Somatic Cell Nuclear Transfer (Cloning): Implications for the Medical Practitioner

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ABSTRACT

The current century will bring tremendous changes to the science and the practice of medicine. This century will be acknowledged as the century of Biology as the fusion of molecular genetics and experimental embryology pushes the barriers of science beyond perimeters that we have thought existed, as much as the past century was the century of Physics, with all the exact scientific calculations and predictions, resulting in electricity, nuclear power and quantum physics.

The first major breakthrough has been the pioneering work of Wilmut and Campbell, first with the birth of Megan and Moran in 1995[1], followed by the birth of Dolly the sheep, the first reported mammalian clone from a fully differentiated adult cell, reported in July 1996[2]. However, current cloning techniques are an extension of over 40 years of research using nuclei derived from non-human embryonic and fetal cells. However, following the birth of Dolly, the prospects of cloning technology have extended to ethically hazier areas of human cloning and embryonic stem cell research.

Cloning is derived from the Greek word "klon" which means a twig which can replicate itself and grows eventually into a tree. Cloning occurs naturally in many plant species by vegetative means and apoximis. To clone is to reproduce asexually or to make a copy or a set of copies of an organism following the fusion or insertion of a diploid nucleus into an oocyte[3]. A true clone is an individual which has all the components that make up the individual including nuclear genetic material (genome) and other maternally derived factors that is derived from a single unique embryo as a result of sexual reproduction. In the laboratory, cloning in mammals involves replacing the genetic material of an egg with the genetic material of a somatic cell from an embryo or adult which will eventually develop into a full organism or being.

This review hopes to bring the reader closer to the science and the ethics of this new technology, and what the implications are for the medical practitioner.

Keywords: somatic cell nuclear transfer, cloning, review

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DEFINITIONS AND TECHNIQUES

A biological clone refers to an organism genetically identical to another organism. In the case of Dolly, and possible attempts at human cloning, the American Medical Association defines cloning as the production of genetically identical organisms via somatic cell nuclear transfer, although a broader definition is often used to include the production of tissue and organs from cell or tissue cultures using stem cells. Somatic cell nuclear transfer refers to the transfer of the nucleus from an existing organism into an enucleated oocyte. Contrary to what one frequently reads in the popular press, nuclear transfer is not synonymous with DNA transfer. The nucleus is not just a bag of DNA, but an organelle with organisational capacity. This distinction brings to mind Sydney Brenner's famous statement "Chemistry as organisation, not just information".

There are several reasons why current techniques involving only nuclear transfer do not strictly produce individuals with 100% identical DNA compositions. Firstly, the recipient oocyte cytoplasm contributes the majority of mitochondrial DNA and ribosomal NA. Secondly, random DNA mutations in the clone will occur, and are likely to be increased due to procedures such as when electric shocks are applied to fuse the nucleus to the recipient oocyte. Thirdly, genomic imprinting further alters the DNA of the cloned embryo. And finally, and most importantly, the clone will be exposed to a different environment, and will hence develop differently from the original organism.

Cloning a whole animal leads researchers one step nearer the more specialised task of cloning stem cells, particularly embryonic ones, which have a much greater capacity for differentiation than adult stem cells. Embryonic stem cell research, is a hotly debated topic

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Table I. Successful mammalian clones produced by somatic cell nuclear transfer.

Species	Donor Cell	Offspring (%)	Reference
Sheep	Adult mammary	1/29 (3%)	Wilmut et al, 1997[2]
Mouse	Cumulus	31/1315 (2%)	Wakayama et al, 1998[5]
Goat	Transgenic fetal fibroblast	3/112 (3%)	Baguisi et al, 1999[6]
Cattle	Adult male fibroblast	2/7 (7%)	Kubota et al, 2000[7]
Pig	Granulosa cell line	5/401 (1.3%)	Polejacva et al, 2000[8]

often mentioned in conjunction with cloning, is the cloning of undifferentiated cells and shares many techniques with reproductive cloning. However, the intent is different as research involving the cloning of stem cells provides numerous possibilities in disease treatment. Hence, ethical and legal discussions and guidelines regarding stem cell research should be kept separate from those concerning human reproductive cloning.

