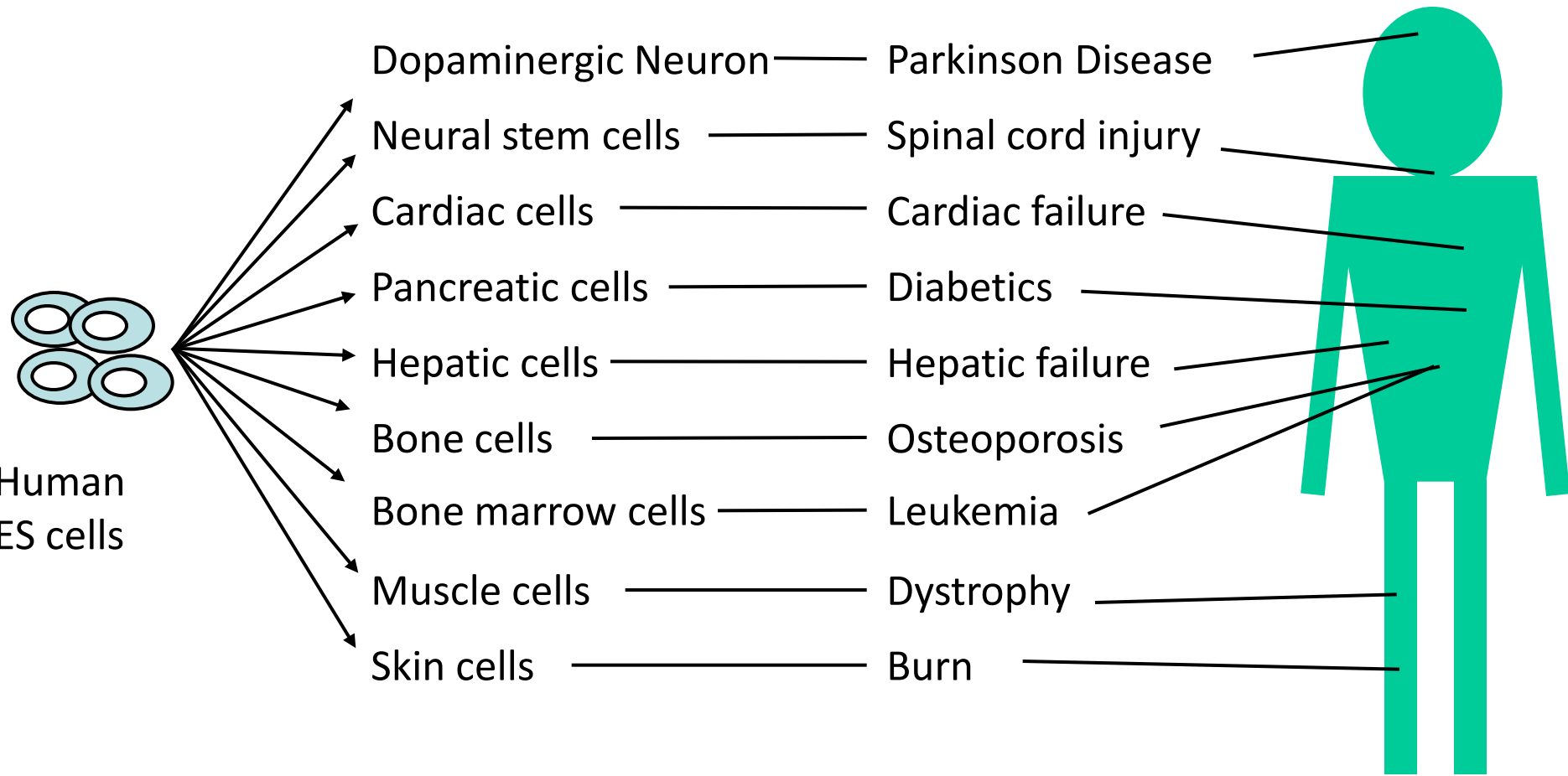
Human ES cells

hES cell



Dr. James Thomson, 1998

Regenerative Medicine & ES Cell

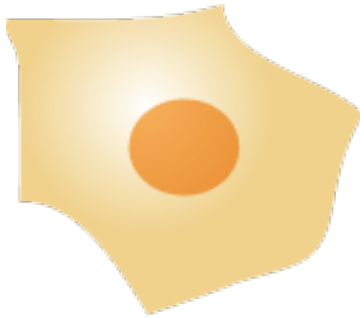




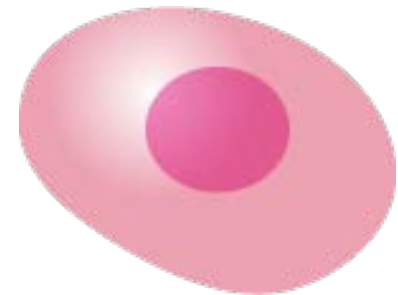
Became a principle investigator in Nara (Dec., 1999)



Our Research Goal



Somatic cells



ES-like
Stem cells

Moral hurdle of human ES cells



Ethical no-go. In 2001, US President George W. Bush and Pope John Paul II made clear that the destruction of embryos for the purpose of generating new ES cell lines violated their ethical principles.

