Researchers piggyback to safer reprogrammed stem cells

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Austin Smith and his research team at the Centre for Stem Cell Research in Cambridge have just published in the journal *Development* a new and safer way of generating pluripotent stem cells - the stem cells that can give rise to every tissue of the body.

Rapid developments in stem cell research in recent years have provided a way for stem cell scientists to convert specialised cells, such as skin cells, into stem cells that can form numerous cell types of the body. Research into the creation of these 'reprogrammed' cells - so-called induced pluripotent stem (iPS) cells - is of vital importance because it could lead to new ways of creating human stem cells from adult tissues for the study and treatment of disease. But there is one key problem with the techniques currently used to generate such stem cells: they rely on potentially harmful viruses to deliver the reprogramming factors that change specialised cells into iPS cells.

Now Austin Smith and his team report in the journal *Development* an approach that avoids the use of such viruses. They successfully persuaded partly specialised mouse cells, called Epi-stem cells, to reprogram into iPS cells using a single reprogramming factor called Klf4. Instead of relying on viruses to introduce Klf4 into the Epi-stem cells, they turned to a special type of DNA, called a transposable element, which can insert itself into an organism's DNA and carry a cargo with it, in this case Klf4. The transposable element Smith and colleagues used in their study is called Piggybac, which delivered a single copy of Klf4 into the Epi-stem cells, causing them to reprogram

into iPS cells. The researchers then used an enzyme to cut the Klf4 out of Piggybac.

In doing so, they discovered that the iPS cells could maintain themselves using their own Klf4 gene, which had been switched on during the reprogramming process. Once the Piggybac Klf4 is removed, they report, iPS cells can go on to create normal mice when introduced into newly developing mouse embryos and can give rise to the offspring of these mice by contributing to their reproductive cells. This is the most stringent test of the normality of iPS cells. As Professor Smith explains below, this is a significant advance in the field.

"The paper we've published in *Development*, together with two other publications in Nature', says Professor Smith, ' is a significant technical development in the field as together these papers present a more reliable and precise method for generating iPS cells. The method allows for greater control over the genetic modification process and this is fully reversible once reprogramming is complete. Therefore, the final iPS cells carry no potentially damaging foreign DNA. Our findings show that this approach produces perfectly reprogrammed mouse cells. The Nature papers show that it can also work in human cells. These studies provide a new tool to help advance basic research into reprogramming and pave the way to the creation of human iPS cells suitable for biomedical applications."

More information: dev.biologists.org/

Source: The Company of Biologists

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