Bon (hydroxyl)apatite

The mineral portion of bones and teeth is a substance called hydroxylapatite. There is more of it in teeth, which makes teeth harder than bone. It has an unusual property in that when it is exposed to ionizing radiation, it instantly forms a free radical—the carbonate anion. Free radicals can be detected and quantified by a technique called electron paramagnetic resonance (EPR) spectroscopy. Most biological free radicals are extremely short-lived, but the carbonate anion is stabilized in the crystal structure of hydroxylapatite, making it exceptionally long-lived. In fact, it is detectable centuries after it has been formed and has been used for the archeological dating of ancient teeth in human and animal remains.

But the substance has a very contemporary purpose as well. Dartmouth radiologist Harold Swartz, M.D., Ph.D., has found it a useful marker for measuring radiation exposure—an application of interest in military and counterterrorism as well as in medical settings.

Record: Swartz first used the technique on extracted teeth in 1968, but advances in EPR now allow the measurements to be made in teeth that are still attached to their owner's jaw. That makes an individual's teeth a permanent record of exposure to cosmic radiation, dental x-rays, and other sources of radiation.

However, Swartz and his team are especially interested in assessing doses that are orders of magnitude larger than the sum of these everyday exposures—such as might be encountered during the detonation of a "dirty" bomb or the meltdown of a nuclear reactor. Such exposures make people physically ill and often require treatment. The sign most often used to triage victims of exposure to dangerous levels of radiation is vomiting, which is indicative of damage to the gastrointestinal tract. But vomiting is one of the most nonspecific of all medical complaints. Another sign is depression of the white blood cell count, indicating damage to the bone marrow. But the drop may not occur for several critical days.

So Swartz's group is developing an instrument that can be used in the field to allow triage of patients into those who do not need treatment, those who need only supportive care (such as fluids and electrolytes), and those who will need bone marrow transplantation. Their pilot model requires wheeled transportation, but eventually they hope to develop a hand-held instrument that could be widely available in case of radiological emergencies.

Irradiation: The methods will be tested and the instruments calibrated on DHMC radiation oncology patients whose treatment targets include appropriate doses to the teeth. They will be further refined at the University of Rochester Medical Center, on patients receiving whole-body irradiation for disseminated cancers. The work is being supported by the counterterrorism unit of the National Institute for Allergy and Infectious Disease—which one could say makes the agency Swartz's tooth fairy. ROGER P. SMITH, PH.D.

FLYING SQUIRREL GRAPHICS

Charles Brenner, right, and Pawel Bieganowski, center—pictured with grad student Huan Liu—were authors of a *Journal of Biological Chemistry* "Paper of the Week."

Protein paper is picked from pack

Of the more than 6,600 articles published in the *Journal of Biological Chemistry* (*JBC*) each year, fewer than 100 are featured as a "Paper of the Week." One of the papers recently selected for that honor features work from the lab of Dartmouth researcher Charles Brenner, Ph.D. The paper focuses on a particular protein associated with a rare neurological disease.

"We want to feature the exciting work our authors publish," says Robert Simoni, Ph.D., deputy editor of the *JBC* and chair of biological sciences at Stanford. "Reviewers are asked to nominate papers they judge to be in the top one to two percent of papers to be published in the *JBC* each year." Brenner's paper was selected, he adds, because of its "broad interest, novelty, and impact."

"We were the first people to identify an enzymatic activity of the Aprataxin protein," says Brenner, an associate professor of genetics and of biochemistry and a researcher at Dartmouth's Norris Cotton Cancer Center. It was already known that certain mutations in the gene that codes for Aprataxin result in malfunctioning versions of a protein that cause a rare inherited neurological disease called ataxia-oculomotor apraxia syndrome 1 (AOA1). AOA1 is characterized by loss of control over the movement of the head, eyes, and limbs.

Genes: But until now, no one understood how this protein worked. Then Brenner and his research colleagues—postdoctoral fellows Heather Seidle, Ph.D., and Pawel Bieganowski, Ph.D.—recognized similarities between a family of cancer-related genes and the ataxia-producing gene and decided to investigate further. They found that mutated Aprataxin lacks a certain enzymatic function and that the "loss of that enzymatic activity leads to changes in the developing brain that produce the ataxia," Brenner explains.

Brenner hopes the attention generated by the "Paper of the Week" designation will "stimulate research into this very interesting protein in order to identify other molecules that are regulated by Aprataxin." Some of the molecules, he believes, "may turn out to be drug targets to treat the kids that are born with this disease." KRISTEN GARNER