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Committee on Health and Aging, Ohio House
June 15, 2011

Mr. Chairman, the Distinguished Ranking Member, and Honored Members of the Committee.

Thank you for the opportunity to testify on this important legislation.
I am testifying in SUPPORT of HB 171

I am a cell biologist, currently working for a policy think tank in Washington, D.C. For the previous 20 years I was Professor of Life Sciences at Indiana State University and Adjunct Professor of Medical & Molecular Genetics at Indiana University School of Medicine, and I have done federally-funded laboratory research, lectured, and advised on these subjects extensively, in the U.S. and internationally. I was selected by the Bush President's Council on Bioethics to write the comprehensive review of adult stem cell research for the Council's 2004 publication "Monitoring Stem Cell Research".

Human cloning is human asexual reproduction, termed "asexual" because it does not involve the combining of egg and sperm to form an embryo. The focal technique to accomplish this is somatic cell nuclear transfer (SCNT)—introducing the nuclear genetic material from one or more human somatic (body) cells into a fertilized or unfertilized egg cell whose nuclear genetic material has been removed or inactivated, producing a human embryo who is virtually genetically identical to an existing or previously existing human being.

Proponents of human cloning hold out two hopes for its use: (1) creating live born children for infertile couples or those grieving over the loss of a loved one, so-called "reproductive cloning" (live birth cloning), and (2) promises of medical miracles to cure diseases by harvesting embryonic stem cells from cloned embryos created from patients, euphemistically termed "therapeutic cloning" (more properly termed research cloning.)

Biologically the process of cloning (somatic cell nuclear transfer; SCNT) produces a zygote, a one-celled embryo, at the starting point for development. As the **President's Council on Bioethics** noted, "The first product of SCNT is, on good biological grounds, quite properly regarded as the equivalent of a zygote, and its subsequent stages as embryonic stages in development."[1]

Likewise, the **National Institutes of Health** has affirmed that SCNT cloning produces an embryo.[2]

The **National Academy of Sciences** noted the following:

> "**The method used to initiate the reproductive cloning procedure is called nuclear transplantation, or somatic cell nuclear transfer (SCNT)**. It involves replacing the chromosomes of a human egg with the nucleus of a body (somatic) cell from a developed human. In reproductive

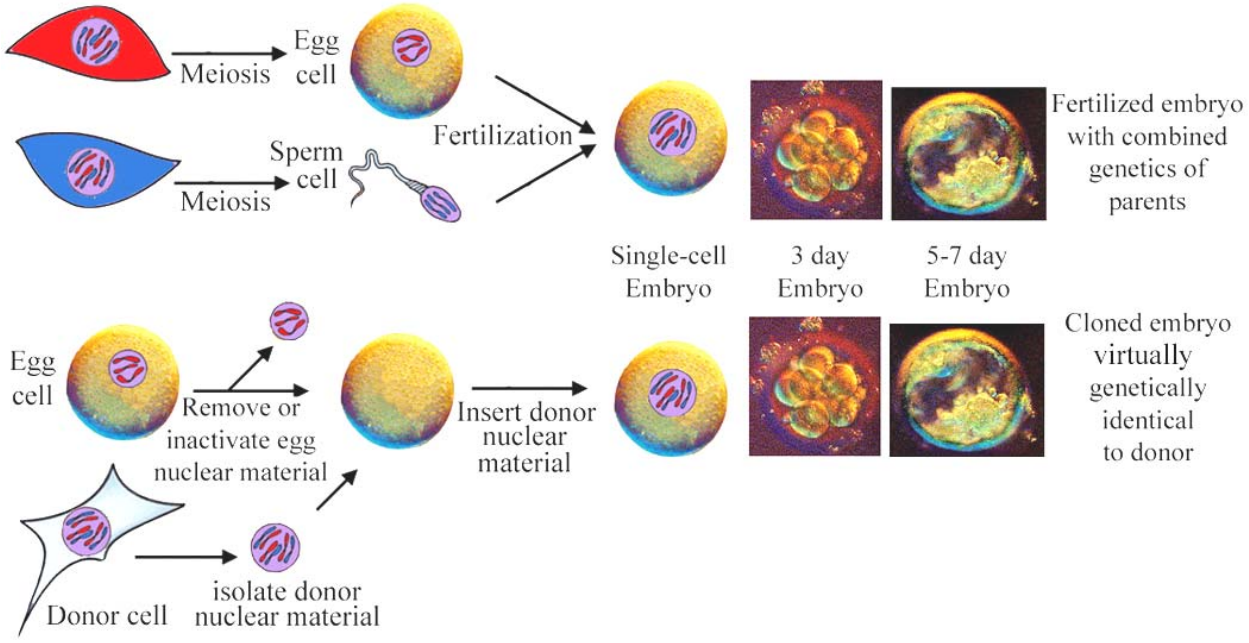
[1] "Human Cloning and Human Dignity: An Ethical Inquiry", Report of the President's Council on Bioethics, July 2002; p.50

[2] See NIH Glossary, under "Therapeutic Cloning" and "Reproductive Cloning"; http://stemcells.nih.gov/info/glossary.asp

cloning, the egg is then stimulated to undergo the first few divisions to become an aggregate of 64 to 200 cells called a blastocyst. The blastocyst is a preimplantation embryo that contains some cells with the potential to give rise to a fetus and other cells that help to make the placenta. If the blastocyst is placed in a uterus, it can implant and form a fetus. If the blastocyst is instead maintained in the laboratory, cells can be extracted from it and grown on their own."[3]

The equivalence of the embryo, as zygote and blastocyst, has also been noted by the National Academy of Sciences,[4] which has noted that the embryos produced by fertilization and the embryos produced by SCNT cloning are **indistinguishable**.[5]

Fertilization compared to Cloning (Somatic Cell Nuclear Transfer, SCNT)



Both sexual reproduction (fertilization, egg+sperm) and asexual reproduction (cloning, *i.e.*, somatic cell nuclear transfer) produce a human embryo, a living human organism, species *Homo sapiens*.

