From frogs to humans, brains form the same way

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It's a critical juncture in an embryo's development: the moment that a brain and nervous system begin to form from a mass of unspecialized cells. Scientists had believed that mammals and amphibians, distinctly different animals, have distinctly different developmental patterns when it comes to the nervous system. But new research suggests that their processes of neural development are actually quite similar.

Rockefeller University scientists say that their model of "mammalian neural induction," presented this summer in Developmental Biology, provides a bridge across the evolutionary gap between amphibians and mammals. The research has implications for scientists working to understand how mammalian stem cells might be efficiently converted into brain cells to someday treat disorders such as Parkinson's disease.

"We have found that there are more similarities than differences between species, and what is nice about this is that it gives a lot of people a way to hang their data on a broad idea," says the study's lead author, Ariel J. Levine, an M.D.-Ph.D. student in the Laboratory of Molecular Vertebrate Embryology. The lab's director, Ali H. Brivanlou, is the study's other co-author.

Levine and Brivanlou analyzed classic and cutting-edge findings on neural induction in the mouse, a vertebrate, and found that the data supports the model of neural induction that Brivanlou pioneered in the 1990s to explain nervous system development in the frog, an amphibian. "We believe these findings represent the most elemental first step in the

formation of the amazingly complex nervous system of vertebrates," Levine says.

Amphibians and mammals are conspicuously different. One lives partially in water, the other on land. One was once called cold blooded, before that name fell out of scientific favor. And, between them, embryogenesis is critically distinct. Amphibians produce streamlined embryos that develop in water, whereas "amniotic" mammalian embryos have extra embryonic tissue to direct and support growth; such tissue later morphs into the placenta.

Both types of embryos form a spherical layer of cells called a blastula, or blastocyst, after initial division. It is during the next stage, gastrulation, that cells start to move to establish the organism's polarity – head and tail, front and back, left and right. The signals they respond to are the critical embryonic development genes (BMP, Nodal, Wnt, FDF) that help pattern cells to assume their future roles in the organism – the heart, liver, etc.

In 1924, scientists discovered that signals responsible for nervous system development come from the so-called "organizer," a tiny collection of cells next to the future "head." Brivanlou's contribution was the discovery that, in frogs, the organizer actually sends out inhibitors of BMP signals; cells protected from these growth factors become the nervous system. This became the well-accepted "default model of neural induction" in amphibious vertebrates.

The story seemed to be different for mammals, possibly due to their extra embryonic tissue. It appeared that two signaling centers were necessary for mammalian neural induction — the "node" (cells similar to the frog organizer) and the "anterior visceral endoderm" or AVE, the extra embryonic tissue that sits over the spot where the brain forms. Because embryos without AVE do not develop a brain, researchers

believed that the node induced a normal spinal cord, but that the signals from the AVE were required to create a brain.

But after examining a wide spectrum of research on mouse embryos, Levine and Brivanlou concluded that the first neural tissue is induced by signal inhibition mediated by the mouse organizer and is anterior, or in the head, and subsequent neural tissue is "posteriorized" to form the midbrain, hindbrain and spinal cord. The AVE works to protect anterior tissue from becoming posteriorized, and so allows a forebrain to develop. "This model is very similar to the default model of neural induction in the frog, and suggests an evolutionarily conserved strategy for this important step in development," Levine says.

One signaling system, instead of two, focuses the molecular players involved in mammalian neural induction and might mean that it could be easier to coax stem cells to form into the type of replacement nerve cell so desired to treat such neurodegenerative disorders as Parkinson's disease, she says. Although more experimentation is needed to validate the model, "it is very testable," she says. "All the data seem to fall in place now."

Source: Rockefeller University