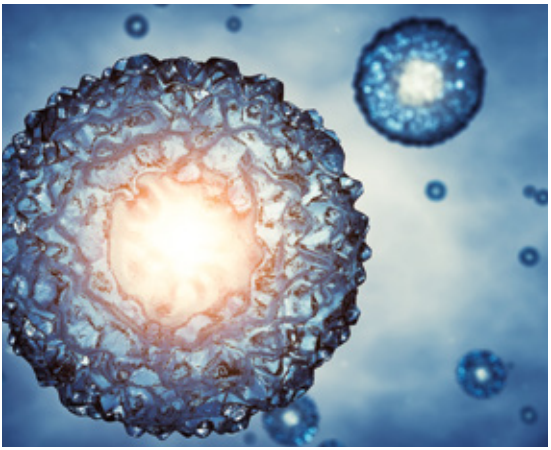
Research Councils UK

Regenerative medicine



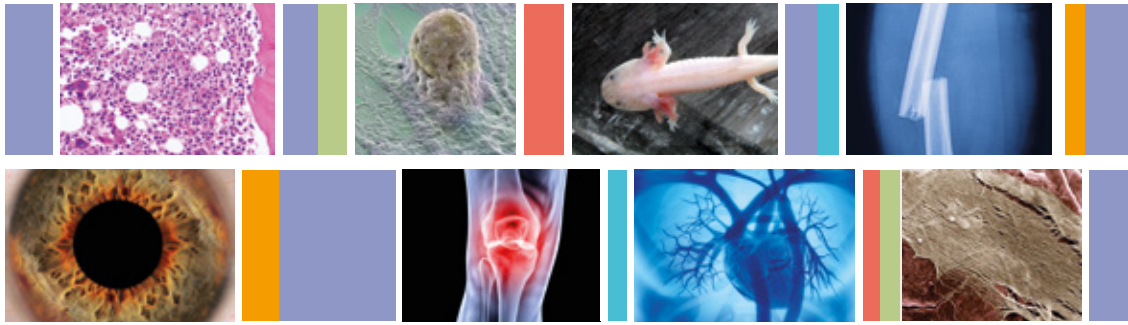
RESEARCH COUNCILS UK

Research funded by the Research Councils makes a vital contribution to the UK's economic growth, prosperity and well-being.

We take a variety of approaches to support innovation and deliver impact from research, including the development of collaborative research programmes, investment in major research capabilities, such as national research facilities, and the support of impact-related capabilities.

Often the impact of research is realised through the combination of several investments over time. The Research Councils seek to ensure that the outputs and outcomes of their funded research have significant long-term benefits for the economy and society. This timeline, one of a series, highlights how investments made in research over the long term combine to create a significant impact in particular areas. In addition, research in one area can combine with that from another to drive innovation and make a key contribution to UK growth. The field of regenerative medicine is inherently interdisciplinary. That the specialisation of cells is reversible and that somatic cell nuclei can be reprogrammed into an embryonic state are discoveries that have led to translational successes in bioengineering, requiring the skills of engineers, materials scientists, chemists, biologists, and clinical scientists, such as the first transplantable windpipe.

A key part of the Government's Industrial Strategy is supporting technologies where the UK has the depth of research, expertise and the business capability to develop and exploit them commercially. Regenerative medicine is one of 'Eight Great Technologies' identified by the Chancellor of the Exchequer in autumn 2012 when he announced an additional £600 million to help support their development. These eight are: Big data and energy-efficient computing, Satellites and commercial applications of space, Robotics and autonomous systems; Synthetic biology, Regenerative medicine, Agri-science, Advanced materials and nanotechnology, and Energy and its storage.



Regenerative medicine

Regenerative medicine, the approach that seeks to replace or regenerate human cells, tissues or organs, to restore or establish normal function, is not a new discipline. Decades of RCUK-funded research has led to successes in the fields of tissue engineering, gene therapy, stem cell biology and bio-materials that have already had a huge impact on healthcare and society, but which also offer fundamental potential in areas of unmet medical need, such as hea rt and neurological diseases, and economic benefits for the UK.

