

Scientists on the meaning of the adult cell reprogramming (iPS cell) advance

In November 2007, researchers discovered a way to reprogram ordinary adult human cells into cells with the versatility and other properties of embryonic stem cells, without using eggs or embryos (“induced pluripotent stem cells” or “iPS cells”). Further advances have quickly followed to make this approach safer and more efficient, creating a new paradigm for stem cell research. Leading researchers and science writers have been commenting on the implications:

Dr. Keisuke Kaji of the Medical Research Council Centre for Regenerative Medicine, University of Edinburgh, where his team discovered a new and safer way to produce these cells without using viruses:

BBC News, March 1, 2009

<http://news.bbc.co.uk/1/hi/health/7914976.stm>

“It is a step towards the practical use of reprogrammed cells in medicine, perhaps even eliminating the need for human embryos as a source of stem cells.”

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New biotechnology company Fate Therapeutics, announcing that MIT’s prestigious embryonic stem cell researcher Dr. Rudolf Jaenisch has become a founding member of its scientific team exploring the potential of adult cell reprogramming:

Business Wire, February 25, 2009

www.businesswire.com/portal/site/topix/index.jsp?ndmViewId=news_view&newsId=20090225005434&newsLang=en&ndmConfigId=1000639&vnsId=41

“Dr. Jaenisch is credited with being one of the first to discover the revolutionary mechanisms for ‘reprogramming’ fully-mature adult cells to a stem-like state. The creation of these ‘reprogrammed’ cells, known as induced pluripotent stem (iPS) cells, **provides numerous advantages over stem cells sourced from human embryos** and has **ushered in a new paradigm in stem cell research** for modeling human diseases, discovering and testing conventional pharmaceuticals and developing personalized cell replacement therapies.”

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Arnold R. Kriegstein, director of the Eli and Edythe Broad Center of Regeneration Medicine and Stem Cell Research at the University of California at San Francisco:

The Chronicle of Higher Education, February 4, 2009

Mr. Obama's anticipated reversal of policy “won’t be a boon the way some people might think... Time has moved on, and so has the field.”

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David T. Scadden, co-director of the Stem Cell Institute at Harvard University:

Id.

Dr. Yamanaka's breakthrough [in producing iPS cells] "is absolutely changing the field... It may be that we'll be able to get away from embryonic stem cells completely. That's something we're all hoping will happen."

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Harry Moore, head of reproductive biology at Sheffield University, on why human embryo cloning experiments using animal eggs are not receiving public funds in the United Kingdom despite being approved on ethical grounds:

The Guardian, 13 January 2009

www.guardian.co.uk/science/2009/jan/13/hybrid-embryos-stem-cells

"What has happened is the field has moved on. You could argue that iPS cells are a more important area than hybrids now."

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Sir Leszek Borysiewicz, chief executive of the United Kingdom's Medical Research Council, explaining this same point:

Id.

"The MRC must make the best use of taxpayers' money and there is no better way to decide what should be funded than to use tried-and-tested peer review systems where scientists assess applications on their merits.... Fighting for the right to carry out such research [obtaining embryonic stem cells from hybrid cloned embryos] does not mean that it should get priority over other applications which *score higher* and *hold more promise*" (emphasis added).

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University of Wisconsin researcher Dr. James Thomson, leading one of the two teams announcing the breakthrough in creating "induced pluripotent stem" [iPS] cells (and the first researcher, in 1998, to isolate embryonic stem [ES] cells by destroying human embryos):

Science, 21 December 2007 (p. 1919)

"The human iPS cells described here meet the defining criteria that we originally proposed for

human ES cells, with the notable exception that the iPS cells are not derived from embryos. Similar to human ES cells, human iPS cells should prove useful for studying the development and function of human tissues, for discovering and testing new drugs, and for transplantation medicine. For transplantation therapies based on these cells, with the exception of autoimmune diseases, patient-specific iPS cell lines should largely eliminate the concern of immune rejection.”

Dr. Thomson on how this advance means “the beginning of the end” for human embryonic stem cell research:

The New York Times, November 22, 2007

<http://www.nytimes.com/2007/11/22/science/22stem.html?ref=science&pagewanted=print>

“The fact is, Dr. Thomson said in an interview, he had ethical concerns about embryonic research from the outset, even though he knew that such research offered insights into human development and the potential for powerful new treatments for disease. ‘If human embryonic stem cell research does not make you at least a little bit uncomfortable, you have not thought about it enough,’ he said. ‘I thought long and hard about whether I would do it.’....

