Cellular conversion turns brain into blood

Talk about a career change. The unspecialized cells that normally give rise to the various cell types in the brain can also act as bone marrow, the crucial source of an adult body's blood cells.

Scientists discovered this remarkable ability when they injected these so-called neural stem cells into the blood of mice whose own bone marrow had been almost completely destroyed by irradiation. The neural stem cells, whose progeny were identifiable by means of a genetic marker previously slipped into them, engrafted as normal bone marrow transplants do and began producing blood cells.

"We really had a hard time convincing ourselves of our own data," notes Angelo L. Vescovi of the National Neurological Institute in Milan, Italy. He, Christopher R.R. Bjornson of the University of Washington in Seattle, and their colleagues describe the neural stem cell transplants in the Jan. 22 SCIENCE.

The experiments suggest that a cell's lot in life, usually determined during the growth of an embryo, isn't as hard and fast as once thought. "Even when a cell seems to have committed to a particular organ, there are still some cells that can switch that fundamental identity. That's an intriguing biological concept," says Evan Y. Snyder of Children's Hospital in Boston, who has isolated human neural stems cells (SN: 11/7/98, p. 293).

Until recently, scientists assumed that most adult cells had made irreversible commitments to a particular fate, becoming heart cells or liver cells, for example. The cloning of Dolly the sheep and other animals from various adult cells challenged that dogma, however. Still, those experiments involved removing the genes of an adult cell and placing them into an egg, a transfer that somehow reverted the genes to their embryonic state (SN: 4/5/97, p. 214). In the new experiments, the researchers have shown that they can directly change the role of some adult cells simply by placing them in a new environment.

Vescovi notes that his unusual experiment was prompted in part by reports of brain tumors that contained muscle cells in addition to brain cells. Those cases hinted that brain cells could develop into very different cell types.

After injecting the neural stem cells into mice, the researchers showed that the cells seeded the animals' bone marrow and spleens, which also produce new blood cells. They also showed that individual white blood cells from the animals had the genetic marker belonging to the neural stem cells.

Although the researchers are confident that the transplanted neural stem cells produced new red blood cells, they haven't proved that point. Mature red blood cells have no DNA-containing nuclei, making it impossible for the investigators to detect the genetic marker used to label the neural stem cells and their progeny.

Vescovi's team is now testing whether human neural stem cells can also act as bone marrow when injected into mice. "If the principle holds for human cells, we'd like to try therapy," says Vescovi. Noting that hematopoietic stem cells, the bone marrow cells that give rise to blood, are difficult to grow and manipulate, the researcher suggests that neural stem cells might substitute for the treatment of many blood disorders.

"We have no problems expanding endless supplies of neural stem cells, and we even have human neural stem cells now," comments Snyder. "I'd be ecstatic if . . . the cells I've isolated with one intent can now address a magnitude-greater level of diseases."

Neural stem cells may have a future outside the bloodstream as well. "We're actively investigating whether our [neural] stem cells can give rise to other solid organs. For instance, can they give rise to muscle or liver?" asks Snyder.

In addition to searching for the chemical cues that switch neural stem cells into blood producers, Vescovi plans to study whether hematopoietic stem cells or other nonneural tissues can give rise to brain cells. —*J. Travis*

A bug's kiss has chemistry in humans

Euphemistically known in tropical climates as the kissing bug, the insect *Rhodnius prolixus* lives in cracks and crevices but crawls out to suck human blood. As it feeds mosquitolike, the bug dribbles saliva into its victim's tissues. Proteins in the saliva somehow deliver nitric oxide (NO), a molecule that opens up blood vessels and prevents clotting (SN: 10/17/98, p. 246). The effect allows *R. prolixus* to finish its feast.

Now, a team of researchers from the University of Arizona in Tucson and the University of Amsterdam has found that these proteins, known as nitrophorins, are unique in the way they hold NO in the insect's saliva—and then release it in human tissues.

In South America, the kissing bug is responsible for transmitting Chagas' disease, a parasitic infection that causes heart-muscle damage and sometimes death. Learning about nitrophorins might not shed light on how to prevent this illness, says Arizona chemist F. Ann Walker, but it could have an impact on human health in other ways. Compounds that either soak up or deliver NO could be used as drugs to fight cardiovascular disease or the effects of bacterial infections, for example.

Walker and her colleagues performed several experiments on nitrophorin 1, the most abundant of the kissing bug's four nitrophorins, to explore the way it binds to NO. They found that in the insect, NO binds tightly to an iron atom in nitrophorin 1, but not so tightly that it can't break free once in target tissue, Walker explains. "This is a nice balance . . . . You want it to be stable but not too stable." The researchers report their findings in the Jan. 13 JOURNAL OF THE AMERICAN CHEMICAL SOCIETY.

The researchers predict that nitrophorins can store NO in the kissing bug's acidic saliva for up to one month. In the more neutral environment of a victim's tissues, NO breaks free and diffuses into the tissues.

"It's the only known natural NO storage and transport protein," says Donald E. Champagne of the University of Georgia in Athens, who cloned the gene for nitrophorin 1 in 1994. "These molecules are pretty unique."

Walker and her colleagues are also looking at how nitrophorins corral histamines, itch-inducing compounds released by the body's immune response. Blocking these chemicals facilitates the blood sucking by preventing the victim from noticing the bug until it's done feeding, says Champagne.

"These insects are darned clever," Walker notes. "They'll probably be around long after mammals have left the face of the Earth"—provided, of course, that they find something new to eat. —*C. Wu*

Walker

Components forming the three-dimensional complex nitrophorin 1. A heme molecule (red) sits at the opening of a barrel-shaped protein (green and blue ribbons). A molecule of nitric oxide (blue- and red-ball figure) binds to an iron atom (black) in the heme.