Sir John B Gurdon's discovery in 1962 that the specialisation of cells is reversible is ultimately enabling the engineering of tissues and organs, including skin, arteries, cartilage and retinal pigment epithelium. This has the potential to transform the lives of many people, for example by restoring vision or repairing damaged brains, nerves and hearts. Understanding how to re-programme cells has also expanded the opportunities for drug toxicity testing to make safer medicines.

Success in this research field has also led to economic growth for the UK. The Regenerative Medicine Programme was set up by the Research Councils in 2008 to support the emergence of new industries, funding 76 different projects. ApaTech, an RCUK spin-out company, was sold for $330 million in 2010.

The Research Councils have also provided the regulatory framework to this research, issuing guidance on the use of stem cells, and conducting public and stakeholder dialogue, helping to increase public confidence and strengthening the case for investment in research of this kind, both in the UK and internationally.

Basic Biology

1960: Research Council-funded scientist Sir Peter Medawar is awarded the Nobel Prize in Physiology or Medicine for early insights into antibody-mediated transplant rejection and tolerance, paving the way in addressing the immune challenges of regenerative medicine..

1962: Sir John B Gurdon discovers that the specialisation of cells is reversible and demonstrates that somatic cell nuclei can be 'reprogrammed' into an embryonic state.

1964: Researchers culture the first embryonic carcinoma cells.

1978: Haematopoietic stem cells are discovered in human cord blood.

1981: Sir Martin Evans is the first to derive embryonic stem cells from mouse embryos, with funding from the UK Research Councils.

1996: Dolly the sheep is created by Research Council scientists using somatic cell nuclear transfer. Dolly is the first mammal to be cloned from an adult somatic cell.

1998: Scientists derive the first human embryonic stem cell (hESC) line.

1999: Research Council-funded scientists are the first to produce hESC in the UK.

2006: Professor Shinya Yamanaka shows that adult, fully specialised mouse cells can be reprogrammed to become cells that behave like embryonic stem cells (induced pluripotent stem cells).

2007: The receptor-ligand interaction that reproduces the two aspects crucial for limb regeneration in the salamander – pattern formation and growth – is discovered by Research Council scientists.

2010: Research Council scientists discover that a gene called Sox9 plays a critical role in how stem cells behave in the central nervous system. These results could help researchers manipulate stem cells in the brain and develop new treatments for stroke, Alzheimer's disease or brain tumours.

2011: The UK's first 'clinical grade' stem cells created without the help of animal products, a product of RCUK-funded research, are donated to the UK Stem Cell Bank. These are expected to become the gold standard for developing new embryonic stem cell-based therapies for serious medical conditions.

2011: Scientists supported by the Research Councils and the pharmaceutical industry discover a simple method to transform stem cells into the precursors of liver cells, which can be used to test the safety of new medicines.

2011: Research Council scientists demonstrate that a small, naturally-occurring, molecule, thymosin beta4, can stimulate cell-mediated repair of a damaged mouse heart, offering the longer term potential to activate dormant stem cells in the adult body.

2012: RCUK-funded researchers discover a patient-friendly and efficient way to make stem cells out of blood, increasing the hope that scientists could one day use stem cells made from patients' own cells to treat cardiovascular disease.

2012: The Nobel Prize in Physiology or Medicine is awarded jointly to Sir John B Gurdon and Shinya Yamanaka *"for the discovery that mature cells can be reprogrammed to become pluripotent"*.

2013: A Research Council-funded study finds that macrophages help trigger the regeneration of myelin, the protective sheaths around nerve fibres in the brain. This could help identify new drug targets for the treatment of multiple sclerosis.

2013: A protein discovered by RCUK-funded researchers that kick-starts the process by which stem cells develop into different cell types could help scientists improve techniques to turn stem cells into other cell types. These cells could then be used to test drugs or help create therapies for degenerative conditions.

Translational Medicine

1963: Dr Georges Mathé pioneers the use of bone marrow transplants in the treatment of leukemia.

1997: Dermagraft, a tissue-engineered human donor skin replacement therapy, is marketed in the UK for the treatment of diabetic foot ulcers.

