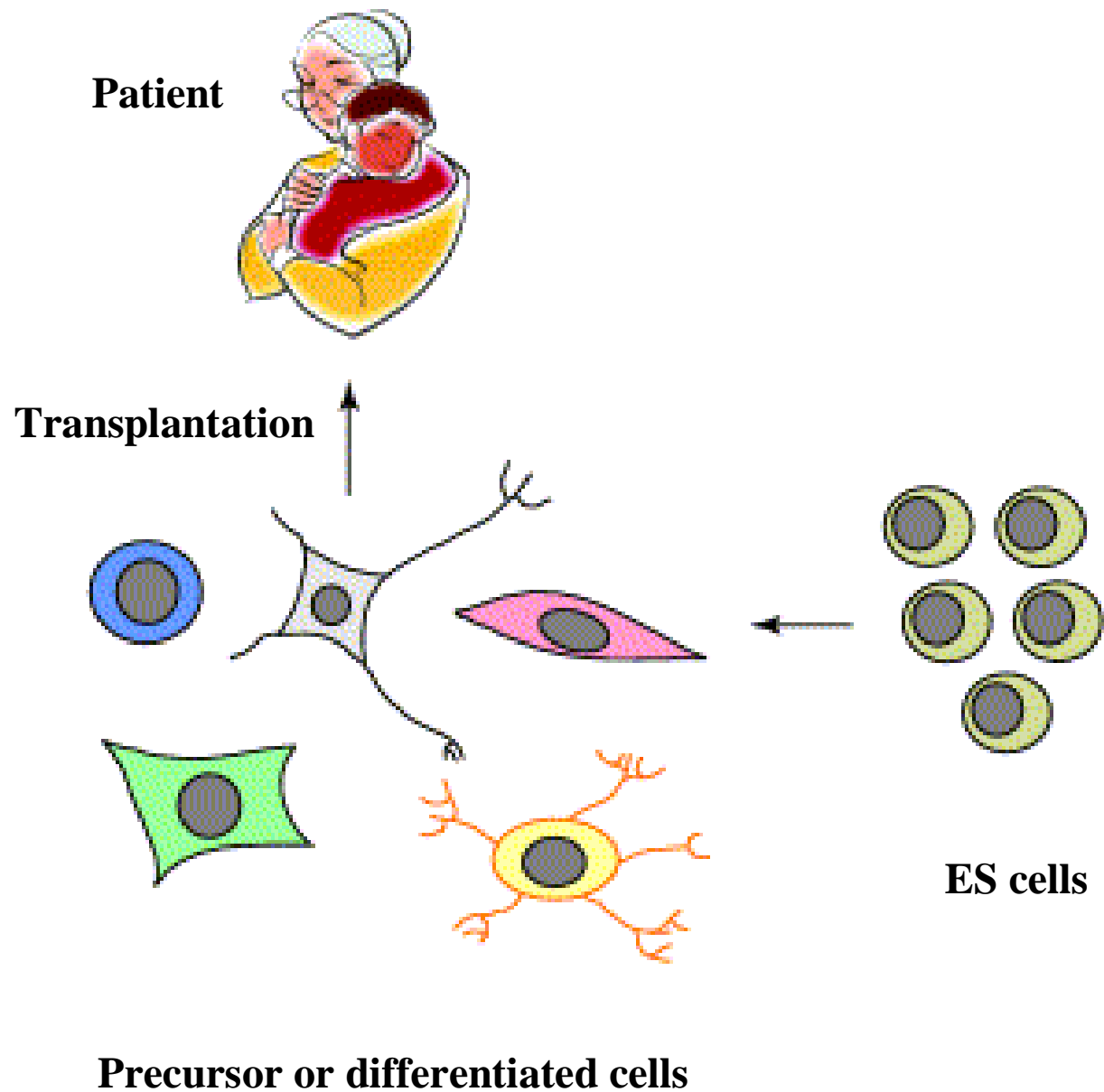


A fluorescence microscopy image of human embryonic stem cells. The cells are stained with DAPI (blue) to highlight nuclei, and a green fluorescent marker is visible throughout the cells. Small red puncta are scattered within the cells, likely representing specific proteins or organelles. The background is dark, making the stained cells stand out.

