Statement Supporting Funding for Stem Cell Research in Horizon 2020

Stem cell research is one of the most exciting and promising fields of biomedical research today. We call on the European Parliament, European Commission and Member States to maintain the provisions of the current framework for funding stem cell research in Horizon 2020. European Commission funding must be available to continue to support scientists investigating all types of stem cells (including human embryonic stem cells) with potential to make advances in regenerative medicine.

Stem cell research has the potential to lead to the development of treatments and therapies for patients suffering from a host of diseases and illnesses including incurable neurodegenerative conditions such as Parkinson’s, motor neurone disease and multiple sclerosis, as well as type 1 diabetes, cardiovascular conditions, liver damage, spinal cord damage and blindness. Many of these conditions will increase in prevalence with an ageing population.

Stem cell research is improving our understanding of biological development, tissue repair and regeneration. Researchers are making progress in determining which illnesses and diseases are amenable to being treated with stem cell-based therapies. Stem cell technologies are also opening up exciting new approaches to disease modelling and drug development.

This field of research is complex. To enable scientists to best understand the massive potential of stem cells, scientists must be able to continue research in all avenues of stem cell research: this includes using adult, induced pluripotent, embryonic and fetal stem cells. It is too early to tell which route will be the most effective, for ultimate clinical use, so it is essential to keep all avenues of research open. Any move to make human embryonic stem cell research ineligible for Horizon 2020 funding would risk holding back progress across the entire field.

To maintain its global edge in this area of research, Europe must ensure all avenues of stem cell research continue to be financially supported, including through Horizon 2020. Europe’s strengths in this field present valuable opportunities to attract skilled scientists, biopharmaceutical companies and international investment in stem cell research to Europe, to drive the translation of basic research towards clinical benefits, and to influence the international agenda. The UK has recently committed significant funding for stem cell research as part of its Regenerative Medicine Strategy.

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Background Information

What are stem cells?

Stem cells are ‘master cells’, which can divide and renew themselves almost indefinitely, but can also mature into specialised cells such as muscle and nerves.

There are three main kinds of stem cell:

- **Human embryonic stem (hES) cells**: these cells, taken from blastocysts\(^1\), can become almost any type of specialised cell – they are pluripotent\(^2\). The most common source is currently from early-stage embryos donated by couples undergoing IVF.

- **Adult stem cells**: these cells, found in many organs and tissues, can only develop into a limited number of specialised cell types. Some recent research has focused on ‘reprogramming’ adult cells to regain the properties of pluripotent cells. These stem cells are referred to as induced Pluripotent Stem (iPS) cells.

- **Fetal stem cells**: taken from fetal tissue, these stem cells have similar characteristics to adult stem cells and can develop into a limited number of specialised cell types.

What might stem cell research achieve?

Regenerative medicine provides a promising avenue to TREAT or CURE:

- **neurodegenerative diseases** such as Parkinson’s and age-related macular degeneration (the most common form of blindness) which are set to increase with an ageing global population.

- **chronic conditions** such as cardiovascular disease, through stimulating repair of vasculature or heart muscle; diabetes, by introducing functional beta-islet cells to make insulin in patients or through wound repair for diabetic ulcers; and for the repair of joints and fractures through regenerating bone material and cartilage.

In the long-term it is hoped that methods will be developed to harness the existing stem cells within patients’ bodies to repair in response to disease or injury. It is envisaged that this could use small molecules to simulate dormant repair processes, thereby avoiding the need to maintain stem cells outside of the body prior to transplant back into patients.

Although not regenerative themselves there are several associated technologies using stem cells with great therapeutic potential.

- Stem cell therapies are being developed to be used as drug delivery systems e.g. stem cells could bring chemotherapeutic agents directly to targeted cancerous cells.

- iPS cells can be used to make models of human disease to investigate their causes at a cellular level. Well-characterised models can provide platforms for screening new drug candidates, accelerating pharmaceutical drug development, and they can provide better

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\(^1\) **Blastocyst**: a developing ball of 50-150 cells which can give rise to an embryo if implanted in a human.

\(^2\) **Pluripotent**: the ability of a stem cell to form any type of specialised cell, such as muscle or nerve.
models for toxicology testing than the traditional animal ones used. Importantly, iPS cells can be used to generate cell types that are currently inaccessible to researchers, such as neural cells representative of patients with neurological or psychiatric conditions.

**Why we need to continue research using human embryonic stem cells**

Although much progress has recently been made in the development of iPS cells, coupled to the promise of new approaches using direct (trans) differentiation, research with all types of stem cells is still required for the foreseeable future.

The reasons for this are:

**Safety and function:** hES cells are normal human embryonic cells, whereas iPS and trans-differentiated cells are created by reprogramming adult cells using molecular engineering. There are subtle but important differences in the behaviours of these different cell types, most likely reflecting epigenetic differences that are not fully understood. More critically, the engineering technologies currently being utilised to create iPS cells do not leave them safe enough to transplant into people. hES cells are therefore required to test the safety and differentiation of iPS cell therapies as they are being developed.

