## Cobweb biotech

Silk proteins confer both elasticity and strength to spider webs. A recent report (*J. Mol. Biol.* 275:773–784, 1998) by Cheryl Hayashi and Randy Lewis of the University of Wyoming, Laramie, provides insights into how the structure of one of these proteins mediates its remarkable properties. The authors describe the cDNA cloning of flagelliform (FLAG), a protein that forms the core thread of an orb web's "capture spiral." Sequencing of FLAG revealed the predicted protein to consist of several repeated amino acid modular arrays, the most prevalent being Gly-Pro-Gly-Gly-X. This motif forms type II β turns that when repeated, are thought to form β spirals. Hayashi and Lewis hypothesize that these β spirals function as molecular "springs" conferring elasticity, in a manner similar to spirals found in gluten, a well-characterized wheat protein. Comparison of FLAG to the seven other known spider silk proteins revealed a direct correlation between the number of these repeats and the elasticity of the silk fiber. "Using the modules, one can explain the mechanical properties of the three known spider silk proteins," says Lewis. WyBiGen (Laramie, WY), a company he has formed to exploit this research, aims to create designer "artificial silk proteins with specific elasticity and tensile strengths" for potential use in high-performance fabrics.

## Self-assembling combinatorials

Combining the principles of molecular self-assembly with those of affinity chromatography, researchers have selected and amplified a DNA-binding compound from a combinatorial library. In a report in *Tetrahedron Letters* (38:8639–8643, 1998), Benjamin Miller and colleagues of the University of Rochester, New York, describe the synthesis of six different salicylaldimines with different side-chain functionality, which were then allowed to form coordination complexes with $Zn^{2+}$. The resulting combinatorial library of 36 unique bis(salicylaldiminato)zinc complexes was then passed through an affinity column prepared from incubating poly (dT)-cellulose resin with oligo $(dA)_{12-18}$. Analyses of the eluate, normalized to amounts eluted from the column in the absence of $Zn^{2+}$, indicated that only two of the salicylaldimine complexes bound to the double-stranded DNA, and further control experiments indicated that one of these two complexes bound to the cellulose column alone. According to Miller, "The self-assembly strategy could be used to select for drugs with specific targets," and the Rochester team is currently examining its use in creating drugs that inhibit the *ras* and *her-2* oncogenes.

*Research News Briefs written by Alexander Castellino, Alan Dove, and Margret Einarson.*

## Truncating tumor growth

Researchers at the Scripps Research Institute in La Jolla, California have used a truncated form of matrix metalloproteinase 2 (MMP-2) to selectively block new blood vessel growth in tumors. Full-length MMP-2 binds to the integrin receptor α-v-β-3 on the surface of angiogenic blood vessels. A naturally occurring carboxy-terminal fragment of MMP-2, dubbed PEX, can bind to the receptor, but lacks the full-length protein's catalytic activity. In a report in *Cell* (92:391–400, 1998), the team demonstrates that PEX inhibits new blood vessel growth in a chick egg system. Tumors injected into the chick embryos were significantly inhibited by PEX compared with a control enzyme. "Our observation that a naturally occurring PEX fragment is present in angiogenic tumors as well as vascularizing eyes suggests there is a common mechanism regulating the development of new blood vessels," says Martin Friedlander, an author on the new study. "There can't be just one pathway by which angiogenesis proceeds. The greater number of shotgun pellets we can use. . .the better chance we have of hitting the target," he adds. Merck KGaA (Darmstadt, Germany) has licensed the technology and hopes to add PEX to the growing arsenal of recombinant angiogenesis blockers, such as the recently described Tie2 pathway inhibitors.

## DNA gets wired

Using a segment of DNA as a scaffold, a team of researchers at the Technion-Israel Institute of Technology in Haifa have constructed a silver wire three times thinner than can be produced by conventional means. The scientists attached short oligonucleotides complementary to the ends of a piece of DNA from bacteriophage lambda to adjacent electrodes, then allowed the phage DNA to anneal to the oligonucleotides, forming a bridge between the electrodes. Next, the team chemically deposited silver on the DNA bridge to form a wire. In addition to carrying a current, the wire can be made to act as a diode, permitting electricity to flow easily in one direction, but not the other. "The silver wire with its hysteresis may serve in principle as a 'memory' device, but more work is needed to understand the mechanism," states Erez Braun, a physicist at the Technion-Israel Institute and lead author of the study. Braun and his colleagues have also produced gold wires with this technique, and they expect to find many other applications for future nanometer-scale electronic devices. The work is reported in *Nature* (391:775–778, 1998).

## Chewed up plant defense

Plants often produce defensive chemicals when damaged by herbivorous insects, but the effectiveness of this response has not been rigorously characterized. Work reported recently in *Science* (279:1201–1202, 1998) reveals that these defense responses confer considerable selective advantage to the plants. Anurag Agrawal, a professor in the department of entomology, University of California, Davis, allowed caterpillars to feed on the leaves of wild radish plants early in the growing season. Plants that received this treatment were healthier, more resistant to attack by chewing herbivores, less prone to colonization by green peach aphids, and produced larger and more numerous seeds than controls in which a leaf was cut off with scissors. "My feeling is that both saliva and the amount of tissue damage are important [in inducing the response]," says Agrawal. In addition to applying chemicals to induce this reaction in commercial crop plants, he suggests a more counterintuitive approach might prove beneficial: "If you can have early-season herbivores [feed on crops]. . .we actually see very strong resistance to later-season herbivores, which are much more economically important."