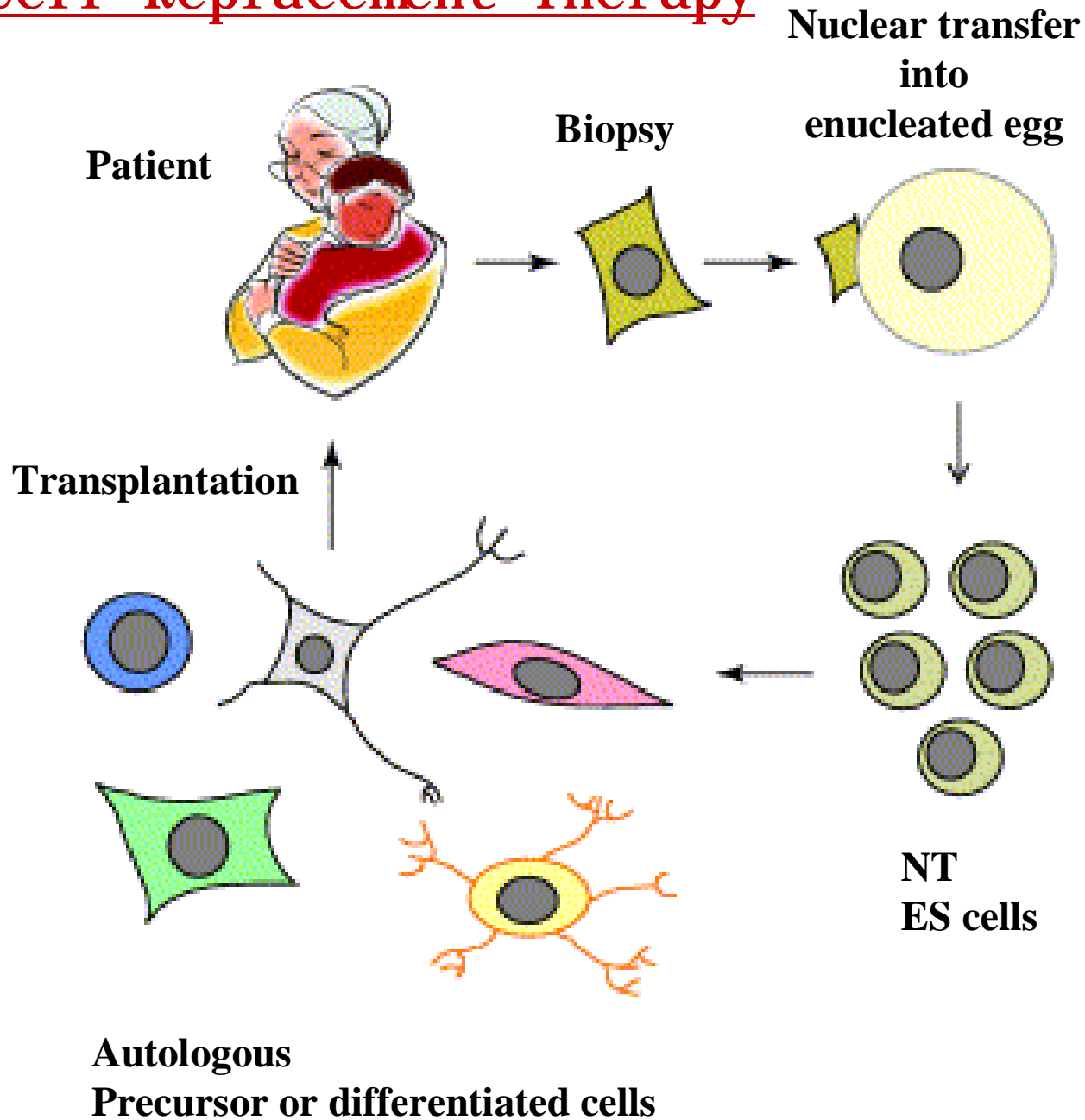
# SCNT and the utility of human embryonic stem cells

Kevin Eggan, Ph.D.  
The Stowers Medical Institute,  
The Harvard Stem Cell Institute  
The Department of Molecular and  
Cellular Biology, Harvard University

