Major stem cell discovery to boost research into development and regenerative medicine

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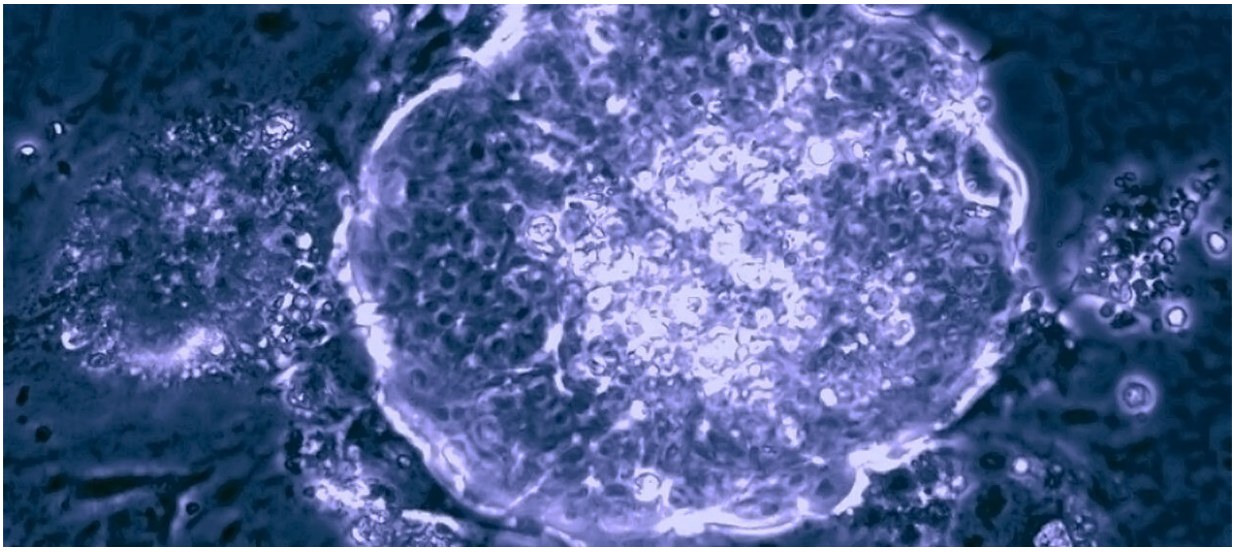

Pig EPSCs (expanded potential stem cells). Credit: Xuefei Gao

A new approach has enabled researchers to create Expanded Potential Stem Cells (EPSCs) of both pig and human cells. These stem cells have the features of the first cells in the developing embryo, and can develop into any type of cell. The research from LKS Faculty of Medicine at The University of Hong Kong (HKUMed), the Wellcome Sanger Institute, and the Friedrich-Loeffler-Institut in Germany offers incredible potential for studying human development and regenerative medicine.

The study published in *Nature Cell Biology* represents the first time scientists have been able to derive stem cells from early pig embryos. Domestic pigs have great potential for biomedical research because of their genetic and anatomical similarities to humans, including comparable organ sizes. Being able to genetically modify pig stem cells will also be beneficial for animal health and food production.

Stem cells have the ability to develop into other cell types, and existing stem cell lines are already extremely useful for research into development, disease and treatments. However, currently available types of stem cell lines have limitations, and until now it has also not been possible to create embryonic stem cells from pigs and many other farm animals.

Professor Pentao Liu, the leader of the study from the School of Biomedical Sciences and Stem Cell and Regenerative Medicine Consortium, HKUMed, and previously of the Wellcome Sanger Institute, said: "Scientists have been attempting to derive porcine embryonic stem cells for decades without much success. With our Expanded Potential Stem Cell technology, we have now successfully derived and characterised stem cells from porcine preimplantation embryos. We have also established similar human stem cells. Our study represents a significant advance in stem cell research."

Since human EPSCs can produce large numbers of placenta cells—called trophoblasts—they offer new opportunities to investigate pregnancy complications such as pre-eclampsia and miscarriages.

EPSCs come from culturing cells from the earliest stage of development, when the fertilised egg has only divided into 4 or 8 cells and the cells retain some totipotency—the ability to produce all cell types.

Dr. Xuefei Gao, a first author on the paper from HKUMed, and

previously from the Wellcome Sanger Institute, said: "These EPSC stem cells possess developmental potency that is not generally seen in conventional embryonic or induced pluripotent stem cells. They have the potential to produce all embryonic and extra-embryonic cell lines—including those in the placenta and yolk sac, turning back the development clock to the very earliest cell type. These cells will enable researchers to study early embryonic development, miscarriage and developmental disorders."

The first EPSCs were created in 2017, when the group targeted key molecular pathways during very early development in mice. At these very earliest embryonic developmental stages, mammalian species are very similar and the cells are like a blank sheet of paper. This study has shown that it is possible to use the same approach to create human EPSCs and also to establish EPSCs from pigs—mammals that had previously been elusive to stem cell researchers.

Dr. Monika Nowak-Imialek, an author on the paper from the Friedrich-Loeffler-Institut (FLI) in Germany, said: "Our porcine EPSCs isolated from pig embryos are the first well-characterized pig cell lines worldwide. EPSC's great potential to develop into any type of cell provides important implications for developmental biology, regenerative medicine, organ transplantation, disease modeling, and screening for drugs."

More information: Establishment of porcine and human expanded potential stem cells, *Nature Cell Biology* (2019). DOI: 10.1038/s41556-019-0333-2 , www.nature.com/articles/s41556-019-0333-2

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