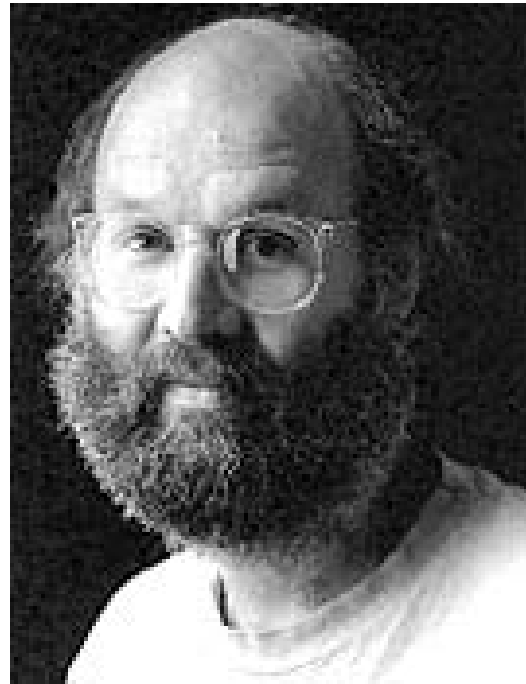
Sir John Gurdon



Somatic cells can be reprogrammed into the embryonic state

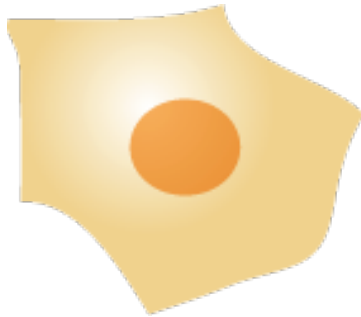


Dr. Harold Weintraub

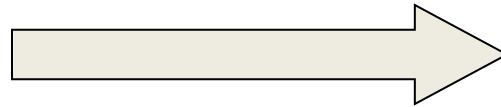


The transcription factor MyoD turns fibroblasts into muscle

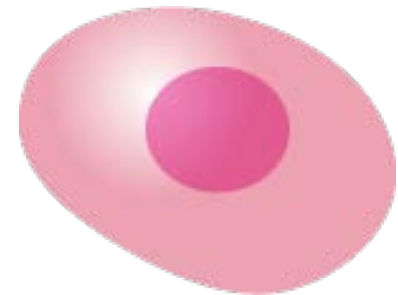
Our Research Goal



Somatic cells

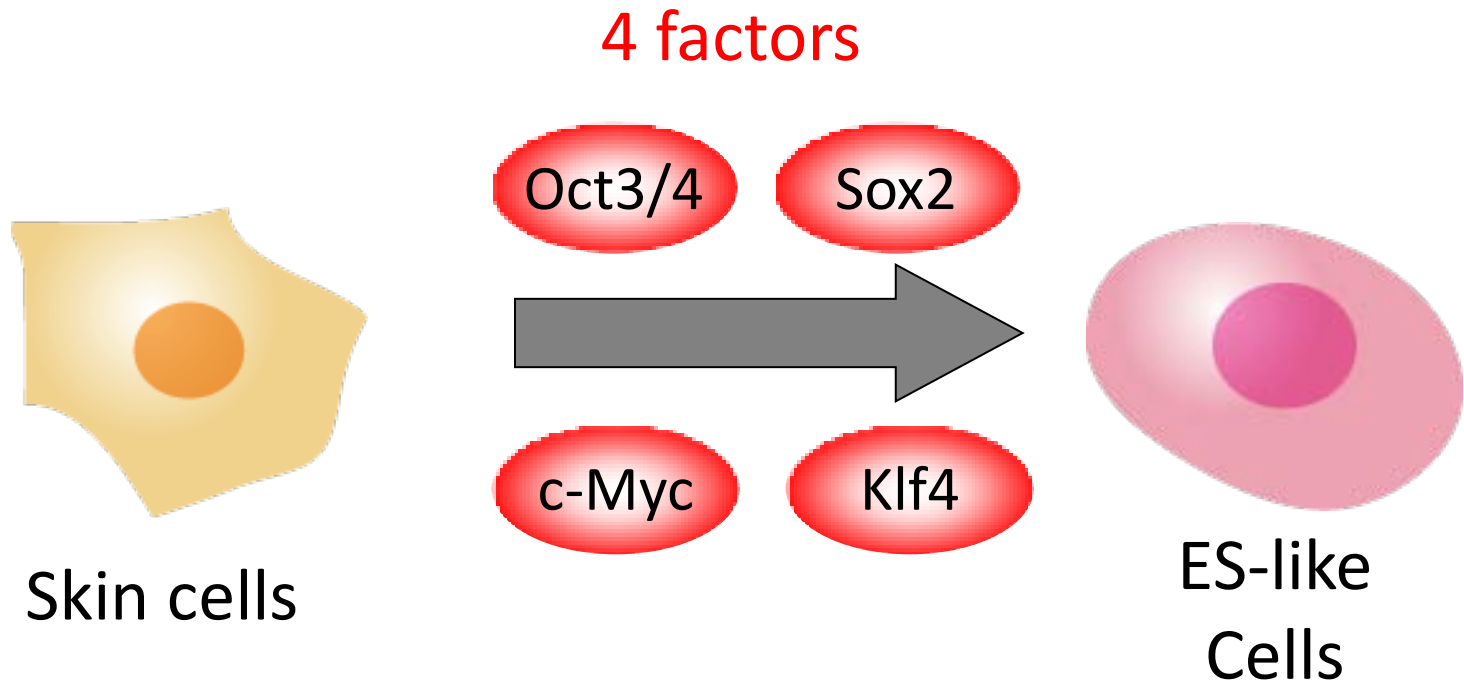


Reprogramming
factors



ES-like
Stem cells

Induced Pluripotent Stem (iPS) Cells

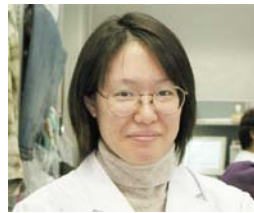
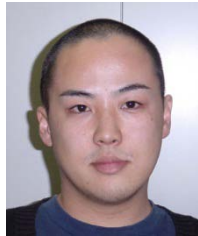