# Cell Replacement Therapy



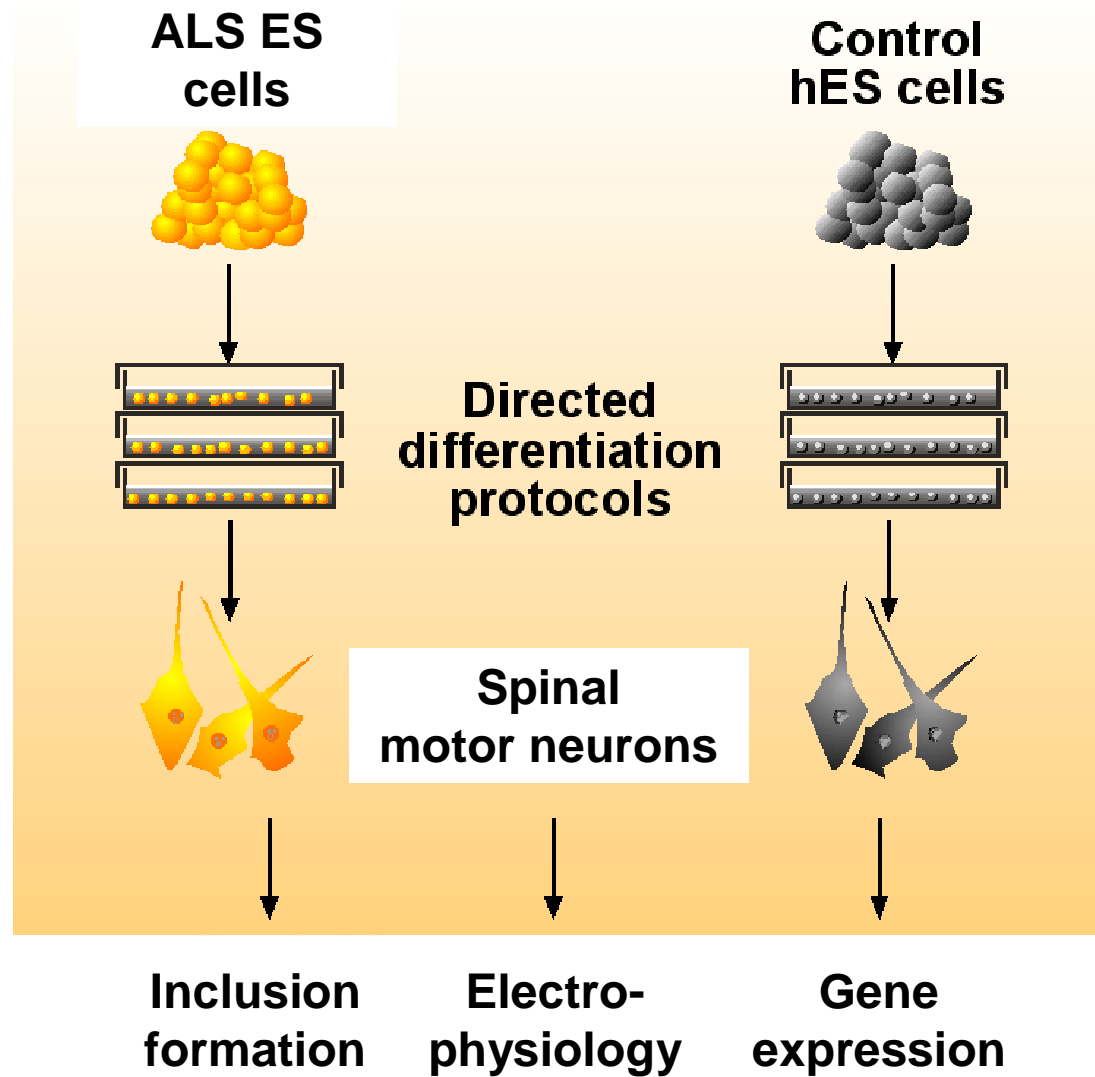
# Cell Replacement Therapy



# Challenges in Disease research

- § Patient material remains difficult for scientists to obtain.
- § Samples from patients represent endpoint of disease.
- § Complex genetic nature of disease compounds with environmental factors to confound studies.
- § Complex nature of many common forms of disease has made it difficult to engineer cell lines or animals to provide models of most common forms of disease.

