New biomarker to assess stem cells developed

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A research team led by scientists from UCL have found a way to assess the viability of 'manufactured' stem cells known as induced pluripotent stem cells (iPSCs). Published today in *Nature Communications*, the team's discovery offers a new way to fast-track screening methods used in stem cell research.

iPSCs are derived from cells, usually taken from skin or blood, that have been genetically reprogrammed to revert back to an embryonic-like state, which enables the cells to differentiate into any cell type in the body. iPSC technology is a hugely important new platform for the study of human diseases in the laboratory, and, offers the potential to develop transformative cell replacement therapies, for example, by creating hepatic cells to treat liver disease and stem cells to treat leukaemia and other blood cancers.

It is the ability of iPSCs to differentiate to other cell types that makes them so valuable for laboratory research, however not all iPSCs offer the same differentiation capacity, some cell lines are markedly defective.

"When generating iPSCs it is clearly beneficial to identify 'good' and 'bad' cell lines" explains Dr Lee Stirling, who led the research team whilst a Research Associate at the UCL Cancer Institute. "Good cell lines offer optimal differentiation capacity and are therefore the most useful for research. However establishing the quality of these cell lines using traditional ways of assessment is costly and time-consuming. We were looking to find a way to expedite this process and we think part of the solution lies in using DNA methylation as a biomarker for

differentiation capacity".

DNA methylation is a physical modification to the genetic material (DNA) of a cell, which can alter the behaviour of that cell. In this study, the team were looking for a particular type of methylation that only occurs in stem cells, known as non-CG methylation, to see if they could identify a link between non-CG methylation and differentiation capacity of iPSCs.

Dr Stirling says: "The role of a pluripotent stem cell is to generate all three germ layers: mesoderm, endoderm and ectoderm. These germ layers then develop into all cells of the body. For this study, we focussed specifically on a pluripotent stem cell's ability to differentiate into the endodermal lineage - the lineage for organs such as liver, pancreas and thyroid gland. Once we had collected and examined our data we were immediately struck by a link - we could confidently report that a reduction in non-CG methylation is associated with impaired differentiation capacity into endodermal lineages."

"The main point of this study is that we have found an epigenetic biomarker that can help us distinguish iPSCs that have a diminished capacity for differentiation. This discovery can be used to reduce costly and time-consuming analysis methods, while simultaneously offering improvements in large-scale assessment of iPSC lines for clinical and therapeutic applications." adds Dr Stirling.

The research team hope that not only will their discovery be used in the short-term as an efficient analysis method of cell lines for research purposes but, going forward, findings can be used as a starting point for discovering the developmental processes associated with methylation patterns in iPSCs. Dr Stirling concludes: "In time, I'm confident that understanding these principles will impact our understanding of cancer cell behaviour and, eventually, form a solid base for regenerative

medicine strategies."

This study was a collaboration between UCL, Cambridge University, Cellcentric and the Wellcome Trust Sanger Institute (HipSci).

More information: Lee M. Butcher et al. Non-CG DNA methylation is a biomarker for assessing endodermal differentiation capacity in pluripotent stem cells, *Nature Communications* (2016). DOI: 10.1038/ncomms10458

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