Mouse 2006

Human 2007

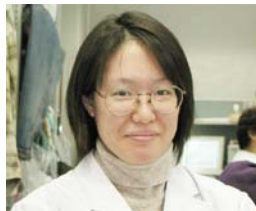
In search of reprogramming factors

1. Collection of 24 candidate factors

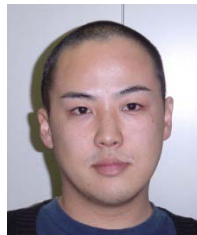


and others

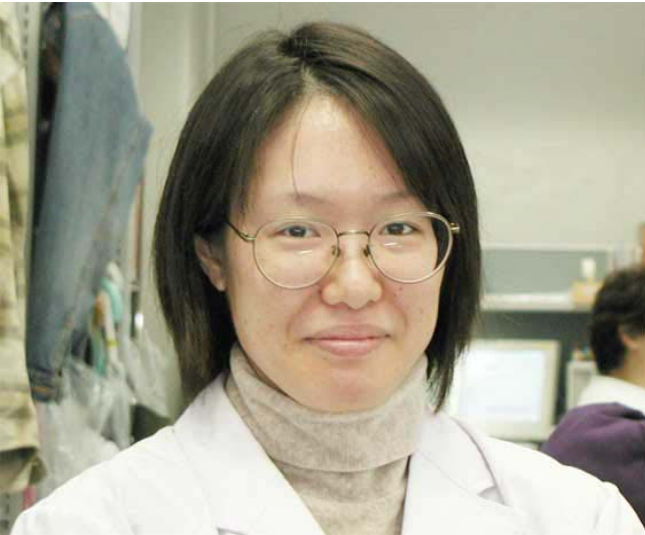
