

## The tooth's connected to the jawbone...

At least, that's how dentists would amend the old ditty. Two connective tissues—the periodontum and the cementum—hold the pearly whites in place. When periodontal disease strikes, those tissues can start to lose their grip.

A. Hari Reddi, a biochemist at the Johns Hopkins Medical Institutions in Baltimore, says that he and his colleagues are using a bone growth protein they've just cloned to successfully treat periodontal disease in baboons. Working with Ugo Ripamonti, an oral surgeon at the University of the Witwatersrand Medical School in Johannesburg, South Africa, Reddi has applied the protein to coax damaged bone and tooth-anchoring connective tissues to repair themselves.

Because similar proteins have proved effective in orthopedic surgery, "initially, we thought that the [new protein] would just regenerate jawbone," Reddi says. "Yet we found, to our surprise, connective tissues were repaired too."

"This may have important clinical implications, though we have yet to test it in humans," Reddi adds. The researchers are currently preparing clinical trials. They also suggest that the technique may prove useful in treating damaged cartilage.

## A mouthful of gene therapy

Bruce Baum wants to help people salivate. As part of that unusual effort, the investigator at the National Institute of Dental Research in Bethesda, Md., has for the last few years applied the emerging tools of gene therapy to salivary glands.

In 1994, Baum and his colleagues showed in test-tube experiments that certain viruses can ferry functioning genes into the two primary cell types of the salivary glands, the acinar and ductal cells. Acinar cells release salt and fluids, while ductal cells absorb salt and are impermeable to water.

Baum's research may be useful for patients who lack acinar cells and consequently can't produce enough saliva. Radiation treatments given for head and neck tumors are deadlier to acinar cells than ductal cells, for example. An autoimmune disorder called Sjögren's syndrome vigorously targets acinar cells as well.

Baum's group has taken the first steps toward restoring such ravaged salivary glands to health. Using viruses as delivery vehicles, they've added a gene to ductal cells that may transform them into acinarlike cells. The gene encodes a protein called a water channel, which normally resides within the outer membranes of cells. If ductal cells made these proteins, they might secrete water and salts, as acinar cells do.

In the test tube, the genetically engineered ductal cells indeed become water permeable, reports Baum. His group next plans to transfer the gene into the ductal cells of live animals and monitor their saliva production.

In addition to more saliva, Baum would like to make better saliva. His group has recently begun attempts at therapy with a gene encoding a small protein called histatin. Histatin is secreted into saliva and protects against fungal infections, says Baum. The team aims to have the salivary glands make more of the protein, which might protect people with devastated immune systems, such as AIDS patients, from the many mouth infections they suffer.

The investigators have already engineered cells in the lab to make large quantities of histatin. "We get buckets of the stuff," says Baum. The next question is whether mice that make extra histatin in saliva will be protected from infection.

## Bacteria on ice

Kangaroos bounce around the arid lands of Australia, but they don't make anywhere else their home. This geographic isolation results, in part, from the inability of large animals to disperse easily to other suitable environments around the world.

Bacteria, whose microscopic size allows them to spread by

water, air, seeds, and a variety of mobile organisms, shouldn't have that problem, notes James T. Staley of the University of Washington in Seattle. At least that's what microbiologists have speculated, he says. Anywhere bacteria can survive, they should probably exist, goes the theory.

Staley's research over the last 5 years offers evidence to the contrary, however. His group has collected bacteria from the bottom of sea ice that builds up every winter at the North and South Poles. "Nobody else has really looked in this environment. Most of the organisms are brand-new," says Staley.

Despite almost identical habitats, none of the bacteria so far found under the North Pole ice has been collected at the South Pole, and vice versa. Understanding this surprising geographic diversity of bacteria should help investigators estimate the true number of bacterial species, of which we know perhaps 1 percent, says Staley.

## Delivering drugs directly to brain tumors

Malignant brain tumors are extremely tough to treat. The blood-brain barrier often prevents anticancer agents in the bloodstream from entering the brain to attack tumor cells. Physicians therefore want to deliver cancer-killing drugs directly to brain tumor cells.

Henry Brem, a neurosurgeon at the Johns Hopkins Medical Institutions in Baltimore, is developing small polymer disks containing anticancer drugs for implantation at tumor sites. After removing a tumor, a surgeon can line the cavity with dime-size disks that slowly release tumor toxins directly to cancerous tissue.

This method increases the drug dose at the cancer site while minimizing side effects on the patient's system.

In the laboratory, Brem's team is testing various slow-release polymers, including two polyanhydrides, in conjunction with several FDA-approved anticancer drugs. In the first clinical trial, which included 222 patients at 27 medical centers, polymers containing the anticancer agent carmustine, or BCNU, "significantly prolonged patient survival," says Brem.

"In marked contrast to the many toxic effects commonly experienced by patients treated with systemic or intra-arterial BCNU therapy, no significant adverse effects were associated with these implants," he adds.

Researchers are now planning further clinical studies of polymer implants, using other drugs and stronger doses of BCNU.

## Electric currents that merely flow

One doesn't normally expect to find electric currents with no identifiable source.

Richard A. Webb, a physicist at the University of Maryland at College Park, and his colleagues have been studying magnetically induced currents in tiny gold rings at low temperatures. Strangely, even when the magnetism is turned off, they find a minuscule, inexplicable "persistent current," which is less than one-billionth of an ampere.

"It's real," Webb says. "The existence of this persistent current is no longer in question. The size of the signal, in my experiments and ones being conducted at other laboratories, is about 100 times larger than what was theoretically predicted."

Despite a lot of bickering among theoreticians to explain the puzzling current, "there's no consensus about its origin," he adds. "We're collecting more data to unravel this mystery."

More than mere trivia for physicists, these results may prove relevant to the microelectronics industry as computer processors continue to shrink, Webb believes. There may come a point, he says, when components are so small that aberrant electrical effects like these small currents will cause computer memories to leak information.