# Analysis of Disease Specific Embryonic Stem Cells



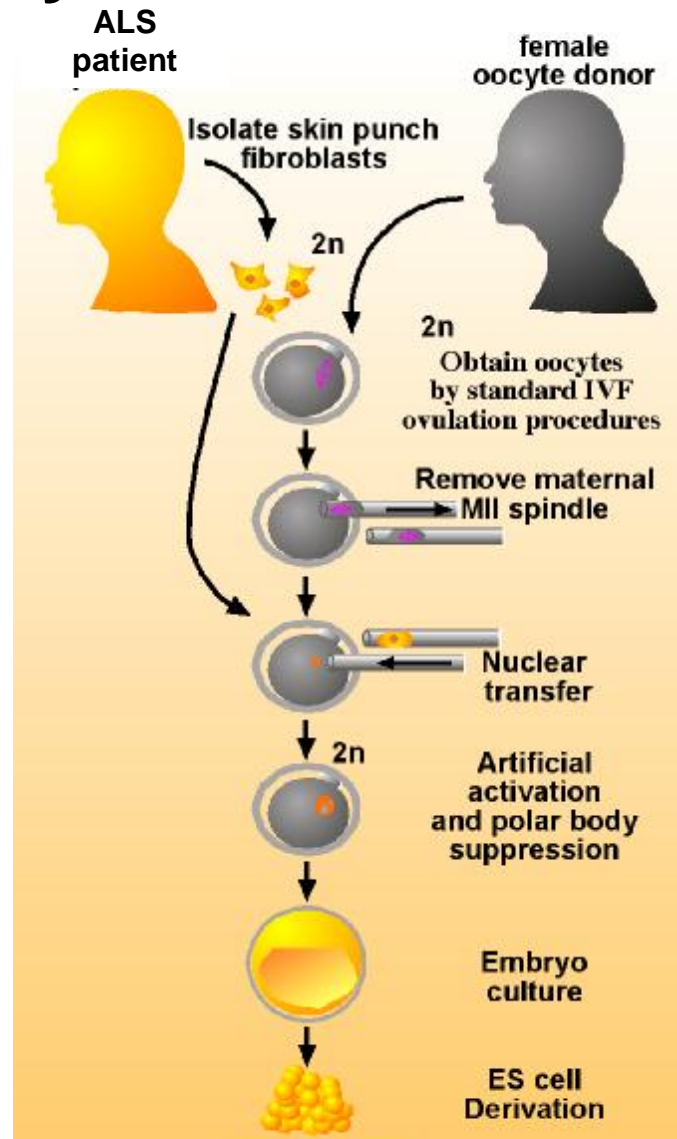
# Challenges in using human embryonic stem cells to model disease

- § Can we generate hES cell lines with the pathological genotype?
- § Can we produce a large number of the appropriate affected cells for study?
- § Can we maintain these cells in culture long-enough for them to manifest disease?
- § Can we create "environments" for the cells that will best represent those in which they reside and function?
- § Can we design assays for assessing the functionality of these cells and their progression towards a disease phenotype?

# Producing “disease specific” ES cell lines for *in vitro* studies

- § Genetic modification of existing hES cell lines
- § Derive hES cell lines from PGD embryos
- § Human SCNT