2001: The first transplantation of a tissue-engineered pulmonary artery takes place in a child suffering from congenital heart disease.

2006: Scientists engineer the first autologous bladders using urothelial and muscle cells obtained from bladder biopsies grown and expanded in culture. The use of autologous cells negates the need for immunosuppression.

2008: A Colombian woman receives the first human windpipe reconstructed using stem cells. The transplant team was jointly led by RCUK researcher Professor Martin Birchall.

2009: Research Councils support four early stage clinical trial projects using stem cells for bone repair and for treatment of leukaemia, Addison's disease and blindness.

2009: ChondroCelect®, an autologous cell therapy where a patient's cartilage cells are grown in the laboratory and used to treat cartilage defects in knees, is approved for commercial use by the European Medicines Agency.

2010: Research Council scientists engineer Mirococept proteins, to coat the cell surfaces of donor kidneys and act as artificial 'complement regulators', to help control organ transplant rejection. Mirococept may also be able to help the body accept 'non-self' cells or engineered organs used in regenerative medicine.

2012: RCUK-funded researchers show that it is possible to restore coordinated limb movement in dogs with severe spinal cord injury, using olfactory ensheathing cells to regenerate parts of nerve cells. This work might have a future role in the treatment of human patients with similar injuries.

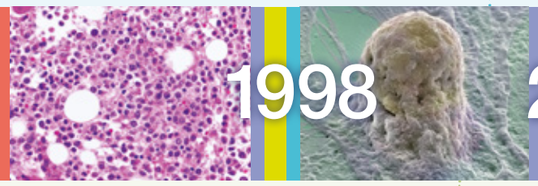
2012: For the first time, transplanted light-sensitive photoreceptors are used to restore vision to visually-impaired mice. The discovery, made by Research Council scientists, could form the basis of a new treatment to restore sight in people with degenerative eye diseases.

2012: Retinal pigment epithelium (RPE), made from stem cells, is transplanted into a patient with Stargardt's disease - the first UK transplantation of hESC.

2012: Glybera® is approved by the European Union for the treatment of lipoprotein lipase deficiency - the first gene therapy treatment to be approved for clinical use in either Europe or the United States.

2013: The first bioengineered tooth is produced from human gum cells by Research Council scientists, offering hope that this method can one day be used to replace a person's missing teeth with ones grown from their own gum cells.

2013: RCUK-funded scientists develop a potential cure for chronic back pain through hydrogel injections that can regenerate damaged discs. The injection contains stem cells, growth factors and inhibitors and is injected directly into the intervertebral discs of patients.



Society and Industry

2001: The Human Fertilisation and Embryology Act is amended to permit research on hESC for strictly regulated purposes.

2003: Research councils establish the UK Stem Cell Bank to provide a repository of human embryonic, foetal and adult stem cell lines.

2003: Biopharmaceutical company Q Chip Ltd is launched to commercialise the microsphere technology that not only makes it possible to control a drug's release rate throughout the body, but ensures it is only active in the target area. The company arose from RCUK-funded research.

2003: International Stem Cell Forum (ISCF), convened by RCUK, brings together nine international research agencies. It quickly expands to include representatives from 16 countries.

2004: The ISCF launches the Ethics Working Party, its primary purpose being to assist countries to undertake stem cell research within a transparent ethical framework. Work still on-going today, it seeks to identify prospective strategies to foster the scientific and ethical integrity of research in a global context.

2005: The ISCF launches the International Stem Cell Initiative (ISCI) to draw up globally agreed criteria for characterising stem cell lines. This forms the basis of an international hESC registry, the first attempt to properly catalogue the hESC lines derived so far.

2008: Research Councils conduct the largest ever public and stakeholder dialogue on stem cell research in the UK, helping to increase public confidence and strengthening the case for investment in research of this kind.

2008: The Regenerative Medicine Programme is set up by the Research Councils to support the emergence of new industries. Over its lifetime, the programme funds 76 different projects and enables Tissue Regenix, a University of Leeds spin-out company, to achieve AIM listing, raising £4.5 million.

2010: A Eurobarometer poll concludes that 59% of those questioned in the UK support the use of human embryos for the development of medical treatments.

