Cloning Technologies and Stem Cell Research

The Issue

In February 1997 scientists at the Roslin Institute in Edinburgh announced that they had successfully 'cloned' an adult sheep. A number of additional developments in cloning higher animals were subsequently reported. These developments, coupled with the isolation, in late 1998, of human embryonic stem cells, generated considerable public interest in cloning and stem cell research. Particular attention has focussed on the potential for cloning entire human beings and the benefits of cloning for therapeutic (rather than reproductive) purposes. This paper outlines GSK's views on the importance of these technologies in medical research and our uses of them.

GSK Position

<u>Cloning Technologies</u>

- GSK uses cloning technologies to replicate molecules and cells for drug discovery and development. This technology has accelerated the testing of life-saving compounds which has meant that new medicines are reaching patients faster. This research is critical to future advancements in biomedical research.

- GSK does not use cloning technologies with the intention of reproducing entire human beings and we do not see a medical or research case for doing so.

<u>Stem Cell Research</u>

- GSK recognises that recent advances in stem cell research herald a new approach for producing human tissues for transplantation and for the treatment of many debilitating diseases and injuries, including Parkinson's disease, Alzheimer's disease, diabetes and spinal cord injuries.

- GSK currently uses <u>adult</u> human stem cells to advance research in our own research centres and in collaboration with academic centres of excellence. For example, blood stem cells are used by GSK as part of the safety assessment process to ensure that new medicines are not toxic to human blood cells. GSK's use of adult stem cells, like that of other pharmaceutical companies, has been conducted for many years and is recognised as an integral element of research for new medicines.

- <u>Foetal</u> stem cells can have a role in discovering therapies for serious and debilitating diseases such as depression and psychosis. GSK has external collaborative agreements in place where they are used to advance research into medicines for serious medical disorders.

- GSK believes that human <u>embryonic</u> stem cells (HESCs) have a promising place in medical research and drug discovery. In appropriate instances, GSK makes use of such cells in its own research and in collaboration with academic institutions or other external partners.

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- Any current, or future, use of human embryonic or foetal stem cells by GSK or by outside collaborators follows established ethical requirements, such as ensuring that the provider of the cells has obtained informed consent from the donor.

- The use of foetal and/or embryonic human stem cells by GSK R&D or in collaboration with an external partner requires the approval of the Chairman of GSK's R&D Compliance Board.

Legislative Environment

- GSK is committed to working with governments to support appropriate legislation or regulation that addresses societal concerns while allowing research to continue so the full potential of cloning technologies and stem cell research can be realised.

- An all-embracing ban on "human cloning" must be avoided. Any ban should be specifically restricted to the "cloning of entire human beings"; otherwise, there is a real danger of inhibiting research into currently untreatable or incurable diseases and medical conditions.

BACKGROUND

Cloning Technologies

Cloning is the process of producing an identical copy of something – in the case of biomedical research, a gene, cell, or entire organism. Biomedical researchers have used cloning technology for almost three decades. The technology has improved our understanding of human biology and led to innovative medical breakthroughs.

There are three main applications of cloning technology in biomedical research: molecular cloning, cellular cloning, and animal cloning. There is also a distinction between "therapeutic" and "reproductive" cloning.

Molecular cloning: Molecular cloning is an essential tool in research at GSK and other research institutions. Molecular cloning involves placing a new piece of DNA into a cell in such a way that every time the cell divides, the DNA is reproduced. This process generates many copies of identical genetic material that can be studied and used in the research process. It also enables production in industrial quantities of the specific protein encoded by a gene.

One important example of a disease application of molecular cloning is the production of a human protein needed to treat a disease. Since the discovery of the gene associated with insulin production, for example, molecular cloning has been used to enable bacteria to produce human insulin. The human gene is inserted into bacterial cells that in turn mass-produce human insulin. Prior to this breakthrough, patients with diabetes had to rely on cow or pig insulin, often requiring higher doses and increasing the risk of adverse reactions.

Cellular cloning: Cellular cloning is used to produce and perpetuate cell lines of identical cells and is also a fundamental tool in research and development used by GSK. A combination of cellular cloning and molecular cloning enabled the sequencing of the human genome, which is providing researchers with the ability to investigate the underlying causes of diseases in order to develop better prevention, treatments, and cures.

Animal cloning: Animal cloning involves a wholly different technique called somatic cell nuclear transfer (SCNT). This technique removes the nucleus of an unfertilized egg cell, replaces it with material from the nucleus of a "somatic cell" (a skin cell, for example), and then stimulates this hybrid cell to begin dividing. The technique is the basis for cloning animals, and in theory could be used to clone humans.

GSK does not clone animals. However, in common with the rest of the pharmaceutial industry, we do use genetically modified rodents (ie. rats & mice) as research models for Alzheimer's disease, cancer, diabetes, obesity, and cardiovascular disease. Specific genes in these rodents are targeted and then either turned off or increased in number to achieve a better understanding of metabolic pathways and discover potential drug targets. GSK sources these rodents from external suppliers as well as producing some in-house.

