# Exploring ceramic vaccines, drug carriers

Make a bunch of virus-sized ceramic particles. Now coat them with a laboratory-designed, carbohydrate-like goo, and then let proteins derived from health-wrecking microbes or viruses stick to it. What have you got?

"We may have here a way of making vaccines that nobody has been able to make," says medical pathologist Nir Kossovsky of the University of California, Los Angeles. His tiny particles also might redeem hundreds of mothballed drug candidates — ones that showed early promise in test tubes but fizzled in animal or human trials.

The key to such applications — none of them even close to human trials — rests in the apparent ability of the coated microscopic crystals to preserve the precise, medically important shape of the delicate proteins adhering to them. That's encouraging, Kossovsky says, because in the body, proteins encounter many molecule-manipulating influences. And the most subtle changes in the shape or structure of a protein can spell dramatic shifts — sometimes with toxic consequences — in its biological behavior or therapeutic potential.

The UCLA researchers suspect that as drug and vaccine designers increasingly turn to protein-based agents for disarming viruses, diseased cells or health-threatening biochemicals, stabilizing the proteins' shapes will prove paramount.

In the winter JOURNAL OF APPLIED BIOMATERIALS, Kossovsky, Rointan F. Bunshah and seven collaborators describe experiments using ensembles of specially coated tin oxide ceramic crystals, each about 25 nanometers in diameter. The proprietary sticky coating — dubbed GF292 — prevents protein-deforming surface interactions between the particles and the attached molecules, Kossovsky explains.

Antibodies — the biochemical champs at finding and binding to specific molecular shapes — had no trouble latching onto transferrin molecules bound to the particles, the UCLA team found. This showed that transferrin, a protein carrier for iron in the blood, retained its precise antibody-attracting structure despite its attachment to the nano-particles, Kossovsky says.

The Epstein-Barr virus (EBV) causes mononucleosis and has been implicated in other ailments. With backing from a Toronto-based technology-development firm, which Kossovsky and Bunshah help manage, the UCLA researchers have begun attaching surface proteins from EBV to the nano-particles with the goal of making safer vaccines from "sterile" decoy viruses.

On rare occasions, vaccines made from real but "killed" viruses have initiated the disease they were designed to prevent. The UCLA researchers expect the immune system will respond to nano-particles robed in the surface proteins of a virus by making antibodies against the virus. Because the cores of the new vaccines are purely ceramic, these decoy viruses cannot cause infection.

Kossovsky also envisions coating the crystalline ceramics particles with oxygen-carrying hemoglobin molecules to make artificial blood.

Acknowledging that biological complexity makes most drug ideas bite the dust, Kossovsky nonetheless asserts, "We have something that is awfully promising." — *I. Amato*

# New and primordial role for ribozymes?

According to some origin-of-life theories, the DNA-based genetic machinery found in almost all modern organisms arose from an ancient "RNA world" (SN: 10/7/89, p.229). Evidence for this scenario stems mainly from the recent discovery of ribozymes: RNA molecules capable of carrying out biochemical tasks that scientists once believed only protein enzymes could perform.

Unlike proteins, which can act as catalysts to direct the cell's complex workings, all ribozymes found so far chemically transformed only RNA (ribonucleic acid). But a new report hints ribozymes may be capable of altering non-RNA molecules as well. If confirmed, the work would enlarge the known range of reactions in which ribozymes participate and strengthen support for the concept of a primitive RNA world.

In the Nov. 27 BIOCHEMISTRY, Japanese scientists report that RNA from a yeast catalyzed the transfer of electrons from one non-RNA molecule to another. Such electron-shuffling processes, known as "redox" reactions, play a crucial role in the metabolism of organisms. Researchers at Mitsubishi Kasei Institute of Life Sciences in Tokyo and Tohoku University in Sendai identified the catalytic agent as 5-hydroxycytidine, a modified form of one of the four basic nucleoside building blocks making up every RNA chain.

The finding "indicates new possibilities for RNA as a living molecule," coauthor Hiroshi Yanagawa told SCIENCE NEWS. That an RNA can assist in redox reactions might mean that before proteins evolved, primordial RNAs served as catalysts driving life-sustaining metabolic processes, the Mitsubishi Kasei scientist suggests. His team proposes that 5-hydroxycytidine may be a vestige of such ancient RNAs.

But others say these claims lack supporting evidence. "Linking [5-hydroxycytidine] to an RNA world is a little premature" because such modified nucleosides are not necessarily "old" in an evolutionary sense, says biochemist Andrew D. Ellington at Massachusetts General Hospital in Boston. Moreover, he notes, scientists have long known that molecules containing modified nucleosides can help drive metabolic reactions.

Thomas R. Cech of the University of Colorado in Boulder also points out that the enzyme-like agent is *only* a modified nucleoside — not a "proper ribozyme," or folded chain of RNA nucleosides that binds a substance to foster a specific biochemical reaction. The Japanese team has yet to show that a yeast RNA containing the isolated agent meets this definition, suggests Cech, the 1989 Nobel laureate who coined the term "ribozyme."

However, Cech acknowledges, the new work does carry important implications. Until now, research has indicated that catalytic RNAs perform only a "limited range of reactions" — making and breaking bonds in RNA. But if a modified nucleoside within an RNA enabled that chain to alter substrates other than RNA, that would "extend the enzymatic repertoire [of ribozymes] beyond the currently known examples," he says. — *I. Chen*

# Rat removal converts shrublands to grass

James H. Brown wasn't looking for greener pastures, but he found them anyway. When he and his colleagues fenced off sections of the Chihuahuan Desert in 1977, excluding certain rat species from small plots of shrubland in southeastern Arizona, they had but a single goal: assessing the rats' ability to compete with native ants for the area's supply of large plant seeds.

But 13 years after initiating the desert study and four years after his original associates published their last report on the project, Brown has doggedly stayed on the job to record a remarkable transformation among eight of 24 small plots of land — each surrounded by fine-mesh fences adjusted to exclude either all rodents or at least three species of kangaroo rats native to the sites. Each of these

Margaret Kurzius

Dipodomys merriami, *the most abundant of three species of kangaroo rats banished from desert study areas.*



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