The cells used in cloning are either embryos or differentiated cells. Embryonic blastomeres are more successful in the creation of clones as these cells are totipotent. The techniques using embryonic blastomeres are many. Following fertilisation of the egg by the spermatozoon it will undergo cleavage and start to divide. Different species have different embryonic stages when the genetic material of the embryo becomes active (ie onset of RNA synthesis), eg two-cells for the mouse, four-cells for humans, pigs and rats; and eight to 16 cells for sheep and cattle[4]. Individual blastomeres before this stage have the potential to develop into entire beings. These cells can be separated and each can give rise to full beings. Thus techniques have been developed to separate individual cells (the "Twinning Technique"), to split blastocysts, to inject into trophoblastic vesicles or to re-program its nucleus by an enucleated oocyte.

However, use of differentiated adult cells is not as successful, as there is a need for the cell nucleus to undergo reprogramming. There are two basic techniques:

Roslin Technique[2]

The cloning of Dolly was a breakthrough in several ways. It demonstrated that the full genetic complement of somatic cells derived from adult animals could be reactivated well into the chronical life of the cell. Dolly was the first animal to contain the genetic material of only one parent nucleus, unlike previous attempts to create identical offspring. The introduction of a crucial step needed to synchronise the cell cycles of both donor and recipient cells was critical; the donor cell was transferred from 10% fetal calf serum to 0.5% fetal calf serum for five days, causing it to become quiescent or enter the G0 stage. This allowed for enucleation and subsequent implantation of the somatic cell nucleus into an enucleated oocyte of a different organism. Another critical step was the use of an electrical pulse to fuse the two cells, and to activate embryonic development. This step is thought to mimic the stimulation normally provided by sperm during sexual reproduction.

Honolulu Technique[5]

The team from of the University of Hawaii led by Ryuzo Yanagimachi created three successive generations of over 50 cloned mice in July 1998, used a slightly different technique. Prior to this success, it was thought that the early stage at which rodent embryonic genome takes over (two-cell in mice) made it difficult for nuclear reprogramming to occur. Mice are one of the hardest subjects to clone as unlike sheep, the egg begins mitosis almost immediately after fertilisation, allowing researchers little time to reprogram the new nucleus. This experiment also showed that clones are reproductive viable by allowing cloned mice to reproduce normally over three successive generations. It was also more successful (3%), compared to the Roslin technique. No in vitro culturing was done on donor or egg cells before nuclear transfer, unlike the Roslin technique. Sertoli and brain cell, which naturally remain in G0 stage and cumulus cells that remain in G0 or G1 phase were used instead of udder cells, thus voiding starving donor cells in minimal medium to synchronise cell cycles.

Since the birth of Dolly was announced in 1997, there have been numerous other attempts at mammalian somatic cell nuclear transfer. Some herald very real benefits to agriculture, medicine and wildlife conservation. This is summarised in Table I.

Of non-human primates, cloning has been achieved with cleavage-stage blastomere nuclei into enucleated oocytes[9], but not with somatic cell nuclei. Two healthy rhesus monkeys, one male and one female, were delivered.

There are two main issues on the technical aspects of SCNT; introduction of donor cell and type of donor cell and its cell-cycle phase. Donor nuclei can be introduced by electro-fusion (as with the Roslin technique) or by direct micro-injection (as with the Honolulu technique); data seems to suggest that the latter technique is more efficient (eg. in the goat)[10]. The most favoured cell with the highest cloned births is the granulose cell, which is naturally at G0 to G1 stage at collection, but that results in only females; the most commonly used cell is the fibroblast, cultured and starved to reach G0 phase.

REPRODUCTIVE & THERAPEUTIC CLONING

Now, with successful SCNT, there is increasing interest in the use of the technique to produce human tissues

("therapeutic cloning"). While there is an interest in cloning of entire beings ("reproductive cloning"), many societies believe that there is no role for such cloning in humans.

