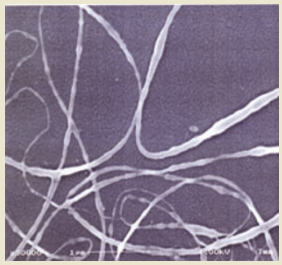
Siliconized spider silk



What do you get if you cross a cobweb with plankton? The answer is probably something similar to what Kaplan and colleagues have obtained through genetic engineering: hard, crystal-like threads that could be useful in the design and engineering of biomaterials for bone regeneration and other applications. In the quest for ever more complex and easier-to-assemble 'natural' materials, the authors created chimeric proteins consisting of a self-assembling portion of the silk protein from the banana spider, *Nephila clavipes*, and a silica-nucleating protein from the marine diatom *Cylindrotheca fusiformis*. After expression and polymerization of the chimeric protein in the bacterium *Escherichia coli*, the resulting 'silk' threads could be spun under silicon-depositing conditions to obtain highly homogenous threads of crystal-like silk (see illustration). Similar strategies using mineral-nucleating proteins could be applied to generate other materials of interest containing hydroxyapatite or titanium dioxide. However, the most important advantage of developing chimeric proteins such as the one described here is that the mineral-like structures obtained are generated under mild chemical conditions resembling the *in vivo* environment of a cell—a far cry from the high-temperature, high-pressure conditions required to make silica-based components in the chemistry laboratory. This approach may thus open the door to the development of *in vivo* self-assembling biomaterials for therapeutic applications. (*Proc. Nat. Acad. Sci. USA*, **103**, 9428–9433, 2006) *GTO*

Diversifying chemical arrays

Small-molecule arrays are increasingly being used to screen for ligands to proteins of therapeutic and research interest. Until now, however, their widespread adoption has been limited by the lack of a universal chemistry for attaching compounds to the array surface. In addition, some arrays are plagued by false positives, and most work best when probed with purified proteins, which can require onerous purification schemes. To solve these problems, Branford *et al.* have developed arrays on isocyanate-functionalized glass slides, on which they capture as many as 10,000 small molecules from a variety of sources, natural and synthetic. The arrayed molecules do not require special functional groups for attachment, produce no acidic by-products that can obscure or degrade the molecules, and can be sampled in different orientations. The researchers demonstrated that they could detect known targets as well as structural analogs to antibodies of known specificity. Most importantly, they showed that they could detect proteins directly from cell lysates, whether a protein was overexpressed and hence at high concentration or endogenously produced. Over 50 proteins have been screened on the arrays, yielding interactions that, upon retesting, were 86% positive. This method should significantly expand the possibilities for screening to those proteins not easily purified, or that require synthesis in mammalian cells for proper folding. (*Chem. Biol.* **13**, 493–504, 2006) *LD*

Research Highlights written by Kathy Aschheim, Laura DeFrancesco, Peter Hare, Gaspar Taroncher-Oldenburg & Jan-Willem Theunissen

Cyclohexanehexols thwart amyloid

Amyloid α peptide (Aα) oligomerization and fibril formation is promoted by phosphatidylinositol lipids and might play a significant role in the development and pathogenesis of Alzheimer disease. McLaurin *et al.* demonstrate that oral administration of two derivatives of these phosphatidylinositol lipids, epi-cyclohexanehexol and scyllo-cyclohexanehexol, inhibit Aα oligomeric assembly in the brain of a transgenic Alzheimer disease mouse model. Whereas both compounds were prophylactically effective, only scyllo-cyclohexanehexol exhibited a therapeutic effect. Transgenic mice treated with scyllo-cyclohexanehexol before or after onset of disease displayed significant behavioral improvements and reductions in Aα plaque formation, synaptic loss, glial inflammation and animal death. Reduced abundance of high molecular weight Aα oligomers and coincident increased presence of low molecular weight trimeric and monomeric Aα species in soluble fractions of brain homogenates of scyllo-cyclohexanehexol–treated transgenic mice further indicated that this cyclohexanehexol might directly inhibit and/or disaggregate high molecular weight Aα oligomers. This study shows that accumulation of high molecular weight Aα oligomers might contribute to Alzheimer disease pathology and that certain cyclohexanehexols might have therapeutic potential. (*Nat. Med.* **12**, 801–808, 2006) *JWT*

Deciphering self-renewal

Elucidation of the molecular pathways that control the self-renewal and differentiation of embryonic stem (ES) cells will facilitate the development of cell therapies. Although several genes involved in ES cell self-renewal are already known, Lemischka and colleagues undertook a search for self-renewal genes using a more systematic approach. A microarray study of mouse ES cells showed that 901 genes were downregulated as the cells undergo differentiation. The authors then selected 65 of these genes, many of which encode DNA-binding proteins, for further study. Each gene was silenced using RNA interference, and the effect on self-renewal was assessed with a fluorescence-based competition assay and by monitoring cell morphology and alkaline phosphatase activity. Six genes were identified: three that are already known to have critical roles in self-renewal (*Nanog*, *Oct4*, *Sox2*) and three novel genes (*Tbx3*, *Esrrb*, *Tcl1*). Further studies showed that *Tbx3* and *Esrrb* prevent differentiation to mesoderm, ectoderm and neural crest cells, whereas *Tcl1* blocks expression of certain neural crest genes. (*Nature*, published online 11 June 2006; DOI: 10.1038/nature04915) *KA*

Flu virus hitchhikes to Newcastle

An affordable vaccine that can protect commercial poultry from avian influenza virus (AIV) would help to control bird flu. Every year, billions of birds are vaccinated against Newcastle disease virus (NDV) by administering live strains either as spray or in drinking water. Two independent groups use reverse genetics to exploit this routine, and often mandatory, practice by creating chimeric viral strains that protect against both NDV and AIV. Whereas Veits *et al.* confer protection against lethal doses of both viruses by incorporating the hemagglutinin gene from the AIV strain H5N2 into the NDV genome, Park *et al.* report comparable success by a single immunization with an attenuated NDV expressing hemagglutinin from the H7N2 AIV strain. Besides the convenience of targeting two important viral diseases simultaneously without changing current mass immunization practices, another advantage of using hybrid strains instead of regular AIV or NDV vaccines is that vaccinated poultry can be distinguished from birds exposed to wild-type viruses. (*Proc. Natl. Acad. Sci. USA* **103**, 8197–8202, 2006; *Proc. Natl. Acad. Sci. USA* **103**, 8203–8208, 2006) *PH*