Keeping a step ahead of immunity

The most powerful attribute of the human immune system is its ability to custom-tailor antibodies to attack a wide variety of invaders. But some troublesome microbes keep a jump ahead of the immune system by changing their surface characteristics more rapidly than the body can mount an attack – and much more rapidly than medical researchers can devise new vaccines. Now biologists report that the mechanism underlying surface changes of at least one species of bacterium closely resembles the very mechanism the immune system uses to generate its wide range of antibodies.

Neisseria gonorrhoeae, the bacterium responsible for gonorrhea, often has hairlike structures called pili, which help attach it to a human cell during infection. Each pilus comprises a stack of many copies of a single "pilin" protein. But that protein is quite variable within a strain.

The pilin protein, like an antibody molecule, can be divided into regions that are constant (invariant), characterized by single amino acid changes (semivariable) and characterized by larger insertions and deletions (hypervariable). Magdalene So and her colleagues at the Scripps Clinic and Research Foundation in La Jolla, Calif., report that these regions are encoded in gene segments at different "silent" locations in the bacterial DNA. Before pilin protein is produced, a set of these segments must be brought together at one of the two "expression" sites in the DNA.

"This arrangement of constant and variable pilin sequences is reminiscent of that of immunoglobulin [antibody] gene segments," the scientists say in the April PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES (No. 7). "To our knowledge, this complex assembly of genetic information has not been observed in prokaryotes [bacteria] until now." However, recent work indicates the same mechanism underlies surface changes of protozoan *Trypanosoma equiperdum,* which causes a venereal disease in horses.

In changeability, *N. gonorrhoeae* may have an advantage over the immune system. To bring together the appropriate segments of an immunoglobulin gene, a white blood cell snips out the intervening DNA, producing a permanent rearrangement. All cells that are descendants of an antibody-producing cell make the same antibody.

But the bacterium appears to rearrange its DNA in a more reversable manner, known as multiple recombination. Therefore a bacterium with pili can be the progenitor to bacteria with different pilin proteins. — *J.A. Miller*

Stopping a killer with interferon?

By name alone, chronic myelogenous leukemia (CML) might not sound as serious as acute leukemia. But CML moves quickly from chronic to fatal, generally killing its victims within three-and-a-half years after diagnosis, regardless of chemotherapy. In an effort to halt that progression, researchers at the M.D. Anderson Hospital in Houston have treated patients with a genetically engineered form of interferon. While it is too early to tell if the treatment reverses the disease, it did normalize blood and genetic changes, they report in the April 24 NEW ENGLAND JOURNAL OF MEDICINE.

The researchers, led by Moshe Talpaz and Jordan Gutterman, treated 17 patients. In the 13 responders, who have been on the therapy for up to 15 months, blood cell counts returned to normal. Side effects were relatively minor. "We just don't know the impact on survival yet," says Gutterman. "But that you can use a natural substance to get the blood counts and [genetics] normal is exciting."

More than 90 percent of CML cases are marked by a jump of genetic material from one chromosome to another; in six of the 13 responders, cells with the abnormality disappeared (though in one of these patients it returned after the paper had gone to press).

"That's very impressive," comments Ken Foon, a cancer researcher at the University of Michigan in Ann Arbor. "Whether that will translate into a cure or prolonged survival I don't know, but we can't do that with [conventional] drugs." Ezre Raze, head of the CML program at Roswell Park Memorial Institute in Buffalo, N.Y., says it is not known yet if the genetic abnormality is a cause of CML. "If it is," she says, "then getting rid of it should eradicate the disease." But if the change is a result rather than a cause, normalizing it won't help. "I think only time will tell," she says.

— *J. Silberner*

The attraction and repulsion of gravity

Newton and Einstein together did not settle the question of gravity; it continues to weigh on physicists' consciousness. The latest of several attempts to amend or extend the two historic theories comes from three physicists at the Los Alamos (N.M.) National Laboratory, Terry Goldman, Richard Hughes and Michael Nieto. Working from what Hughes calls generic characteristics of recently formulated quantum theories of gravity, they have concluded that gravity can be partially repulsive, that its strength may vary for different substances and that gravity may be weaker for moving bodies than it is for the same bodies when they are still.

Early this month their proposal was accepted by the management of the CERN laboratory in Geneva, Switzerland, for an experiment with falling (or rising) antiprotons. The procedure will not only test their ideas but will also be the first experiment to directly measure the earth's gravitational force on antimatter.

The quantized theories are called supergravity, and though they differ among themselves, they all come up with a three-component gravity, whereas Newton and Einstein had only one.

Two of these components are attractive for all things, but the third depends on the number of neutrons and protons in a given substance (its baryon number) and so may differ for different chemical elements and may be repulsive between matter and matter. The strengths of two of the components are altered by motion in different ways, leading to a complicated relationship between velocity and gravity. Although the earth always attracts, in the net result antiprotons should weigh more than protons, and bodies may weigh less when moving than when still. Furthermore, the weights of different elements will not accord exactly with the number of atomic mass units they possess.

This last provision violates the classic principle of equivalence that both Newton and Einstein adopted, Hughes told SCIENCE NEWS. The principle of equivalence states that a body's inertial mass, which determines how it responds to forces, is the same thing as its gravitational charge, the quality that determines the size of the gravitational force it exerts. A good deal of the science of dynamics and the philosophy of physics is based on the equivalence principle. The inertial mass of an given atomic nucleus is the atomic mass units it possesses, but this atomic mass is not exactly equivalent to the total of neutrons and protons. The forces that hold the neutrons and protons together make a contribution to the inertial mass – that is, the atomic mass – but for at least one component of supergravity, they make no contribution to the gravitational charge – that is, the weight. The difference is about 1 part in 1,000, but it's enough to kill the equivalence principle.

Thus, Hughes stresses, the CERN experiment will test both the quantum theories of supergravity, which are difficult to reach experimentally, and the principle of equivalence. — *D.E. Thomsen*