ADVANTAGES & FUTURE APPLICATIONS OF CLONING TECHNOLOGY

Proponents argue that cloning technology and research will undoubtedly improve the overall quality of science and life by answering critical biological questions, and leading to advances in animal husbandry, genetics and medical science. A key reason behind the usefulness of cloning is that by producing near-identical genetic copies of an organism, results are faster and more predictable than in previous reproductive techniques like artificial insemination, which involve costly and potentially harmful procedures such as cryopreservation. Many of these procedures require the use of stem cells.

There are three main areas in which the cloning technology is useful: agriculture, conservation and therapeutics. Whilst only the last is directly relevant to medicine, the first two are important as they illustrate the extent in which the technology can be applied; hence they are briefly discussed.

Agriculture

The first application of SCNT has been with agriculture, SCNT ensures the rapid production of genetically modified herds or elite individuals with desirable traits, eg. for milk containing extra nutrients or meat more consistent in taste and quality. It also allows genetic conservation of local breeds with unique tolerance for regional diseases or local climates. Wells et al (1998)[11] reported two calves born of an endangered breed of cattle, adapted to sub-Antarctic conditions, following adult somatic cell nuclear transfer. This approach was used to clone the last surviving Enderby Island cow from mural granulosa cells. SCNT also allows spread of disease resistance faster than traditional techniques. For instance, herds of clones lacking the prion protein gene will no longer be susceptible to *bovine spongiform encephalitis*.

Conservation

Conservation has been highlighted recently as an area where the SCNT technique may be useful[12]. It may preserve and propagate endangered species that reproduce poorly in zoos until their habitats can be restored and populations reintroduced to the wild. Attempts have been made with the Giant Panda for instance[13]. The technique allows maintenance or increase of the overall genetic diversity of a species by introducing new genes from preserved specimens or animals in other wild and captive populations of the same species back into a diminishing gene pool. SCNT may even recreate extinct species, if viable tissues/cells have been banked or are available. An example is the mammoth, where an intact animal was discovered frozen in the Tundra recently; the closely related elephant can be used as both oocyte donor as well as surrogate mother.

The work requires interspecies embryo transfer, as the surrogate female is usually a different but closely related species. The 1st interspecies nuclear transfer in this field was between a gaur, an endangered species of cattle and a domestic cow[14]. Unfortunately, the calf died 48 hours after birth.

Medicine: Therapeutics

The greatest potential of the SCNT technique is in medical therapeutics and this is therapeutic cloning. The source cell can be human or animal, though the patient's own cells will be the most likely source for therapeutic cloning.

Therapeutic cloning can be categorised into:

a. Replacement tissues & organs;
b. Prevention of immunological tissue rejection, to allow for more successful organ transplantation;
c. Enhancement of immunological surveillance, to prevent cancers; and
d. Gene therapy, to correct genetic defects by introducing the functional gene (probably through stem cell re-population)

Clinical Applications include the ability to prevent, treat and overcome: Aging, Disease, Cancers, Myocardial infractions and Genetic disorders amongst many others. They can be grouped into two categories: fine-tuning of existing strategies, eg. production of and screening for new drugs; and new strategies, also known as "cell-based therapy", and their use is in a rapidly growing field of medicine, known as regeneration medicine.

"Pharming" the production of pharmaceuticals by extracting and purifying desired molecules from the milk of genetically modified livestock is an example of the *production of new drugs and proteins*[15]. Cloning ensures the presence of a transgene by introducing the DNA into the somatic cell lines in culture instead of by the more traditional and tedious process of altering individual genotypes. Cattle producing insulin in their milk are an example. The first example published was Polly, another lamb cloned by the Roslin Institute. She was derived from fetal skin cells, genetically modified to contain a human gene. This has resulted in a valuable sheep that secretes human factor IX in its milk. The blood-clotting protein is extracted, purified, and used to treat haemophilia B[16].

Cell-based therapies based on stem cells hold the most exciting prospects. These cells will form the basis

of new therapies in the battle against death and disease – cell-based therapies will be the next major approach in medicine. The simplest approach is to seed satellite cell clusters of healthy donor progenitor cells in a diseased or dystunctioning organ and this may be all that is necessary. The next level is to produce primordial or rudimentary organs with primordial cells which can replace the diseased organ in part or in whole. The final step is to develop the organ completely ex-vivo, probably in conjunction with xenotransplantation, before transplant.

