New method for generating human stem cells is remarkably efficient

September 30 2010

The ability to efficiently generate patient-specific stem cells from differentiated cells and then reliably direct them to form specialized cells (like neurons or muscle) has tremendous therapeutic potential for replacing diseased or damaged tissues. However, despite some successes, there have been significant limitations associated with existing methods used to generate human induced pluripotent stem cells (iPSCs).

Now, a study published by Cell Press on September 30th in the journal *Cell Stem Cell* presents a novel strategy for creating iPSCs that exhibits some significant advantages when compared with current iPSC technologies. The new method does not require risky genetic modification and holds great promise for making the reprogramming process more therapeutically relevant.

"Clinical application of iPSCs is currently hampered by low efficiency of iPSC generation and protocols that permanently alter the genome to effect cellular reprogramming," explains senior study author, Dr. Derrick J. Rossi from Harvard Medical School. "Perhaps even more importantly, safe and effective means of directing the fate of patient-specific iPS cells towards clinically useful cell types are lacking."

In the current study, Dr. Rossi and colleagues did not take the standard approach to permanently alter the genome to achieve expression of protein factors known to reprogram adult cells into iPSCs. Instead, they developed synthetic modified messenger RNA molecules (which they termed "modified RNAs") that encoded the appropriate proteins but did

not integrate into the cell's DNA.

Repeated administration of the modified RNAs resulted in robust expression of the reprogramming proteins in mature skin cells that were then converted to iPSCs with startling efficiency. "We weren't really expecting the modified RNAs to work so effectively, but the reprogramming efficiencies we observed with our approach were very high," says Dr. Rossi.

Importantly, the modified RNA method was also used to successfully to control the fate of the iPSCs. "Creation of iPSCs is the critical first step towards patient-specific therapies, but to truly realize the promise of iPS cell technology for regenerative medicine or disease modeling, we must harness the potential of iPS cells to generate clinically useful cell types," notes Dr. Rossi. RNA-induced iPSCs with an RNA associated with muscle cell development caused the cells to differentiate into muscle cells —again simply, efficiently and without the immediate risk of inducing genetic mutations.

These findings demonstrate that the novel RNA-induced iPSC technology offers significant advantages over existing methodologies. "Our technology represents a safe, efficient strategy for somatic cell reprogramming and directing cell fate that has wide ranging applicability for basic research, disease modeling and regenerative medicine," concludes Dr. Rossi. "We believe that our approach has the potential to become a major and perhaps even central enabling technology for cell-based therapies."

More information: Cell Stem Cell: http://www.cell.com/cell-stem-cell/home
Information on iPS cells: http://bit.ly/dvGaqN

Provided by Cell Press