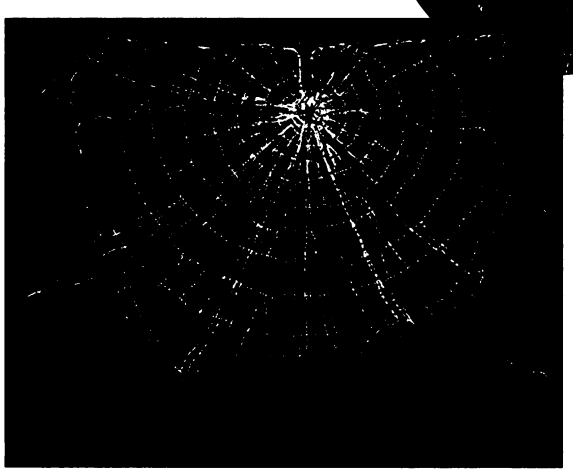
MOLECULAR GENETICS

Spider Genes Reveal Flexible Design

As engineers, spiders leave most other creatures in the dust. Dragline silk, which the eight-legged acrobats use for bungee jumping or rigging webs, is fabulously strong; a cable not much thicker than a garden hose could support two fully loaded Boeing 737 jetliners without breaking. And yet the so-called flagelliform silk used in web spirals is elastic enough to stretch over 200%. With seven kinds of silk, many spiders weave complex and resilient works of art.

Now, the most extensive look yet at spider-silk DNA, reported on page 1477, reveals that the gene for flagelliform silk has some marvelous architecture of its own. Like other silk genes, the DNA that codes for flagelliform silk is a repetitive string of nucleotides. But these nucleotides are grouped in a way that may be an engine for generating diversity. Although the finding may not have an immediate impact on the way artificial silk is designed, it has excited people who think about spider evolution. "This structure is totally different from anything we've seen in spiders," says Catherine Craig, an evolutionary biologist at Tufts University in Medford, Massachusetts. "It looks like a system that could allow considerable variation in the composition of flagelliform silk proteins."



Nice threads. *Nephila clavipes* dabs sticky silk onto a framework of elastic flagelliform silk (blue).

Many arthropods make silk: spiders, silkworms, butterflies, and even some honeybees. Trying to mimic and improve this wonder fiber, outfits from the U.S. Army to DuPont have investigated its biomechanics and genetics. Since 1990, several teams have discovered 10 spider silk genes. But no one had looked at the genetics of the highly elastic flagelliform silk, so called because the glands that produce it resemble whips. So evolutionary biologist Cheryl Hayashi and molecular biologist Randolph Lewis of the University of Wyoming, Laramie, sequenced genes for the flagelliform silk of the tropical spiders *Nephila clavipes* and *Nephila madagascariensis*.

Silk proteins are made of repeating amino acid motifs. Some researchers think this chain of springlike helices is a key to the strength and elasticity of silk, and the regularity may help the liquid proteins self-assemble into fibers as they are pulled out of the silk glands. Not surprisingly, as Hayashi and Lewis sequenced the *Flag* gene, they found repeated stretches in the DNA that coded for three regular amino acid motifs. Curiously, these motifs kept turning up in the same order.

But Hayashi and Lewis also came across a stretch that didn't code for amino acids. Such noncoding sequences, or introns, are common in other genes but had never been seen before in spider silk DNA. Then Hayashi found another, and another—almost all the same size. "That's when I started to be surprised," she says. The 12 introns take up about half the gene, and they alternate with active coding regions called exons. Even more unusual, most of the introns are very similar—two of them are 99.9% identical—suggesting that the introns are more highly conserved than the exons, which code for amino acids. That's like taking better care of your CD cases than the compact discs themselves.

Hayashi and Lewis believe that all these peculiarities are tied to the monotony of the exons. When a sequence is highly repetitive, enzymes that copy the DNA can lose their place and make an error. That could explain why the exons tend to vary more in length than do the introns, which are less repetitive. The exons are also rich in the nucleotides cytosine and guanine, which when found in strings may increase the chance of genetic mistakes. Either factor might have led to new genetic diversity, the researchers say.

On the other hand, the repetitive architecture may lead to "homogenization" of the gene, which occurs when one repeat overwrites another repeat. Such rewriting is more likely when the repeats are similar in sequence. "The amazing similarity across the *Flag* introns almost certainly means that this kind of recombination event led to the redundancy of the motifs," says Andrew Clark, an evolutionary geneticist at Pennsylvania State University, University Park.