2. Simple and sensitive assay system



3. Identification of the four factors



iPSC Trio



Yoshimi
Tokuzawa



Kazutoshi
Takahashi

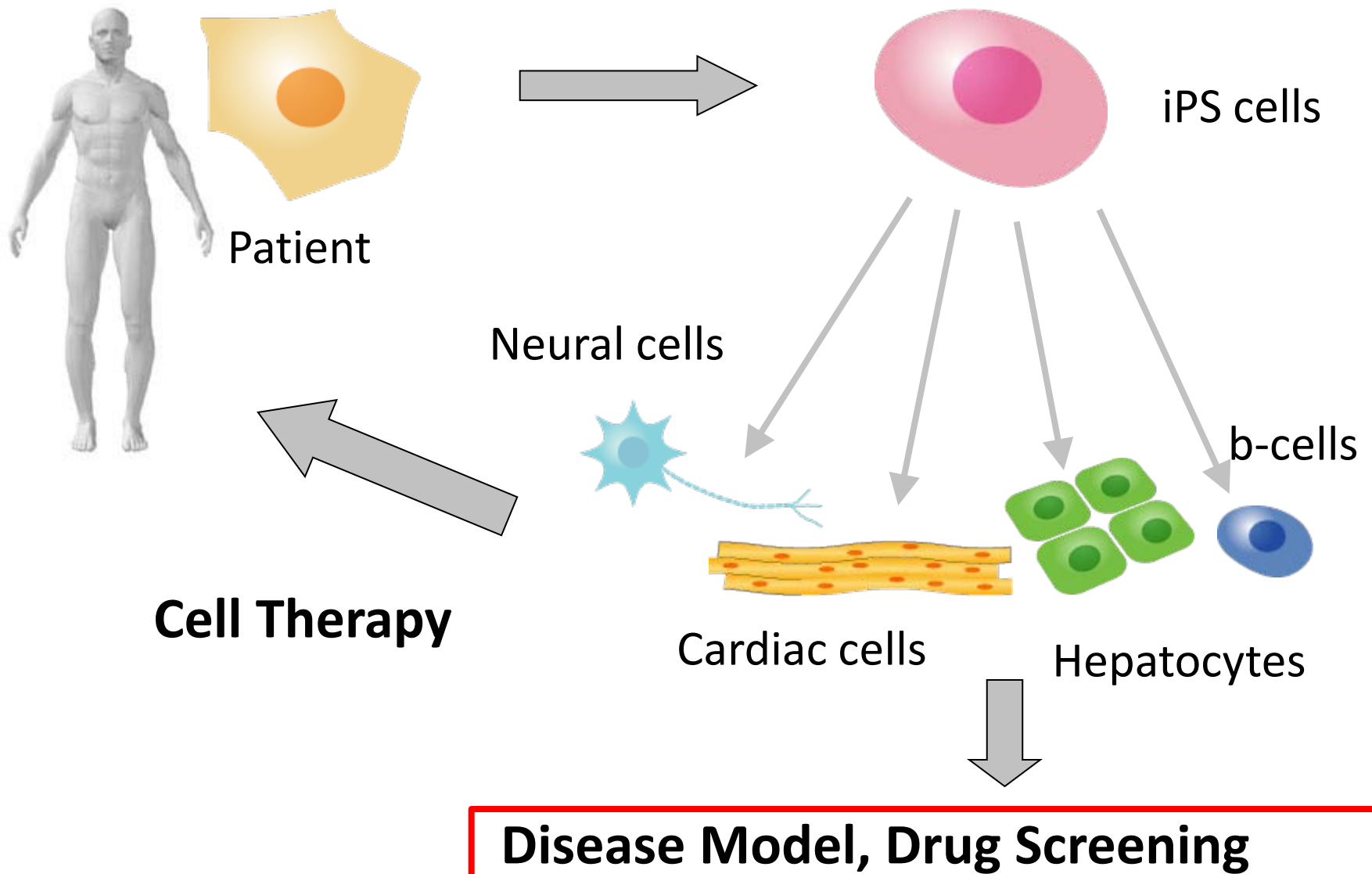


Tomoko
Ichisaka

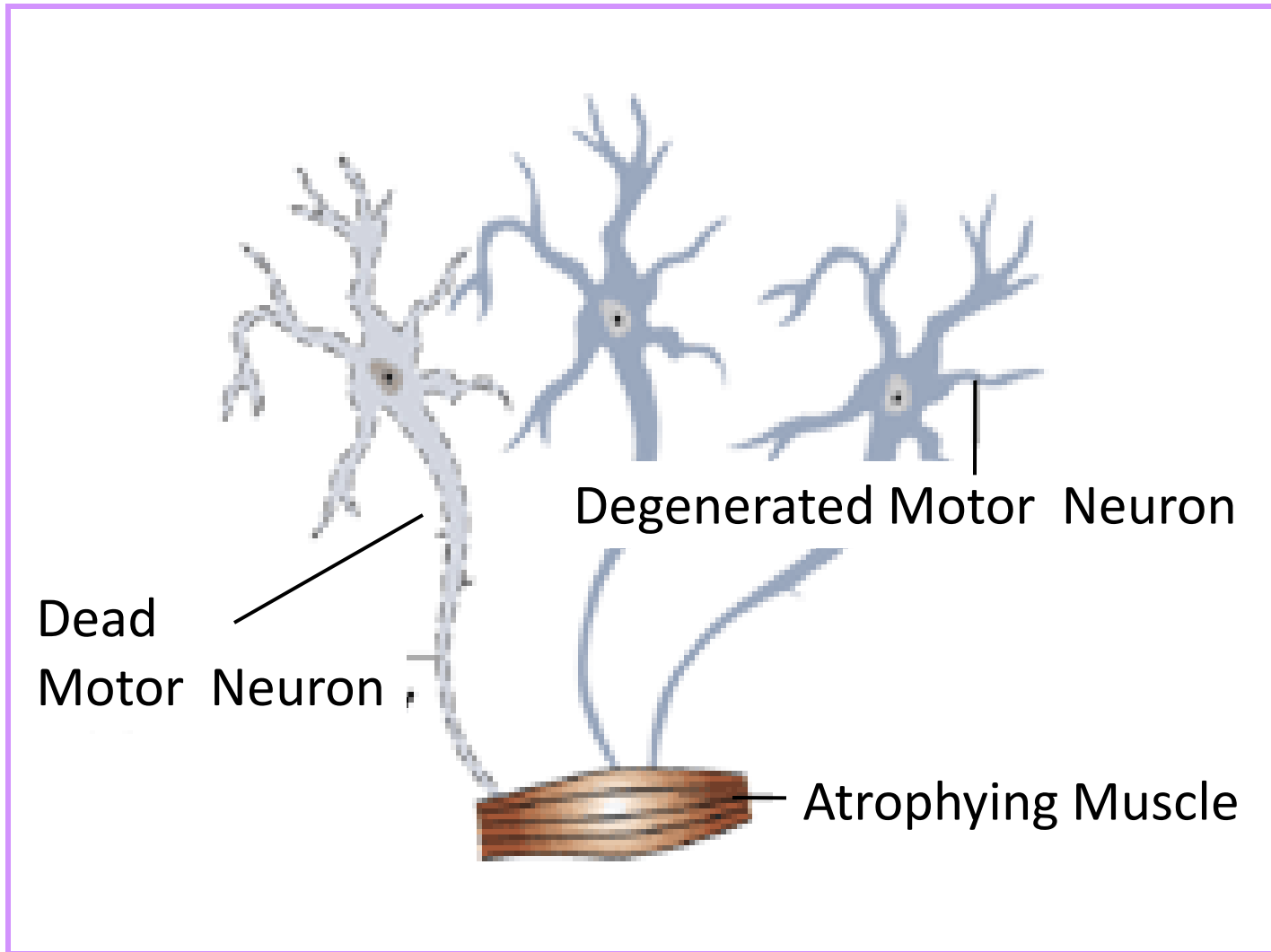


