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Stem cells without genetic defects heralded as breakthrough

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The prospect of treating genetic diseases with corrected stem cells grown from patients' own bodies has moved closer, after the results of a remarkable experiment.

Scientists have successfully reprogrammed skin tissue from people with a rare form of anaemia to create powerful stem cells, while at the same time rectifying the genetic defect that causes the condition.

The corrected stem cells could be grown into blood precursor cells for therapy. As these would carry a patient's own DNA, except for the mutation responsible for the illness, they could be transplanted without risk of rejection by the body's immune system.

Though the research team, from Spain and the United States, has yet to use the cells to treat patients, and several important hurdles still remain, the achievement has been hailed as a significant advance for stem cell research.

It suggests that it should eventually be possible to treat many inherited conditions by making disease-free stem cells from their own bodies.

The experiment offers "proof of concept" that the technique "can be used for the generation of disease-corrected, patient-specific cells with potential value for cell therapy applications," the researchers write in the journal *Nature*.

In the study, a team led by Juan Carlos Izpisua Belmonte, of the Salk Institute in La Jolla, California, took cells from six patients with Fanconi anaemia, a recessive genetic disorder that causes bone marrow failure and leukaemia. It is often fatal unless a bone marrow transplant is available from a perfectly matched donor.

The cells were infected with a genetically modified virus to correct the gene that causes Fanconi anaemia. These were then reprogrammed into an embryo-like state by modifying further genes, to create versatile master cells known as induced pluripotent stem cells (IPS cells).

When these IPS cells were grown in culture, they developed into blood progenitor cells of the sort that are required for transplant in Fanconi anaemia therapies.

As the IPS cells' DNA had been corrected, they did not have the mutation that causes the disease, but they were otherwise genetically identical to the patients' own tissue.

The reprogrammed, corrected cells are not yet suitable for transplanting into patients, because it is not yet known whether IPS cells can be safely given to patients.

The reprogramming technique currently relies on modifying genes with a virus, and there are fears that this could promote cancers. Several new reprogramming methods that do not rely on viruses, however, have recently been developed.

"The recent implementation of reprogramming protocols that do not rely on viral integration, if their

applicability to human cells was confirmed, would bring the realisation of this possibility closer," the researchers said.

The combination of reprogramming cells and correcting their DNA could also have potential for treating many other conditions with a genetic component, such as Parkinson's disease, motor neuron disease and diabetes.

Chris Mathew, Professor of Molecular Genetics at King's College London, said: "This is an important development for families with this rare, inherited blood disorder. The patients have low numbers of blood stem cells in their bone marrow, so there are very few target cells to correct by gene therapy.

"The new research shows that it is possible to reprogramme skin cells from these patients into stem cells in which the genetic defect has been corrected. In future it may become possible to transfer the corrected stem cells back into the patient, but much work remains to be done."