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New in Cerebrum: Induced Pluripotent Stem Cells

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What are induced pluripotent stem (IPS) cells and how do they relate to the brain? The topic is the focus of “[Your Brain Under the Microscope: The Promise of Stem Cells](#),” our *Cerebrum* feature for January.

Until recently, scientists primarily worked with two kinds of stem cells: embryonic stem cells and non-embryonic “somatic” or “adult” stem cells from animals and humans. They are just now beginning to improve their understanding of IPS cells, believing that they may help unlock the mystery behind a number of brain disorders.

The authors of our story are Dana Alliance member [Fred H. Gage](#), Ph.D., and Maria C. Marchetto, Ph.D., at the Salk Institute in La Jolla, CA. Gage, the Adler Professor in the [Laboratory of Genetics](#), is one of the world’s foremost authorities on IPS cells. Marchetto is a senior staff scientist in Gage’s lab and is involved in understanding the mechanisms by which human embryonic stem cells and induced pluripotent stem cells become a fully developed functional neuron.

“We all begin our lives with one major stem cell: a fertilized egg,” write the authors, adding that the one stem cell divides, forms new cells, and become increasingly varied over time. The process is known as cell differentiation as cells become specialized for their locations in the body. “As we develop in the womb, our cells differentiate into nerves, muscles, and so on, and the organs begin to organize and function together,” they explain.

Scientists long believed that a mature or specialized cell could not “reprogram,” or return to an immature state, but a major breakthrough occurred in 1997 when Ian Wilmut electrofused nuclei of cultured sheep adult mammary gland cells into enucleated (surgical removal of the nucleus) sheep eggs. The genetic engineering procedure resulted in a single cloned sheep named Dolly. It showed the promise of reprogramming adult cells to an immature state by exposing them to a yet-unknown combination of factors that were present inside enucleated eggs. These reprogrammed cells became pluripotent again, meaning they were capable of going through a new process of maturing and specializing.

Even though there was now proof that reprogramming was possible, cloning experiments were difficult and controversial. An important piece of the puzzle was solved in 2006 when Japanese researcher Shinya Yamanaka and his postdoc Kazutoshi Takahashi induced an adult skin cell (fibroblast) to become an IPS cell in just a month’s time.



Their speedy outcome played a major role in popularizing and disseminating stem cell research. By uncovering the basic factors and principles of the reprogramming process, they made it possible for researchers from other fields, including neuroscience, to work more efficiently with IPS cells. Their research earned them the Nobel Prize in Physiology or Medicine in 2012.

“Reprogramming technology has opened the door for many new insights into the brain and brain-related conditions,” write the authors. “The recapitulation of early stages of human neural development made possible by using IPS cells is an invaluable tool that can reveal the exact moment of the disease onset, thus fostering the generation of new diagnostic tools and potentially optimizing novel therapeutic interventions.” IPS cells have the potential to impact diseases and disorders such as autism, schizophrenia, Parkinson’s disease, Alzheimer’s disease, and Lou Gehrig’s disease.

How important are IPS cells to the future of neuroscience? A meeting of the International Society for Stem Cell Research (ISSCR) in 2003 attracted a mere few hundred researchers. Just 10 years later, 4,000 scientists from all over the world were on hand.

–Bill Glovin

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