# Generation of Disease Specific Embryonic Stem Cells by NT



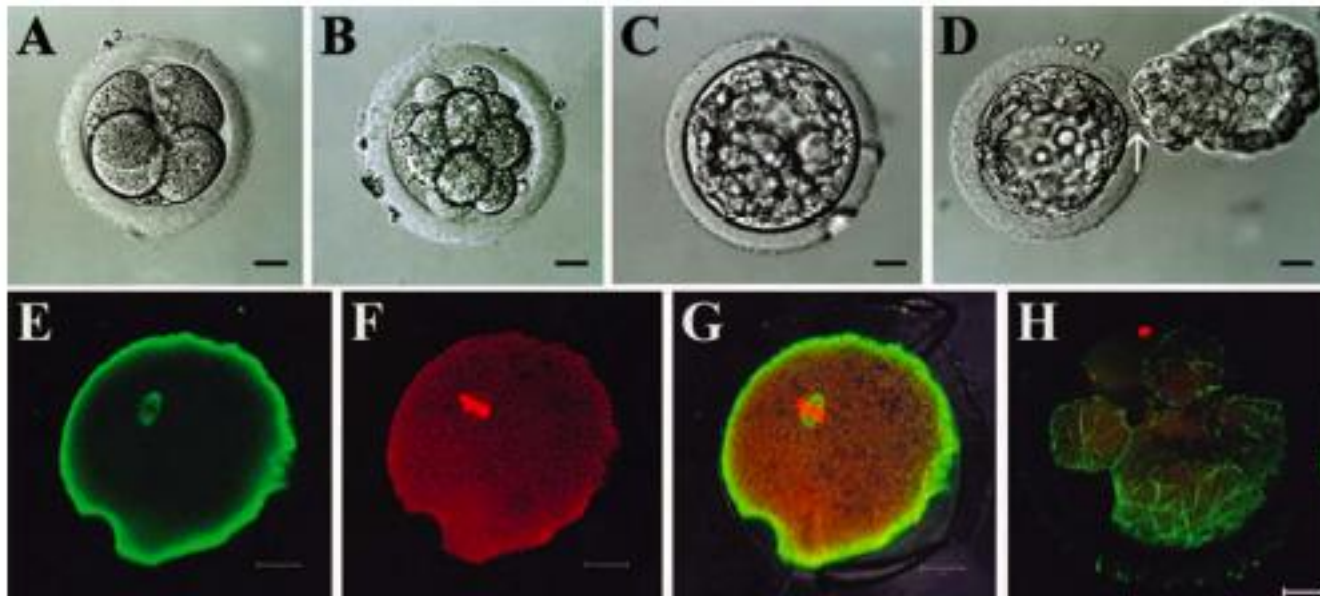
ALS Embryonic Stem Cell Line

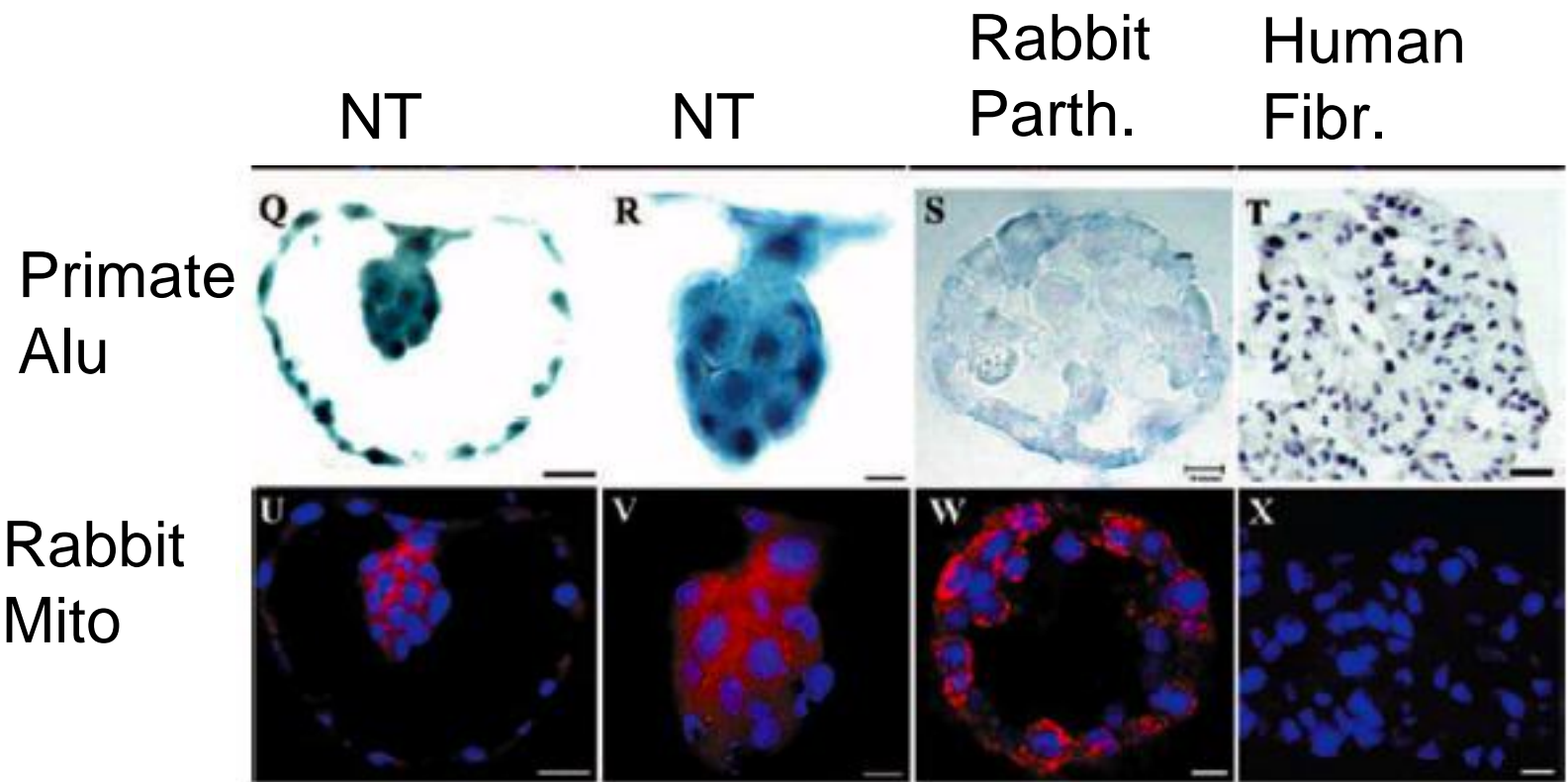
# Overcoming logistical difficulties of human SCNT

- § Human oocytes donated specifically for research.
- § Use immature or failed to fertilize eggs.
- § Produce human eggs from discarded ovarian material or from germ-line stem cells.
- § Produce human oocytes from mES or hES cells.
- § Xeno-NT to produce “human” ES cell lines.
- § Use material from existing hES cell lines as a source of “reprogramming” activities.

