

## Gene cloned for stretchiest spider silk

To snag a speeding insect, the resilient silk at the center of a spider's web may stretch to almost three times its original length. Now, researchers have cloned the gene for this most elastic of spider silks and unraveled its protein structure.

The extreme elasticity of this natural miracle fiber, called capture silk, comes from long spirals in the protein's configuration, propose researchers from the University of Wyoming in Laramie. Figuring out what makes silk stretchy and what makes it strong will ultimately enable scientists to design genes to control the manufacture of silks, says Randolph V. Lewis, a coauthor of the report in the Feb. 6 *JOURNAL OF MOLECULAR BIOLO-*

*gy*. This finding, he says, "Gives us the tools to say, 'If you want to make an elastic silk, this is what you've gotta have.'"

The researchers obtained the gene from a gland of the golden orb-weaving spider, *Nephila clavipes*. They found that capture silk protein, a chain of thousands of amino acids, contains regions in which a sequence of five amino acids is repeated over and over, as many as 63 times.

The researchers suggest that the segments of the protein with the repeating blocks form long, springlike shapes. At the end of each five-amino-acid block, the protein kinks back on itself in a 180° turn, Lewis says. The series of turns eventually forms a spiral that "looks



Capture silk threads spiral between the spokes of a web spun by a spider in the genus *Nephila*.

## Electromagnetic fields may trigger enzymes

Though numerous epidemiological studies have hinted that exposure to the electromagnetic fields (EMFs) associated with power lines, home wiring, and appliances may cause leukemia or other malignancies, researchers have lacked any explanation of how EMFs could produce such effects. The fields seem incapable of delivering enough energy into the body to damage DNA or bring about other harmful changes.

Now, in a pair of studies, an international team reports what may be the first EMF-triggered change in a cascade of events that could result in cancer. The cascade begins with the activation of enzymes—tyrosine kinases—produced by tumor-promoting genes.

For about 6 years, pediatric oncologist Fatih M. Uckun of the Wayne Hughes Institute in St. Paul, Minn., reviewed radiation research proposals, including those focusing on EMFs, from people seeking grant money from the National Institutes of Health. He was highly skeptical of the link between EMFs and cancer. Without a mechanism for suspected EMF risks, he says. "I had thought it was voodoo."

That assessment is now coming back to haunt him, he says. His latest test-tube studies show that magnetic fields with a frequency of 60 hertz and a strength of 1 gauss—on the high end of exposures that might be encountered in the home or workplace—trigger a cascade of enzyme-driven cell-signaling events. These short-distance communications serve as a means by which cells can relay operational directions to their DNA.

A year ago, Uckun and his team reported that ionizing radiation could prompt cell membranes to initiate a similar signaling cascade. Those data, he says, suggested that events triggered by the enzyme tyrosine kinase "are responsible for the final DNA damage that ionizing

radiation induces." Out of curiosity, the team decided to look at EMFs, expecting that they would prove ineffective.

Instead, the EMFs activated a tyrosine kinase dangling from the inner surface of the cell membrane. By alternately removing and inserting the gene that makes the enzyme, Uckun and his colleagues report in the Feb. 13 *JOURNAL OF BIOLOGICAL CHEMISTRY*, they showed that cells exhibit a response to EMFs only when the kinase is present. This suggests that activation of the enzyme represents the initial manifestation of EMFs' biological influence, Uckun says.

In a second report, slated to appear in the journal in April, the team details the cascade of events triggered by EMFs' activation of that enzyme. It includes the turning on of a second tyrosine kinase, known as BTK. Studies in people have shown that excessive activation of BTK can lead to leukemia, lymphomas, and other cancers, Uckun observes.

Because "you don't have any hormone production without activation of tyrosine kinases," Uckun says, the new findings may also explain provocative hormonal perturbations linked to EMF exposures (SN: 1/10/98, p. 29).

"Uckun's work provides key information for beginning to understand how magnetic field exposure may lead to biological effects," observes Jerry L. Phillips of the Veterans Administration Medical Center in Loma Linda, Calif. However, he adds, "it does not tell us how magnetic field exposure may lead to leukemia or other cancers" because the cells studied "were already cancerous."

Clearly, "if the effects can be repeated, they are significant," says Steven C. Miller of SRI International in Menlo Park, Calif. While he has attempted to copy Uckun's study, to date he has "gotten no [EMF] effect." Miller says the two labs should now work closely to resolve their contradictory findings. —J. Raloff

exactly like a molecular spring."

Spiders make as many as seven different types of silk, says coauthor Cheryl Y. Hayashi. Insects get entangled in the sticky web, she explains, because the stretchiness of capture silk lets the web oscillate back and forth after the insect hits it. If the web were stiff, the insect might just bounce off.

Researchers have cloned several genes for dragline silk, the type that the nursery rhyme spider must have spun to lower itself down beside Miss Muffet. Spiders use dragline silk to form the gylines and framework for wheel-shaped orb webs. It is stronger than capture silk but less flexible (SN: 3/9/96, p. 152). In fact, Lewis says, dragline silk is only one-fifth as elastic as capture silk.

Dragline silk proteins and capture silk proteins have similar turn-forming blocks of amino acids. However, the researchers found that these blocks repeat an average of 43 times in the capture silk, compared to only 9 times in the dragline silk. That fivefold difference in length corresponds to the difference in elasticity between the two proteins, Lewis says.

"When you put the math to it," he notes, "it looks pretty good."

The stretchy section of the protein may not spiral in the way Lewis describes, cautions John Gosline, a biomechanic at the University of British Columbia in Vancouver.

An alternative theory suggests that the zigzag turns may simply allow the protein to flex and bend, Gosline says. Rather than assuming a specific, organized shape, the stretchy parts of the protein may flop around at random.

Gosline adds that he has no doubt that the Wyoming group has identified the correct gene for capture silk protein.

"I think it's interesting," he says. "We're actually a bit jealous." —M. Jensen