“Now with the new technique, which involves adding just four genes to ordinary adult skin cells, it will not be long, he says, before the stem cell wars are a distant memory. ‘A decade from now, this will be just a funny historical footnote,’ Dr. Thomson said in the interview.....

“More work remains, but he is confident that the path ahead is clear. ‘Isn’t it great to start a field and then to end it,’ he said.”

The Boston Globe, November 21, 2007

www.boston.com/news/science/articles/2007/11/21/breakthrough_on_stem_cells?mode=PF

“‘The world has changed,’ said James Thomson, head of the University of Wisconsin lab where scientist Junying Yu led the effort to form the new cells, called induced pluripotent stem cells. ‘It is the beginning of the end of the controversy that has surrounded this field,’ Thomson told a news conference. ‘Over time, these [induced] cells will be used in more and more labs. And human embryo stem cell research will be abandoned by more and more labs.’”

The Washington Post, November 20, 2007

www.washingtonpost.com/wp-dyn/content/article/2007/11/20/AR2007112000546_pf.html

“Thomson, a shy and laconic laboratory researcher whose 1998 discovery made him the focus of religious opprobrium and repeated congressional hearings, expressed relief that he may now be able to work without being at the center of what had become America's other abortion debate.

‘What a great bookend,’ Thomson said in an interview. ‘Ten years of turmoil and now this nice ending. I can relax now.’”

The Detroit Free Press, November 21, 2007

www.freep.com/apps/pbcs.dll/article?AID=/20071121/NEWS07/711210405/1009

“While ducking ethical debate wasn't the goal, Thomson said this is ‘probably the beginning of the end of the controversy’ over embryonic stem cells.”

Medical News Today, November 26, 2007

www.medicalnewstoday.com/printerfriendlynews.php?newsid=89799

“Speaking about this latest breakthrough, Thomson said: ‘The induced cells do all the things embryonic stem cells do. It's going to completely change the field.’....

“The other advantage of the new method is the fact that using cells drawn from the patient’s own skin, the stem cells can be customized to the patient, bringing numerous benefits, such as the elimination of immune system rejection. Thomson put it like this: ‘They are probably more clinically relevant than embryonic stem cells.’”

The Daily Cardinal (newspaper of the University of Wisconsin), November 26, 2007

www.dailycardinal.com/article/1282

“‘I believe that these new results, while they don’t eliminate the controversy, it’s probably the beginning of the end of that controversy,’ Thomson said.”

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Dr. Shinya Yamanaka, leader of the other (Japanese) team and first discoverer of the “induced pluripotent stem cell”:

TIME, December 3, 2007

www.time.com/time/magazine/article/0,9171,1686833,00.html

“‘We can now for sure begin to generate patient-specific stem cells. And we should be able to use them in cell-transplant therapy.’”

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Dr. John Gearhart of Johns Hopkins University, a leading stem cell researcher who first isolated “embryonic germ cells” from fetal reproductive tissue:

CNN, November 21, 2007

www.cnn.com/HEALTH/blogs/paging.dr.gupta/2007/11/new-stem-cells-what-they-could-mean-to.html

“‘This opens this up to a huge field,’ according to Dr. John Gearhart, a long-time stem cell researcher at Johns Hopkins School of Medicine. He says now researchers ‘don’t have to learn how to work with embryonic stem cells’ because it’s a simple process to create these new stem cells. ‘This is going to become a very common technology.’”

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Dr. Ian Wilmut, pioneering cloning researcher who cloned “Dolly” the sheep:

The London Telegraph, November 16, 2007

www.telegraph.co.uk/earth/main.jhtml?xml=/earth/2007/11/16/scidolly116.xml&page=1

“Prof. Ian Wilmut's decision to turn his back on ‘therapeutic cloning’ ... will send shockwaves through the scientific establishment....

“Prof. Wilmut, who works at Edinburgh University, believes a rival method pioneered in Japan has better potential for making human embryonic cells which can be used to grow a patient’s own cells and tissues for a vast range of treatments, from treating strokes to heart attacks and Parkinson’s, and will be less controversial than the Dolly method, known as ‘nuclear transfer.’

