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IN-DEPTH FOCUS:
iPS cell research

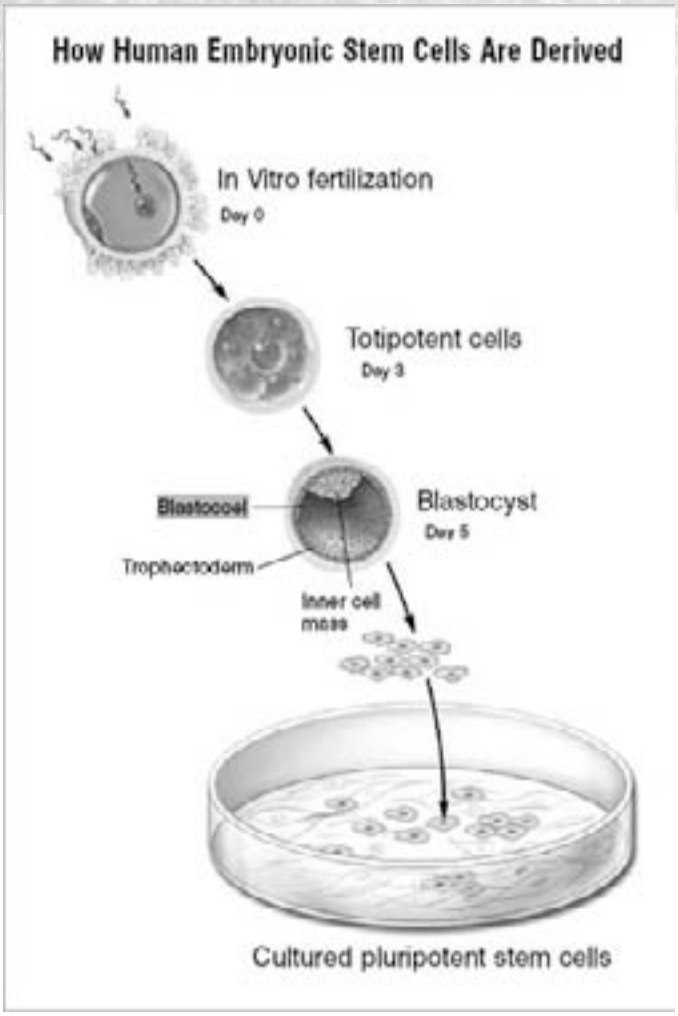
Synthetic RNA for Cell Reprogramming

The field of induced pluripotent stem cells (iPSCs) is moving with breathtaking rapidity (1). *Cell* has recently published a landmark finding by Derrick Rossi's laboratory at the Harvard Stem Cell Institute, promising to push the field to new horizons. Rossi's team engineered synthetic mRNA-transfected cells in order to generate iPSCs, which they called RiPSCs. Instead of using the established method of transfecting cells with retroviruses encoding the reprogramming factors, mRNA was specifically constructed to encode factors. The researchers also modified the mRNA in order to decrease its susceptibility to degradation, increase reprogramming efficiency, and decrease the immune response (2).

RiPSCs have major advantages over virally-derived iPSCs. First, mature cells are reprogrammed to a pluripotent state at an efficiency of 1.4%, whereas retroviruses are reprogrammed at an efficiency of 0.04%, a 36-fold improvement. Also, gene expression arrays show that RiPSCs are more similar to true pluripotent stem cells (embryonic stem cells) than virally-derived iPSCs. Lastly, and perhaps most importantly, mRNA is non-integrating, unlike retroviruses. Thus, there are no permanent changes to the genome of the host cell, reducing its oncogenic risk (2).

The Rossi laboratory's results have implications on directed differentiation and transdifferentiation, as scientists may now manipulate cellular identity with greater precision, higher efficiency, and without permanent genomic changes. The ability to make RiPSCs is also a step forward in making clinically-viable induced pluripotent cells, offering hope for cellular therapy methods. H

—Seth Cassel '13 is a Human Developmental and Regenerative Biology concentrator in Leverett House.



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▲ **Figure 1**: Culturing human embryonic stem cells

1. Takahashi, K. et al. (2006) Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. Cell. 126: 663-676.
2. Warren, L. et al. (2010) Highly efficient reprogramming to pluripotent and directed differentiation of human cells with synthetic modified mRNA. Cell Stem Cell. 7(5):618-630.