Their use in therapeutic cloning would require production of stem cells from SCNT. Such therapics are particularly useful in the treatment of degenerative diseases such as Parkinson's, AIDS, diabetes and muscular dystrophy. This is also the basis for a new field of medicine known as "regenerative medicine". According to James Thomson of the University of Wisconsin and John Gearhart of Johns Hopkins University, stem cells could potentially be used for such things as: growing nerve cells to repair spinal injuries and restore function to paralysed limbs; growing heart muscle cells to replace useless scar tissue after a heart attack; making brain cells that would secrete dopamine for the treatment and control of Parkinson's disease; and growing pancreatic cells that make insulin, creating a lifelong treatment for diabetes.

SCNT can also be used to grow autologous haematopoietic stem cells and bone marrow to replace blood-forming organs damaged by disease or radiation.

SCNT can be used in cancer treatment by cloning cells from cancerous tissue and introducing specific characteristics leading to early cell death (eg. short telomeres). Reintroducing the altered cells could decrease the capacity for division and replication in the tumour.

SCNT can also be used in xenotransplantation in which pig hearts, amongst other organs, engineered to lack the enzyme alpha-galactosyl transferase that creates proteins triggering hyper acute immune reactions may then be tolerated in human bodies. This has recently been reported[17].

SCNT can also be used to make haematopoietic cells genetically altered to resist specific disease, such as HIV, to replace diseased blood cells.

A limitation of the SCNT technique for human therapeutic cloning is the need for human oocytes. Hence, the "universal donor" oocyte. Animal oocytes have been postulated for use with human somatic cells to create hybrid embryos, but this approach has not been accepted by many. Another limitation is the need for feeder cells to maintain the stem cells in an undifferentiated state (see below).

The main strategy in regenerative medicine is the creation of universal human donor stem cells that can be differentiated in culture and be used to replace damaged tissue or aging cells. Using the patient's own somatic cells for nuclear transfer voids triggering an immune response as the resultant stem cells are autologous. In the future, skin stem could be directly reprogrammed into insulin-producing cells, and then introduced into the pancreas. At present, however, it is more feasible to create stable human embryonic stem cell lines from cloned embryos using the patient as the donor. Stem cell lines or compatible organs and even specific body parts could then be grown from the embryonic cells.

Other uses of "Therapeutic cloning" include developing of models, for instance allergen-free no-sneeze cats currently being developed.

SCNT can also be useful in biomedical research. Large animals can be genetically modified to carry genetic defects mimicking human illnesses such as cystic fibrosis. The similarities in organ size and life span allow for improved monitoring of factors such as the long-term consequences of treatment. Another use is to reduce genetic variability in animal experiments, so that fewer animals are needed in each trial. It can be used to investigate the possibility of curtailing the transmission of hereditary diseases by testing a clone of the fertilised ovum or transferring nuclei into eggs from modified embryonic cells.

The technique is also useful in basic scientific research by facilitating the study of cell development and differentiation and mechanisms causing and controlling them; by investigating the role of the oocyte and cytoplasm vs. nucleus in cell and embryonic development. An immediate possible application is increase in the understanding of the causes of miscarriages and possibly the development of new contraceptives.

Medicine: Reproductive

The only possibility here is reproduction for infertile couples. However, this is highly clouded by emotional and ethical issues (see below) and most countries have put a ban on it and others have considered legislation against its use.

STRATEGIES TO PRODUCE STEM CELLS

All cells contain the genetic material and instructions in its DNA to form all the proteins and enzymes in the life of the animal or person from whom it comes. There is now a major research effort in unravelling the time sequence and relational positioning to understand developmental processes. With this understanding and knowledge it will be possible to produce progenitor cells that can develop into specific tissues that are needed.

It is now appreciated that adults have stem cells in certain tissues to enable repair and re-population and that these stem cells can de-differentiate to re-populate

tissues of different types. Hence, one strategy is to de-differentiate adult stem cells from tissues that have them in abundance, eg. adipose and bone marrow. Because the age of the individual may have a bearing on the telomerase length of the stem cell, it is logical to move to stem cells which can be collected at birth. Umbilical cord stem cells are found in the umbilical cord and the placenta that are usually discarded following the birth of the child. Many institutions are now realising the potential benefits to collect such cells, which can be stored for the child's own use in the future or matched for donation if necessary. These cells, obtained from a fully formed individual, though at different ages, are multipotent, in that they can form several types of cells[18].

