When is a stem cell not really a stem cell?

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Working with embryonic mouse brains, a team of Johns Hopkins scientists seems to have discovered an almost-too-easy way to distinguish between “true” neural stem cells and similar, but less potent versions. Their finding, reported this week in *Nature*, could simplify the isolation of stem cells not only from brain but also other body tissues.

What the researchers identified is a specific protein “signal” that appears to prevent neural stem cells – the sort that might be used to rebuild a damaged nervous system – from taking their first step toward becoming neurons. “Stem cells don’t instantly convert into functional adult tissue,” says author Nicholas Gaiano, Ph.D., assistant professor at the Institute for Cell Engineering. “They undergo a stepwise maturation where they gradually shed their stem cell properties.”

The first step turns stem cells into “progenitor” cells by dictating how signals downstream of a protein called Notch, which regulates stem cells in many different tissues, are transmitted. One well known target of Notch is a protein called CBF1. To help study Notch signaling further, Gaiano and his team created genetically engineered mouse embryos that glow green when CBF1 is turned on.

To their surprise, they noticed that during brain development some of the brain cells generally thought to be neural stem cells stopped glowing, indicating that the CBF1 protein was no longer active in them. A closer look revealed that those cells that went dark were in fact no longer true neural stem cells, which can form all major brain cell types, but instead had aged into progenitor cells, which form mostly neurons.

They tested whether CBF1 was the critical switch by chemically knocking out the protein in neural stem cells. The knockout got the stem cells to rapidly convert to progenitor cells. “However, if we activated the CBF1 protein in progenitor cells we couldn’t get them to shift back into stem cells,” says Gaiano. “So whatever happens biochemically once CBF1 is turned off seems to create a one-way street.”

Another recent study, using the mouse line generated by the Gaiano group, found that CBF1 signaling may play the same role in blood stem cells, leading Gaiano to suspect that his team’s discovery might be a general “switch” distinguishing stem cells from progenitors in many different tissues.

Source: Johns Hopkins Medical Institutions