Cybrid Embryos: GSK notes the UK Government's decision to allow research into life-saving diseases using cytoplasmic embryos, or cybrids. These are made by using eggs from animals, such as rabbits or cows, which have had their nuclei replaced with genetic code from human cells. This is not an area of research currently conducted by GSK; however, we recognise its potential value in supporting discovery of novel medicines. Any decision to apply the technology to future GSK research programmes, or those of its academic partners, would be made following the same stringent internal guidelines established for embryonic and foetal stem cell use.

"Therapeutic" and "Reproductive" Cloning: The main distinction between these two types of cloning - both of which involve SCNT - is intent. "Reproductive cloning", as currently practiced, seeks to produce entire animals, whereas "therapeutic cloning" produces human embryonic stem cells for use in research.

Human Stem Cell Research

Stem cells are unspecialised cells that can renew themselves indefinitely and develop into specialised, more mature cells. For example, stem cells give rise to blood, skin, liver, muscle and a variety of other tissues and organs.

The two defining features of stem cells – their potential for differentiating into various specialised cells and their capacity for self-renewal – make them the logical focus of research into tissue regeneration.

A better understanding of how these cells develop, divide and give rise to differentiated cells, could lead to innovative ways to treat burns, stroke, spinal-cord injuries, neurodegenerative disease, cancer and diabetes, among other medical conditions.

Stem Cell Definitions

Embryonic Stem Cells: Embryonic stem cells, which come from the inner cell mass of an early stage human embryo, have the potential to develop into all or nearly all of the tissues in the body. The scientific term for this characteristic is "pluripotentiality." This unique feature of embryonic stem cells gives scientists optimism that stem cell research will result in new ways of treating disease.

A common source of embryos from which stem cells are obtained are surplus embryos from in vitro fertilisation (IVF) programmes. Another potential source is SCNT. GSK's corporate policy allows for the use of SCNT-sourced cells if they are required for research intended to lead to new medicines. Currently, however, GSK and its academic collaborators only make use of embryonic stem cells originating from IVF programmes. These are obtained or derived from a number of cell banks, including those run by the Medical Research Council in the UK and the National Institutes of Health in the US.

Foetal Stem Cells: Foetal stem cells are derived from foetal tissue, the transition from embryo to fetus being generally defined as at 9 weeks. Scientists in many research institutions are using foetal stem cells because of the scientific limitations of animal cells and adult human stem cells. For example, scientists have found a way of implanting human foetal stem cells into the brains and spinal cords of rats as a step toward creating new therapies for neurodegenerative diseases like Parkinson's disease and Alzheimer's disease. Foetal stem cells used by GSK external collaborators are obtained from hospitals with the consent of a woman after she has decided to terminate a pregnancy, for personal reasons unrelated to the research objectives.

Adult Stem Cells: Adult stem cells are "multipotent". After cells differentiate to become tissues and organs in a human body, some tissues retain a group of these versatile cells to replace mature cells that are damaged or aged. Adult stem cells can divide in two, one cell differentiating into the cell type needed by the damaged tissue, the other cell remaining undifferentiated (as a stem cell). One example is blood stem cells serving to replenish mature blood cells, which are short lived.

Although scientists believe that some adult stem cells from one tissue can develop into cells of another tissue, no adult stem cell has been shown in culture to be "pluripotent". It is hoped that once the processes of cell differentiation and tissue regeneration are understood more clearly, researchers will be able to work directly with stem cells derived from adults, or perhaps to induce differentiated cells to 'redifferentiate' in a new direction.

Adult derived stem cells can be collected from both adults and children, they include blood stem cells, which are found in the bone marrow continuously replenish the body's red blood cells, white blood cells, and platelets.

Adult vs Embryonic and Foetal Stem Cells: Based on scientific understanding to date, it appears unlikely that human adult stem cells alone will provide all the necessary cell types required for the most clinically important areas of research. These uncertainties are such that work should continue on all fronts (that is with adult, embryonic and foetal stem cells) to ensure that the full potential of stem cell research is realised for the benefit of patients.

Examples of Promising Research with Human Stem Cells

There are many areas where stem cell research is currently being conducted and where continued research is warranted. A few examples are given below. None of these examples apply to areas of research undertaken by GSK.

- Tests on paralysed rats, involving the injection of embryonic stem cells into the spinal cord, have resulted in the renewed functioning of the rats' legs. This is an encouraging step towards helping humans suffering from spinal injuries once thought irreversible.

- Scientists have successfully used adult stem cells harvested from patients' bone marrow to repair or limit the often-debilitating damage caused by heart attacks. The research involved injecting stem cells into the heart at the site of the original blockage that caused the heart attack.

- Scientists at the University of Wisconsin have turned human embryonic stem cells into blood cells. This is one of the first examples of cells being turned into other human tissues and may one day lead to the development of treatments for leukaemia, lymphoma and other blood disorders.

Revised : September 2007