Smart Molecules May Enhance Images

In medicine, a good picture is often worth more than a thousand words.

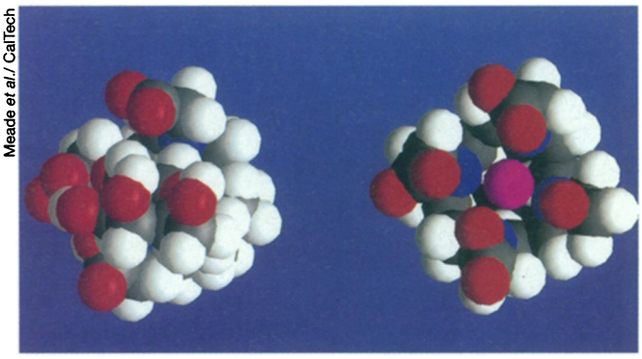
For that reason, physicians have invested heavily in high-tech systems to image the body's interior by means of X rays, magnetic resonance imaging (MRI), and positron emission tomography (PET).

Today, such systems provide three-dimensional color images of living tissues without the need to cut into a patient's tender flesh. What remains tricky, though, is producing detailed images that show how organs perform their biological duties.

To enhance MRI's capacity to track biological activities as they happen, Thomas J. Meade, a chemist at the California Institute of Technology, and his colleagues are developing a series of what they call smart contrast agents. They hope to make injectable compounds that can light up specific biological actions during MRI, Meade said in Baltimore this week at the annual meeting of the American Association for the Advancement of Science.

"These contrast agents could allow researchers to get the same kind of functional data about a person that they usually obtain with PET, except that MRI has higher resolution and is easier to use than PET," Meade says.

PET excels in observation of biological processes, but it requires radioactive materials and particle accelerators, making the technique clinically unwieldy. MRI, on the other hand, is highly effective at structural imaging and has found widespread clinical use, but it is less effective at gathering live-action information.



Meade *et al.*/ CalTech

A molecule of the MRI contrast agent (left) shows up on the image when an enzyme cuts a hole in one side, exposing a gadolinium atom (right).

The new contrast agents offer the potential to help physicians identify disease processes as they occur—highlighting, for example, tissues damaged during a heart attack or stroke, says Meade. Such timely data could give physicians a head start in treatment, increasing a patient's chances of benefiting from speedy intervention.

The prototype contrast agents use gadolinium atoms encased in molecular shells tailored to trigger a specific enzyme, Meade says. Inside the body, the enzyme takes a bite out of the shell. This enzymatic chomp exposes the gadolinium atom within, enabling the MRI to pinpoint enzymatic activity.

The effect, he adds, is to illuminate the image of body tissues where specific metabolic processes are taking place. Though gadolinium on its own has toxic effects, it shows no toxicity in mice when processed this way, Meade says.

"These agents could also prove useful for mapping the brain and identifying hard-to-diagnose diseases," Meade says. Patients suffering from Alzheimer's disease, schizophrenia, and manic depression, for example, often present similar symptoms despite their vastly different brain disorders. Meade's team thinks that the smart agents could someday help clinicians distinguish such diseases on the basis of crisp brain images rather than interpretations of symptoms.

"Contrast agents have a lot of potential," says James V. Haxby, a neuroscientist at the National Institute of Mental Health in Bethesda, Md., "though they need to be tested carefully to make sure they don't have unwanted pharmacological activities."

Moreover, the contrast agents can help researchers track cell and neuron growth as organisms develop, Meade says, perhaps replacing the "slice-and-dice" methods required when using a microscope to follow embryonic development. — *R. Lipkin*

DNA vaccine set to tackle HIV infection

The Food and Drug Administration has for the first time given researchers permission to inject a vaccine made from simple DNA into healthy, uninfected volunteers. The small trial, involving a potential AIDS vaccine, should begin in the next few months and will be conducted by investigators from the University of Pennsylvania in Philadelphia and the biotech firm Apollon in Malvern, Pa.

The experiment marks another major milestone for the emerging technology of DNA vaccines. In ongoing trials, people with advanced cancer and people infected with HIV, the AIDS virus, have received DNA injections.

The new HIV trial will be the first conducted with the hope of preventing infection. Investigators suggest that it sets the stage for the testing of DNA vaccines against a wide array of viruses and bacteria.

"This really opens up the field," says David B. Weiner of the University of Pennsylvania, who announced news of the trial at an international meeting on DNA vaccines held in Bethesda, Md.

Over the last few years, investigators have found, to their surprise, that simply injecting a gene into an animal elicits an immune response to the protein that the gene encodes (SN: 1/1/94, p. 6; 6/3/95, p. 343).

The vaccine in the new trial is made from a gene that codes for one of the proteins that form the surface of the AIDS virus. Consequently, this DNA vaccine should generate antibodies to the AIDS virus and activate immune cells that kill the virus.

Though investigators hope that the vaccine will prevent HIV infection, the primary purpose of this initial study is to assess the safety of injecting the pure DNA. All available data suggest that injected genes survive only briefly in the body, but there are still concerns that this genetic material may become permanently integrated into a person's genome, with undesired consequences.

Since the cancer and HIV-positive patients already injected with DNA have reported no major side effects after several months, FDA decided it would allow the new trial in uninfected volunteers.

"Now that we've gathered more data, we're ready to move forward. We're all very excited," says Kathryn Zoon, director of FDA's Center for Biologics Evaluation and Research.

Researchers have a number of reasons to hope that the DNA-based AIDS vaccine might be more effective than injection of the HIV protein itself. The two approaches, according to animal data, sometimes provoke different immune responses.

DNA-based vaccines, for example, appear to stimulate a stronger, longer-lasting response from infection-fighting immune cells. — *J. Travis*