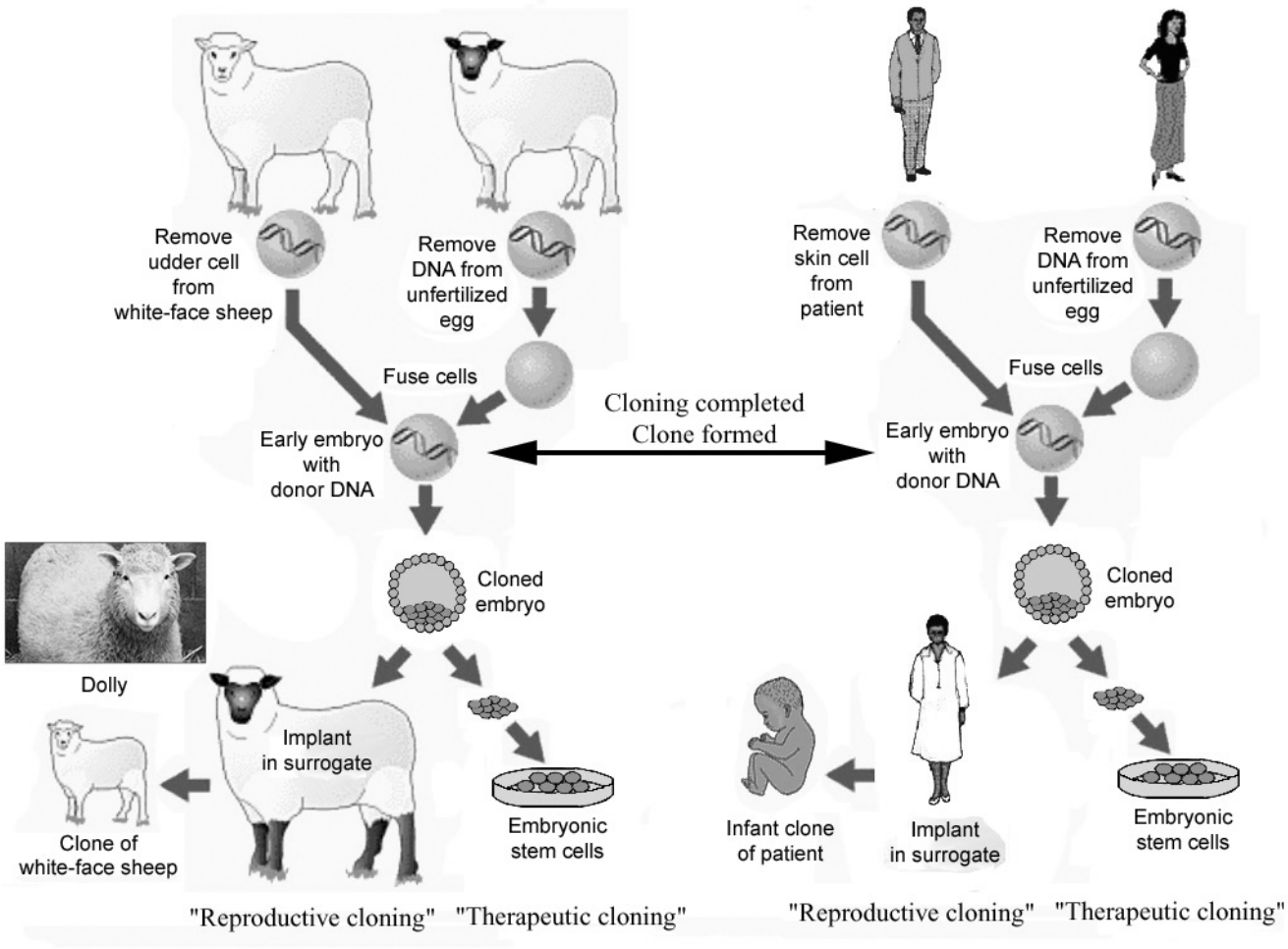
Cloning (SCNT) creates an embryo, not stem cells.

[3] Scientific and Medical Aspects of Human Reproductive Cloning, Report of the National Academy of Sciences and the Institute of Medicine, National Academy Press, Washington, DC, Jan 2002; Preface page xii

[4] Stem Cells and the Future of Regenerative Medicine, Report of the National Academy of Sciences and the Institute of Medicine, National Academy Press, Washington, DC, Sept 2001; pp 10, 11, 26.

[5] National Academy of Sciences, Guidelines for Human Embryonic Stem Cell Research (2005), p. 29

This is the same cloning technique, **somatic cell nuclear transfer (SCNT), that was the process used to create the cloned sheep Dolly**.



We need to be clear on the terms. **Both "reproductive" and "therapeutic" cloning use exactly the same techniques to create the clone, and the cloned embryos are indistinguishable**. The process, as well as the product, is identical. The only distinction is the purpose for use of the embryo—either transfer to a uterus in the hopes of a live birth, or destruction in the hopes of a medical miracle.

The technique of cloning is finished once that first cell, the one-celled embryo (zygote) is formed. Anything beyond that step is simply growth and development. And despite attempts to employ various euphemisms, scientifically, genetically, what is created is a human being; its species is *Homo sapiens*, it is neither fish nor fowl, monkey nor cow—it is human. The use of disingenuous euphemisms to describe the embryo as something other than an embryo likewise are not scientific, and diverge from the accepted definitions as put forth by the National Academy of Sciences, the National Institutes of Health, and others, including well-known proponents of human cloning.

This fact is also made clear by leading proponents of embryo research:

> "Moreover, because therapeutic cloning requires the creation and disaggregation ex utero of blastocyst stage embryos, this technique raises complex ethical questions."

"[Therapeutic cloning] requires the deliberate creation and disaggregation of a human embryo."[6]

Q: The people who use nuclear transfer generally say that the technique is optimized for producing the stem cells rather than making babies. They would not want to equate this with the process that produces embryos that were fit for implantation, and they'd argue that they're using the reproductive process differently … A: (**James Thomson**) "See, you're trying to define it away, and it doesn't work. If you create an embryo by nuclear transfer, and you give it to somebody who didn't know where it came from, there would be no test you could do on that embryo to say where it came from. It is what it is. It's true that they have a much lower probability of giving rise to a child. … But by any reasonable definition, at least at some frequency, you're creating an embryo. If you try to define it away, you're being disingenuous."[7]

The assumption that cloning (SCNT) will produce matching tissues for transplant that will not be rejected is still theoretical. When tested in mice in 2002,[8] the ES cells from the cloned mouse embryo were rejected by the genetically-identical host:

> "Jaenisch addressed the possibility that ES clones derived by nuclear transfer technique could be used to correct genetic defects… However, the donor cells, although derived from the animals with the same genetic background, are rejected by the hosts."[9]

In 2008, another lab attempted to treat Parkinson's in mice, first cloning the mice, then harvesting stem cells from the cloned embryos. When placed back into the mice, there was some improvement in their condition, but 1 out of 6 mice showed "graft overgrowth" in their brains, most of the cells produced showed chromosomal abnormalities, and the authors noted that it was "technically complex" and required a huge number of eggs to get a single dish of cells.[10] It is unknown whether tumors might have developed later in other animals as the experiment was terminated early. Moreover, the data are equivocal in terms of transplant matching, due to the fact that the brain is an immuno-privileged site (very little immune reaction).

In fact, the best results to date (even though equivocal) in animal studies actually come from gestating cloned animals to the fetal stage and then harvesting tissue stem cells.[11,12,13]

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[6] Robert P. Lanza, Arthur L. Caplan, Lee M. Silver, Jose B. Cibelli, Michael D. West, Ronald M. Green; "The ethical validity of using nuclear transfer in human transplantation"; *The Journal of the American Medical Association* 284, 3175-3179; Dec 27, 2000.

[7] Stem-cell pioneer does a reality check. James Thomson reflects on science and morality, By Alan Boyle Science editor MSNBC Updated: 4:13 p.m. ET June 22, 2005

[8] Rideout WM *et al*., "Correction of a genetic defect by nuclear transplantation and combined cell and gene therapy," *Cell* 109, 17-27; 5 April 2002 (published online 8 March 2002)

[9] Tsai RYL, Kittappa R, and McKay RDG; "Plasticity, niches, and the use of stem cells"; *Developmental Cell* 2, 707-712; June 2002.