This tug-of-war between mutation and homogenization may put the spider in a bit of an evolutionary tangle, Hayashi and Lewis say. Although the gene structure may be good for allowing mutations—and coming up with an even better type of silk—the same architecture means that those improvements might be weeded out. "Purely because of the repetitiveness, it might be very hard to stabilize these genes and maintain an optimal sequence," Hayashi says.

Silk is crucial for spiders; aside from catching insects, they also use it as a safety line and to make egg cases. That makes spiders great animals for exploring the link between the evolution of an important behavior and the evolution of a family of proteins, Craig says. And because the protein is directly extruded—rather than hidden inside the body like most proteins—the physical effects of mutations on silk proteins and spider survival are much easier to study. Those kinds of experiments may be far off, but probing the genes behind the proteins is a key step. "Now we know the structure of the gene," Craig says, "and that's fantastic." —ERIK STOKSTAD

PLANETARY SCIENCE

NEAR Finds a Battered But Unbroken Eros

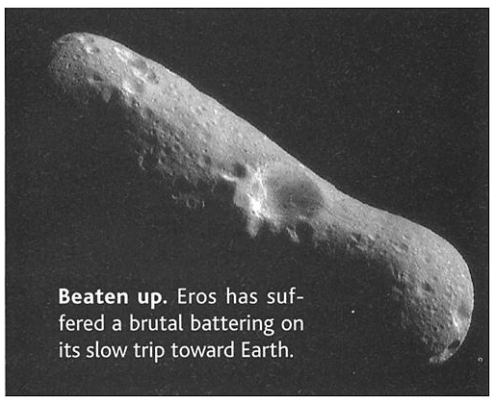
When the Near Earth Asteroid Rendezvous (NEAR) spacecraft went into orbit around the asteroid Eros last Monday, planetary scientists were expecting to see a body little worn by the ravages of time. According to conventional theory, Eros had escaped from the main belt of asteroids between Mars and Jupiter shortly after it was formed in a catastrophic collision of two larger asteroids. With little time spent in the cosmic shooting gallery of the main belt, Eros should have arrived near Earth less blemished by impacts than siblings that remained behind. But data from NEAR reveal that the asteroid took a heavier beating than expected, NEAR team members announced last week; the pitted surface suggests a slower, unconventional passage out of the main belt. Early NEAR returns also hint at Eros's innermost nature.

Every image returned by the NEAR spacecraft on its arrival shows a surface almost covered with impact craters. The more craters, the longer a body has been exposed to the interplanetary elements, so "Eros does have an ancient surface," says NEAR project scientist Andrew Cheng of the Applied Physics Laboratory (APL) in Laurel, Maryland, which built the space-

CREDITS: (TOP) N. ROTENBERG/ANIMALS ANIMALS; (BOTTOM) SAMUEL ZSCHOKKE

craft and is running the mission for NASA.

A group of planetary dynamicists is suggesting that Eros suffered such a battering because it was slow getting out of the main asteroid belt following the impact that tore it from its parent body. Most asteroids that escape toward Earth are blasted by a collision into one of two narrow zones, as William Bottke of Cornell University and Alessandro Morbidelli of the Observatory of the Côte d'Azur in Nice, France, point out. They usually remain in these regions for less than about a million years before Jupiter's powerful gravity slings them inward, so near-Earth asteroids like Eros should look relatively young. Instead, they argue, a gentle push from sunlight may have nudged Eros gradually into one of numerous, weaker "escape hatches" created by Jupiter and Saturn or even by little Mars (*Science*, 13 August 1999, p. 1002). Such a route would have taken Eros hundreds of millions of years longer to approach Earth.



Beaten up. Eros has suffered a brutal battering on its slow trip toward Earth.

Despite the prolonged pounding, Eros still seems to be in one solid piece. Impacts have pummeled the asteroid Mathilde, which NEAR flew by in 1997, into a flying bunch of boulders. Such collections can appear solid when covered with fine debris. But by combining NEAR estimates of the volume and mass of Eros, the radio science team led by Donald Yeomans of the Jet Propulsion Laboratory in Pasadena, California, calculates that the asteroid has a density of 2.4 grams per cubic centimeter, about the same as Earth's crust. That doesn't leave much room for the nooks and crannies of a rubble pile, Yeomans says: "It now looks like we have a fairly solid object" in Eros.

