Scientists unveil the UK's largest resource of human stem cells from healthy donors

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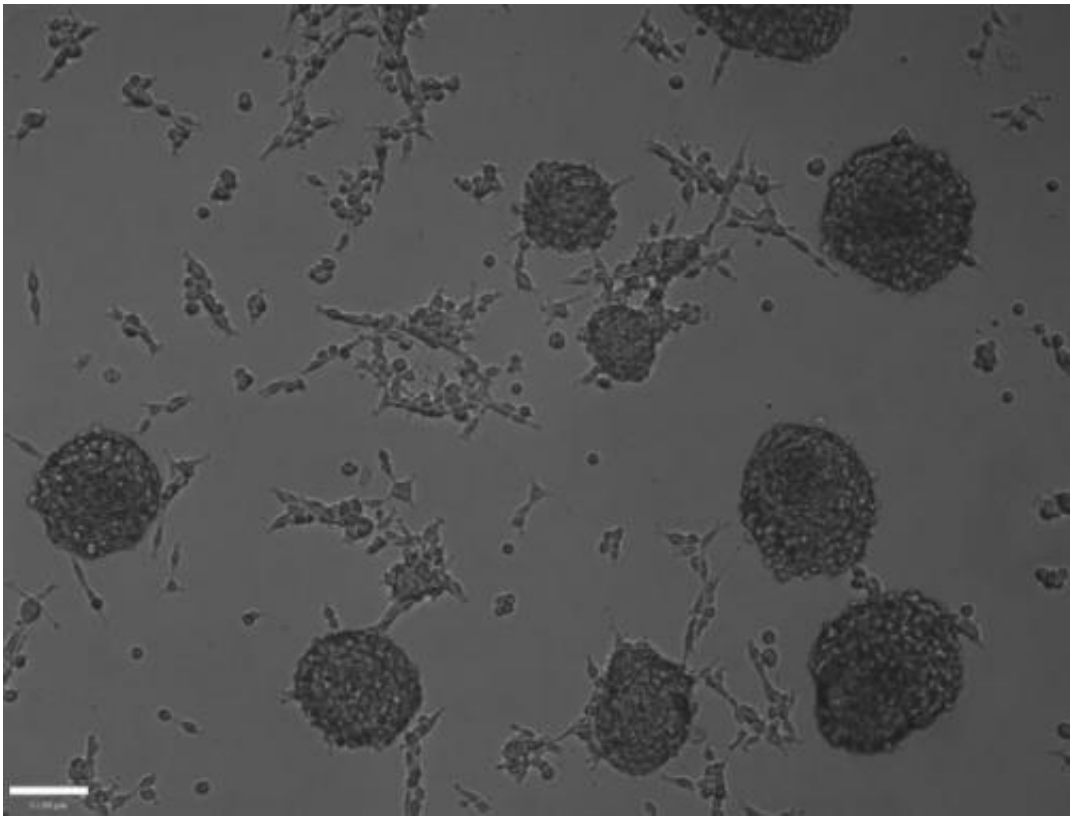

Eye stem cells. Credit: University of Southampton

Reported in *Nature* today, one of the largest sets of high quality human induced pluripotent stem cell lines from healthy individuals has been produced by a consortium involving the Wellcome Trust Sanger Institute. Comprehensively annotated and available for independent

research, the hundreds of stem cell lines are a powerful resource for scientists studying human development and disease.

With collaborative partners from King's College London, the European Bioinformatics Institute, the University of Dundee and the University of Cambridge, the study also investigates in unprecedented detail the extensive variation between stem cells from different healthy people.

Technological advancements have made it possible to take an adult cell and use specific growth conditions to turn back the clock - returning it to an early embryonic state. This results in an induced pluripotent stem cell (iPSC), which can develop into any type of cell in the body. These iPSCs have huge scientific potential for studying the development and the impact of diseases including cancer, Alzheimer's, and heart disease.

However, the process of creating an iPSC is long and complicated and few laboratories have the facilities to characterise their cells in a way that makes them useful for other scientists to use.

The Human Induced Pluripotent Stem Cell Initiative (HipSci) project used standardised methods to generate iPSCs on a large scale to study the differences between healthy people. Reference sets of stem cells were generated from skin biopsies donated by 301 healthy volunteers, creating multiple stem cell lines from each person.

The researchers created 711 cell lines and generated detailed information about their genome, the proteins expressed in them, and the cell biology of each cell line. Lines and data generated by this initiative are available to academic researchers and industry.

Dr Daniel Gaffney, a lead author on the paper, from the Wellcome Trust Sanger Institute, said: "We have created a comprehensive, high quality reference set of human induced pluripotent stem cell lines from healthy

volunteers. Each of these stem cell lines has been extensively characterised and made available to the wider research community along with the annotation data. This resource is a stepping stone for researchers to make better cell models of many diseases, because they can study disease risk in many cell types, including those that are normally inaccessible."

By creating more than one stem cell line from each healthy individual, the researchers were able to determine the similarity of stem cell lines from the same person.

Prof Fiona Watt, a lead author on the paper and co-principal investigator of HipSci, from King's College London, said: "Many other efforts to create stem cells focus on rare diseases. In our study, stem cells have been produced from hundreds of healthy volunteers to study common genetic variation. We were able to show similar characteristics of iPS cells from the same person, and revealed that up to 46 per cent of the differences we saw in iPS cells were due to differences between individuals. These data will allow researchers to put disease variations in context with healthy people."

The project, which has taken 4 years to complete, required a multidisciplinary approach with many different collaborators, who specialised in different aspects of creating the cell lines and characterising the data.

Dr Oliver Stegle, a lead author on the paper, from the European Bioinformatics Institute, said: "This study was only possible due to the large scale, systematic production and characterisation of the stem cell lines. To help us to understand the different properties of the cells, we collected extensive data on multiple molecular layers, from the genome of the lines to their cell biology. This type of phenotyping required a whole facility rather than just a single lab, and will provide a huge

resource to other scientists. Already, the data being generated have helped to gain a clearer picture of what a typical human iPSC cell looks like."

Dr Michael Dunn, Head of Genetics and Molecular Sciences at Wellcome, said: "This is the fantastic result of many years of work to create a national resource of high quality, well-characterised human induced pluripotent stem cells. This has been a significant achievement made possible by the collaboration of researchers across the country with joint funding provided by Wellcome and the MRC. It will help to provide the knowledge base to underpin a huge amount of future research into the effects of our genes on health and disease. By ensuring this resource is openly available to all, we hope that it will pave the way for many more fascinating discoveries."

More information: Helena Kilpinen et al, Common genetic variation drives molecular heterogeneity in human iPSCs, *Nature* (2017). DOI: 10.1038/nature22403

www.yourgenome.org/facts/what-is-a-stem-cell

Provided by Wellcome Trust Sanger Institute