Scar wars: Designing a chemical weapon

When a back injury causes the spongy cushion between two vertebrae to protrude from its encasement, spinal nerves may feel the pinch. To fix the slipped disk, a surgeon must cut through skin, slide past muscle, drill through bone and then push aside the outer wrapping of the spinal cord to remove the peanut-butter-like packing material that squeezed out of place.

But the problem doesn't always end there. The surgical invasion triggers fibrous scar tissue that contracts around the spinal cord, often yanking on nerves once again. The pain returns.

"The very same nerves that were freed by surgery now become pinched—that's the classic 'failed back' syndrome," explains surgeon Shafik Ahmad. In subsequent operations, he says, it takes three times longer to cut through the tough, blood-rich scar tissue, and the risk of hemorrhage increases.

Now, he and his co-workers at Gliatech Inc. in Cleveland report that they have developed a nontoxic sugar polymer that prevents this internal scarring in rats for at least six months.

"It's something surgeons have waited for for a very long time," says Ahmad. The new molecule, to be patented under the name GL402, might one day minimize the internal scars and fused tissues (adhesions) that plague thousands of people after back, knee or gynecological surgery, he suggests.

To test their designer sugar, the researchers performed disk surgery on rats and inserted a gelatin sponge — soaked in either GL402 or an inactive solution — into each spinal site. Two weeks later, they reopened the wounds to compare the scars. The GL402-treated sites healed well, with only a very thin layer of scar tissue, but the untreated sites were crowded with fibrous, quick-to-bleed scar tissue.

The team also compared GL402 with two of its chemical relatives, heparin and hyaluronic acid (SN: 9/30/89, p.222). The new sugar outperformed both of these naturally occurring compounds, they found. "GL402 appears to be the most potent anti-fibrotic [anti-scarring] agent yet discovered," Ahmad and his coauthors assert in the November EXPERIMENTAL NEUROLOGY.

GL402's synthesis grew out of earlier work led by study coauthor Jerry Silver, a Gliatech researcher and professor at Case Western Reserve University. Silver and his university colleagues reported five years ago that star-shaped cells called astrocytes guide nerve growth by producing chemicals that promote nerve-fiber elongation, while also producing "competing" chemicals that inhibit the same process (SN: 11/21/87, p.324). The chemical inhibitors, it turned out, also discourage fibroblast cells from migrating to wound sites and forming scars.

The Case Western group identified these inhibitors as proteoglycans — members of a diverse family of molecules with protein cores and sugar sidechains. When the team discovered that the sugar portion performs the inhibitory function, Gliatech began designing its own scar-deterring sugar.

Meanwhile, Silver and his university colleagues continued their search for the body's own nerve-growth inhibitors. In the November JOURNAL OF NEUROSCIENCE, they report that chondroitin-6-sulfate proteoglycan (CS-PG), produced by astrocytes, appears to deter nerve regeneration in rats after injury to the central nervous system.

Adult and newborn mammals develop different kinds of brain and spinal scars, and only the young can regrow nerve fibers after injury, Silver explains. His team suspected these differences traced to proteoglycan production during adulthood. To test that hypothesis, they implanted filter papers into the brains of newborn and adult rats to create lesions and to collect the chemical soup produced by astrocytes in the resulting scar tissue.

Only the filter papers removed from the adult rats contained CS-PG, they found. Furthermore, when the researchers used these same pieces of paper to create "scars in a dish," only the papers taken from the adult brains failed to encourage the growth of added nerve cells.

These findings support the view that chemical barriers play a role in limiting nerve growth in adults, says Silver. Until a few years ago, neuroscientists attributed the growth inhibition entirely to mechanical barriers, such as scars, or to a shortage of growth-promoting chemicals.

Diane Snow, who studies nerve-growth inhibition at the University of Minnesota in Minneapolis, calls the new studies "the beginning of something good." This kind of knowledge, she says, could someday enable physicians to manipulate nerve-growth inhibitors and promoters to encourage nerve regeneration after injury or to discourage painful scar formation.

Although scientists still don't know why the adult brain begins producing proteoglycans that limit nerve regeneration, "we're getting to know the molecules — the players — and what they do," Silver says. "That's what's so exciting."

— K. Schmidt

Detecting Jupiter's tug on radio waves

The gravitational deflection of starlight when it grazes the sun's limb has become a standard test of Einstein's general theory of relativity. With the help of sophisticated instrumentation stretched to its limits, researchers have now confirmed that an object as small as Jupiter also has a discernible effect on the paths of radio waves from a distant source as they speed past the planet.

These observations "constitute the first measurement of the deflection of electromagnetic radiation by a planetary gravitational field," Robert N. Treuhaft and Stephen T. Lowe of the Jet Propulsion Laboratory in Pasadena, Calif., report in the November ASTRONOMICAL JOURNAL. The findings also demonstrate the usefulness of a new approach for locating and tracking distant objects — including spacecraft on deep-space missions — observed within a wide field of view.

"It's a nice result," says physicist Clifford M. Will of Washington University in St. Louis. "It illustrates that we can now measure radio waves accurately enough to see the deflection caused by a planet."

To make such a measurement possible, Jupiter in the course of its passage across the sky had to come nearly in front of a strong celestial source of radio waves, an event that happens only once or twice in a decade. Such a close encounter occurred on March 21, 1988. On that day, Treuhaft and Lowe measured the differences between the arrival times of radio waves at receiving stations at each end of two lines stretching between California and Australia. They repeated the measurements 13 days later, after Jupiter had moved farther away from the radio source's point in the sky.

Careful data analysis, which took nearly three years to complete, revealed a tiny deflection consistent with theoretical predictions of the gravitational effect Jupiter would have on electromagnetic radiation. This deviation of 300 microarcseconds corresponds to a shift of only about 1 kilometer in the radiation's path when measured at Jupiter's distance from Earth. "Our measurement agrees with general relativity," Treuhaft says.

Although this planetary measurement doesn't test gravitational theory as well as solar-deflection measurements, "it shows that we can now detect the deflection due to Jupiter's warping of space-time," Will says. "Modern VLBI [very long baseline interferometry] has reached the stage where we can really see the curvature of space-time essentially everywhere."

Further development of VLBI techniques will allow more accurate measurements of such deflections in the future.

— I. Peterson