Medium is the message for stem cells in search of identities

July 5 2006

Embryonic stem cells, prized for their astonishing ability to apparently transform into any kind of cell in the body, acquire their identities in part by interacting with their surroundings - even when they are outside of the body in a laboratory dish, University of Florida scientists report.

Using an animal model of embryonic stem cell development, researchers with UF's McKnight Brain Institute have begun to answer one of the most fundamental questions in science - how does a batch of immature cells give rise to an organ as extraordinarily complex as the human brain?

The findings, to be published this week in the *Proceedings of the National Academy of Sciences*, may one day help scientists create laboratory environments to grow specialized cells that can be transplanted into patients to treat epilepsy, Parkinson's, Huntington's and Alzheimer's diseases or other brain disorders.

Scientists observed that when embryonic stem cells from mice were plated on four different surfaces in cell culture dishes, specific types of cells would arise.

"The medium and the molecular environment influence the fate of the cell," said Dennis Steindler, Ph.D., executive director of the McKnight Brain Institute. "We simulated some events that occur while the brain is developing and challenged them with different environments, and the effects are profound. Ultimately both nature and nurture influence the

final identity of a stem cell, but in early stages it seems nurture is very important."

In experiments, scientists confirmed a cell culture surface molecule called laminin activates a common developmental pathway that is crucial for the generation and survival of particular types of brain cells.

The laminin-influenced stem cells are a kind that goes on to generate a brain structure called the medial ganglionic eminence, which in turn is believed to give rise to a population of early neurons in the developing cerebral cortex, a structure that helps coordinate sensory, motor and cognitive function.

"This is significant because this molecule is frequently used to secure cells onto culture dishes in stem cell labs all over the world," said Bjorn Scheffler, M.D., a neuroscientist with UF's College of Medicine. "Everyone believes this molecule is purely growth supportive, but now we've shown it changes the fate of cells it is working with. When you grow the cells in a culture dish you are actually educating them to become something very special."

In that respect, the discovery sheds light on how embryonic stem cells diversify to form various neural structures, one of the fundamental mysteries of brain development, the researchers say.

Since the 1980s, Steindler has studied the effect of certain molecules in the extracellular matrix, a mixture that surrounds developing brain cells. Transiently appearing and disappearing, these molecules apparently cordon the brain into different regions.

If molecules from the matrix activate genes in stem cells responsible for generating neural components, potentially any of the molecules can be tested to find its specific role during development of the brain, according

to UF neuroscientist Katrin Goetz, M.D., first author of the paper.

In addition, the discovery reinforces a notion that rodent embryonic stem cell biology can be used to understand basic brain mechanisms, potentially leading to treatments where adult stem cells are taken from patients, cultured and transplanted into damaged brain environments to restore functions lost to disease or injury.

"We largely keep the brain cells we are born with for life, but we also have stem cells in our brain that can divide and make new neurons for maintenance," said Gordon Fishell, Ph.D., a professor of cell biology with the Skirball Institute of Biomolecular Medicine at New York University Medical Center who was not involved in the research. "Stem cells continue to proliferate because they are in a specialized 'niche' that nurtures them and keeps them dividing. Previous studies have shown that factors in the niche are important for stem cell proliferation. Less studied are the means by which these cells are directed to become specific types of neurons useful in the adult brain. This work is the first to systematically look at how components in the extracellular matrix affect the fate of these cells. It seems the niche doesn't just support these cells, it tells them what to become. It educates stem cells for a bright future."

Source: University of Florida