CHEMICAL TOOLS

Chemical nano-corking

Silica nano test tubes used as delivery vehicles can be 'corked' with nanoparticles using chemical self-assembly.

Researchers across all scientific and engineering disciplines have been jumping on the nano bandwagon. The intriguing material properties of nanotubes are being explored for many practical applications, even in biomedicine, and some material-minded biomedical scientists are hoping to use nanotubes as drug or gene delivery vehicles *in vivo*.

That is just one 'small' problem that nanotube expert Charles Martin is pursuing with his biochemistry collaborator Jon Stewart at the University of Florida. The Martin laboratory previously developed a method using template synthesis to construct nano test tubes, which unlike traditional nanotubes are closed on one end (Gasparac *et al.*, 2004). "We thought these would be really cool for cargo delivery, but it would sort of be like trying to ship wine in a wine bottle without a cork," says Martin. Recently, they took the first step toward a solution to this problem by using chemical self-assembly to 'cork' silica nano test tubes with an appropriately sized nanoparticle (Hillebrenner *et al.*, 2006; **Fig. 1**).

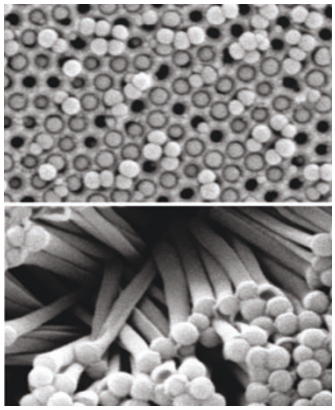

Figure 1 | Scanning electron micrographs of nanoparticle-corked silica nano test tubes. Template-embedded (top) and freed (bottom) nano test tubes. Reprinted with permission from *J. Am. Chem. Soc.* Copyright 2006, American Chemical Society.

The silica nano test tubes can be functionalized at the mouth with amino groups, which spontaneously react with aldehyde-functionalized nanoparticles to form imine linkages (by what is known as the Schiff base reaction), thus capping the tubes. "The beauty of template synthesis is that you can develop nanotubes that are easy to functionalize, chemically or biochemically," explains Martin. Moreover, the template synthesis method can be adapted to almost any material, from carbon to silica to polymers. Their long-term goal is therefore to make the corked nano test tubes out of a biodegradable material safe for use in living systems.

The very next step in Martin and Stewart's work is more within reach, however, and that is to develop labile chemistry to be able to uncap the nano test tubes and let the cargo out under different conditions. Martin says: "It's tough pulling a cork out.... I've destroyed many corkscrews trying to get corks out of wine bottles, and we certainly don't want to develop the nano equivalent of that!"

Allison Doerr

RESEARCH PAPERS

Hillebrenner, H. *et al.* Corking nano test tubes by chemical self-assembly. *J. Am. Chem. Soc.* **128**, 4236–4237 (2006).

Gasparac, R. *et al.* Template synthesis of nano test tubes. *Nano Lett.* **4**, 513–516 (2004).

MICROBIOLOGY

MY ENEMY'S ENEMY IS MY FRIEND

Bacteriophages form the foundation for a rapid and sensitive bacterial detection assay, capable of revealing the presence of a few dozen cells in a milliliter sample.

Bacteriophages could offer an excellent weapon against pathogenic bacteria—they can exhibit exquisite host preference and could also prove valuable for dealing with antibiotic-resistant strains. National Institutes of Health researcher Sankar Adhya has been exploring the use of these viruses for antibacterial therapeutics, but recently came to realize that even the best therapies require a good diagnostic tool first. "Detecting [bacteria] earlier, when the bacterial counts are less, is invaluable for therapies," says Adhya.

And so his group set about developing rapid and sensitive diagnostic assays. Bacteriophages remained the tool of choice, and Adhya's team also took advantage of the highly conserved bacterial biotinylation metabolic pathway. They engineered T7 phage in which the coat protein was tagged to allow processing by bacterial biotinylation enzymes. When these phage encounter target bacteria, infection will lead to the production of phage that are at least partially biotinylated before host lysis. These phage can then be detected by fluorescence microscopy using streptavidin-conjugated quantum dots.

The method tested successfully both in the laboratory and in the real world—using T7, Adhya's team found that they could detect as few as 10 *Escherichia coli* cells intermixed with other nontarget bacteria, and they were able to detect roughly 20 *E. coli* cells in a milliliter of Potomac River water. The sensitivity and speed of the assay (roughly an hour from start to finish) compared favorably with existing assays—a standard *E. coli* detection system took nearly 24 hours to detect coliform cells in river water.

Adhya is now looking into improving the assay's sensitivity by developing methods to improve the efficiency of phage biotinylation. In general, however, he believes the method should be broadly applicable because of the wide variety of bacteriophage types with different host preferences, even though engineering the phage could be difficult if genome data are lacking for a given strain. In the end, Adhya hopes that the system's usefulness will grow as more people adapt it for themselves: "We're [using this assay] with the model organisms we work with in our lab, but if people use it, I'm sure they'll succeed... with other bacteria."

Michael Eisenstein

RESEARCH PAPERS

Edgar, R. *et al.* High-sensitivity bacterial detection using biotin-tagged phage and quantum-dot nanocomplexes. *Proc. Natl. Acad. Sci. USA* **103**, 4841–4845 (2006).