

A major breakthrough in generating safer, therapeutic stem cells from adult cells

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The new technique solves one of the most challenging safety hurdles associated with personalized stem cell-based medicine because for the first time it enables scientists to make stem cells in the laboratory from adult cells without genetically altering them. This discovery has the potential to spark the development of many new types of therapies for humans, for diseases that range from Type 1 diabetes to Parkinson's disease.

The study was published in an advance, online issue of the journal *Cell Stem Cell* on April 23, 2009.

"We are very excited about this breakthrough in generating embryonic-like cells from fibroblasts [cells that gives rise to connective tissue] without using any [genetic material](#)," says Scripps Research Associate Professor Sheng Ding, who led the research. "Scientists have been dreaming about this for years."

Normally, cells develop from stem cells into a myriad of increasingly more specialized cell types during early development and throughout a lifetime. In humans and other mammals, these developmental events are irreversible. This means that when tissues are damaged or cells are lost, there is usually no source from which to replenish them. Having a source of the most primitive stem cells available would be useful in many medical situations because these cells are "pluripotent," having the ability to become any of the body's cell types—potentially providing doctors with the ability to repair damaged tissues throughout the body.

However bright this promise, the use of stem cells in medicine has faced many hurdles. One strategy has been to work towards a therapy where doctors could take a patient's own [adult cells](#) and "reprogram" them into stem cells. This not only avoids potential ethical problems associated with the use of human [embryonic stem cells](#), it also addresses concerns about compatibility and immune rejection that plague therapies such as [organ transplantation](#).

A few years ago, a team of researchers in Japan made a breakthrough in this general approach by converting mouse skin cells into mouse stem cells. The Japanese team accomplished this remarkable transformation by inserting a set of four genes into these skin cells. While the study was a powerful proof-of-principle, the therapeutic potential of genetically reprogrammed cells is limited because of safety issues. One obvious problem is that the four required genes and their associated foreign DNA sequences permanently reside in the cells when transplanted. Moreover, the specific genes in question are problematic because, in living tissue, they are linked to the development of cancerous tumors.

Many scientists have been trying to find safer ways to generate stem cells from adult cells -- developing methods that require fewer genes, or techniques that can put genes in and then take them out. However, to date all of these have still harbored significant safety concerns due to the nature of the genetic manipulations. Ding and his team previously reported the discovery of drug-like small molecules to replace some of those genes, but have also hoped to go even further and find ways to reprogram adult cells into stem cells without using any genes or genetic manipulations at all.

The team of scientists accomplished this extraordinarily challenging feat by engineering and using recombinant proteins, that is proteins made from the recombination of fragments of DNA from different organisms. Many different recombinant proteins have been therapeutically and

routinely used to treat human diseases. Instead of inserting the four genes into the cells they wanted to reprogram, the scientists added the purified engineered proteins and experimented with the chemically defined conditions without any genetic materials involved until they found the exact mix that allowed them to gradually reprogram the cells.

The scientists found that those reprogrammed embryonic-like cells (dubbed "protein-induced pluripotent stem cells" or "piPS cells") from fibroblasts behave indistinguishably from classic embryonic [stem cells](#) in their molecular and functional features, including differentiation into various cell types, such as beating cardiac muscle cells, neurons, and pancreatic cells.

Source: The Scripps Research Institute ([news](#) : [web](#))

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