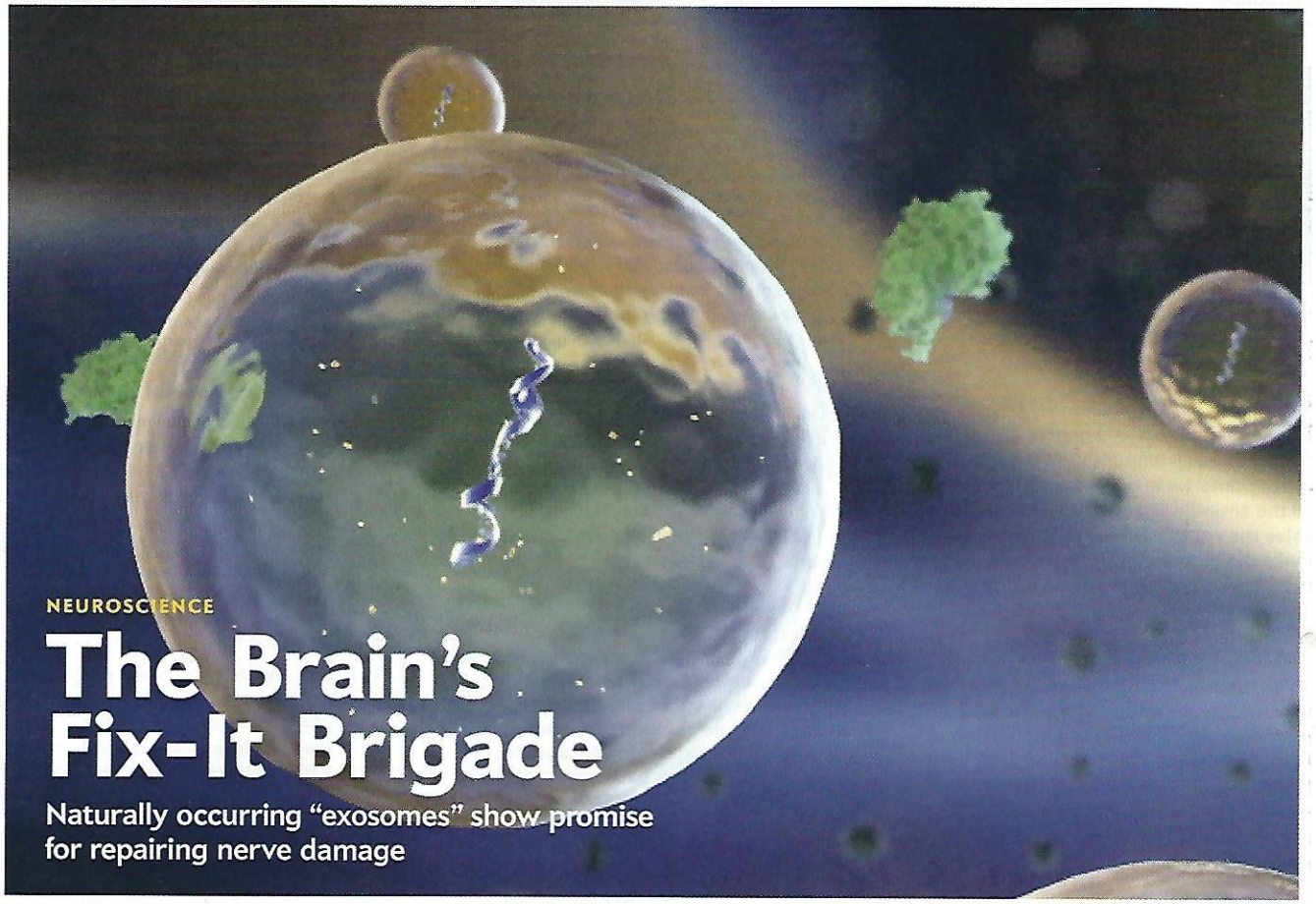
ADVANCES

Dispatches from the frontiers of science, technology and medicine



NEUROSCIENCE

The Brain's Fix-It Brigade

Naturally occurring "exosomes" show promise for repairing nerve damage

An active lifestyle improves brain health, scientists have long believed. The studies bear this out: physical, intellectual and social activity—or "environmental enrichment," in the parlance—enhances learning and memory and protects against aging and neurological disease. Recent research suggests one benefit of environmental enrichment at the cellular level: it repairs brain myelin, the protective insulation surrounding axons, or nerve fibers, which can be lost because of aging, injury or diseases such as multiple sclerosis. But how does an enriched environment trigger myelin repair in the first place?

The answer appears to involve naturally occurring membrane-wrapped packets called exosomes. A number of different cell types release these little sacs of proteins and genetic material into the body's fluids. Loaded with signaling molecules, exosomes spread through the body "like messages in a bottle," says R. Douglas Fields, a neurobiologist at the National Institutes of Health. They target particular cells and change their behavior. In animal studies, exosomes secreted by immune cells during environmental enrichment caused cells in the brain to start myelin repair.

Researchers think exosomes might find use as biomarkers for diagnosing diseases or as vehicles to deliver cancer drugs or other therapeutic agents.

The exosomes produced during environmental enrichment carry microRNAs—small pieces of genetic material—which appear to instruct immature cells in the brain to develop into myelin-making cells called oligodendrocytes. When researchers at the University of Chicago withdrew exosomes from the blood of rats and administered them to aging animals, the older rats' myelin levels rose by 62 percent, the team reported in February in *Glia*.

The researchers also discovered how to generate exosomes outside the body, making them on demand for potential therapies. By stimulating immune cells from bone marrow, the group was able to "mimic Mother Nature's environmental enrichment in a dish," says Richard Kraig, a professor of neurology at Chicago.

Kraig's team is now exploring how to craft exosomes into a treatment for multiple sclerosis. The lab-grown exosomes stimulated myelin production in a sample of rat brain tissue intended to simulate multiple sclerosis damage, returning myelin levels to 77 percent of normal, Kraig and his colleagues recently reported in the *Journal of Neuroimmunology*.

The next step is to see if exosomes harvested from immune cells work as effectively in live animals with the disease, says team member Aya Pusic, a Ph.D. candidate in neurobiology. With any luck, Pusic says, the research could progress to human tests in five years. —*Debra Weiner*

FURTHER READINGS AND CITATIONS ScientificAmerican.com/mar2014/advances