[10] Tabar *et al.*, *Nature Medicine* 14, 379, April 2008

[11] Lanza R *et al*. Long-term bovine hematopoietic engraftment with clone-derived stem cells. *Cloning Stem Cells* 7, 95-106, 2005

[12] [12] Lanza R *et al*. Regeneration of the infarcted heart with stem cells derived by nuclear transplantation. *Circ Res* 94, 820-827, 2004

[13] Lanza R *et al*. Generation of histocompatible tissue using nuclear transplantation. *Nat Biotechnol* 20, 689-696, 2002

The idea of therapeutic cloning—cloning an individual to create embryos, from whom stem cells are harvested—was already outdated in 2008 and the science superseded by better, easier scientific methods for matching stem cell production.

Moreover, the assertion that cloning is the only method for preventing immune rejection of transplanted embryonic stem cells is completely false. In an article published March 18, 2002 (Abate, San Francisco Chronicle), researchers with Geron Corp. and with Advanced Cell Technologies admitted that there are ways to prevent rejection of transplanted cells without therapeutic cloning, but that "that message has not gotten out," and that "the need for cloning to overcome immune system rejection has been overstated." The report goes on to note **"the scientific community has put out the message that a ban on therapeutic cloning will prevent researchers from solving the immune-system problem—an argument that seems at best a stretch, and at worst, a deception."**

Other scientists have admitted in testimony that therapeutic cloning will not prevent transplant rejection of cloned tissues:

> "There is no question in my mind that the possibility exists that if you are doing an egg donor, and nuclear transfer into an egg, that there possibly exists that that cell -- that the embryonic stem cells derived from that could be rejected. Absolutely." Dr. John Gearhart, Johns Hopkins[14]

> "I should say that when you put the nucleus in from a somatic cell, the mitochondria still come from the host." He concluded, "And in mouse studies it is clear that those genetic differences can lead to a mild but certainly effective transplant rejection and so immunosuppression, mild though it is, will be required for that." Dr. Irving Weissman, Stanford[15]

Dr. James Thomson, who originally isolated human embryonic stem cells, has stated in one of his published papers that cloning is unlikely to be clinically significant.

> "[T]he poor availability of human oocytes, the low efficiency of the nuclear transfer procedure, and the long population-doubling time of human ES cells make it difficult to envision this [therapeutic cloning by SCNT] becoming a routine clinical procedure…"[16]

Other leaders in the embryonic stem cell field have also published similar views, including Australia's Alan Trounson:[17]

> "However, it is unlikely that large numbers of mature human oocytes would be available for the production of ES cells, particularly if hundreds are required to produce each ES line… In addition, epigenetic remnants of the somatic cell used as the nuclear donor can cause major functional problems in development, which must remain a concern for ES cells derived by nuclear transfer. …it would appear unlikely that these strategies will be used extensively for producing ES cells compatible for transplantation."

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[14] Dr. John Gearhart; transcript of the April 25, 2002 meeting of the President's Council on Bioethics; p.47; http://www.bioethics.gov/meetings/200204/0425.doc

[15] Dr. Irving Weissman, Stanford, before the President's Council on Bioethics on February 13, 2002

[16] Odorico JS, Kaufman DS, Thomson JA, "Multilineage differentiation from human embryonic stem cell lines," *Stem Cells* 19, 193-204; 2001

[17] Trounson AO, "The derivation and potential use of human embryonic stem cells", *Reproduction, Fertility, and Development* 13, 523-532; 2001

The evidence from animal studies indicates that it will indeed require a tremendous number of human oocytes (eggs) to produce even one ES cell line from cloned embryos. Dr. Peter Mombaerts, who was one of the first mouse cloners, estimates that it will require a minimum of 100 eggs.[18] The reports from South Korea[19] of human embryo cloning have been **shown to be a fraud**, but even so the news stories indicate that the researchers obtained over 2,200 human eggs for use in their unsuccessful experiments, through paying women to go through the risky procedures of egg harvesting, as well as through coercion of students. At a rate of 100 eggs per patient, to treat, theoretically, the 18 million diabetics in the U.S. by this technique would require at least 1.8 billion human eggs.

The 2008 report of the first and only documented success at cloning human embryos was by the California company Stemagen (in which one of the scientists, Wood, admitted that he cloned himself), and **did not result in any cells** obtained from the clones;[20] they attributed this sole cloning success to use of fresh, high-quality human eggs from a nearby fertility clinic with which they were associated. The only reported case of obtaining any embryonic stem cells from cloned primate embryos was in 2007 with monkeys.[21] In this case it took **over 100 eggs each** to produce only 2 ESC lines (one of which had chromosomal problems.) The group had worked for almost 10 years, using around 15,000 monkey eggs.[22] Dr. Rudolph Jaenisch, a cloning scientist at Massachusetts Institute of Technology, noted:

> "The procedure is very complicated, he said, and has ethical implications because the embryos have to be destroyed to obtain the stem cells. **"Nobody in their right mind would think this is useful for therapies," Dr. Jaenisch said.** He also noted that the process requires more than 100 oocytes to create a single stem-cell line and that the supply of human oocytes available for research is limited."[23]

In a recent profile of Dr. Jaenisch,[24] he discussed the uselessness of so-called "therapeutic cloning" and how the technique is of no practical relevance:

> "Ten years ago, we talked about the potential of nuclear transfer for therapy. But it turns out the technique was of no practical relevance. You would never do it in humans for a number of reasons. First, it's very inefficient. With mice, that doesn't matter because we can do hundreds of transfers to get a few mice. But human cloning is another order of magnitude more difficult than in mice. And people can't even get the eggs to practice [on]. My former student Kevin Eggan, along with his colleagues at Harvard, spent years putting in place a protocol to get volunteer egg donors. They spent a couple hundred thousand dollars just in advertising. And I think they got one or two donors.

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18 Mombaerts P, "Therapeutic cloning in the mouse", *Proceedings of the National Academy of Sciences USA* 100, 11924-11925; 30 Sept 2003 (published online 29 August 2003

19 Hwang WS *et al.*, Patient-specific embryonic stem cells derived from human SCNT blastocysts, *Science* published online 19 May 2005

20 French AJ *et al.*, "Development of human cloned blastocysts following somatic cell nuclear transfer (SCNT) from adult fibroblasts", *Stem Cells* published online Jan 17, 2008; DOI: 10.1634/stemcells.2007-0252

21 Byrne JA *et al.*, Producing primate embryonic stem cells by somatic cell nuclear transfer, *Nature* 450, 497, 22 Nov 2007; published online 14 November 2007, doi: 10.1038/nature06357

22 Cyranoski D, Cloned monkey stem cell produced, *Nature* published online 14 November 2007, doi: 10.1038/news.2007.245

23 The Chronicle of Higher Education, Thursday, November 15, 2007

24 Hopkin K, "Ready, Reset, Go" The Scientist 25, 52, 2011

> Kevin's postdoc, Dieter Egli, who went to Columbia, told me that he got a couple [of] human nuclear transfers going, but they all arrested at the 6- or 8-cell stage."

The problem with finding enough human eggs for cloning experiments has led to an interesting alliance of pro-choice and pro-life feminists, forming a group called Hands Off Our Ovaries (see http://handsoffourovaries.com). The group spans the political and ideological spectrum, but are united against this risk of using women and their bodies as raw materials for experiments, including harvesting eggs for cloning experiments.

