Missouri Roundtable For Life

Scientific Advances Render Embryo-Destructive Research Obsolete

Paid for by Missouri Roundtable For Life, F. Sauer, Treasurer

Scientific advances have transformed stem cell research

Rapid scientific advances in the past five years have transformed the stem cell field.

Scientist can now produce ***human pluripotent stem cells from easily obtainable adult human cells, without using human embryos, cloning human embryos, or destroying human embryos.***

In other words, we can obtain cells that behave like embryonic stem cells without the moral evil of manipulating and killing our littlest brothers and sisters.

These so-called induced pluripotent stem cells (iPS cells or iPSCs) are both easier to obtain than embryonic stem cells and more flexible tools for research and potential therapeutics. For example, genetically-matched patient-specific iPS cells can be easily generated, while producing such cells from human embryonic stem cells would require human cloning that has never been done.

Here is an outline of scientific advances since 2006. For a more thorough discussion, see "Harnessing the potential of induced pluripotent stem cells for regenerative medicine" by Wu & Hochedlinger (Nature Cell Biology, 2011).

Producing pluripotent stem cells without using human embryos

In 2006, Takahashi and Yamanaka showed that could generate mouse pluripotent stem cells from fibroblasts by the introduction of 4 factors (oct3/4, sox2, c-myc, and klf4). They termed these cells induced pluripotent stem (iPS) cells. iPS cells express embryonic stem (ES) cell marker genes and behave like ES cells.

> "These data demonstrate that pluripotent stem cells can be directly generated from fibroblast cultures by the addition of only a few defined factors." (Takahashi & Yamanaka, Cell 2006)

In 2007, two groups—Takahaski et al, and Yu et al.—demonstrated that human pluripotent stem cells could be generated from adult human cells using a similar technique.

> "These findings demonstrate that iPS cells can be generated from adult human fibroblasts." (Takahashi et al., Cell 2007)

> "We show that four factors… are sufficient to reprogram human somatic cells to pluripotent stem cells that exhibit the essential characteristics of embryonic stem (ES) cells." (Yu et al., Science 2007)

Improvements in induced pluripotent stem cell production

The techniques first used to produce iPS cells involved the use of viral vectors that integrate into the cell genome, which creates the potential for mutations in the cell. This limited the potential therapeutic uses of iPS cells.

But in 2009, Yu et al. produced human iPS without the use of integrating viral vectors.

> "Human iPS cell derivation previously required vectors that integrate into the genome, which can create mutations that limit the utility of the cells in both research and clinical applications. We describe the derivation of human iPS cells with the use of nonintegrating episomal vectors. After removal of the episome, iPS cells completely free of vector and transgene sequences are derived… These results demonstrate the reprogramming human somatic cells does not require genomic integration or the continued presence of exogenous reprogramming factors and removes one obstacle to the clinical application of human iPS cells." (Yu et al., Science 2009)

Shortly thereafter, in June 2009, Kim et al. reported the production of human iPS cells with the use of any viral or other DNA vectors at all. Instead, they delivered the reprogramming proteins themselves, rather than the DNA that encodes them, directly into human fibroblasts to generate human iPS cells.

> "[W]e report the generation of stable iPS cells from human fibroblasts by directly delivering four reprogramming proteins (Oct4, Sox2, Klf4, and c-Myc)… This system eliminates the potential risks associated with the use of virues, DNA transfection, and potentially harmful chemicals, and in the future could potentially provide a safe source of patient-specific cells for regenerative medicine." (Kim et al., Cell Stem Cell 2009).

Induced pluripotent stem cells from multiple easily obtainable cell types

Recent research has demonstrated that iPS cells can be derived from multiple human cell types, making them readily available.

> "iPSCs have been derived at increased efficiencies from several easily accessible human cell types, including blood cells, keratinocytes and dermal fibroblasts." (Wu & Hochedlinger, Nature Cell Biology 2011).

For example, in 2008, iPS cells were produced from human dermal fibroblasts (skin cells).

> "[W]e describe methods to use dermal fibroblasts easily obtained from an individual human to generate human induced pluripotent stem (iPS) cells…" (Lowry et al., PNAS 2008)

Later in 2008, researchers reported the generation of iPS cells from human keratinocytes, that is, cells from the outermost layer of the human skin.

