Introduction

As we enter the 21st century, we face numerous social, technical, scientific and ethical challenges. Of these, research on stem cells looms on the horizon as a particularly difficult issue. It will most likely emerge as one of the great debates of the years ahead, ranking in comparison with the controversies surrounding nuclear arms proliferation, deployment of biological and chemical weapons, in vitro fertilization, contraception, recombinant DNA technologies, and abortion.

Research on stem cells aims to provide an understanding about organismic development from a single cell to a complex being, about the repair and replacement mechanisms required to counteract the ravages brought on by damaged cells and tissues, and to provide alternative means for bringing life forth in cases where doing so is not possible through normal procreation. There exists a clear and present moral and ethical divide between those who condone stem cell technology research and the benefits to health care and perhaps even life itself that it might provide and those who consider the harvesting of stem cells from developing embryos to be nothing less than murder. The intersection of religion, belief systems and faith, fundamental values assigned to the human condition, the natural curiosity stoked by unanswered
questions about the universe in which we coexist, all conspire to create a tangled network of philosophical chaos, political conflict, legal innuendoes and scientific misinformation. Is the key issue really the question of when life begins, as many believe it to be, or is it a question of ancient values unable to cope with 21st century reality? Scientists, engineers, philosophers, lawyers, ethicists, religious leaders and the proverbial “man on the street” all seem to hold opinions related to stem cell technology that are steeped in deep rooted cultural beliefs that transcend the facts. What is right? What is wrong? What is the moral high ground? What is best for the human condition? All these questions and many others swirl around the controversies, myths, ethos and pathos of stem cell technology. In the end, how do we define the risks and the benefits of going forward with this technology, knowing full well that at some point in the not to distant future we will transform from a state of essentially random to deterministic human architecture? Are we prepared to unleash the era of “designer” humans?

**What are stem cells?**

All cells in our bodies emerge from primitive early cells known as stem cells. Two primary features characterize such cells. First, they have the ability to divide and renew themselves without differentiation for indefinite periods of time. Second, they are pluripotent, that is they have the capability to differentiate into any one of the over 200 tissue types that comprise a mammalian organism. Indeed, any group or collection of cells possessing these two features are often times referred to as a stem cell line.
Where can stem cells be obtained?

There are six primary sources for stem cells.

- Adult tissues
- Fetal tissues
- Umbilical cord blood
- Parthenogenesis
- Embryos from *in vitro* fertilization [IVF] clinics
- Blastocysts produced using somatic cell nuclear transfer [SCNT]

At present it is thought that only embryos and blastocysts offer the potential for obtaining truly pluripotent stem cells. Stem cells isolated from adult and fetal tissues or umbilical cord blood appear not to have the capability to develop into all possible tissue types. Rather they have already undergone some degree of differentiation and are therefore limited in the spectrum of tissue types into which they might develop. Adult stem cells are certainly readily available but there are risks to the donor associated with extraction, risks to the recipient due to disease transmission for allogeneic patients, and they have a low proliferative capacity. The volume of collected blood limits umbilical blood stem cell utility. Fetal tissue sources are inexorably linked to the abortion issue. Parthenogenesis involves taking immature eggs that still contain the full complement of 46 chromosomes and coaxing them to develop into blastocysts. This approach would exclude males. In mammals, such parthenogenetic eggs do not produce offspring, so taking stem cells from them does not result in destroying an embryo that theoretically could survive in a woman. The
odds are low however, as demonstrated by experiments in monkeys where 77 eggs were needed to produce one parthenogenetic egg that produced stem cells that were in turn prodded to grow into brain cells, heart cells, and other tissues. As such, there is great interest among the scientific community to press for advancing the state of knowledge of stem cells obtained from both IVF and SCNT means.

There is something on the order of 300 IVF clinics in the United States and many more worldwide. In the US alone, there are around half a million unused fertilized embryos residing in liquid nitrogen. Each of these has the potential of developing into a human being should they be implanted into a woman's uterus. The legal and moral status of these embryos is unclear. Nonetheless, it is expected that most will be discarded and this gives rise to the question as to whether or not they should or could be used in scientific research.

What is reproductive cloning?

