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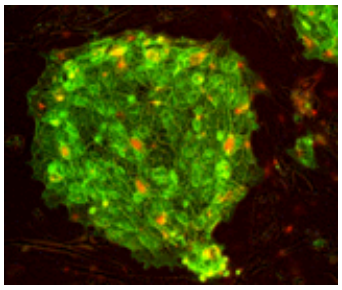
University study sheds light on human embryonic stem cells´ DNA changes

A study on the genome of human embryonic stem cells (hESCs) has brought scientists closer to identifying and avoiding the adverse DNA changes that naturally occur when these cells are multiplied in laboratory. The findings could help researchers to prevent deleterious changes in cultured hESCs - a factor that may hamper their future medical use - advancing towards more reliable applications of stem-cells-based regenerative treatments.



Colonies of Shef 1 human embryonic stem cells (green) with feeder cells (dark red)

The collaborative study, coordinated through an EU-funded project ESTOOLS and involving experts at the University of Sheffield, is published by the peer-review journal Nature Biotechnology.

Embryonic stem cells are studied for potential applications in regenerative cell replacement therapies because of their unique capacity to self-renew and turn into a variety of cell and tissue types, including neurons, blood cells, bone and muscle.

However, it is known that genetic changes take place in various hESC lines as they multiply in the laboratory, some of which resemble the DNA abnormalities typical of cancer cells. hESCs may also undergo other genetic changes undetectable by conventional methods, raising concerns over their medical use.

To address this issue, researchers used high resolution DNA analysis to plot the genetic changes in 17 hESC lines cultured over many generations, from the ESTOOLS consortium -the largest cluster of hESCs laboratories in Europe. Authors of the study include several partners of the ESTOOLS consortium, including Prof Riitta Lahesmaa and colleagues in Turku, Finland.

The study mapped hundreds of copy number variations (CNV) and loss of heterozygosity (LOH) after prolonged passages in culture. Both CNV and LOH are genetic variations that that may be associated with tumour transformation.

For the first time, researchers could shortlist a number of genes that map inside or near the mutated sites, and that could therefore be affected by these potentially deleterious changes.

Professor Peter Andrews, from the University of

Sheffield's Department of Biomedical Sciences and a leading author of the study, said: "When we know which genes are involved, it will be easier to reject those hESC lines in which those genes are more likely to mutate."

Authors point out that the study will also help to dig into the so-called culture adaptation process, i.e. the accumulation of genetic changes typical of malignant transformation that is mimicked by hESCs in culture, potentially providing clues to some of the genetic mechanisms underlying cancer development.

For further information please contact the Media Team on 0114 222 5338 or email mediateam@sheffield.ac.uk or ESTOOLS Media Relations, Sergio Pistoi +39-3478735664 or email press@sergiopistoi.com

- Read the full paper
- ESTOOLS International Scientific Symposium

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