Another strategy is to go even earlier into a developing embryo or fetus to obtain stem cells that are pluripotent. However, this has generated much emotional reaction and heated ethical debate, mainly because of the need to destroy the embryos in order to collect these embryonic stem cells.

The last strategy is to produce a cell that is completely totipotent, and that can only come from an embryo that is able to produce a complete individual, ie. with the cells that can produce the placenta and membranes in addition to the fetus. This is different from embryonic stem cells that can only produce the embryo, and not the placenta. This is achieved through somatic cell nuclear transfer to re-program its nucleus to "go-back" completely to its very first division ("cloning"). The added advantage of this approach is that the genetic material is that of the donor, and hence, there is no ethical repulsion of a donated cell/organ, or immunological rejection.

The best strategy with the least controversy is to re-instruct an adult differentiated somatic cell to form a progenitor cell of a specified tissue type without the need to form an embryo.

EMBRYONIC STEM CELLS

Stem cell sources can be Wild-type ES cells; Genetically-altered ES cells; and ES cells from SCNT; ES cells from SCNT can be further genetically altered. Recently Wakayama et al (2001)[19] reported the generation of 35 embryonic stem cell lines from murine cumulus and tail tip (skin) cells that were transferred into enucleated oocytes.

Clinical use of such cells have to overcome the following problems:

1. President Bush (USA) has said publicly on 10 August 2001 that he will support the use of federal funds for embryonic stem cell research, but this is to be limited to the existing cell-lines that have been obtained based on the NIH guidelines. To limit ES cells to a few cell-lines can have potential repercussions. These ES cells are genetically identical to the donor. Widespread use of these cells would be similar to producing a large number of chimeras with a link to only a few donors; as there is no one without any form of recessive genes, it would be tantamount to allowing widespread propagation of a gene mutation. A possible solution to overcome this is to use ES cells that have been obtained from one's own tissues, through SCNT; the ethical issue is then confined to one's own embryos.
2. Another potential problem is the propensity of ES cells to form teratomas; in fact, it is this property that characterises an ES cell. Hence, introduction of ES cells which are not properly differentiated into a particularly cell line may result in formation of a tumour[20]. Ability to direct the ES cells along definite developmental pathways or lineages will overcome this problem.
3. Embryonic stem cells have to be maintained on mouse embryonic fibroblast feeder layers, otherwise they tend to differentiate and therefore lose their ability to form progenitor cells of specific tissues[21]. This need to use animal cell-lines to maintain their undifferentiated state has resulted in concerns of possible xenobiosis. Development of cell-free media cocktails (fully defined media, without animal proteins) will be the next step and this has just been reported[22].

POTENTIAL DISADVANTAGES & ETHICAL IMPLICATIONS OF CLONING

Apart from a few vehement opponents of cloning, including several religious sects such as the Roman Catholic Church that condemns the cloning of all life, most societies appear to accept animal cloning for agricultural, scientific and medical purposes. However, most people including scientists and governments object to human reproductive cloning on the grounds that there is currently too little knowledge and too much risk to be considered ethically acceptable[23]. The cloning of human stem cells, tissues or organs is still very much a controversial affair. The debate which in fact parallels the abortion debate as a moral argument, turns on whether one considers an embryonic stem cell a human being or more simply the means to develop any type of cell or tissue in the human body and so in time be able to replace or repair damaged organs in sick people. Central to the entire issue of human cloning is whether we wish to view human life in terms of its utilitarian or intrinsic value.