Moreover, **allowing "therapeutic" cloning while trying to ban reproductive cloning is unfeasible, and will simply hasten development of the process supposedly to be banned, reproductive cloning**. Again, honest proponents of cloning have noted this themselves:

> "It is true that the techniques developed in CRNT [cell replacement through nuclear transfer, aka therapeutic cloning] research can prepare the way scientifically and technically for efforts at reproductive cloning."[25]

The American Society for Reproductive Medicine (ASRM), the largest professional organization with expertise in reproductive technologies, says that SCNT is simply the procedure that clones embryos for whatever purpose (whether for starting a pregnancy or destroying for research). And ASRM concedes that if cloning for research is allowed, that research will be used to refine the process and will make it easier to perform "reproductive" cloning:

> "If undertaken, the development of SCNT for such therapeutic purposes, in which embryos are not transferred for pregnancy, is likely to produce knowledge that could be used to achieve reproductive SCNT."[26]

In terms of the egg issue and numbers involved, one proposal has been to use animal eggs instead, to produce a human-animal hybrid or "chimera". Some have claimed that this is improbable science, yet in 2003 a Chinese lab reported success using rabbit eggs to produce cloned animal-human hybrids,[27] and the U.K. in fact issued three licenses to begin such research and in 2008 one lab reported success at creating human-animal hybrid embryos using this technique with cow eggs, though they did not obtain any cells from the cloned embryos.[28] Some laboratories, such as Advanced Cell Technology, have failed to produce cells from human-animal hybrid embryos and concluded that the technique is implausible.[29] It should be noted that the same lab also failed to produce cells from fully-human clones. Such experiments, while ethically questionable and unlikely to produce useable results, are still not impossible, as noted above.

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[25] Robert P. Lanza, Arthur L. Caplan, Lee M. Silver, Jose B. Cibelli, Michael D. West, Ronald M. Green; "The ethical validity of using nuclear transfer in human transplantation"; *The Journal of the American Medical Association* 284, 3175-3179; Dec 27, 2000.

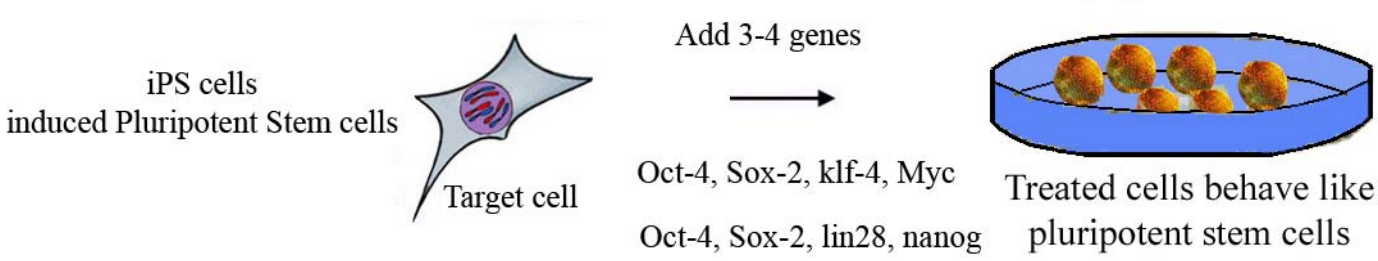
[26] The Ethics Committee of the American Society for Reproductive Medicine; "Human somatic cell nuclear transfer (cloning)"; *Fertility and Sterility* 74, 873-876; November 2000.

[27] Chen Y *et al.*, *Cell Research* 13, 251, 2003

[28] Highfield R, "Hybrid embryos made by UK scientists", http://www.telegraph.co.uk/earth/main.jhtml?view=DETAILS&grid=&xml=/earth/2008/04/01/sciembryo101.xml

[29] Chung Y *et al.*, *Cloning and Stem Cells* 11, 1, 2009;

Recent advances in stem cell research have overtaken the efforts at cloning. Scientists have now shown that there is an easier, less expensive and more direct method to produce embryonic-type stem cells from a patient's own tissue, with a real potential for a tissue match.. These cells, termed iPS cells (induced Pluripotent Stem cells) were first developed in 2006 in mice by the Japanese scientist Shinya Yamanka.[30] Yamanaka's lab and the lab of Thomson in the U.S. showed in November 2007 that this same technique could work for humans as well, easily producing human iPS cells directly from human tissue.[31] The straightforward technique involves adding 3-4 genes directly to a human cell such as a skin cell, reprogramming the cell such that it behaves like an embryonic stem cell, yet without use or production of an embryo, eggs, or cloning.



Thomson's group in their paper showing this first production of human iPS cells noted:

> "The human iPS cells described here meet the defining criteria we originally proposed for human ES cells (14), with the significant exception that the iPS cells are not derived from embryos."

In a subsequent report, Thomson (who was the first successfully to grow human embryonic stem cells in the lab) noted:

> "Recently, adult human cell lines were reprogrammed to an ES cell state (induced pluripotent stem cells, iPS cells) (40, 41). These cells possess the therapeutically desired characteristics of ES cells, namely indefinite self-renewal and pluripotency, without the requirement of human embryo destruction."[32]

Hearing of the impending announcement about iPS cells in 2007, Prof. Ian Wilmut, cloner of Dolly the sheep, publicly forsook cloning technology and his UK license allowing him to clone human embryos, to work on the new iPS cell technology.[33]

Subsequently, other groups have verified the ability to obtain iPS cells, including from human tissue, and improved on the technique, making it even safer.[34]

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[30] Takahashi K and Yamanaka S, Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors, *Cell* 126, 663-676, 25 August 2006

[31] Takahashi K *et al.*, Induction of pluripotent stem cells from adult **human** fibroblasts by defined factors, *Cell* 131, 861-872, 30 November 2007; published online 20 November 2007; Yu J *et al.*, Induced pluripotent stem cell lines derived from **human** somatic cells, *Science* 318, 1917-1920, 21 Decmber 2007, published online 20 November 2007

[32] Swaney DL *et al.*, *Proceedings of the National Academy of Science USA* 106, 995-1000, 27 January 2009

[33] Roger Highfield, Dolly creator Prof Ian Wilmut shuns cloning, The Telegraph, November 16, 2007

Jaenisch's group has also shown that iPS cells are effective at improving the health of mice with sickle cell anemia. The iPS cells succeeded where cloning had previously failed.[35]

Discussing this real advance with iPS cells in mice, the researchers noted:

> "This demonstrates that IPS cells have the same potential for therapy as embryonic stem cells, without the ethical and practical issues raised in creating embryonic stem cells," says Jaenisch.[36]

And

> Townes says he and Jaenisch initially collaborated on a project that used nuclear transfer to make corrected stem cells, a process called therapeutic cloning. But the experiments failed, he says, because nuclear transfer was too inefficient to produce the needed cells. The iPS cell technique "is amazingly efficient," he says.[37]

Thus, iPS cells fulfill the desire to create embryonic-type stem cells, with the potential for transplant match, but do so without the use of embryos, eggs, or cloning.