Potential of iPS cells

Potential of iPS Cells

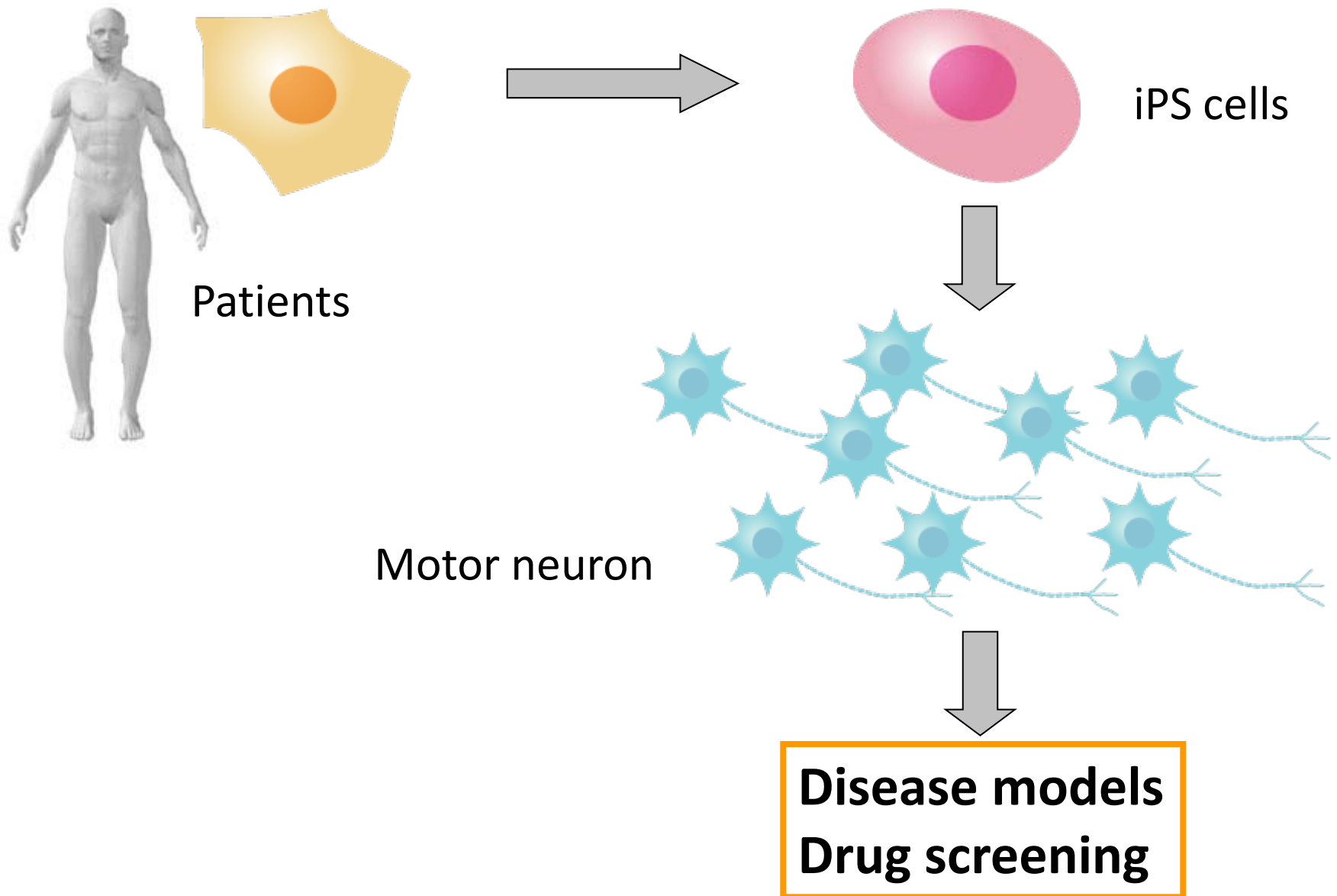


Motor Neuron Disease



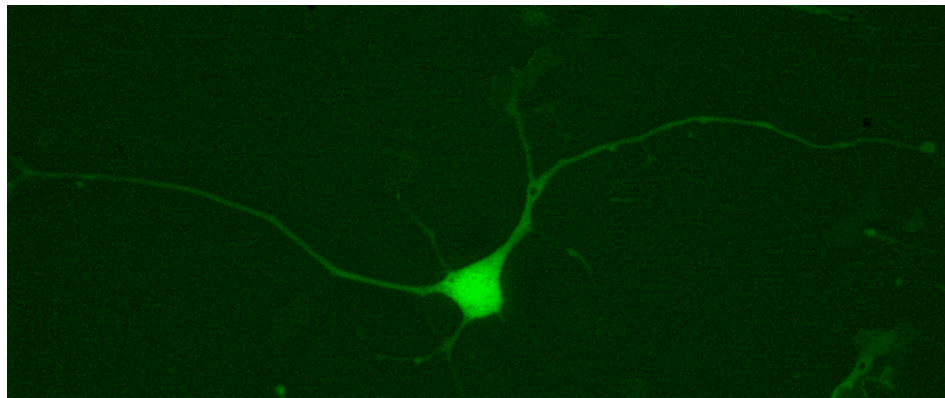
No effective treatment, because no good disease model

