Stem cell research in the UK reaches significant milestone

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Stem cell scientists at King's College London will today announce they have submitted to the UK Stem Cell Bank (UKSCB) their first clinical grade human embryonic stem (hES) cell lines that are free from animal-derived products, known as 'xeno-free' stem cells.

The cells, which have the potential to become the 'gold standard' lines for developing new stem cell-based therapies, will be the first deposited in the UKSCB based at the National Institute for Biological Standards and Control, under arrangements that will ensure they are freely accessible to the wider research community. The expectation is that these cells will be grown and processed by the UKSCB to provide stem cell stocks that will be used for clinical research and treatment to benefit patients.

Researchers say this is a significant milestone; this first batch of cells is the culmination of nearly ten years of research funded strategically by the Medical Research Council (MRC) that will keep the UK at the forefront of regenerative medicine.

Embryonic stem cells can be grown in the laboratory indefinitely while retaining their capacity to develop into specialised cell types, such as nerve or heart muscle cells, which can then be used in clinical trials. More than 20 'research grade' stem cell lines have been provided by King's to the UKSCB since it derived the first research grade hES cell lines in the UK in 2003, but the challenge to date has been to establish appropriate derivation and growing conditions for the cells without the

presence of any animal products, such as porcine enzymes, bovine serum or mouse feeder layers.

Clinical use of hES cells is already being explored in a number of phase 1 safety trials, such as spinal cord injury and macular degeneration. However, the hES cell lines used in these trials were reclassified from 'research grade' to 'clinical grade' for specified short-term clinical studies in selected disease states, as a matter of expediency. This route is not considered appropriate for the future of cell therapy because of the expense of the required testing and reclassification, and the significant risk of using cell lines derived on unqualified feeders, using unqualified reagents under undocumented environmental conditions in the embryology and stem cell labs and storage facilities. While it might be reasonable to incur additional risks for these early pioneering studies, it is not reasonable to accept these risks for the long-term future of cell therapy. Therefore the highest standard of xeno-free lines are urgently needed, and the development of these lines by King's represents a major step forward.

The hES cells were grown from frozen embryos donated by patients who had previously undergone IVF treatment and no longer wished to use their remaining stored embryos. These embryos would otherwise have been discarded in line with HFEA requirements.

The work took place in the purpose-built stem cell laboratory at King's, in collaboration with the Assisted Conception Unit at Guy's and St Thomas' NHS Foundation Trust, as part of King's Health Partners Academic Health Sciences Centre, and licensed by the Human Fertilisation and Embryology Authority (HFEA) and the Human Tissue Authority (HTA). The laboratory is compliant with Current Good Manufacturing Practices (cGMP).

The team developed a comprehensive methodology and standards for

derivation of the xeno-free hES cell lines that will be appropriate for studies in human subjects after suitable additional testing and processing by the UKSCB. Developed in line with these rigorous standards, researchers, physicians and industry can be reassured of the reliability of the seed stock – the essential base for translational applications. It is hoped that these standards will be recognised across academia, future users and policy agencies operating in and monitoring the field.

As the research that underpinned this work was funded by the MRC, the decision has been taken to submit these to the UKSCB for open-access therapeutic use for the public good. A number of additional xeno-free lines will follow shortly from King's and from the stem cell team at the University of Manchester/Central Manchester NHS Trust, who have been similarly supported by MRC and have also developed clinical grade hES cells to submit to the UKSCB in the same way.

Professor Peter Braude, Emeritus Professor of Obstetrics and Gynaecology, King's College London; former director of the Stem Cell Programme and the Pre-Implantation Genetic Diagnosis Programme, Guy's and St Thomas' NHS Foundation Trust, said:

'This is a significant achievement of the team, one which we have been working towards for many years with the support of the University, our local hospital, and most importantly the Medical Research Council. We have succeeded where many substantial commercial companies have not. Many more xeno-free lines should follow, which demonstrates the validity and foresight of this and previous governments in this important endeavour.'

Dr Dusko Ilic, Senior Lecturer in Stem Cell Science at King's, said:

'I'm pleased that we have finally been able to supply the UK Stem Cell Bank with well-characterised hES cell lines for public use, and can

therefore contribute to the ongoing consolidation of the UK as a leading international player in the stem cell field. In the future, patients hoping for the benefit of regenerative medicine for serious medical conditions caused by illness, injury and ageing, can expect improved progress on cures or amelioration from hES cell-based therapy.'

Dr Rob Buckle, Head of Regenerative Medicine at the MRC, said:

'The MRC is delighted that this investment into regenerative medicine research is beginning to bear fruit. The development of xeno-free hES cells lines is a major step forward in the field as it paves the way for 'gold standard' clinical-grade cell lines suitable for use in humans. This is essential in demonstrating proof-of-concept for stem-cell therapies, which have the potential to treat many diseases that currently have no effective cure. Furthermore, the distribution of these high quality and ethically-sourced lines through the UK Stem Cell Bank will ensure these are widely available to the research community as we seek to accelerate progress in this area.'

Dr Glyn Stacey Head of the UK Stem Cell Bank, based at the National Institute for Biological Standards and Control, a centre of the Health Protection Agency, said:

'These lines will be an important resource to fulfill our plan to make available a panel of characterised and tested clinical grade lines within the next three years. The process of testing will be rigorous and not all cells lines received will make the grade. We will need significantly more lines submitted to reach these targets, especially those that are to be made available for universal use.'

Professor Daniel Brison, Scientific Director of the IVF unit at St Mary's and Co-Director of the Manchester stem cell group, said:

'This is the first step towards a number of clinical lines from King's and from ourselves which should reframe and enhance the initiative established in the UK, and lead the way to important new therapies in regenerative medicine.'

More information: An early online paper on the methodology and standards developed by King's College London for the derivation of xeno-free hES cells is available from Cytotherapy, the official journal of the International Society for Cellular Therapy (www.celltherapysociety.org) www.ncbi.nlm.nih.gov/pubmed/22029654

Provided by King's College London