New genetic technique converts skin cells into brain cells

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A research breakthrough has proven that it is possible to reprogram mature cells from human skin directly into brain cells, without passing through the stem cell stage. The unexpectedly simple technique involves activating three genes in the skin cells; genes which are already known to be active in the formation of brain cells at the foetal stage.

The new technique avoids many of the ethical dilemmas that stem cell research has faced.

For the first time, a research group at Lund University in Sweden has succeeded in creating specific types of nerve cells from human skin. By reprogramming connective tissue cells, called fibroblasts, directly into nerve cells, a new field has been opened up with the potential to take research on cell transplants to the next level. The discovery represents a fundamental change in the view of the function and capacity of mature cells. By taking mature cells as their starting point instead of stem cells, the Lund researchers also avoid the ethical issues linked to research on embryonic stem cells.

Head of the research group Malin Parmar was surprised at how receptive the fibroblasts were to new instructions.

"We didn't really believe this would work, to begin with it was mostly just an interesting experiment to try. However, we soon saw that the cells were surprisingly receptive to instructions."

The study, which was published in the latest issue of the scientific journal *PNAS*, also shows that the skin cells can be directed to become certain types of nerve cells.

In experiments where a further two genes were activated, the researchers have been able to produce dopamine brain cells, the type of cell which dies in Parkinson's disease. The research findings are therefore an important step towards the goal of producing nerve cells for transplant which originate from the patients themselves. The cells could also be used as disease models in research on various neurodegenerative diseases .

Unlike older reprogramming methods, where skin cells are turned into pluripotent stem cells, known as IPS cells, direct reprogramming means that the skin cells do not pass through the stem cell stage when they are converted into nerve cells. Skipping the stem cell stage probably eliminates the risk of tumours forming when the cells are transplanted. Stem cell research has long been hampered by the propensity of certain stem cells to continue to divide and form tumours after being transplanted.

Before the direct conversion technique can be used in clinical practice, more research is needed on how the new nerve cells survive and function in the brain. The vision for the future is that doctors will be able to produce the brain cells that a patient needs from a simple skin or hair sample. In addition, it is presumed that specifically designed cells originating from the patient would be accepted better by the body's immune system than transplanted cells from donor tissue.

"This is the big idea in the long run. We hope to be able to do a biopsy on a patient, make dopamine cells, for example, and then transplant them as a treatment for Parkinson's disease", says Malin Parmar, who is now continuing the research to develop more types of brain cells using

the new technique.

More information: 'Direct conversion of human fibroblasts to dopaminergic neurons', publ. *PNAS* 2011; 6 June 2011: www.pnas.org/content/early/201 … /1105135108.abstract

Provided by Lund University