Potential of iPS Cells

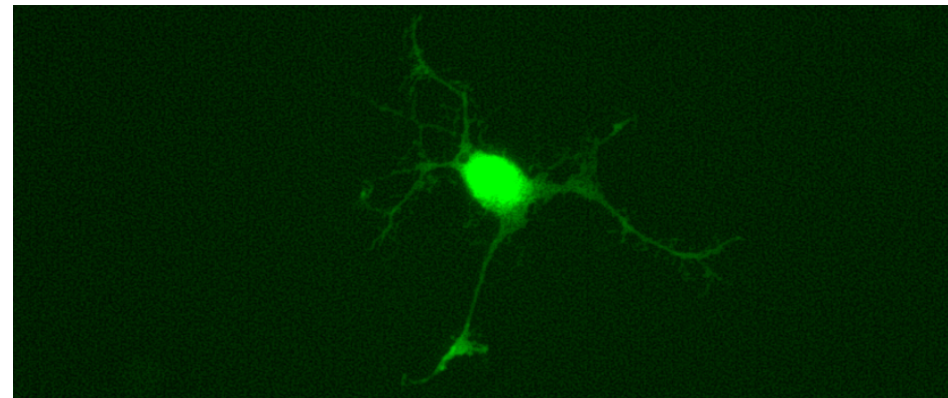


Motor Neurons from iPS Cells

Control



Patient

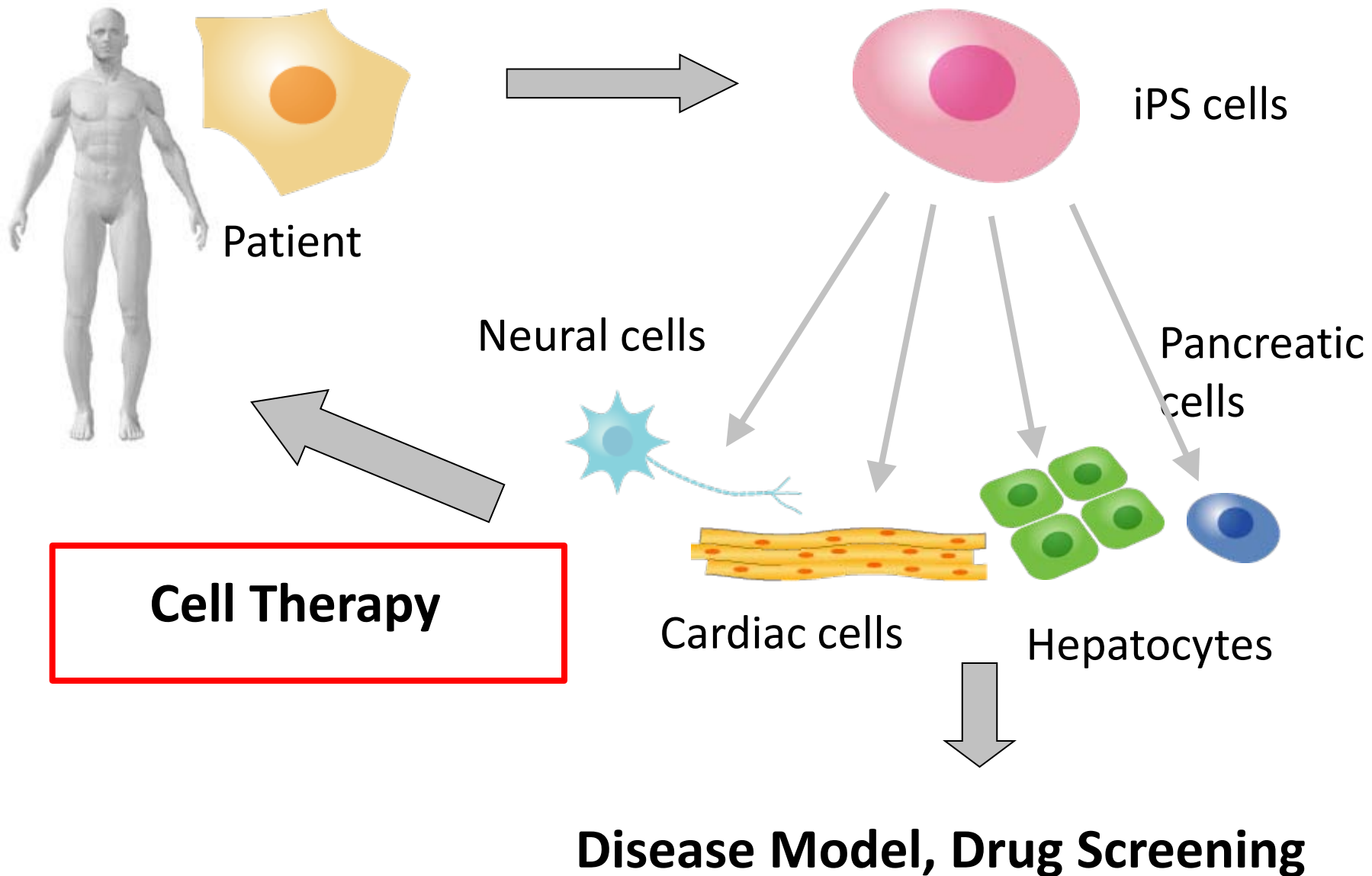


Dr. Haruhisa Inoue, *Science Translation al Med 2012*