Since November 2007 and the first human iPS cells, groups have created over 600 different human iPS cell lines, including over 50 different lines directly from patients with different diseases. In 2008, a Japanese news agency announced that Dr. Yamanaka was preparing to produce iPS cells from a group of 60 patients with various diseases, in order to study disease development and potential treatments in the laboratory.[38] Ian Wilmut (cloner of Dolly the cloned sheep) has created iPS cell lines from patients with motor neuron disease, to study the disease in the laboratory and possibly to match the patient. Prof. Wilmut had been trying to obtain such cells from cloned human embryos for years, yet succeeded in a short period of time with the iPS cell technique. According to Wilmut:

[Footnote continued from previous page]

[34] Kim D *et al.*, *Cell Stem Cell* 4,472, 5 June 2009; Nakagawa M *et al.*, Generation of induced pluripotent stem cells without Myc from mouse and **human** fibroblasts, *Nature Biotechnology* 26, 101-106, January 2008, published online 30 November 2007; Park I-H *et al.*, Reprogramming of **human** somatic cells to pluripotency with defined factors, *Nature* 451, 141-147, 10 January 2008, published online 23 December 2007; Wernig W *et al.*, C-Myc is dispensable for direct reprogramming of mouse fibroblasts, *Cell Stem Cell* published online 28 December 2007; Yamanaka S, Induction of pluripotent stem cells from mouse fibroblasts by four transcription factors, *Cell Proliferation* 41 (suppl 1), 51-56, January 2008; Brambrink T *et al.* Sequential expression of pluripotency markers during direct reprogramming of mouse somatic cells, *Cell Stem Cel*l 2, 151–159, February 2008, online 6 February 2008; Aoi T *et al.*, Generation of pluripotent stem cells from adult **mouse liver and stomach** cells, *Science* published online 14 February 2008, doi:10.1126/science.1154884; Stadtfeld M *et al.*, Defining molecular cornerstones during fibroblast to iPS cell reprogramming in mouse, *Cell Stem Cell* 2, __, March 2008, published online 14 February 2008, doi:10.1016/j.stem.2008.02.001; Lowry WE *et al.*, Generation of **human** induced pluripotent stem cells from dermal fibroblasts, *Proc. Natl. Acad. Sci. USA* 105, 2883-2888, 26 February 2008; published online 16 February 2008

[35] Hanna J *et al.*, **Treatment of sickle cell anemia mouse model** with iPS cells generated from autologous skin, *Science* 318, 1920-1923, 21 December 2007, online 6 Dec 2007

[36] Reprogrammed adult cells treat sickle-cell anemia in mice, published 14:10 EST, December 06, 2007, http://physorg.com/news116172622.html

[37] Gretchen Vogel, Reprogrammed Skin Cells Strut Their Stuff, ScienceNOW Daily News, 6 December 2007

[38] "Scientists to create iPS cells from Japanese patients", The Yomiuri Shimbun, Mar. 10, 2008, http://www.yomiuri.co.jp/dy/features/science/20080310TDY02301.htm

"This is so much simpler a procedure, quite apart from the ethical issues.[39]

Some have claimed that SCNT cloning is needed to replace stocks of human embryonic stem cells from IVF embryos. In March 2009, President Obama issued an executive order, and NIH issued guidelines, that allow many more human embryonic stem cell lines to be produced, and allowing federal taxpayer dollars to fund embryonic stem cell research with these newly-established ESC lines. It is worth noting, however, that scientists were most concerned that the oldest, best characterized and reliable stem cell lines, previously funded, be approved;[40] the stocks of those cells obviously did not need to be replaced. The NIH has at this date approved 122 embryonic stem cell lines for federal funding, including the oldest and best characterized lines.[41]

Stem cell science has moved beyond the outdated cloning technique. The only reason at this point to practice SCNT cloning would be if the researcher wished to produce cloned embryos for gestation and birth.

Stem cell science has also moved well beyond cloning and hybrids in terms of real treatments for patients. A wealth of scientific papers published over the last few years document that **adult stem cells are a much more promising source of stem cells for regenerative medicine**. Some adult stem cells actually do show **pluripotent** flexibility in generation of tissues, meaning that they can generate most or all of the different tissues of the body. These include adult stem cells from various sources, including bone marrow,[42,43,44] peripheral blood,[45] inner ear,[46] umbilical cord blood,[47,48] nasal mucosa,[49] amniotic fluid,[50,51] and placental amniotic membrane.[52] As just one example, Wake Forest researchers found that amniotic fluid and placenta contains stem cells that can be easily harvested, show extended growth in culture, show

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39 John von Radowitz, Scots team's innovation may help to beat 'shocker of a disease', http://news.scotsman.com/health/Scots-team39s-innovation-may-help.6314149.jp

40 See, e.g., http://blogs.nature.com/news/thegreatbeyond/2010/04/key_bushera_stem_cell_lines_wi_1.html

41 See http://grants.nih.gov/stem_cells/registry/current.htm

42 Jiang Y *et al.*; "Pluripotency of mesenchymal stem cells derived from adult marrow"; *Nature* 418, 41-49; 4 July 2002

43 D'Ippolito G *et al.*, "Marrow-isolated adult multilineage inducible (MIAMI) cells, a unique population of postnatal young and old human cells with extensive expansion and differentiation potential", *J. Cell Science* 117, 2971-2981, 15 July 2004

44 Yoon Y-s *et al.*, "Clonally expanded novel multipotent stem cells from human bone marrow regenerate myocardium after myocardial infarction", *Journal of Clinical Investigation* 115, 326-338, February 2005

45 Zhao Y *et al.*; "A human peripheral blood monocyte-derived subset acts as pluripotent stem cells"; *Proceedings of the National Academy of Sciences USA* 100, 2426-2431; 4 March 2003

46 Li H *et al.*, "Pluripotent stem cells from the adult mouse inner ear", *Nature Medicine* 9, 1293-1299, October 2003

47 Kögler G *et al.*, "A new human somatic stem cell from placental cord blood with intrinsic pluripotent differentiation potential", *J. Experimental Medicine* 200, 123-135, 19 July 2004

48 McGuckin CP *et al.*, Production of stem cells with embryonic characteristics from human umbilical cord blood, *Cell Proliferation* 38, 245-255, August 2005

49 Murrell W *et al.*, "Multipotent stem cells from adult olfactory mucosa", *Developmental Dynamics* published online 21 March 2005

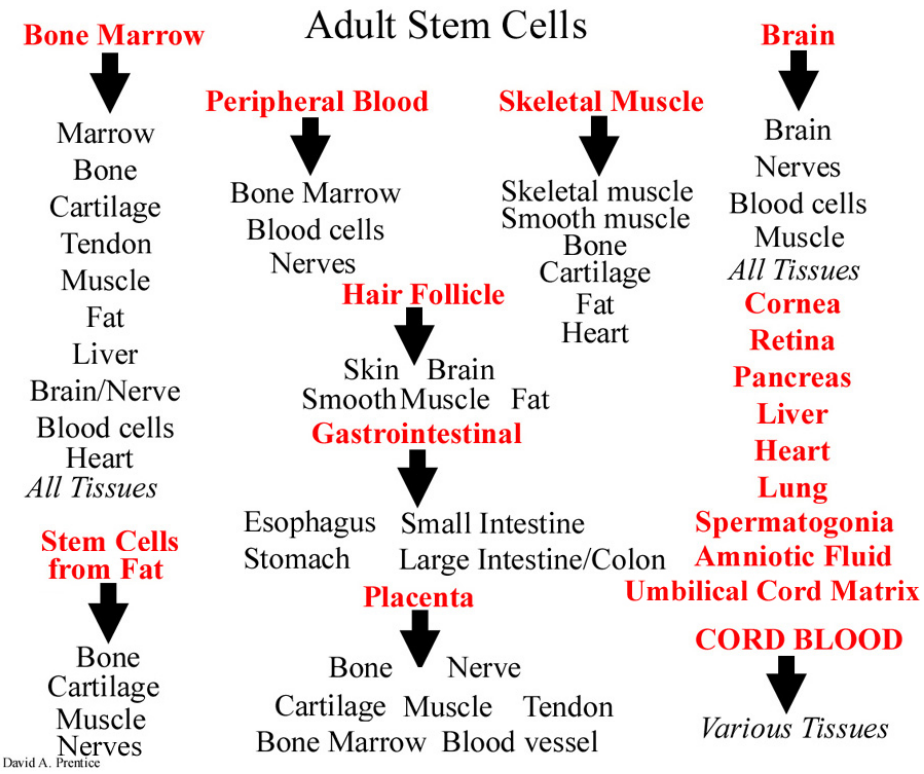
50 Prusa A-R, Marton E, Rosner M, et al. Oct-4-expressing cells in human amniotic fluid: a new source for stem cell research? *Hum Reprod* 18, 1489-1493, 2003

