Battling Evolution to Regrow Nerves

Humans may have paid a stiff price for their complex brains: the well-known inability of the brain and spinal cord to generate new connections between nerve cells after an injury.

To help explain how the mammalian central nervous system (CNS) evolved, researchers have theorized that it had to develop special means to protect its intricate circuits from inadvertent remodeling by immune cells, especially macrophages. As evidence, they point out that the CNS is one of the few sites in the body where mammals actively suppress their immune cells.

A study now suggests that suppression of macrophage activity provides the main barrier to nerve cell regeneration in mammals. "Macrophages may be the missing link in the process of wound healing in the CNS," Michal Schwartz of the Weizmann Institute of Science in Rehovot, Israel, and her colleagues conclude in the September FASEB JOURNAL.

In a provocative experiment supporting this idea, Schwartz' group induced nerve cell regeneration by artificially stimulating macrophages and transplanting them to injured areas of the CNS.

This surprising result, observed so far only in rats, may one day lead to new strategies to treat spinal cord injuries, suggests Schwartz.

Schwartz's group only recently began to study seriously the role of macrophages. They had found that the mammalian CNS makes a molecule that limits macrophage recruitment into the injured brain or spinal cord. The same molecule seems to prevent activation of macrophages, says Schwartz.

In the peripheral nervous system of mammals, which can regenerate after injury, activated macrophages are vital to healing. They rush to the wound and, among other duties, clear away debris, including dead cells and myelin, the fatty insulation around nerve cells. Previous studies had shown that myelin contains molecules that thwart nerve cell regeneration. Because the CNS has a macrophage-inhibiting molecule, the myelin cleanup process doesn't proceed efficiently there, and nerve cell regeneration stalls, asserts Schwartz.

To overcome that obstacle, her group exposed rat macrophages to peripheral nerve tissue excised from a rat. They then placed those activated immune cells on the severed optic nerve of the same rat.

After the macrophage transplant, the researchers report, new nerve extensions started to grow across the lesion. Macrophages exposed to CNS tissue or to nothing at all stimulated little or no regeneration.

Schwartz envisions two potential treatment strategies emerging from her research. As in the current study, investigators could harvest macrophages, artificially activate them, and transplant them into damaged spinal cords or other injured CNS sites. Alternatively, researchers might use antibodies or other compounds to block the macrophage-inhibiting actions of the CNS.

The work of Schwartz's group, and that of a few other research teams, offers a startling new perspective on the role of macrophages in the brain and spinal cord. Macrophages in the CNS have largely been considered a hazard, since they can also kill existing brain cells by releasing toxic substances.

"Most of the time when you encounter activated macrophages in the CNS, they're contributing to local inflammation, dysfunction, and disease," notes William Hickey of Dartmouth Medical School in Lebanon, N.H.

Whether CNS macrophages are good or evil may ultimately depend upon how they are activated and how long they persist, says Schwartz.

Indeed, Ira B. Black of the Robert Wood Johnson Medical School in Piscataway, N.J., and his coworkers have shown that activated CNS macrophages can make several compounds that promote nerve cell growth and survival.

"There is a story emerging here. It may hold the key to a lot of different diseases," says Black. —*J. Travis*

Better and cheaper porous carbon filters

Although activated carbon has been used for more than half a century to filter contaminants from air and water, scientists have only now imaged the twisting and turning pores that enable the adsorbent to do its job.

Christian L. Mangun and James Economy of the University of Illinois at Urbana-Champaign and their colleagues at Southern Illinois University at Carbondale used scanning tunneling microscopy to look at cross sections of carbon fibers that had been activated by heat to make them porous. By understanding the microstructure, they can tailor the fibers' properties to filter specific contaminants. "We can not only control pore size and shape but also pore chemistry," Economy says. The group's findings will appear in the October CARBON.

Although low-cost carbon granules, not fibers, are used in most applications, no one has yet sliced granules into thin sections that would show the tiny pores, which are often only a few tenths of a nanometer wide, Mangun says.

That pore size is small enough to filter out contaminants like sulfur dioxide, butane, and trichloroethylene. The researchers have changed the chemistry of the pores by lining them with different compounds, thus improving further the fibers' ability to trap passing molecules. For example, acidic pores remove ammonia gas, and basic pores filter out hydrochloric acid, they find.

The researchers' analysis also showed that conventional wisdom about greater surface area leading to greater adsorption wasn't completely correct, Mangun says. At high contaminant concentrations, total pore surface area matters most. But at low concentrations, measured in parts per million, pore size takes precedence.

The activated carbon fibers, invented by Economy in the early 1970s, perform 10 times better than granules, he says, but at $100 a pound, they are 100 times as expensive. Only one company, Nippon Kynol, located in Osaka, Japan, manufactures them.

To address this cost difference, the group developed a cheaper fiber that performs as well as the original. Currently, the carbon fibers are made by heating a weave of plastic fibers to about 800°C with steam. The heat turns the plastic into a fabric of pure, porous carbon strands. The new process begins with much cheaper glass fibers, coats them with plastic resin, and then activates the resin carbon by heating it.

The product costs only a few dollars a pound, which "brings the cost into a range competitive with activated granules" and other molecules designed for filtering, Economy says. The group filed for a patent last summer.

Economy envisions many applications for these fabrics. Made into face masks, they could protect city dwellers from pollution or civilians from chemical warfare. About 10 companies have expressed interest in the new fibers, he says, as components of air filtration systems for cars, home water purification devices, and industrial waste filtration equipment. —*C. Wu*