> "[W]e show that reprogramming of juvenile human primary keratinocytes… is at least 100-fold more efficient and twofold faster compared with reprogramming of human fibroblasts." (Aasen et al., Nature Biotechnology 2008)

Then in 2009, researchers generated induced pluripotent stem cells from human cord blood.

> "[W]e report the generation of human iPSCs from cord blood (CB)… CBiPSCs show characteristics typical of embryonic stem cells and can be differentiated into derivatives of all three germ layers, including functional cardiomyocytes [heart cells]." (Haase et al., Cell Stem Cell 2009)

Also in 2009, researchers produced iPS cells from peripheral blood, which is of course easily obtainable.

> "[W]e describe the derivation of induced pluripotent stem cells from… human peripheral blood cells..." (Loh et al., Blood 2009)

Disease-specific induced pluripotent stems cells

Induced pluripotent stem cells have been produced from patients with various diseases. In some cases, these iPS cells have then been used to generate more fully differentiated cells of the type relevant to the particular disease, an advance that has the potential to facilitate disease modeling and development of novel treatments.

> "[R]ecent studies have described the generation of iPSC lines from patients with a full range of genetially inherited as well as sporadic diseases… In most cases, *in vitro* differentiation of iPSCs to the cell type relevant to the disorder has been reported, and there are now many studies that suggest that patient-specific iPSCs exhibit certain disease features." (Wu & Hochedlinger, Nature Cell Biology 2011)

For example, in 2009, researchers reported both the production of iPS cells from a patient with spinal muscular atrophy and then the production of motor nerve cells from the iPS cells.

> "Spinal muscular atrophy is one of the most common inherited forms of neurological disease leading to infant mortality. Patients have selective loss of lower motor neurons resulting in muscle weakness, paralysis, and often death… [W]e report the generation of induced pluripotent stem cells

> from skin fibroblast samples taken from a child with spinal muscular atrophy. These cells expanded robustly in culture, maintained the disease genotype and generated motor neurons that showed selective deficits compared to those derived from the child's unaffected mother… [This study] represents a promising resource to study disease mechanisms, screen new drug compounds and develop new therapies." (Ebert et al., Nature 2009)

Direct conversion of adult skin cells into other types of cells

Recently, scientists have converted skin cells directly into other cell types, including blood progenitor cells, heart cells, and nerve cells, without even having to first produce iPS cells.

For example, in 2010, researchers converted human skin cells into blood progenitor cells.

> "[W]e demonstrate the ability to generate progenitors and mature cells of the haematopoietic fate directly from human dermal fibroblasts without establishing pluripotency… These unique fibroblast-derived cells gave rise to granulocytic, monocytic, megakaryocytic and erythroid lineages… These findings demonstrate restoration of multipotency from human fibroblasts, and suggest an alternative approach to cellular reprogramming for autologous cell replacement therapies that avoids complications associated with the use of human pluripotent stem cells." (Szabo, Nature 2010)

Also in 2010, scientists converted skin cells into functional heart cells.

> "[W]e report that a combination of three developmental transcription factors… rapidly and efficiently reprogrammed postnatal cardiac or dermal fibroblasts directly into differentiated cardiomyocyte-like cells. Induced cardiomyocytes expressed cardiac-specific markers had a global gene expression profile similar to cardiomyocytes, and contracted spontaneously." (Ieda, Cell 2010)

And researchers have converted skin cells into functional nerve cells.

> "[W]e identified a combination of only three factors… that suffice to rapidly and efficiently convert… postnatal fibroblasts into functional neurons in vitro. These induced neuronal (iN) cells express multiple neuron-specific proteins, generate action potentials and form function synapses." (Vierbuchen, Nature 2010)

Summary

Scientists can now easily produce pluripotent stem cells without using human embryos, cloning human embryos, or killing human embryos.

These induced pluripotent stem cells behave like embryonic stem cells, but are easier to obtain. They can be generated from multiple easily available adult cell types, including skin cells and blood cells.

And these induced pluripotent stem cells are more flexible tools for research and potential therapeutics. For example, patient-specific and disease-specific induced pluripotent stem cells can be easily produced. This is not possible with embryonic stem cells using current technology.

And the field of cell reprogramming is advancing rapidly—indeed, scientists have recently converted adult skin cells directly into other cell types, including heart cells and nerve cells, bypassing the pluripotent cell stage entirely.

Thus, cloning or destroying human embryos for their stem cells is not only immoral, it is also scientifically obsolete. The field is advancing rapidly without the need to clone or kill human embryos for research purposes.

References

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