51 De Coppi *et al.*, Isolation of amniotic stem cell lines with potential for therapy, *Nature Biotechnology* published online 7 January 2007; doi:10.1038/nbt1274

52 Miki T *et al.*, Stem cell characteristics of amniotic epithelial cells, *Stem Cells* published online 4 Aug 2005; doi:10.1634/stemcells.004-0357

similar flexibility to form other tissues of the body, and can be transplanted without tumors, emphasizes the range of abilities that adult and tissue stem cells possess.

Many references also show that adult stem cells can multiply in culture, retaining their ability to differentiate, and providing sufficient numbers of cells for clinical treatments. Two 2010 papers document factors that stimulate adult stem cells from bone marrow and cord blood to significant growth in numbers. The factor **pleiotrophin** significantly stimulated growth and expansion of bone marrow and cord blood adult stem cells, describing it as a "regenerative growth factor."[53] And Boitano *et al.* discovered a factor they called StemRegenin1 (SR1)[54] that produces robust expansion of bone marrow and cord blood stem cells, what some experts labeled the "holy grail" of hematopoietic transplant medicine.[55]



The chart shows examples (not all-inclusive) of tissues from which adult stem cells have been isolated, as well as some of the derivatives from those stem cells. Many references also show that adult stem cells can multiply in culture, retaining their ability to differentiate, and providing sufficient numbers of cells for clinical treatments. Adult stem cells have been shown to be effective in treating animal models of disease, including such diseases as diabetes,[56] stroke,[57] spinal cord injury,[58] Parkinson's disease,[59] and retinal degeneration.[60]

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[53] Himburg HA *et al.*, Pleiotrophin regulates the expansion and regeneration of hematopoietic stem cells, *Nature Medicine* 16, 475-482, April 2010

[54] Boitano AE *et al.*, Aryl Hydrocarbon Receptor Antagonists Promote the Expansion of Human Hematopoietic Stem Cells, *Science* 329, 1345-1348, 10 Sept 2010

[55] Sauvageau G and Humphries RK, The Blood Stem Cell Holy Grail?, *Science* 329, 1291-1292, 10 Sept 2010

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[Footnote continued on next page]

But of even greater significance, **adult stem cells are already being used clinically to treat many diseases in human patients**. These include published results with patients, using adult stem cells as reparative treatments with various cancers, autoimmune diseases including multiple sclerosis, lupus, juvenile diabetes and arthritis, anemias including sickle cell anemia, and immunodeficiencies. Adult stem cells are also being used to treat patients by formation of cartilage, growing new corneas to restore sight to blind patients, treatments for stroke, and several groups are using adult stem cells with patients to repair damage after heart attacks. Early clinical trials have shown initial success in patient treatments for Parkinson's disease[61] and spinal cord injury (for a list of conditions already treated in human patients by adult stem cells and cord blood stem cells, please see http://www.stemcellresearch.org/facts/treatments.htm). An advantage of using adult stem cells is that in many cases the patient's own stem cells can be used for the treatment, circumventing the problems of immune rejection, and without tumor formation. The citations given above for adult stem cells are only a sampling, including some more recent references. Other listings can be found in the 2004 President's Council Report[62] and in a January 2006 review in the Journal of Investigative Medicine.[63]

In terms of *setting the record straight*, the complete and accurate record from peer-reviewed publications shows that adult stem cells have already successfully improved patient health. A completely-referenced defense of the use of adult stem cells for treatments that improve patient health has been published recently by the journal *Science* This information has been validated by several other peer-reviewed papers documenting improvement in patient health after adult stem cell treatment, including a paper published

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of autoimmune diabetes in NOD mice", *Science* 302, 1223-1227; 14 Nov 2003; Hess D *et al.*, "Bone marrow-derived stem cells initiate pancreatic regeneration", *Nature Biotechnology* 21, 763-770; July 2003

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[58] Hofstetter CP *et al.*, "Marrow stromal cells form guiding strands in the injured spinal cord and promote recovery", *Proc Natl Acad Sci USA* 99, 2199-2204; 19 February 2002; Sasaki M *et al*., "Transplantation of an acutely isolated bone marrow fraction repairs demyelinated adult rat spinal cord axons," *Glia* 35, 26-34; July 2001; Ramón-Cueto A *et al*., "Functional recovery of paraplegic rats and motor axon regeneration in their spinal cords by olfactory ensheathing glia," *Neuron* 25, 425-435; February 2000

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[61] Levesque MF *et al.*, Therapeutic Microinjection of Autologous Adult Human Neural Stem Cells and Differentiated Neurons for Parkinson`s Disease: Five-Year Post-Operative Outcome, *Bentham Open Stem Cell Journal* 1, 20-29, 2009; doi: 10.2174/1876893800901010020

[62] Prentice, D, "Adult Stem Cells." Appendix K in Monitoring Stem Cell Research: A Report of the President's Council on Bioethics, 309-346. Washington, D.C.: Government Printing Office, 2004

[63] Prentice DA, "Current Science of Regenerative Medicine with Stem Cells", *J. Investigative Medicine* 54, 33-37, January 2006

February 26, 2008 in the *Journal of the American Medical Association* reviewing 10 years of 69 published patient trials that document the benefit to patient health of adult stem cells for autoimmune conditions such as multiple sclerosis, juvenile diabetes, systemic lupus, and Crohn's disease, as well as acute and chronic heart damage and peripheral vascular disease.[64]

Peripheral artery disease has now been treated successfully in a number of patients, restoring circulation to limbs and preventing amputation.[65]

Other recent peer-reviewed publications document patient improvement with adult stem cells in treatment of spinal cord injury,[66] multiple sclerosis,[67] as well as type I (juvenile) diabetes[68] and type II diabetes,[69] as well as end-stage liver disease.[70] Adult stem cells have also shown documented success at treating chronic heart failure in 191 patients,[71] and restoring sight to blind patients with corneal blindness, even after 50 years of blindness.[72]

Tissue engineering using the patient's own adult stem cells has been used successfully in the production of a new trachea or windpipe;[73] the group reports unpublished results that within the past year they have improved the technique using *in vivo* regeneration of tissue, successfully treating three more patients,

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[64] Burt RK *et al.*, Clinical applications of blood-derived and marrow-derived stem cells for nonmalignant diseases, *Journal of the American Medical Association* 299, 925-936, 27 February 2008