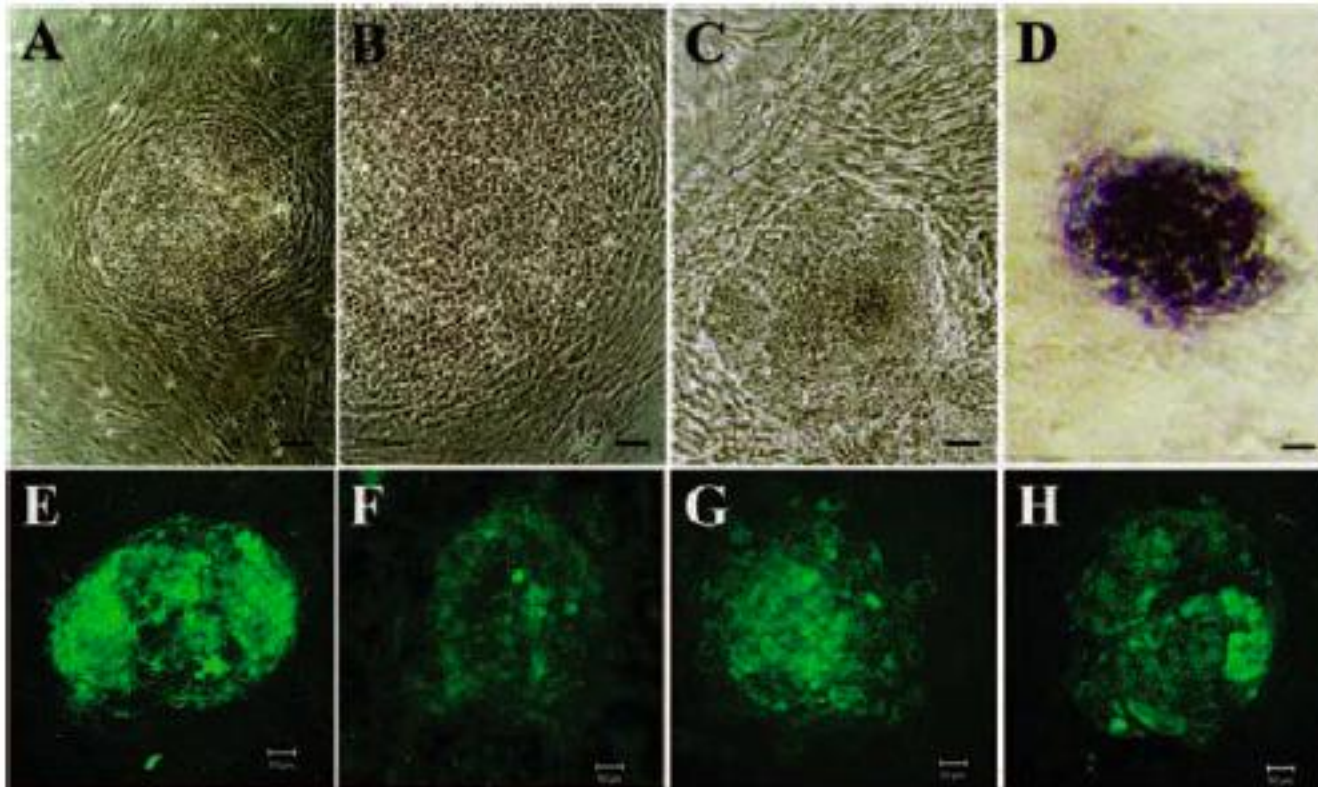
## Embryonic stem cells generated by nuclear transfer of human somatic nuclei into rabbit oocytes

YING CHEN<sup>1,2</sup>, ZHI XU HE<sup>3</sup>, AILIAN LIU<sup>1,2</sup>, KAI WANG<sup>1,2</sup>, WEN WEI MAO<sup>1,2</sup>, JIAN XIN CHU<sup>1,2</sup>, YONG LU<sup>1,2</sup>, ZHENG FU FANG<sup>1,2</sup>, YING TANG SHI<sup>1,2</sup>, QING ZHANG YANG<sup>1,2</sup>, DA YUAN CHEN<sup>4</sup>, MIN KANG WANG<sup>4</sup>, JIN SONG LI<sup>4</sup>, SHAO LIANG HUANG<sup>3</sup>, XIANG YIN KONG<sup>5</sup>, YAO ZHOU SHI<sup>5</sup>, ZHI QIANG WANG<sup>5</sup>, JIA HUI XIA<sup>6</sup>, ZHI GAO LONG<sup>6</sup>, ZHI GANG XUE<sup>6</sup>, WEN XIANG DING<sup>7</sup>, HUI ZHEN SHENG<sup>1,2,\*</sup>





