The Fate of Brain Cells

New technique tracks the long life of neural stem cells.

A FOUNTAIN OF YOUTH SPRINGS FROM WITHIN THE BRAIN OF every mammal, report HHMI investigator Alexandra L. Joyner and her former postdoctoral associate Sohyun Ahn in the October 6, 2005, issue of *Nature*. No, the two researchers haven't unlocked the secret to immortality. But their discovery of a method to visualize an elusive population of stem cells that has the potential to regenerate nerves and other brain cells may explain how certain regions of the brain rejuvenate themselves. Moreover, the findings may allow researchers to tap the revitalizing powers of stem cells for repairing injured and diseased brain tissue.

Two regions of the mouse brain—the hippocampus, which controls short-term memory, and the olfactory bulb, which processes odors—contain neurons that are continually replenished throughout adult life. Some neurobiologists have thought that these fresh brain cells arise from a population of rapidly dividing but short-lived stem cells called transient amplifying cells, but others have proposed that these cells must derive from infrequently dividing "quiescent neural stem cells" lurking within the brain. Indirect evidence has hinted that such quiescent cells do exist, but, until now, says Joyner, no one had effectively pinpointed the cells in living brains.

Ahn and Joyner, working at New York University's Skirball Institute of Biomolecular Medicine, devised a method to mark all stem cells and their descendants in the brains of live laboratory mice over the animals' lifetimes. After marking the stem cells, the researchers administered a drug called AraC, which efficiently kills only rapidly dividing brain cells. "We killed off the transient amplifying cells and then showed that there is another population of cells still capable of replenishing," Joyner explains. "And then we did it a year later. We killed off the transient amplifying cells again, and the cells we had marked the year earlier could still replenish," proving the existence of long-lived quiescent stem cells in living animals.

Because the normal life span of a mouse is only about 1 year, the results imply that the quiescent stem cells survive throughout the life of the animal. "The idea in humans is that they would lie mostly dormant for 80 years," says Joyner.

Now she wants to learn how to harness the cells for regenerating new tissue types. "If we could infuse the right type of growth factors into the brain after injury or disease, perhaps we could mobilize them to do more than what they normally do."

Some other potential applications may involve selective destruction rather than harnessing, as Joyner says that similar stem cells elsewhere in the body may be involved in spreading cancer. "There's this idea that there are stem cells in cancers, the ones that allow aggressive tumors to escape therapies. There may be quiescent stem cells in cancers, which produce the rapidly dividing cells that eventually are lethal." ■

– Paul Muhlrad –

IN BRIEF

LEARNING HOW SARS SPIKES ITS QUARRY

Researchers have determined the first detailed molecular images of a piece of the spike-shaped protein that the SARS virus uses to grab host cells and initiate the first stages of infection. The structure, which shows how the spike protein grasps its receptor, may help scientists learn new details about how the virus infects cells. The information could also be helpful in developing antiviral drugs or vaccines.

The research team, led by HHMI investigator **Stephen C. Harrison** at Children's Hospital Boston and Harvard Medical School, and colleague Michael Farzan, also at Harvard Medical School, reported its findings in the September 16, 2005, issue of the journal *Science*.

"One of the critical issues in a SARS epidemic would be to predict whether a given variant of the virus will jump species or move laterally from one human to the other," says Harrison. "Understanding the structure of this complex will help us understand what mutations in the spike protein mean in terms of infectivity."

RACE AGAINST ANTIBIOTIC RESISTANCE

Antibiotic resistance has put humans in an escalating "arms race" with infectious bacteria, as scientists try to develop new antibiotics faster than the bacteria can evolve new resistance strategies. But now, researchers have a new strategy that may give them a leg up in the race—reproducing in the lab the natural evolution of a class of bacterial enzymes that confer resistance.

A team of scientists from Argentina and Mexico identified mutations that increased the efficiency of a bacterial enzyme that renders penicillin and cephalosporin antibiotics useless. The results could lead to more effective enzyme inhibitors by giving drug designers a sneak peek at the next generation of resistance.

Alejandro J. Vila, an HHMI international research scholar, and colleagues at the Institute of Molecular and Cellular Biology of Rosario, in Argentina, and at the Biotechnology Institute of the National Autonomous University of Mexico reported their findings in the September 27, 2005, issue of the *Proceedings of the National Academy of Sciences.*

SUPERCHARGING BLOOD-FORMING STEM CELLS

Researchers studying a colorfully named zebrafish mutant, mind bomb, have discovered a way to replenish blood cells more quickly after exposure to radiation. The studies identify key genetic regulators that boost production of blood-forming stem cells.

The finding could lead to ways to supercharge production of hematopoietic stem cells in cancer patients who have received bone marrow transplants to restore their blood-forming system after chemotherapy or radiation. Supercharging could also enhance effectiveness of such transplantations to treat disorders such as aplastic and sickle-cell anemias, say the researchers.