Reproductive cloning refers to using the SCNT technique for the expressed purpose of creating a new offspring. SCNT is the technique used to create the sheep clone, Dolly in 1998. Dolly was the offspring of a ewe from which an egg was obtained, the nuclear matter removed and replaced with the nuclear material from a mammary gland cell of a six-year-old adult ewe. The egg was then implanted and the offspring was a genetic copy of the six-year-old adult sheep. There is some evidence that Dolly, although phenotypically young, was genetically older. She gave birth to a healthy offspring, Bonnie. Dolly recently died at the age of six. Normally sheep live 11 or 12 years. This appears to have been Dolly's genetic age. This result in and of
itself provides some pause for concern regarding the utility of the SCNT technique for cloning offspring. In addition to these concerns, implanted SCNT embryos are extremely genetically unstable. This explains why most animal clones die before birth and survivors often have respiratory and circulatory problems and growth abnormalities. Currently there are over 5000 cloned animals alive. These include mice, rats, pigs, goats, sheep, cows, monkeys and an Asian guar. At the present stage, reproductive cloning is inefficient and dangerous. Despite this, several scientists and organizations have announced their intentions to clone humans. These include animal-reproduction specialist Panylotis Zavos of Lexington, KY and fertility physician Severino Antinori of Rome. Indeed, Dr. Brigitte Boisselier, president of the biotech company Clonaid, and member of the order of Angels of the Raelian religious cult, announced in January 2003 the birth of Eve, the first human clone. The unidentified mother is claimed to be a 31 year-old American living in Florida. The cult's prophet, Rael, reports that aliens visited him 30 years ago in a French volcano and revealed that all humans are descended from the clones they planted here 25,000 years ago. Rael justifies his human cloning efforts as a means to achieve eternal life.

**What is therapeutic cloning?**

Therapeutic cloning involves the growth of tissues or organs for the expressed purpose of treating diseases by tissue or organ transplant. Providing a patient with healthy tissue derived from their own cellular matter would obviate problems associated with adverse immune responses that accompanies the introduction of foreign or non-self materials. Therapeutic cloning does not involve implantation since
there is no intent to duplicate an entire organism. Instead, cells are withdrawn from the blastocyst or pre-embryo after 6-7 days of cell division and cultured in the laboratory. These cells have undergone no differentiation. At some point, these cells are coaxed into differentiating into the desired cells for therapeutic purposes. These might be, for example, brain, nerve, skin, lung, heart or liver cells. The pre-embryo or blastocyst from which they are derived has no brain, no central nervous system, mouth, heart, lungs or other internal organs. It has no organs to see, hear, touch, taste; it lacks a body, head, arms, legs; it has no self awareness, memory, thought processes, or consciousness. It does have the potential to grow into fetuses and become a newborn, but not unless it undergoes implantation.

What has been accomplished to date with stem cell technologies?

Within the past few years stem cells have been used to repair an immune-system defect in mice. Doctors have used stem cells in an attempt to repair the heart of a 16-year old boy in the US. Prior to that, doctors in Germany and Hong Kong had carried out similar procedures. Other reports include transforming stems cells into blood vessels, into primitive types of blood cells that later develop into more mature types of blood cells, and into brain cells and into pancreatic islet cells. Researchers have reported successes in using stem cells to repair damaged spinal cords and reverse paralysis.

Indeed, it is expected that such diseases as Alzheimer's and Parkinson's might be treated using stem cell treatments.
What is the political stance of the US government?

On August 9, 2001, President Bush declared that no federal funding would be available for embryonic stem cell research conducted on cells obtained from embryos created after that date. He suggested that there were some 64 stem cell lines available worldwide for stem cell research derived from embryos created prior to August 9, 2001. Most experts today believe that less than 10 of these lines are viable stem lines, and even fewer are available for public use because most are held in private hands or are otherwise inaccessible. Indeed, it is thought that all of the lines have been proliferated on mouse feeder cells therefore rendering them useless for human trials. Bush’s policy has brought US human embryonic stem cell research to a halt for all scientists reliant on federal funding. Research can continue in the private sector and there are a number of companies that continue to pursue this kind of work. The results, however, need not be disclosed nor shared to the scientific community at large.

