

## **Update: Breakthroughs in Stem Cell Research**

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In 1998, stem cells were plucked from human embryos for the first time for the purpose of conducting stem cell research. Proponents of this type of research claim that human embryonic stem cells might be useful to understand disease mechanisms, to screen safe and effective drugs, and to treat patients of various diseases and injuries, such as juvenile diabetes and spinal cord injury.<sup>1</sup>

This research sparked an intense ethical debate, mainly because the embryo is destroyed in the process. Why is the destruction of something so small—an 8-cell embryo, for example, a few days old, is only about .2 mm in diameter—opposed by the Catholic Church? Catholic teaching is clear that we must respect the inherent dignity of all human life, which begins at the moment of fertilization.

By comparison, the Church does not oppose adult stem cell (stem cells not taken from embryos, e.g. umbilical cord stem cells) research, because it does not destroy life and offend human dignity. The Church supports ethical science that would achieve the stated goals of adult stem cell research, to achieve cures for serious illnesses and diseases.

Rapid developments in this area may soon make embryonic stem cell experimentation less useful, without forgoing the potential benefits. However, these new developments are not totally free of ethical problems.

To understand the current state of stem cell research, it is helpful to review a major breakthrough in this field credited to Dr

Yamanaka of Japan. Some other recently published breakthroughs in stem cell research are listed below.<sup>2</sup>

### **2006 - 2007**

Dr Yamanaka from Kyoto University and his international team made a significant breakthrough in 2006 when they were able to genetically reprogram mouse skin cells into an embryo-like state.<sup>3,4</sup> These were not embryos, but only embryo-like cells. He called these new cells induced pluripotent stem cells (iPS). (Pluripotent cells have the theoretical potential to develop into any cell type. There are 220 in the human body.) This was accomplished by using a virus to insert four genes of mouse origin, called factors, into the genome (complete DNA) of the mouse skin cell.<sup>5</sup>

In 2007, Dr Yamanaka successfully generated iPS from human adult skin cells. The same four genes and viruses used in 2006 were also used here. A diagram found at this footnote titled “From Skin Cells to Stem Cells” compares Yamanaka’s breakthrough to previously existing techniques.<sup>6</sup>

A review of the methods used by Dr Yamanaka indicates that material from embryos or aborted fetuses was not used in the development of his techniques. However, human embryonic stem cells were used in testing that compared the properties of the iPS with those of human embryonic stem cells, and that use is morally problematic for many people.<sup>7</sup>

Ever since Yamanaka’s breakthrough discovery, researchers have looked for ways to avoid the use of the viruses and genes that

trigger the transformation. The difficulty with viruses is that they also create the potential for cancerous tumors.<sup>8</sup>

#### **MARCH 1, 2009**

On March 1, 2009, *Nature* published on-line a report revealing the latest advance in stem cell research credited to Dr Nagy of Mount Sinai Hospital in Toronto and his international team of researchers.<sup>9</sup> They developed a technique that reprogrammed mouse and human skin cells without using viruses back to an embryo-like state. To accomplish this, these researchers inserted the factors (identified by Yamanaka) into another piece of DNA that was itself inserted into the genome of the target skin cells.<sup>10</sup>

The team then demonstrated that they could remove the factors from the mouse skin cells. Until these factors can be removed from the human skin cells, the technique is not a major advance over viral methods.<sup>11</sup> “The problem is if you leave the factors behind...they could misbehave and could create cancer,” said Nagy.<sup>12</sup>

Using mouse genetic material to reprogram a human skin cell does not appear to be morally problematic. Using material from 12-week-old abortuses is morally problematic, and that was done here. Why is this immoral? Since abortion is wrong, the use of an abortus for any other purpose is also wrong, i.e., it is collusion in evil.

On the other hand, if the use of abortuses does not remain an essential part of this technique, the moral questions may disappear.

#### **MARCH 6, 2009**

On March 6, 2009, *Cell* reported that Dr Jaenisch from The Whitehead Institute in Cambridge, Massachusetts, and his colleagues at other institutions were able to create factor-free iPS with cells taken from five Parkinson’s patients.<sup>13, 14</sup> The

Yamanaka factors were used, but were subsequently completely excised. These iPS then developed into neurons in vitro (in laboratory glassware as opposed to in vivo, in a living organism).

“These don’t yet have therapeutic power,” Jaenisch said, “but are still useful for studying disease in a person-specific way...For the first time, we can generate these cells in a culture dish, and study the mechanisms that led to their disease in the first place.”<sup>15</sup>

As with Yamanaka’s research, Jaenisch used human embryonic stem cells to test the properties of these iPS to determine how embryo-like they were.

