

GSK Public policy positions

Cloning Technologies and Stem Cell Research

The Issue

Over 15 years ago scientists at the Roslin Institute in Edinburgh announced that they had successfully cloned an adult sheep. There have since been a number of developments in cloning technology and the cloning of whole organisms (bacteria, fungi, plants and animals) is now commonplace for research purposes. These developments, coupled with other scientific advances arising from the isolation in the late 1990s of human embryonic stem cells, have subsequently generated considerable public and regulatory interest in a number of aspects of cloning, regenerative medicine and stem cell research. This paper outlines GSK's views on the importance of some of these technologies in medical research and our uses of them.

GSK's Position

Cloning Technologies

- GSK uses cloning technologies to replicate molecules and cells for drug discovery and development. This technology has accelerated the testing of life-saving compounds and 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.

Stem Cell Research

- 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 Rare Genetic Diseases, macular degeneration, Parkinson's disease, Alzheimer's disease, diabetes and spinal cord injuries.
- GSK currently uses pluripotent and adult human stem cells to advance research in our own research centres and in collaboration with academic centres of excellence. For example, stem cells from human blood are used by GSK to evaluate the safety of medicines. GSK's use of pluripotent and 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.
- Foetal stem cells and other foetal material can have a role in discovering therapies for serious and debilitating diseases. GSK has external collaborative agreements in place where these materials are used to advance research into medicines for serious medical disorders.
- GSK believes that human embryonic stem cells (HESCs) have a promising place in medical research and drug discovery. In appropriate instances, GSK makes use of such cells in our own research and in collaboration with academic institutions or other external partners.
- Induced Pluripotent Stem Cells (iPSCs) are genetically and functionally similar to embryonic stem cells and can be isolated from patients allowing advances in personalised medicine approaches. GSK increasingly makes use of iPS cells in our own research and in that carried out in collaboration with academic institutions.
- Any current, or future, use of human embryonic or foetal material, by GSK or by outside collaborators follows established ethical requirements and rigorous scrutiny, including confirmation that the provider of the material has obtained informed consent from the donor.
- The use of embryonic and/or foetal material by GSK R&D or in collaboration with an external partner requires the approval of the Chairman of R&D.

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.
- The cloning of entire human beings should continue to be forbidden. However, other forms of cloning should continue to be applied to research into currently untreatable or incurable diseases and medical conditions.

Background

GSK and 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 a number of 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. Research is also underway in some quarters using cybrid embryos.

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 unfertilised 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.

GSK does not clone animals. However, in common with biomedical researchers in universities and other research institutions, we do use genetically modified rodents (i.e. 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: UK legislation passed in 2008 allows research into life-saving diseases using cytoplasmic hybrids, 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 our academic partners, would be made following the same stringent internal guidelines established for embryonic and foetal stem cell use.

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 and disease relevant cells for drug discovery.

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: Within the first couple of cell divisions after fertilisation, embryonic stem cells are the only cells that are 'totipotent' i.e. they can form all the cell types in a body, plus the extraembryonic, or placental, cells. This unique feature of embryonic stem cells has given scientists optimism that human stem cell research will result in new ways of treating disease.

The most common source of human embryos from which stem cells are obtained are surplus embryos from in vitro fertilisation (IVF) programmes, where a woman's egg is fertilised outside of her body to generate the embryo. Another potential source is human SCNT as described above. GSK's approach allows for the use of SCNT-sourced cells if they are required for research intended to lead to new medicines. Currently, however, GSK and our academic collaborators only make use of embryonic stem cell lines originating from IVF programmes. These are primarily obtained or derived from a number of cell banks, including those overseen by the Medical Research Council in the UK and the National Institutes of Health in the US. Most human embryonic stem cell lines in common usage were generated between 1998 and 2008.

Foetal Stem Cells: Foetal stem cells are derived from foetal tissue, the transition from embryo to foetus in humans being generally defined as at 9 weeks. Scientists in many research institutions use 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 and other foetal material used by GSK and our external collaborators are obtained from hospitals and/or clinics with the consent of the woman. Unlike human embryonic stem cell lines, which can be obtained from stem cell banks, the use of foetal material usually requires access to newly consented tissue. This process is completely separate from a woman's decision whether to terminate her pregnancy and is initiated only after the woman's decision to terminate has been made.

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.

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 replenishing the body's red blood cells, white blood cells and platelets.

Induced Pluripotent Stem Cells: iPSCs are created by the introduction of 3-4 genes into the somatic cells. They have an advantage over HESCs because they can potentially be created from any human cell, for example, skin cells, and used to create all the cell types that HESCs can create. They can then be transplanted back into the person from whom they were taken, via a process called autologous cell therapy and thereby avoid tissue rejection. For drug discovery purposes, iPSC technology allows the creation of banks of human cells with defined genotypes of interest to multiple diseases. As such, they are set to provide a highly sophisticated platform to support preclinical drug development.



GSK and Stem Cell Technologies

GSK uses two distinct scientific approaches to develop new medicines using adult and embryonic stem cells:

1. Regenerative therapeutics – identifying medicines which activate stem cells in patients and regenerate cells lost in the disease process e.g. pancreas cells in diabetes or brain cells in Parkinson's disease. GSK's first regenerative medicine, Promacta™, a bone marrow stem cell activating drug, was approved in 2008 for treating platelet loss in patients with chronic immune (idiopathic) thrombocytopenic purpura (ITP).
2. Cellular tools – using stem cells to generate a range of cell types (many of which cannot be safely or physically collected from patients) to determine drug activity and toxicity, e.g. liver hepatocytes, brain neurons or cultures of contracting heart cells.

In 2008, GSK announced a strategic partnership with leading stem cell researchers at the Harvard Stem Cell Institute (Cambridge, MA). This investment has resulted in new stem cell based tools for drug discovery use within GSK in several key therapeutic areas. The Harvard Stem Cell Institute is a leader in the development and application of human, patient derived induced pluripotent stem cells and research. This important new avenue of research allows focus on personalised medicine and human cell based translational models.

In 2010, we announced a new strategic alliance with the Italian Fondazione Telethon and Fondazione San Raffaele which specialise in research into rare genetic disorders, to develop novel treatments for such conditions using gene therapy carried out on stem cells taken from a patient's bone marrow. Under this agreement, we will develop an investigational gene therapy for Adenosine Deaminase Deficiency – Severe Combined Immune Deficiency (ADA-SCID), a very rare and life-threatening disorder that affects approximately 350 children worldwide. We will also co-develop further stem cell therapies to treat six other rare disorders.

February 2014