**Ready for the clinic:** a number of adult stem cell-based regenerative therapies are undergoing clinical testing, utilising minimally manipulated cell populations, for the most part derived from donor bone marrow stem cells. These offer promise in a limited number of disease-areas, given the restricted ability of such cells to differentiate into other tissue-types, and build on the long-established success of bone-marrow transplantation in leukaemia treatment.

The use of iPS cells offers a much greater range of possibilities for regenerative medicine, as well as the potential for unlimited supplies of donor cells. To be of a standard to be transplanted into people, such cell lines, or their derivatives, must be of a very high quality, purity and stability, otherwise there is a risk of inappropriate behaviour in the recipient of such transplants, with cells either creating the wrong type of tissue or leading to the formation of tumours. The nature of the technology currently being used to generate iPS cell lines means that issues remain before they can be developed to this standard. Unlike iPS cells, human embryonic stem cells (hES) are not derived through procedures involving genetic modification and hence are potentially ready for use in clinical settings. Over the past couple of years, a number of clinical-grade hES cell lines have been generated to support early phase human trials and in the past 12 months hES cell derived therapies have successfully achieved regulatory approval for use in clinical trials to treat age-related macular degeneration (blindness) in the EU and USA, and spinal cord injury (in the USA).

Europe’s first clinical trial using hES cells has commenced in the UK, after being approved by the Medicines and Healthcare products Regulatory Agency (MHRA) in September 2011. Professor Bainbridge at NIHR Biomedical Research Centre, based at Moorfields and the UCL Institute of Ophthalmology, will test the treatment for Stargardt disease (a form of macular degeneration). The cells were developed by US company Advanced Cell Technology (ACT), where the Food and Drug Administration (FDA) approved similar trials in November 2010.
**Discovery and innovation:** It is noteworthy that the basis of iPS cell technology is entirely based on our understanding of human embryonic stem cell biology, and that the potential for new innovations in the field will best be maintained through encouraging parallel approaches in stem cell discovery science.

**Time taken for discoveries**

Critics argue that stem cell research has not delivered therapies over an extended period of funding for the research. However, stem cell research and specifically human embryonic stem cell research is a relatively new field. James Thompson discovered how to isolate human embryonic stem cells in 1998. Comparatively, other therapies currently in use, for example monoclonal antibodies, have taken up to 25 years to develop into large-scale therapeutics. The first reliable sources of monoclonal antibodies were first developed in 1975. The first therapeutic monoclonal antibody was not approved for therapeutic use until 1986. The explosion in the use of monoclonal antibodies for therapeutic use did not occur until 2000 onwards. These therapies are now widely used to treat cancer, and other autoimmune and inflammatory disorders. Indeed the average time for development of a therapeutic drug from the pre-clinical research stage is approximately 15 years.³

It is therefore imperative that all avenues of stem cell research are kept open and proportionately regulated until scientists are able to find the optimal techniques and materials to develop therapies. Limiting the use of hES cells risks cutting off avenues to develop therapeutics and new knowledge which will benefit biomedical developments.

**Patentability of human embryonic stem cell therapies**

The European Court of Justice decision in Brüstle v Greenpeace has called into question the patentability of therapies derived from human embryonic stem cell lines. Critics of this type of research have argued that the inability to patent is reason not to support embryonic stem cell research as it will not bring a commercial return and therefore make Europe uncompetitive. Various legal commentators believe that the Brüstle decision and the inability to patent human embryonic stem cell lines, should not preclude the ability to commercialise and exploit such products for the following reasons:

(a) it will be possible to obtain such patents in other jurisdictions (including the USA);

(b) other aspects of any therapy (such as biomarkers or diagnostics or specific treatments) may still be patentable in Europe; and

(c) crucially, the current regulatory framework will make it virtually impossible for a generic (technically a “biosimilar”) version of a hES cell medicine to be approved, thus the regulatory protection for approved hES cell medicines will be very high.

Legal minds are of the view that regulatory barriers for competing products will be so significant that patents may be a secondary consideration for anyone considering developing a competing product. Further, patents may well cover methods of production rather than the product itself. Finally, innovators should be open to the concept that other barriers to market, such as seeking a conditional marketing authorisation for a new product might offer alternative protection to ensure innovators are fiscally rewarded for their inventions and investment.

More broadly some have argued that the decision of the European Court of Justice in Brüstle v Greenpeace is questionable, given the Court’s interpretation of ‘human dignity’ in the Biotechnology Directive.

**Creation of embryonic cell lines**

Technology has developed to the extent that the destruction of an embryo is not required to undertake research. Embryonic stem cell lines which are initially developed from a blastocyst are kept in stem cell banks all over the world. Scientists are able to use these to grow more embryonic stem cells in the laboratory. Where new cell lines are made, the blastocysts used are those left over from IVF treatments where consent has been given. These blastocysts would otherwise be discarded once an IVF patient has decided that they do not require further blastocysts for fertility treatment. It would seem far better to use these for research where potential treatments for disease for future generations can be developed rather than discarded as biological waste.