Reproductive cloning involves unacceptable risks at present, with a high incidence of malformations

and low fertility rates of 3% at best seen in animal cloning. As such, it would violate the ethical obligations of clinicians and researchers to carry out human reproductive cloning. Clones have proven to be at greater risk from gross developmental abnormalities compared to mammals born of natural methods. Examples from animal research include developmental delays, respiratory abnormalities, malformed fetuses and oversized animals ("Large Offspring Syndrome" LOS) that often die at birth[24]. This my be due to an increase in random DNA errors due to the electric pulse used to jumpstart embryo development. There are also unknown long-term complications such as genetic defects being amplified as successive cloning may cause mutations in a somatic cell to accumulate. There are some concerns on the age of the cloned cells, as Dolly had shortened telomeres[25]. This may contribute to premature aging. However, subsequent reports have shown that this my not be the case[26]; in fact, the report by Lanza et al (2000)[27] in cattle showed that the telomeres were actually longer than age-matched controls. Finally, the risk of disease transfer is increased, particularly through to genes of transgenic animals, as cloning accelerates the propagation of a disease-causing gene as rapidly as a desirable one. Cloning interferes with natural evolution and may easily result in loss of genetic variation.

The other problems associated with human reproductive cloning are ethical and philosophical. Many societies and religions around the world believe that cloning experiments will break a natural barrier that is moral in character. The current reasons for human reproductive cloning are fundamentally selfish and have great potential for vanity. This could create potential problems ranging from legal battles over the intellectual property of cloning technology to a black market of fetuses from desirable donors. The cloning of individual humans also forces society to redefine the boundaries of parenthood and social responsibility, as there are numerous unknown psychosocial harms impacting families and societies. Cloning compromises human autonomy, individuality and possibly, equality, as the creation of a genetic underelass will be possible. As a result, human clones will face a myriad of societal problems, which in turn would be detrimental to their psychological and emotional development.

HUMAN REPRODUCTIVE CLONING

A recurring theme in science fiction for decades, the cloning of live humans is now on the brink of taking place. There are currently three groups that have announced an intention to clone humans, regardless of government or societal disapproval despite the fact that Forbes business magazine has estimated the current cost of a clandestine attempt to clone a human could cost approximately US$1.7 million.

1. Dr Richard Seed a specialist in human infertility practising in the USA, announced his intention to clone humans on 5 Dec 1997.
2. Cloneaid, a company sponsored by the Raelian religious movement, which believes that life on earth was created by aliens, has agreed to attempt to clone a dead child. It will continue to proceed, despite being asked by the US Food and Drug Administration, not to clone a human in the United States, although one of its laboratories is a secret location in the United States.
3. The 3rd group is generally acknowledged to be the best equipped and qualified to clone a human being as it has the necessary funding, location and expertise. At a conference in Rome on 9 Mar 2001, the International Cloning Consortium announced that it was fully prepared to perform therapeutic human cloning for infertile couples. The Consortium is based in one of the Mediterranean countries and is headed by three specialists: Dr Severino Antironi, Dr Avi Ben Abraham and Dr Panayiotis Zavos. It is now in the midst of its 1st project to implant the adult cell of an infertile man into one of his wife's oocytes. Over 700 couple have volunteered to participate in the project and Dr Zavos has stated that embryo screening will greatly reduce the number of abnormal births by insuring only healthy embryos are implanted. There has been suggestions that the work will be done in a Mediterranean country, possibly Libya. Unlike Clonaid, the Consortium does not offer to clone dead people such as children or famous people.
4. Recently Cibelli et al (2001)[28] reported the generation of two embryos from 19 human eggs; the donor cells were from the skin and granulosa. However, this report generated scientific scepticsm as the embryonic genome is not confirmed to take over yet.

LEGISLATION

- In Mar 1997, President Clinton announced a five-year moratorium on human reproductive cloning in the United States. Following the recommendations of the National Advisory Commission, the Cloning Prohibition Act of 1997 prohibits federal funding for human reproductive cloning in the US. Then, cloning is legal in over 170 countries and 45 US states.

