# For First Time, Brain Cells Generated In A Dish

June 15 2005

GAINESVILLE, Fla., June 14 (SPX) -- Regenerative medicine scientists at the University of Florida's McKnight Brain Institute have created a system in rodent models that for the first time duplicates neurogenesis - the process of generating new brain cells - in a dish.

Writing in today's (June 13) Proceedings of the National Academy of Sciences, researchers describe a cell culture method that holds the promise of producing a limitless supply of a person's own brain cells to potentially heal disorders such as Parkinson's disease or epilepsy.

"It's like an assembly line to manufacture and increase the number of brain cells," said Bjorn Scheffler, M.D., a neuroscientist with UF's College of Medicine. "We can basically take these cells and freeze them until we need them. Then we thaw them, begin a cell-generating process, and produce a ton of new neurons."

If the discovery can translate to human applications, it will enhance efforts aimed at finding ways to use large numbers of a person's own cells to restore damaged brain function, partially because the technique produces cells in far greater amounts than the body can on its own.

In addition, the discovery pinpoints the cell that is truly what people refer to when they say "stem cell."

Although the term is used frequently to describe immature cells that are the building blocks of bones, skin, flesh and organs, the actual stem cell

as it exists in the brain has been enigmatic, according to Dennis Steindler, Ph.D., executive director of the McKnight Brain Institute and senior author of the paper.

Its general location was known, but it was an obscure species in a sea of cell types.

"We've isolated for the first time what appears to be the true candidate stem cell," said Steindler, a neuroscientist and member of UF's Program of Stem Cell Biology and Regenerative Medicine.

"There have been other candidates, but in this case we used a special microscope that allows us to watch living cells over long periods of time through a method called live-cell microscopy, so we've actually witnessed the stem cell give rise to new neurons. Possibly a different method may come up to identify the mother of all stem cells, but we're confident this is it."

During experiments, scientists collected cells from mice and used chemicals to induce them to differentiate.

During the process, they snapped images of the cells every five minutes for up to 30 hours and compiled the images into movies.

Traditional ways to attempt neurogenesis have been unable to so closely duplicate the natural process.

They also haven't allowed scientists to monitor the entire sequence of cell development from primitive states to functional neurons and expose the electrophysiological properties of the cells.

A little more than a decade ago, scientists came to realize that the brain continues to produce small amounts of new cells even in adulthood,

overturning the belief that people are born with a fixed amount of brain cells that must last them throughout their lives.

In people, stem cells develop naturally into full-fledged brain cells as they travel through a neural pathway that begins deep within the brain in a region called the subventricular zone. The primitive cells mature along the way, finishing as neurons in a spot called the olfactory bulb.

In the laboratory cultures, the cells still move about, but the pathway is no longer important, showing that neurogenesis does not necessarily require the environmental cues of the host brain.

The natural development of stem cells in the brain is very similar to the lifelong production of blood cells in the human body called hematopoiesis, with "poiesis" derived from the Greek word meaning "to make."

Scientists in Steindler's lab noticed the similarities between primitive cell development in blood and in the brain in the late 1990s, calling the process "neuropoiesis."

"The exciting part is we are actually using methods that researchers involved with hematopoiesis used," Scheffler said. "Those researchers took primitive cells, put them in a dish and watched them perform. From that, they learned vital information for clinical applications such as bone marrow transplants. Now we have a tool to do exactly the same thing."

By watching the cells perform, scientists can make judgments and influence the capacity of the cells to generate specific neurons.

"As far as regenerating parts of the brain that have degenerated, such as in Parkinson's disease, Huntington's disease and others of that nature, the ability to regenerate the needed cell type and placing it in the correct

spot would have major impact," said Dr. Eric Holland, a neurosurgeon at Memorial Sloan-Kettering Cancer Center in New York who specializes in the treatment of brain tumors, but who is not connected to the research.

"In terms of tumors, it's known that stem-like cells have characteristics much like cancer cells. Knowing what makes these cells tick may help by furthering our knowledge of the biology of the tumor."