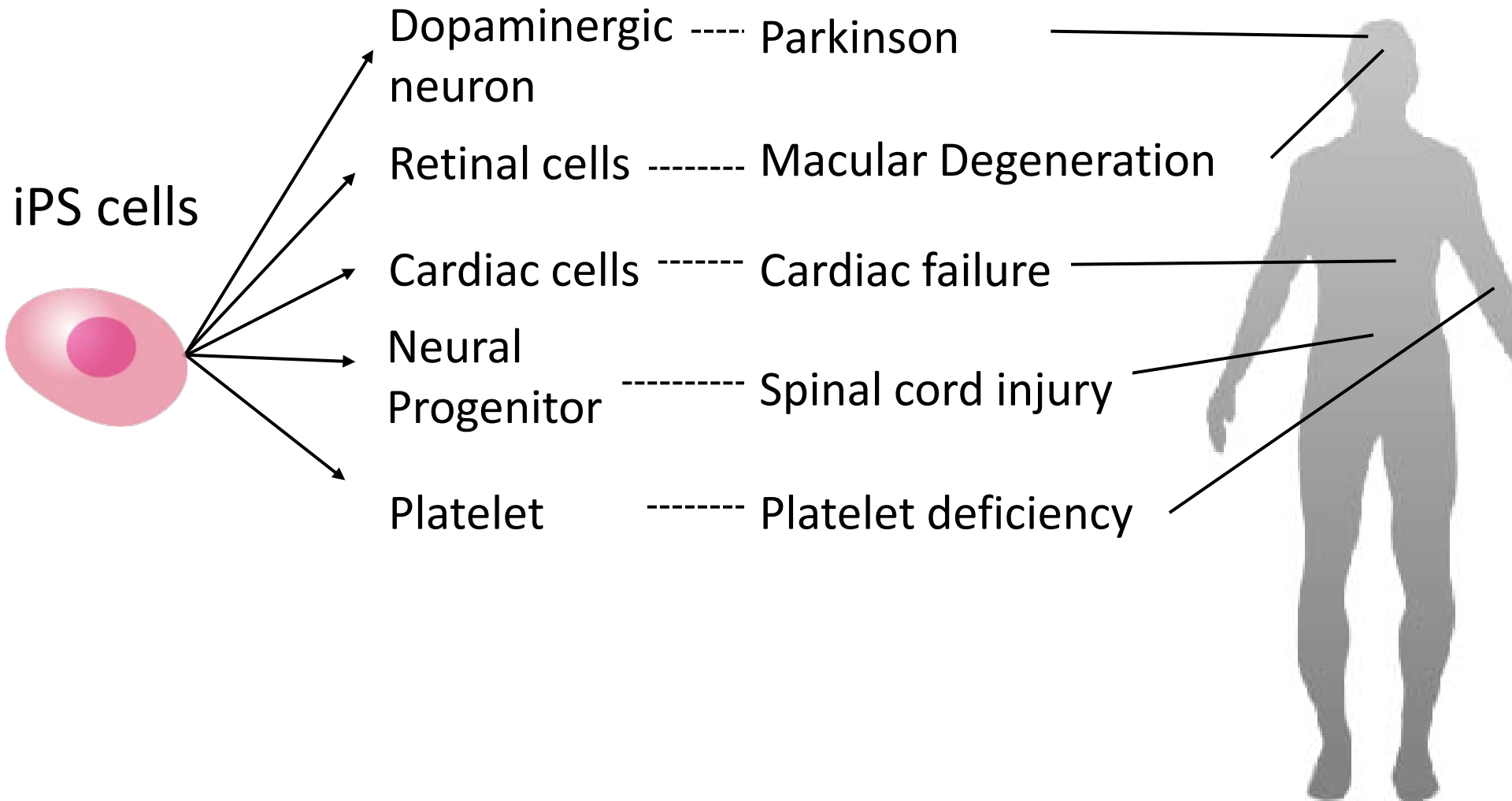
Robotic Drug Screening



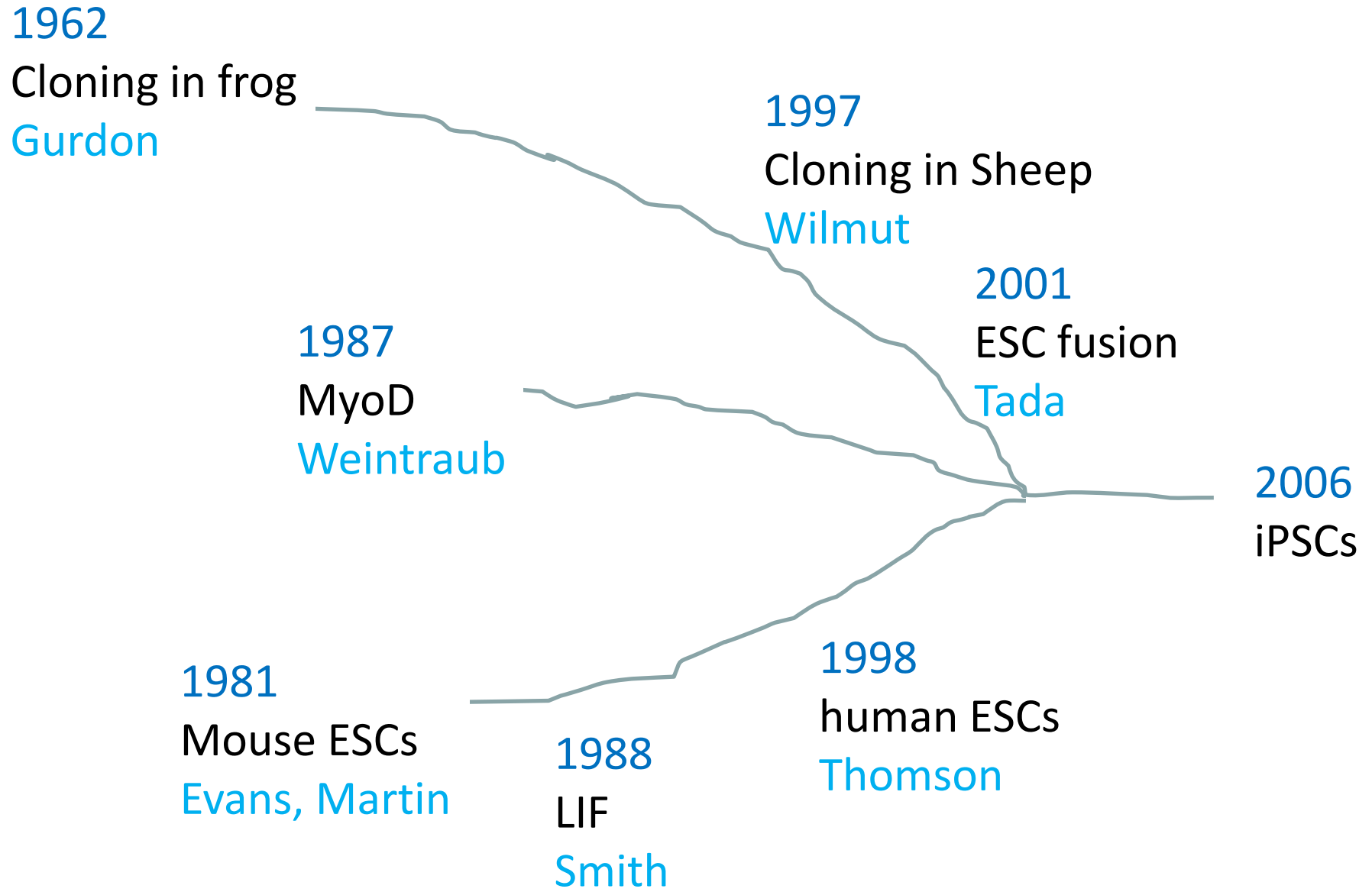
Potential of iPS Cells



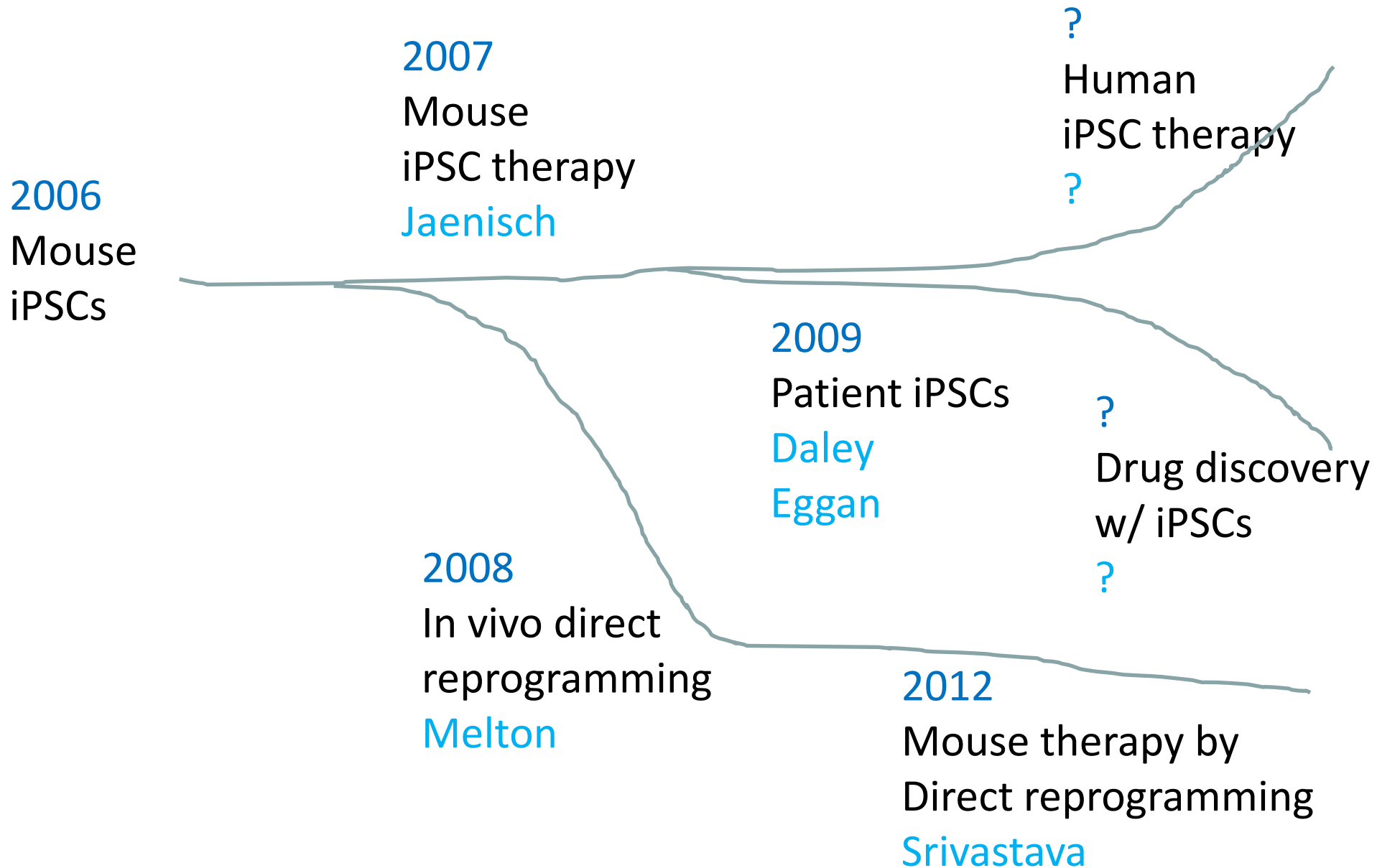
Ongoing preclinical studies in Japan



Three scientific streams that led to iPS cells



New scientific streams from iPS cells



Center for iPS Cell Research And Application (CiRA), Kyoto



Gladstone Institutes, San Francisco





Tusen Tack!