“His announcement could mark the beginning of the end for therapeutic cloning, on which tens of millions of pounds have been spent worldwide over the past decade... Most of his motivation is practical but he admits the Japanese approach is also ‘easier to accept socially.’...

“Prof. Wilmut said [the cell reprogramming advance] was ‘extremely exciting and astonishing’ and that he now plans to do research in this area. This approach, he says, represents the future for stem cell research, rather than the nuclear transfer method that his large team used more than a decade ago at the Roslin Institute, near Edinburgh, to create Dolly.”

TIME, December 3, 2007

www.time.com/time/specials/2007/article/0,28804,1685055_1686349_1686638,00.html

“Ian Wilmut, the scientist responsible for cloning the first mammal, Dolly the sheep, has announced that he is abandoning the egg-hollowing, gene-replacing technique that made him a pioneer, noting that ‘changing cells from a patient directly into stem cells has got so much more potential.’ No embryos, no eggs, no hand-wringing over where the cells came from and whether it was ethical to make them in the first place.”

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Dr. Jose Cibelli, stem cell researcher at Michigan State University, formerly vice president of research at Advanced Cell Technology which pioneered human cloning research:

Science, 21 December 2007, pp. 1879-80 at 1880

“Is human therapeutic cloning no longer needed? The short answer is no, but it is likely a matter of time until all the hypothetical advantages of therapeutic cloning will be implemented with induced pluripotent stem cells. More importantly, the controversial issues (ethical and technical) specific to human therapeutic cloning may well be left behind along with the procedure itself, a refreshing change for the field, indeed.”

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Dr. Richard Boyd, professor of immunology at Monash University and one of Australia’s top stem cell experts, on the new move away from human cloning research:

The Sydney Morning Herald, 21 November 2007

www.smh.com.au/news/National/Study-shows-shift-in-cloning-ommunity/2007/11/21/1195321821901.html

“There is a definite move now towards this new [iPS] area which is potentially so much easier and free of the ethical stresses that surround classical embryonic stem cell research... For one, it allows us to derive stem cells from any patient without the need for human eggs, which is very important in Australia because that has been a major ethical issue here....

“By comparison with the classical embryonic stem cell process, which requires us to use thousands of eggs, this is much more efficient, technically much easier and it solves some of those more emotional dilemmas.”

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Science writer Bruce Goldman, surveying the research field:

“Embryonic Stem Cells 2.0,” *Nature Reports Stem Cells*, published online 1 May 2008

“The fact that making iPS cells does not pose the technical and ethical challenges of working with eggs or embryos is drawing large numbers of researchers into the field and speeding up reprogramming research....

“‘Biologically there’s no difference’ between murine iPS and ES cells, says [Dr. Rudolf] Jaenisch. Both can generate all the tissues in a mouse. Human iPS cells have not been as rigorously demonstrated to be quasi-equivalent to ES cells, and they won’t be, because doing so would require generating human babies or fetuses. Such experimentation is irrelevant anyway,

says Douglas Melton, director of the Harvard Stem Cell Institute in Cambridge, Massachusetts, who has derived multiple human ES cell lines. ‘Nobody’s trying to make people.’....

“No one doubts that iPS cells will eventually be generated from the cells of individuals with known medical history. That was the main advantage claimed for somatic cell nuclear transfer, a technically and ethically challenging procedure that has yet to be achieved in humans. For generating person-matched cells, iPS cells may be not only easier to use but perhaps superior, as they would share both nuclear and mitochondrial DNA with the original patient, whereas cells derived by somatic cell nuclear transfer carry only the same nuclear DNA....

“Like a new computer operating system, iPS cells are muscling into the field as their radically fewer barriers to entry, compared with those for ES cells, accelerate the pace of research. The ten-year head start human ES cells got on human iPS cells has effectively shrunk to zero, says [Dr. James] Thomson, because so much of the legacy of ES cells — reagents, culture media, hands-on expertise and experimental history — is transferable to iPS cells. Tissue culture is simpler than embryology. Skin is cheap. Creating iPS cells that are innately immunologically compatible with the patient from whose cells they were derived presents an attractive alternative to obtaining human eggs, executing difficult nuclear-transfer protocols and destroying embryos.”

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