2010: ApaTech, an RCUK spin out company, and a world-leader in bone graft technologies, is sold for $330 million.

2010: RCUK issues the Code of Practice for the use of Human Stem Cell Lines, providing guidance on best practice for those working with stem cell lines in the UK.

2012: The UK Regenerative Medicine Platform is established, with funding from RCUK, to address the technical and scientific challenges associated with translating promising scientific discoveries in this area towards clinical impact.

2012: RCUK-funded scientists develop a software-based tool to plan an optimal route for the commercialisation of new therapies.

2013: The Research Council Biomedical Catalyst funds the world's first clinical trial of a stem cell-based larynx transplant, 'RegenVox'.

2013: The first lab-grown 'beef' burger, produced from muscle stem cells derived from cows, is cooked and eaten.

Engineering and Technology

1978: In one of the earliest attempts to engineer tissues, scientists use fibroblasts to condense a hydrated collagen lattice to a tissue-like structure.

1988: For the first time, researchers successfully seed living cells onto synthetic scaffolds, producing viable cells, mitotic figures and vascularisation of the cell mass.

2006: Newcastle University scientists create the first ever artificial liver cells using umbilical cord blood stem cells, grown using a microgravity bioreactor, a piece of equipment derived from NASA technology.

2008: Scientists manufacture an ex vivo heart using an extracellular matrix, reseeded with cardiac and endothelial cells.

2007: The RCUK-funded Diamond Light Source underpins research aiming to make stem cell patches to repair amniotic membranes, whose rupture causes up to 40% of premature births.

2009: Electrospun biopolymer nanofibres, consisting of Polycaprolactone, pave the way for future research into tendon repair. The nanofibres were created by RCUK-funded researchers.

2009: A new technique to identify human stem cells using mid-infrared light is developed by researchers at the European Synchrotron Radiation Facility.

2010: Researchers supported by the RCUK Nanoscience Programme use microscopic magnetic particles to bring stem cells to sites of cardiovascular injury in a new method designed to increase the capacity of cells to repair damaged tissue.

2010: Spin-out The Electrospinning Company is formed from Research Council-funded research. It designs and manufactures products with nanostructured 3D scaffolds for cell growth using electrospun nanofibres.

2012: Scaffolds engineered from biodegradable plastics by RCUK-funded researchers could, in combination with skeletal stem cells, replace lost bone in hip surgery. The scaffolds were created using a technique called supercritical CO_2 fluid-foaming.

2012: Biopolymer hydrogels are developed by RCUK-funded scientists for use in the treatment of corneal blindness caused by limbal stem cell deficiency.

2012: Research Council-funded scientists develop a 'nanopattern' pitted plastic that can be used to coat implant surfaces to encourage stem cells to form bone in contact with the new joint. It is hoped that this will be used in the production of a more durable orthopaedic implant.

2013: Using a pioneering technique called 'solvent blending', Research Councils scientists create a degradable polymer that can be inserted into broken bones to encourage real bone to regrow.

Regenerative medicine

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The seven Research Councils are:

- Arts & Humanities Research Council (AHRC)
- Biotechnology & Biological Sciences Research Council (BBSRC)
- Economic & Social Research Council (ESRC)
- Engineering & Physical Sciences Research Council (EPSRC)
- Medical Research Council (MRC)
- Natural Environment Research Council (NERC)
- Science & Technology Facilities Council (STFC)

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Research Councils UK is the strategic partnership of the UK's Research Councils.

We invest annually around £3 billion in research. Our focus is on excellence with impact. We nurture the highest quality research, as judged by international peer review providing the UK with a competitive advantage. Global research requires we sustain a diversity of funding approaches, fostering international collaborations, and providing access to the best facilities and infrastructure, and locating skilled researchers in stimulating environments.

Our research achieves impact – the demonstrable contribution to society and the economy made by knowledge and skilled people. To deliver impact, researchers and funders need to engage and collaborate with the public, business, government and charitable organisations.

Image credits:

Human embryonic stem cell
Annie Cavanagh/Wellcome Images

SEM of meshed skin graft over a burn
David Gregory & Debbie Marshall, Wellcome Images

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