[65] See, *e.g.,* Burt RK *et al.*, Autologous peripheral blood CD133þ cell implantation for limb salvage in patients with critical limb ischemia, *Bone Marrow Transplantation* 45, 111-116, 2010, published online 18 May 2009; Amann B *et al.*, Autologous Bone Marrow Cell Transplantation Increases Leg Perfusion and Reduces Amputations in Patients With Advanced Critical Limb Ischemia Due to Peripheral Artery Disease, *Cell Transplantation* 18, 371-380, 2009

[66] Lima C *et al.*, Olfactory Mucosal Autografts and Rehabilitation for Chronic Traumatic Spinal Cord Injury, *Neurorehabilitation and Neural Repair* 24, 10-22, 2010, published on 30 September; Mackay-Sim A *et al.*, Autologous olfactory ensheathing cell transplantation in human paraplegia: a 3-year clinical trial, *Brain* 131, 2376, September 2008; Lima C *et al.*, Olfactory Mucosa Autografts in Human Spinal Cord Injury: A Pilot Clinical Study, *Spinal Cord Medicine* 29, 191, July 2006

[67] Fassas A *et al.*, Long-term results of stem cell transplantation for MS, *Neurology* 76, 1066-1070, 2011; Rice CM *et al.*, Safety and Feasibility of Autologous Bone Marrow Cellular Therapy in Relapsing-Progressive Multiple Sclerosis, *Clinical Pharmacology & Therapeutics* 87, 679-685, June 2010, published online 5 May 2010, doi:10.1038/clpt.2010.44; Burt RK *et al.*, Autologous non-myeloablative haemopoietic stem cell transplantation in relapsing-remitting multiple sclerosis: a phase I/II study, *Lancet Neurology* 8, 244, March 2009

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[69] Bhansali A *et al.*, Efficacy of Autologous Bone Marrow–Derived Stem Cell Transplantation in Patients With Type 2 Diabetes Mellitus, *Stem Cells and Development* 18, 1407-1415, 2009

[70] Salama H *et al*., Autologous Hematopoietic Stem Cell Transplantation in 48 Patients With End-Stage Chronic Liver Diseases, *Cell Transplantation* 19, 1475-1486, 2010

[71] Strauer B-E, *et al.*, The acute and long-term effects of intracoronary Stem cell Transplantation in 191 patients with chronic heARt .failure: the STAR-heart study; *Eur. J. Heart Failure* 12, 721-729, 2010

[72] Rama P *et al.*, Limbal Stem-Cell Therapy and Long-Term Corneal Regeneration, *New England Journal of Medicine* 363, 147-155, 2010

[73] Macchiarini P *et al.*, Clinical transplantation of a tissue-engineered airway, *Lancet* 372, 2023, December 2008

including two patients with tracheal cancer.[74] A different group has constructed functional urethras for patients.[75]

In another first, Adult stem cells have been used successfully to treat children with a deadly skin disease known as recessive dystrophic epidermolysis bullosa (RDEB; one of the most severe forms of epidermolysis bullosa, a set of genetic skin diseases.) EB affects the skin and lining of the mouth and esophagus, causing skin to blister and scrape off with the slightest friction. The blistering, peeling skin also leads to recurrent infections, and an aggressive form of skin cancer. Most children with EB do not live past their 20′s. Previously, there was no treatment and it was considered incurable. Wagner and colleagues published results in the *New England Journal of Medicine* showing effective treatment of EB using donor adult stem cells.[76] One of the interesting aspects of this treatment is that it documents that bone marrow adult stem cells can travel to sites of injured skin, increasing production of collagen for these patients.

A 2010 article in the *Journal of the American Medical Association* provides a global perspective on adult stem cell transplants.[77] Researchers looked at how many adult stem cell transplants were taking place in various parts of the world. This particular study looked only at hematopoietic stem cell transplants, *i.e.*, transplants of blood-forming cells, obtained from bone marrow, peripheral blood, and umbilical cord blood; and did not survey uses of other adult stem cell types, such as mesenchymal, adipose-derived, or nasal adult stem cells. The published report found that in 2006, a total of 50,417 transplants were performed worldwide using these adult stem cells. Of that total, 57% used the patient's own adult stem cells, and 43% used donor adult stem cells. Almost half (48%) took place in Europe, followed by the Americas (36%), Asia (14%), and the Eastern Mediterranean and Africa (2%). They note that adult stem cell transplants have become "**the standard of care for many patients**" with blood disorders and malignancies, though they are starting to be used for other conditions including autoimmune disorders and heart disease. They also note that their study "**demonstrates that it is an accepted therapy worldwide**".

I am aware that some have criticized HB 171 and similar legislation, claiming that it would preclude stem cell research, or specifically embryonic stem cell research, or even that it would prohibit commonly used animal tests for pluripotent stem cells. Nothing could be further from the truth. The technique used involves injection of stem cells into immunocompromised mice; pluripotent stem cells form a a tumor (called a teratoma) within the mouse, potential data for their ability to form different tissue types. This test is done by injecting the cells into born mice, not mouse embryos.

It has also been hypothesized that patients who might receive injections of stem cells from their clones created and destroyed outside of the state of Ohio would be at risk of arrest upon entering the state of Ohio if HB 171 passes. This interpretation is based on a naïve or willful misreading of the bill. Cells incorporated into a patient's body would not be covered by the bill, just as a patient who eats a hamburger

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[74] UCL surgeons perform revolutionary transplant operation, 19 March 2010, http://www.ucl.ac.uk/news/news-articles/1003/10031903; Transplant advance in windpipe cancer, http://www.physorg.com/news199887055.html; Bader A and Macchiarini P, Moving towards in situ tracheal regeneration: the bionic tissue engineered transplantation approach, *Journal of Cellular and Molecular Medicine* 14, 1877–1889, July 2010

[75] Raya-Rivera A *et al*., Tissue-engineered autologous urethras for patients who need reconstruction: an observational study, *The Lancet* 377, 1175-1182, 2011

[76] Researchers Use Stem Cells to Treat Children with Life-Threatening, Blistering Skin Disease, August 12, 2010, http://www.ahc.umn.edu/media/releases/ebtreatment/index.htm; Wagner JE *et al.*, Bone Marrow Transplantation for Recessive Dystrophic Epidermolysis Bullosa, *New England Journal of Medicine* 363, 629-639, August 12, 2010

[77] Gratwohl A *et al.*, Hematopoietic stem cell transplantation, *JAMA* 303, 1617-1624, 2010

in the U.K. would not be arrested at the state line for transporting hazardous meat that might contain mad cow disease, or who eats sprouts in Germany would not be arrested for potential transport of hazardous microbes.

Internationally, most countries have moved to ban all human cloning, including countries such as France (7 years in jail), Germany (5 years in jail), Canada (5 years in jail), and in March 2005 even the United Nations passed a declaration against all human cloning.

HB 171 only bans production of cloned human embryos and production of human-animal hybrids. It does not address embryonic stem cell research, nor any stem cell research. No stem cell research is prohibited by this bill, whether embryonic, iPS, adult, cord blood stem cells. HB 171 does not restrict any vital or viable medical research. Cloning and nuclear transfer techniques for production of DNA, other molecules, cells other than human embryos, tissues, organs, plants, and animals are all allowed.