Chen et al. (2003) Embryonic stem cells generated by nuclear transfer of human somatic nuclei into rabbit oocytes; Cell Research, Vol. 13



AP  
staining

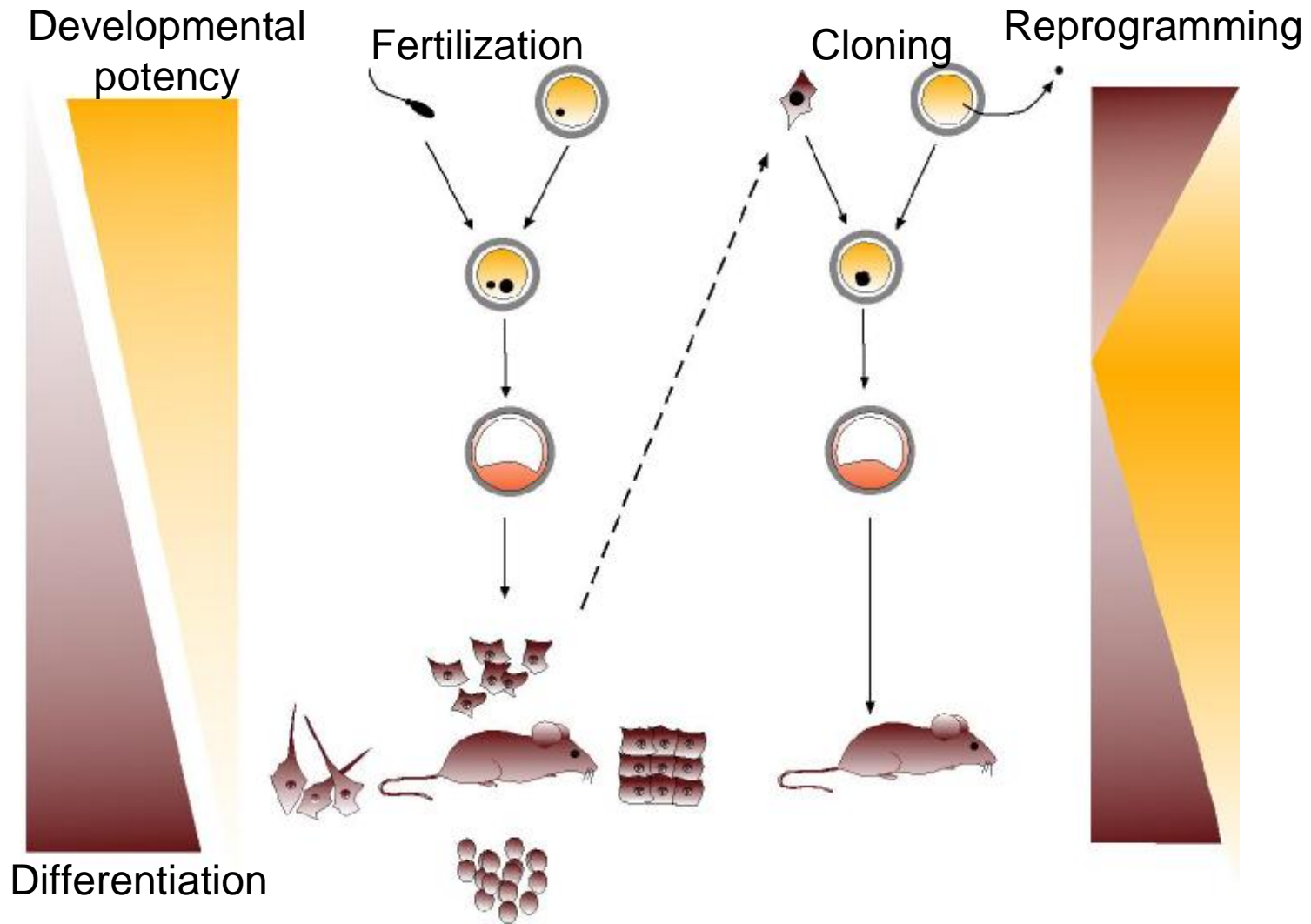
Other  
pluripotency  
markers

Chen et al. (2003) Embryonic stem cells generated by nuclear transfer of human somatic nuclei into rabbit oocytes; Cell Research, Vol. 13

