

# Gene regulating human brain development identified

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With more than 100 billion neurons and billions of other specialized cells, the human brain is a marvel of nature. It is the organ that makes people unique.

Now, writing in the journal *Cell Stem Cell* (July 1, 2010), a team of scientists from the University of Wisconsin-Madison has identified a single gene that seems to be a master regulator of human [brain](#) development, guiding undifferentiated stem cells down tightly defined pathways to becoming all of the many types of cells that make up the brain.

The new finding is important because it reveals the main [genetic factor](#) responsible for instructing cells at the earliest stages of embryonic development to become the cells of the brain and spinal cord. Identifying the gene — known as Pax6 — is a first critical step toward routinely forging customized brain cells in the lab.

What's more, the work contrasts with findings from animal models such as the mouse and [zebrafish](#), pillars of developmental biology, and thus helps cement the importance of the models being developed from human [embryonic stem cells](#).

The new work, conducted in the Waisman Center laboratory of UW-Madison neuroscientist Su-Chun Zhang, reveals the pervasive influence of Pax6 on the neuroectoderm, a structure that arises early in embryonic development and that churns out the two primary forms of [brain cells](#) —

neurons and glial cells — and the hundreds of cell subtypes that make up the human brain.

"This is a well-known gene," says Zhang, a professor of anatomy in the UW School of Medicine and Public Health. "It's been known for a long time from work in mice and other animals, but what Pax6 does in human development isn't very well known."

In animals, the gene is known to play a role in the development of the eye and is seen in some neural cells. In the [human cells](#) used in the new Wisconsin study, Pax6 was observed in virtually all of the cells of the neuroectoderm. "The fact that Pax6 is uniformly expressed in all human neuroectoderm cells was a surprise," Zhang explains. "This is a phenomenon that is a departure from what we see in animals. It seems that in the earliest stages of development, human cells are regulated by different processes."

The finding may help explain why the human brain is larger and, in many respects, more advanced than what is observed in other species. In the laboratory dish, human brain stem cells are chock full of Pax6 and produce a large volume of cortical cells, notes Xiaoqing Zhang (no relation to Su-Chun Zhang), a UW-Madison neuroscientist and the lead author of the Cell Stem Cell paper.

"In human brain development, this plays a really important role," says Xiaoqing Zhang. "In humans, the cortex is a major part of the brain. In the mouse, the cortex is a much smaller part of the brain."

Adds Su-Chun Zhang, "In a way, it makes sense that the human brain is regulated in a different way. The brain distinguishes the human as a unique species."

In practical terms, the new finding will help scientists refine and

improve techniques for making specific types of neural cells. Such cells will be critical for future research, developing new models for disease, and may one day be used in clinical settings to repair the damaged cells that cause such conditions as Parkinson's disease and amyotrophic lateral sclerosis or Lou Gehrig's disease.

"This gives us a precise and efficient way to guide stem cells to specific types of [neural cells](#)," says Xiaoqing Zhang. "We can activate this factor and convert stem cells to a particular fate."

The discovery of the new role of Pax6, says Su-Chun Zhang, is the first time researchers have discovered a single genetic factor in human cells that is responsible for shepherding blank slate stem cells to become a particular tissue stem cell type. "Until now, for any organ or tissues, we didn't know any determinant factors. This is the first," he says.

There are certainly other genes at play in the cells of the developing brain, says Su-Chun Zhang: "You may need additional genes, but they're in a supporting role. Pax6 is the key."

Provided by University of Wisconsin-Madison

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