#### **APRIL 23, 2009**

On April 23, 2009, *Cell Stem Cell* published the work of a group of researchers at The Scripps Research Institute (located in Florida and California) on their new technique of creating embryo-like cells.<sup>16, 17</sup> Instead of using genetic material as other methods do, these researchers relied on recombinant proteins, which are made from the recombination of fragments of DNA from different organisms. These proteins penetrated cells in mouse fibroblasts.<sup>18</sup>

The link to a short video of some beating mouse cardiac cells developed in vitro with this technique can be found in the article referred to in endnote nineteen.<sup>19</sup> Compared to all existing techniques, this new technique is safer, simpler, faster, and potentially more economical in large-scale production not to mention ethical.

Yamanaka’s factors were of mouse origin, but this group of researchers decided to use the human equivalent of these factors in making the recombinant proteins.<sup>20, 21</sup> A major concern for many is whether the genetic material for these factors came from abortuses or human embryos, but since the

factors are obtainable from adult sources, the moral question can be resolved.

## CONCLUSION

The breakthroughs discussed in this article are significant, although some ethical concerns remain. The good news is that given the speed of developments in this field, it is quite likely that these ethical concerns will be resolved soon. ■

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<sup>1</sup> Takahashi et al., Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors, *Cell* (2007), doi:10.1016/j.cell.2007.11.019

<sup>2</sup> [http://www.cell.com/cell-stem-cell/fulltext/S1934-5909\(09\)00159-3](http://www.cell.com/cell-stem-cell/fulltext/S1934-5909(09)00159-3)

<sup>3</sup> Dept of Stem Cell Biology at Kyoto University; CREST, Japan Science and Technology Agency; Kawaguchi, Japan; Gladstone Institute of Cardiovascular Disease at San Francisco; Institute for Integrated Cell-Material Sciences at Kyoto University

<sup>4</sup> *Nature*, published online 1 March 2009 | 458, 19 (2009) | doi:10.1038/458019a

<sup>5</sup> These are identified as Oct3/4, Sox2, Klf4, and c-Myc, and come from mice.

<sup>6</sup> [http://www.nytimes.com/imagepages/2007/06/06/science/07cell\\_graphic.html](http://www.nytimes.com/imagepages/2007/06/06/science/07cell_graphic.html)

<sup>7</sup> These properties include: morphology, proliferation, surface antigens, gene expression, epigenetic status of pluripotent cell-specific genes, and telomerase activity.

<sup>8</sup> [http://www.boston.com/news/nation/articles/2009/03/06/new\\_technique\\_boosts\\_stem\\_cell\\_safety/](http://www.boston.com/news/nation/articles/2009/03/06/new_technique_boosts_stem_cell_safety/)

<sup>9</sup> Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, Canada; Dept of Molecular Genetics, University of Toronto; The Wellcome Trust Sanger Institute, Cambridgeshire, UK; MRC Centre for Regeneration Medicine, Institute for Stem Cell Research, University of Edinburgh, UK.

<sup>10</sup> This piece of DNA is called a cassette, which contains a jumping gene known as piggyBAC. Hence,

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this technique is referred to as piggyBAC transposition.

<sup>11</sup> <http://www.nature.com/news/2009/090227/full/458019a.html>

<sup>12</sup> [http://www.boston.com/news/nation/articles/2009/03/06/new\\_technique\\_boosts\\_stem\\_cell\\_safety/](http://www.boston.com/news/nation/articles/2009/03/06/new_technique_boosts_stem_cell_safety/)

<sup>13</sup> The Whitehead Institute, Cambridge, MA; Dept of Biology, MIT; Udall Parkinson Disease Research Centre for Excellence, McLean Hospital/Harvard Medical School, MA.

<sup>14</sup> The type of cell used in this case was a fibroblast, which is found in connective tissue.

<sup>15</sup> <http://www.wired.com/wiredscience/2009/03/virusfreeips/>

<sup>16</sup> [http://www.cell.com/cell-stem-cell/fulltext/S1934-5909\(09\)00159-3](http://www.cell.com/cell-stem-cell/fulltext/S1934-5909(09)00159-3)

<sup>17</sup> [http://www.scripps.edu/e\\_index.html](http://www.scripps.edu/e_index.html)

<sup>18</sup> The type of cell used was a mouse embryonic fibroblast.

<sup>19</sup> [http://www.cell.com/cell-stem-cell/fulltext/S1934-5909\(09\)00159-3](http://www.cell.com/cell-stem-cell/fulltext/S1934-5909(09)00159-3)

<sup>20</sup> <http://download.cell.com/cell-stem-cell/mmcs/journals/1934-5909/PIIS19345909001593.mmc1.pdf>

<sup>21</sup> Fusing the factors to an IIR protein created the recombinant proteins.

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