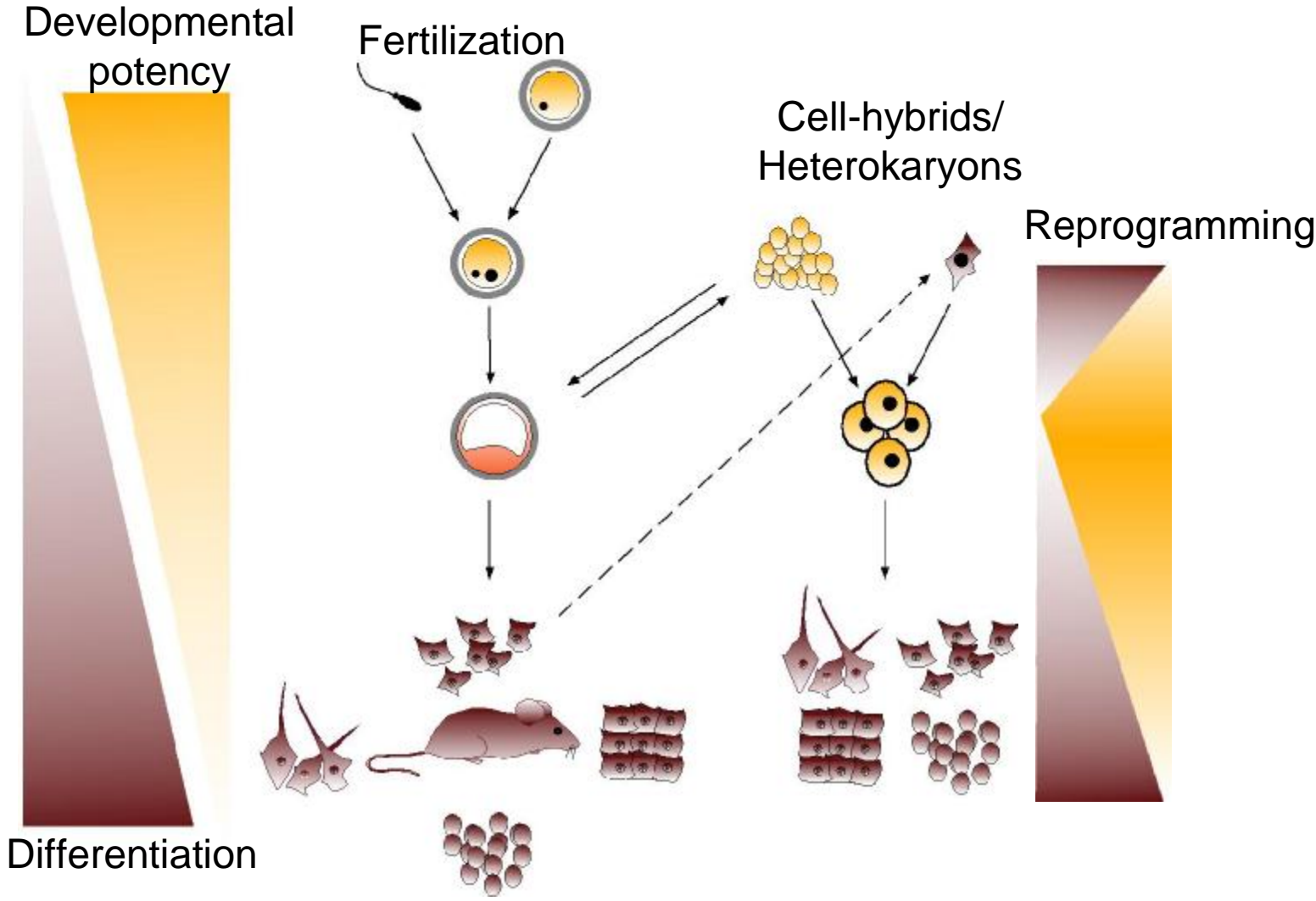
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# Programming and Reprogramming Development



# A Cell Based Method for Nuclear Reprogramming



# Summary

- § Potential utility of patient specific ES cell lines makes their derivation an important scientific priority.
  - § Transplant medicine
  - § Basic disease research
  - § Drug discovery
- § This goal is not yet realized.
- § Work in animals suggests that human SCNT for stem cell derivation should be possible.
- § Alternatives to human SCNT are not yet a reality even in animal models.