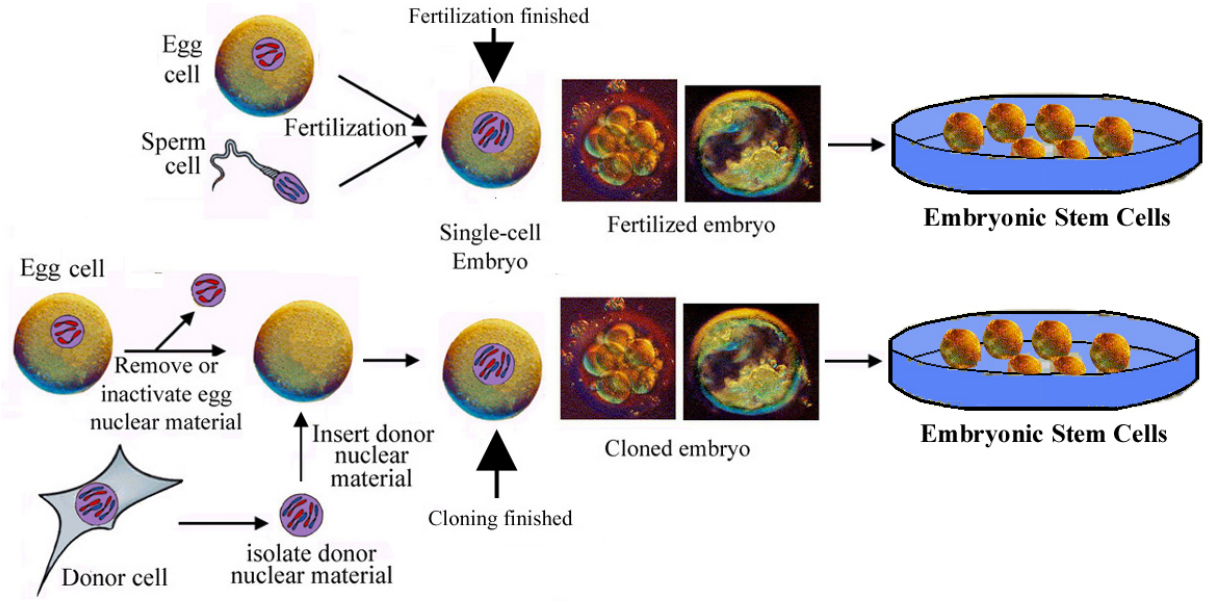
There are no valid or compelling grounds—ethical, scientific, or medical—to allow SCNT cloning of human embryos for any purpose, nor for production of animal-human hybrids. A comprehensive ban is necessary, and HB 171 would accomplish that purpose without limiting any valid medical research. I encourage you to please do all that you can to pass this bill.

Thank you for the opportunity to contribute to the debate on this important issue.

DIFFERENT TYPES OF STEM CELLS

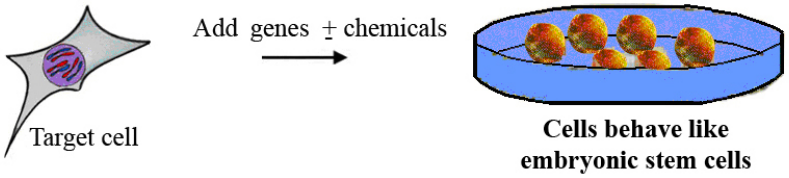
Embryonic Stem Cells

from Embryos created by Fertilization or by Cloning (Somatic Cell Nuclear Transfer)



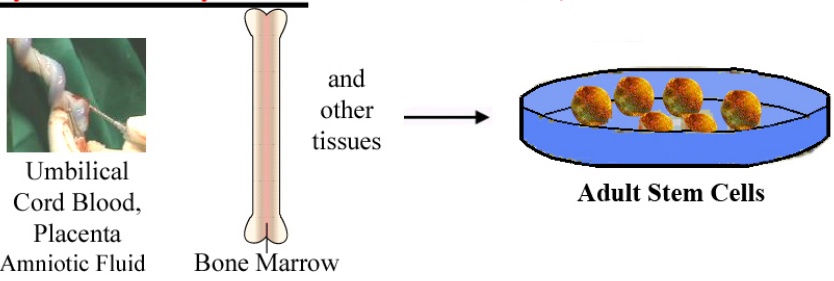
Induced Pluripotent Stem Cells (iPS cells)

from Normal Cells that are Reprogrammed to behave like Embryonic Stem Cells



Adult Stem Cells

Stem Cells normally found in body tissues from birth onward, as well as umbilical cord, etc.



Stem Cell and Cloning Glossary

Adult Stem Cell: A stem cell from organs and tissues, usually after birth (including umbilical cord and placenta), that can renew itself and transform into other specialized cell types.

Assisted reproductive technology: Fertility treatments that involve a laboratory handling eggs or embryos, such as in vitro fertilization.

Blastocyst: Early stage of embryo, approximately 5-7 days after conception (50-250 cells.)

Cloning: Creation of an animal or person that derives its genes from a single other individual; "asexual reproduction". Creating a copy that is virtually identical to the original (can be done with molecules, cells, and whole organisms.)

Chromosomes: Contain genes, working stretches of DNA that carry the genetic code for specific proteins. Normal human cells contain 46 chromosomes; mature normal human gametes have 23 chromosomes.

Differentiation: The process by which early unspecified cells become specialized cells such as heart, liver, muscle, or brain tissue.

DNA: DeoxyriboNucleic Acid. The genetic material that contains the instructions for making an entire organism.

Embryo: The earliest stage of human development, from the single cell zygote up to about 8 weeks.

Embryonic germ cell: A cell in the embryo/fetus that normally develops into mature gametes.

Embryonic stem cell: A cell from the inner mass of cells of a blastocyst, with the potential to become most or all of the body tissues.

Fetus: The human being from 8 weeks after conception to birth.

Gamete: A mature germ cell (egg or sperm), which unites with another in sexual reproduction.

Gene: A unit of heredity that is a segment of DNA located on a specific site on a chromosome.

In vitro: Done outside of the body.

In vivo: Done within the living body.

Multipotent: Capable of giving rise to several specialized cells or tissues of an organism.

Nucleus: The core of a cell that contains the chromosomes (genetic material.)

Pluripotent: Capable of giving rise to most tissues of the adult body.

"Reproductive Cloning" (Live-Birth Cloning): All cloning is reproductive in that it creates – reproduces – a new developing human intended to be virtually identical to the cloned subject. The term "reproductive cloning" has been used to signify the implantation into a womb of a cloned embryo, in hopes of a live birth.

Somatic cell: Cell of the body other than a gamete (other than an egg or sperm.)

Somatic cell nuclear transfer: Cloning. The transfer of a cell nucleus from a body cell into an egg from which the chromosomes have been removed or inactivated; the method used for cloning of an organism. Once the transferred genome is within the egg cell and a one-cell embryo is created, the process of cloning is complete and further development of the clone can occur.

Stem cells: Unspecialized cells with the capacity to self-renew and to transform into other mature cell types

"Therapeutic Cloning" (Experimental Cloning): Creating a cloned embryo for the purpose of destroying it to harvest embryonic stem cells or tissues, or for other experimental studies.

Tissue culture or cell culture: Growth of cells or tissues in a laboratory dish for experimental research.

Totipotent: Capable of giving rise to all tissues and organs, including placenta.

Zygote: A one-cell embryo. Even at this stage the embryo is a human being (species *Homo sapiens*).