Prior to August 9, 2001, two competing bills were introduced into the House and Senate. One bill, the Human Cloning Prohibition Act of 2001 sponsored by Rep. Weldon (R-FL) and Sen. Brownback (R-KS) would have made all cloning a criminal offense. It deliberately makes no distinction between reproductive cloning [aimed at producing new people] and therapeutic cloning [aimed at creating cell lines for medical treatments]. It was passed in the House in July 2001 by a vote of 265 to 162. In a companion vote of 249-178, the House rejected an amendment that would have allowed the limited creation of cloned embryos dedicated solely to research.
Ultimately the bill died in the Senate. Another bill, the *Cloning Prohibition Act of 2001* sponsored by Rep. Greenwood (R-PA) would have banned cloning with the intent of initiating pregnancy, however, it would allow therapeutic cloning. The House rejected the bill 178-249.

In January 2002 a panel of the National Academy of Sciences (NAS) called for legal sanctions against human cloning for reproductive purposes, but reiterated an NAS endorsement of cloning to produce stem cells for research purposes, a process it prefers to call nuclear transplantation. In its final report, this NAS panel—which met publicly during 2001 and was chaired by Irving Weissman of Stanford University, endorsed a "legally enforceable" ban on human reproductive cloning, one that would carry "substantial penalties" and would apply to clinics in the private sector to which other federal regulations have not applied.

In January 2002 President Bush commissioned a Council on Bioethics, a collection of 18 doctors, legal and ethical scholars, scientists and a journalist. Chaired by Leon Kass, a University of Chicago bioethicist, the committee reported their findings in July 2002 and called for a four-year moratorium on human therapeutic cloning and an outright ban on reproductive cloning.

Also, in January 2002 the 12 member California Advisory Committee on Human cloning unanimously recommended that while the state should ban human reproductive cloning, it should not prohibit human therapeutic cloning. This recommendation was made to coincide with the expiration of present state law, which banned human reproductive cloning for 5 years beginning in 1997.
In September 2002 Governor Gray Davis of California signed a bill approving therapeutic cloning in the state.

Senators Arlen Specter (R-PA), Dianne Feinstein (D-CA), Orrin Hatch (R-UT), and Edward Kennedy (D-MA) have joined together to sponsor S. 2439, the Human Cloning Prohibition Act of 2002. The act would ban reproductive cloning to create children, but permit privately funded research involving somatic cell nuclear transfer (SCNT), also called therapeutic cloning. This legislation is widely supported among scientific, medical, and patient groups. Sen. Sam Brownback (R-KS) and Sen. Mary Landrieu (D-LA) have sponsored S. 1899, yet another bill that would ban all cloning including SCNT, put researchers in prison, and deny patients the benefit of any therapies developed from therapeutic cloning outside the United States.

Since the cloning of the sheep Dolly in 1996, at least 26 states and the federal government have introduced bills to ban human cloning - with at least 14 definition of the term "cloning". Five states - California, Rhode Island, Louisiana, Michigan, and Virginia - have succeeded in putting some sort of moratorium in place. California, Louisiana and Rhode Island would have allowed therapeutic cloning however the Virginia and Michigan laws were written in such a way as to ban all forms of cloning.

In January 2003, representatives from several countries, including the US, met in London to consider initiating a Human Genome Project equivalent for stem cells. The idea would be to pool results of stem cell research efforts worldwide into a comprehensive stem-cell program with global reach, avoiding the legal quagmires and inefficiencies of each country moving forward independently. Roger Pederson, a senior stem-cell investigator at the UCSF Medical Center who moved to England to
advantage of the more encouraging regulatory environment is championing the idea most vigorously.

Bush's policy has stimulated considerable interest in the private sector to push for and support stem cell research. The Juvenile Diabetes Research Foundation, the Michael J. Fox Foundation for Parkinson's research, the Wellcome Trust, the Christopher Reeve Paralysis Foundation and others have given tens of millions of dollars to various laboratories, many in Europe. Several universities, teaching hospitals and biotechnology companies have also stepped up their involvement in the field, as have wealthy individuals. Late last year, an anonymous benefactor gave Stanford University twelve million dollars to build a stem-cell research center, and Andrew s. Grove, the Intel chairman, gave the University of California-San Francisco five million dollars for such a center.