- The largest piece of cloning legislation to date is the moratorium on human cloning put forth by the Council of Europe. 19 countries signed it.
- In January 2001, Britain became the 1st country to set down legislation allowing scientists to create early cloned embryos in search of treatment for serious diseases and harvest stem cells from unwanted human embryos created during fertility treatments. Locally, no decision has been made regarding embryonic stem cell research to date.
- In April 2001, Britain became the 1st country to outlaw human reproductive cloning.
- Australia agreed to a national Ban on human reproductive cloning in June 2001, though researchers urged the government to follow Britain's lead in allowing embryonic stem cell research.
- In June 2001, Germany and France sought a UN ban on human cloning, and the Bush Administration refused to endorse a cloning bill, while leading British scientists called for an international ban on human reproductive cloning.
- The US Food and Drug Administration (FDA) has stated that it will not approve any experiments to clone humans at present due to safety concerns. However, the ruling may be unable to withstand a court challenge.
- The US FDA is currently assessing if cloned animals pose hazards to animals, human health or the environment. A report on the results of their investigations is due early 2002.
- The US government issued a legal opinion saying that research on human embryonic stem cells did not fall under a ban on federal funding for human embryo research.
- 27 July 2001: Nearly half the members of the House of Representatives sent President Bush a letter urging him to allow federal funding of embryonic stem cell research. The letter was signed by 202 House members, including 40 Republicans, and follows two similar letters sent to Bush one week before signed by 61 senators, including 13 Republicans.
- 31 July 2001: The United States House of Representatives voted to ban all human cloning. The legislation supported by President George W Bush, passed by a 265-162 vote. The House then went on to reject an amendment to the bill, which would have permitted human cloning for stem cell research, while outlawing it to produce children, by 249-178. The bill is not yet law, as it first has to be passed by the Democratic-led Senate. At present, federal funding for human cloning, including embryonic stem cell research, is prohibited in the US.
- On 7 of August 2001, scientists gathered in the National Academy of Sciences in Washington, USA, to debate the safety of reproductive human cloning. Though the conference did succeed in promoting discussion about human cloning around the world, the anti-human cloning scientists remained anti-human cloning and the pro-human cloning scientists remained pro-human cloning.
- More recently, with the debate that generated from the production of human embryos by Advanced Cell Technology[28], a recently formed US bioethics advisory committee is tasked to examine the issues in human cloning closely. On 20 Jan 2001, the US National Academy of Sciences issued the findings of a panel that recommended a ban on reproductive cloning, but recommended that therapeutic cloning be allowed.

FUTURE ACTION

Issues regarding the cloning of organisms other than humans have been more or less resolved, as most societies agree that the vast advances in medicine and science justify such technology and research. Thus, the current controversy centres around the cloning of humans because of the myriad ethical, social and legal complications it involves.

Human cloning has remained legal in many countries, largely because many politicians and researchers have feared that outlawing whole organism cloning would slow down or halt research on life-saving tissue and organ cloning. Legislation is difficult particularly in the western world, which favours autonomy of choice. However, governments around the world are becoming increasingly aware of the need to engage the issue, for government involvement is necessary to oversee and regulate research and to increase public awareness.

Unless there is an unforeseen technical complication, an international ban, or the disappearance of a market, human reproductive cloning seems to be an inevitable eventuality. Judging by the numerous industries gathered around human reproduction, and the websites of organisations like the Human Cloning Foundation, there is a great demand for human reproductive cloning. Future attitudes are likely to be defined by the 1st human clone.

As it will ultimately fall to society to decide on the fate of cloning, it is important to bear two key points in mind as we struggle to determine long-term policies governing this new technology. Firstly, the need for widespread and continuing education, discussion and deliberation to understand the ethical and social implications of all cloning technology. And secondly,

any current legislation or regulatory action must be carefully defined and should not interfere with other important areas of scientific research.

History teaches us that the implementation of technology is inevitable. Hopefully, we will be successful in facing this unique test of human wisdom, restraint, and institutional development that will define many moral features of the 21st century.

CONCLUSION

SCNT, more commonly known as cloning will have a major impact on the practice of medicine through therapeutic cloning. Reproductive cloning is important in unraveling the basic mechanisms at cellular and molecular levels as a normal offspring is the best evidence for an optimal technique; it is also important in agricultural science to improve stock quality and important breeds; in conservation of endangered species, where SCNT is one of the many approaches to prevent their extinction and in high value animals such as prised race breeds and pets. However, it is through therapeutic cloning that medical advances will make its greatest strides, through production of one's own stem cells for cell-based therapies.

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