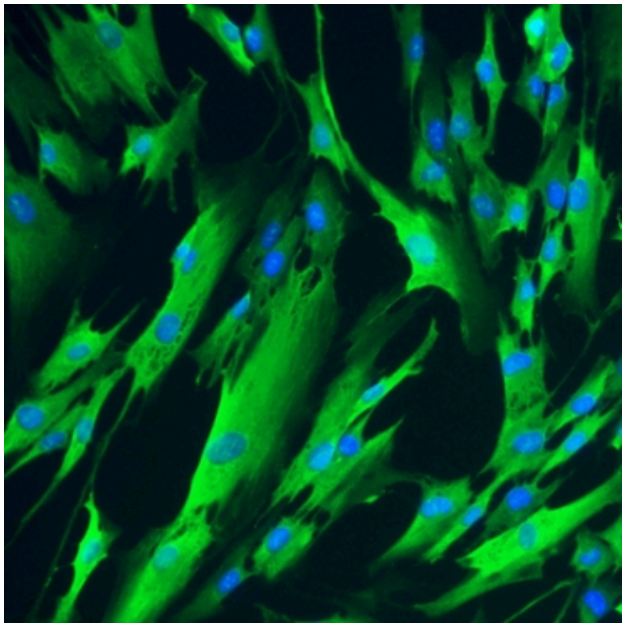
RNA offers a safer way to reprogram cells

New technique holds promise to revert cells to an immature state that can develop into any cell type.

Anne Trafton, MIT News Office

July 26, 2010

email comment print share



MIT researchers used RNA to induce these fibroblast cells to express four genes necessary to reprogram cells to an immature state.
Image: Yanik Laboratory

In recent years, scientists have shown that they can reprogram human skin cells to an immature state that allows the cells to become any type of cell. This ability, known as pluripotency, holds the promise of treating diseases such as diabetes and Parkinson's disease by transforming the patients' own cells into replacements for the nonfunctioning tissue.

However, the techniques now used to transform cells pose some serious safety hazards. To deliver the genes necessary to reprogram cells to a pluripotent state, scientists use viruses carrying DNA, which then becomes integrated into the cell's own DNA. But this so-called DNA-based reprogramming carries the risk of disrupting the cell's genome and leading it to become cancerous.

Now, for the first time, MIT researchers have shown that they can deliver those same reprogramming genes using RNA, the genetic material that normally ferries instructions from DNA to the cell's protein-making machinery. This method could prove much safer than DNA-based reprogramming, say the researchers, Associate Professor of Electrical and Biological Engineering Mehmet Fatih Yanik and electrical engineering graduate student Matthew Angel.

Yanik and Angel describe the method, also the subject of Angel's master's thesis, in the July 23 issue of the journal *PLoS ONE*.

However, the researchers say they cannot yet claim to have reprogrammed the cells into a pluripotent state. To prove that, they would need to grow the cells in the lab for a longer period of time and study their ability to develop into other cell types — a process now underway in their lab. Their key achievement is demonstrating that the genes necessary for reprogramming can be delivered with RNA.

"Before this, nobody had a way to transfect cells multiple times with protein-encoding RNA," says Yanik. (Transfection is the process of introducing DNA or RNA into a cell without using viruses to deliver them.)

Focus on RNA

today's news

Emeritus: On the trail of aflatoxin

Photo: Calvin Campbell

Toxicologist Gerald Wogan has dedicated his career to understanding — and fighting — a deadly carcinogen.

Understanding shape-shifting polymers

December 6, 2010

A hardy Constitution

December 3, 2010

related

Paper: "Innate Immune Suppression Enables Frequent Transfection with RNA Encoding Reprogramming Proteins"

High-Throughput Neurotechnology Group

Research: "Extended transient transfection by repeated delivery of in vitro-transcribed RNA"

PRESS RELEASE: "RNA offers a safer way to reprogram cells"

tags

bioengineering and biotechnology

biology

computer science and technology

electrical engineering and electronics

reprogramming

stem cells

graduate/post-doc

In 2006, researchers at Kyoto University showed they could reprogram mouse skin cells into a pluripotent, embryonic-like state with just four genes. More recently, other scientists have achieved the same result in human cells by delivering the proteins encoded by those genes directly into mature cells, but that process is more expensive, inefficient and time-consuming than reprogramming with DNA.

Funded by a Packard Fellowship in Science and Engineering, Yanik and Angel decided to pursue a new alternative by transfecting cells with messenger RNA (mRNA), a short-lived molecule that carries genetic instructions copied from DNA.

However, they found that RNA transfection poses a significant challenge: When added to mature human skin cells, mRNA provokes an immune response meant to defend against viruses made of RNA. Repeated exposure to long strands of RNA leads cells to undergo cell suicide, sacrificing themselves to help prevent the rest of the body from being infected.

Yanik and Angel knew that some RNA viruses, including hepatitis C, can successfully suppress that defensive response. After reviewing studies of hepatitis C's evasive mechanisms, they did experiments showing they could shut off the response by delivering short interfering RNA (siRNA) that blocks production of several proteins key to the response.

Once the defense mechanism is shut off, mRNA carrying the genes for cell reprogramming can be safely delivered. The researchers showed that they could induce cells to produce the reprogramming proteins for more than a week, by delivering siRNA and mRNA every other day.

Peter Andrews, director of the Centre for Stem Cell Biology at the University of Sheffield, says the MIT team's key advance is suppressing the cell's immune response to RNA. He calls the work an interesting approach, but adds "the jury's out" on whether it will prove better than other methods. "The next step would be to make iPS cells [induced pluripotent stem cells]" using this technique, says Andrews. The MIT researchers agree that determining whether this will work remains an open question.

Comments

mascott - **Very promising!** 2010-07-26 09:37:41

I look forward to seeing those reprogrammed cells in the future!

allen 2010-08-02 04:18:27

The cell is such a complicated system! It's really difficult to transform it! But MIT is a great university! I believe in MIT, and she will transform the cell, the human being and all the creature!

Alex :P - **Very Interesting + Fat-derived pluripotent cells** 2010-10-01 04:40:57

I heard of a method that called for the utilization of fat cells in lieu of those from the skin. The liposuction fat-to-stem cell method was apparently more effective. (I believe that it was discovered by a duo of SF Bay Area scientists; Berkeley?)

I'd be curious to know whether or not the RNA method as described above would be able to increase the efficiency and accuracy of the fat-derived stem cell procedure.