Ethical and Moral Concerns

Proponents and opponents of embryonic stem cell research debate when human life begins, whether destroying embryos amounts to murder, and whether the moral good of deriving medical breakthroughs outweighs the ethical in injunctions. Some ethicists warn that human reproductive cloning is so alluring that any human cloning, such as therapeutic cloning to develop drugs, diagnostics, and tissues for regenerative medicine, should be avoided lest researchers start down a slippery slop that will inevitably lead to reproductive cloning.

The fundamental moral bottleneck, inevitably, is whether even very early stage embryos conceived in a laboratory deserve legal protection. Therapeutic cloning is
unacceptable to those who believe that a human being is created at the instant of fertilization. That belief is sincere and powerful and ultimately transcends scientific disagreement. The question for our democracy is how tightly that spiritual belief should bind the hands of those who disagree with it. There are others who believe that life begins with the emergence of personhood. That is the time when the emerging being first is able to sense its environment and respond to light, pain, pleasure, sound and other external stimuli. This occurs many weeks into gestation in humans and far beyond the 5-6 day period when blastocysts would be harvested for stem cells. Indeed, there was a period that even the Roman Catholic church believed that life began at "quickening", the time at which a mother could sense the movement of an unborn child in the womb. Generally this occurred around 40 days into gestation or 10 weeks after fertilization, just about the same time the organism ceases to be known as an embryo and is referred to as a fetus. This doctrine was modified in the late 19th century and presently it is thought that life begins at the moment of conception for those who ascribe to the Roman Catholic faith. It is interesting to note that Sen. Orin Hatch (R-UT) has personally concluded that life does not begin at the moment of fertilization because there is "zero chance" for becoming a human being until it is implanted. Since implantation happens after the blastocyst stage during which harvesting of stem cells takes place, Hatch is at peace with himself for condoning stem cell research for therapeutic purposes.

Global Positions and Interpretations
While the US position is largely dictated by the present Bush policy of August 9, 2001, how stem cell research proceeds and what rules apply elsewhere varies from nation to nation, reflecting each country’s unique mix of historical, religious, cultural and political influences.

On the one end of the spectrum is China, where scientists have cloned dozens of human embryos with few ethical concerns. On the other end is Ireland, where deeply held religious convictions make all such research repugnant.

The vast majority of nations are between the two extremes. Almost none advocates the cloning of an embryo to create a person. But after much soul searching, most nations are deciding that embryo research aimed at enhancing human health should proceed, with restrictions. Examples include:

- **Ireland**
  
  Bans embryo research

- **Canada, France, Australia, Sweden**
  
  Allows use of surplus embryos from fertility clinics; bans their creation through cloning

- **Germany**
  
  Bans embryo research; allows stem cell research only on imported cell lines

- **Great Britain, Singapore, Israel, Japan, Cuba**
  
  Permits research on surplus, cloned and specially created embryos

- **China**
No restrictions on research on embryos younger than 14 days; allows implantation of human genes into animal eggs

- **India**
  
  Government drawing up policies; private labs doing research on surplus and cloned embryos

- **South America**
  
  Brazil and Peru have passed general laws banning human embryo research. Several nations are developing positions. In others, technology is not advanced enough to warrant policies.

- **Europe**
  
  The European Union and council of Europe consistently opposed the creation of human embryos for research, but supported the use of surplus embryos from fertility clinics

- **Africa**
  
  No formal policies established; in most nations technology is not advanced enough to warrant government action

- **Former Soviet Union**
  
  While embryo research is not banned, the regions' labs do not have the capability to do the work

At this juncture bioethicists agree that the most troublesome scenarios of all may be a deadlock in the Senate on the cloning issue. If Democratic and Republican proposals cannot be reconciled, no regulations will be put in place to govern any type
of cloning research. In an unregulated environment, a nation that often sounds like Ireland may end up looking like China.

Perhaps the outcome of the stem cell debate will turn on whether the projected benefits of stem cell research for health improvements (by providing histocompatible tissues, organs, and implants) will be judged sufficiently great to risk an outcome that could possibly pave the way for downstream genetic trait selection and genetic enhancements, with the latter diluting biodiversity and in the end scuttling the robustness and future of the human race. Or, will ethical objection to the latter outcomes prove so intense and abiding that it will drive the adoption of a course of action so definitive that it even foregoes the projected health benefits? It is these issues that engineers and scientists, together with lawyers, religious leaders and politicians must resolve as we sail into a vast sea of uncharted waters.