NEAR is getting hints about Eros's parent body as well. For decades, planetary scientists have been debating whether asteroids like Eros, whose spectral color makes them the most common type in the main belt, could be the source for the ordinary chondrites, the most common type of meteorite to fall to Earth. That's one reason NEAR was sent to Eros. If so, Eros, like its parent body, would have the same primitive composition throughout. But ground-based observations by Scott Murchie of APL and Carlé Pieters of Brown University had caught a hint of different colors on opposite sides of Eros. The colors, imperceptible to the human eye, suggest different mineral compositions. That implies that Eros's parent became hot enough inside to melt and form different minerals in separate places, a process the parents of ordinary chondrite meteorites never went through.

NEAR team member James Bell of Cornell now tells *Science* that "we do see [color] differences from place to place" on Eros, confirming the ground-based observations. That still doesn't necessarily mean Eros is mineralogically differentiated and an unsuitable source for ordinary chondrites, cautions Bell. Surface colors may have been altered by poorly understood "space weathering" over Eros's ages and ages of exposure (*Science*, 9 February 1996, p. 757). Best to wait, he says, for more NEAR data to get to the heart of Eros.

–RICHARD A. KERR

CREDITS: (LEFT TO RIGHT) NEAR/NASA; DURING *ET AL*

NEUROSCIENCE

New Stroke Treatment Strategy Explored

Strokes are among the most prolific killers in the developed world, claiming about 160,000 lives each year in the United States alone. Those who survive are often left physically and mentally impaired. Although new treatments can limit stroke damage, they have to be administered quickly to work. Now, researchers working with rats have come up with a new strategy that may guard against brain damage by taking advantage of the brain's response to injury.

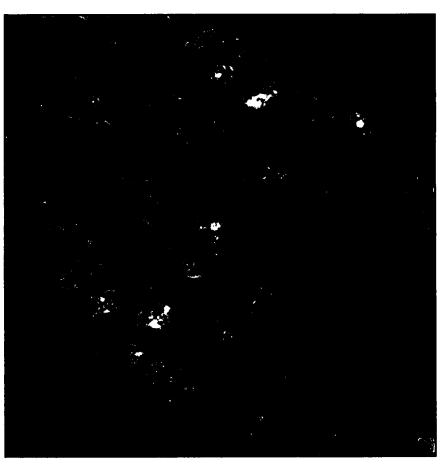
In this work, described on page 1453, neuroscientists in effect immunized rats against the brain nerve cell death caused by stroke and severe seizures. The team, led by Matthew During of the University of Auckland in New Zealand and Thomas Jefferson University in Philadelphia and his colleagues, vaccinated animals with a virus that had been genetically engineered to contain part of the NMDA receptor. Excessive stimulation of this receptor, which occurs when massive amounts of the neurotransmitter glutamate are released in the wake of a stroke, contributes to neuronal death. During's team theorized that the modified virus would stimulate the production of antibodies that could slip into the stroke-damaged brain, seek out NMDA receptors, and prevent them from being excited to death.

In the vaccinated rats, this strategy proved surprisingly effective. The protection against stroke damage "was as good as could possibly be expected," says neuroscientist Brian Meldrum of King's College Institute of Psychiatry in London. But the technique could pose dangers to humans. Neuroscientist James McNamara of Duke University in Durham, North Carolina, cautions that "immunizing people with neural antigens might have unwanted effects," including encephalitis or learning disruptions.

Other NMDA receptor–blocking drugs are already used clinically, but for optimal effectiveness, they have to be given within about an hour of a stroke, and many stroke patients do not reach help so quickly. To develop a treatment that could act almost immediately, During and his colleagues took advantage of the fact that the blood-brain barrier—the membrane that normally prevents large molecules such as proteins from entering the brain—breaks down after a stroke or other trauma. NMDA antibodies circulating in the bloodstream could then steal into the brain.

To test this, his team modified an adeno-associated virus so that it carried a piece of DNA that codes for a portion of the NMDA receptor. The researchers fed rats one dose of the virus and waited 1 to 3 months for antibodies to build up in the blood. Then, to simulate a stroke, they injected an artery leading to the brain with a compound that causes the artery walls to squeeze shut. The resulting lack of blood ordinarily devastates a large portion of the brain. But in the vaccinated rats, the lesion was 70% smaller than in controls.

During's team also induced a state of prolonged, intensifying seizures known as status epilepticus by injecting another set of rats with kainate, a compound that stimulates the release of large amounts of glutamate. In humans, long-lasting status epilepticus seizures can kill cells in the hippocampus. In the group of untreated rats, 68% progressed into full-blown status epilepticus and also suffered major cell death in the hippocampus. But just 22% of the vaccinated



Antibody triggers. Blue-stained immune cells in the gut respond to the NMDA receptor.