Retinitis: Breaking the chain's link

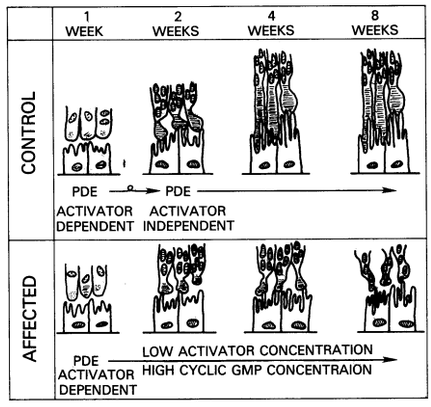
Retinitis pigmentosa, which can lead to partial or total blindness, is an inherited disease of the retina of the eye. It afflicts thousands and is a major health problem in certain areas of the world where persons with the disease often intermarry. There is currently no treatment for retinitis pigmentosa, but now the biomedical defects underlying the disease may have been found, according to a report in the July 5 NATURE. Three researchers with the National Institutes of Health in Bethesda, Md.—Y. P. Liu of the National Cancer Institute, Gopal Krishna of the National Heart, Lung and Blood Institute and G. J. Chader of the National Eye Institute — and Gustavo Aguirre of the University of Pennsylvania School of Veterinary Medicine in Philadelphia suggest that there may be defects in the retinal cell machinery, the producer of the intercellular messenger GMP.

"This is the first definitive linking, we think, between cyclic GMP or cyclic AMP and any disease," Chader told SCIENCE NEWS, adding, "... what we are especially enthusiastic about is the possibility of our finding leading to an effective treatment for retinitis pigmentosa."

The link connecting cyclic GMP with retinitis pigmentosa appears to be related to the amount at birth of calmodulin, a protein that activates at least one form of phosphodiesterase (PDE) — the enzyme responsible for breaking down cyclic GMP in retinal cells. Both PDE and calmodulin help retinal cells adapt to light.

Studies of dogs with inherited red-cone dysplasia (an animal disease comparable to retinitis pigmentosa) and a control group revealed abnormally high retinal levels of cyclic GMP in the dysplastic dogs — levels high enough to damage retinal cells and impair vision. Comparison of the retinas for PDE activity and the effect of calmodulin levels on such activity showed a significant difference in the two groups at seven weeks of age (the onset of photoreceptor maturity). Calmodulin was found to be substantially decreased in diseased retinas as compared with control retinas. In addition, in the diseased dogs calmodulin continued to stimulate PDE activity even after seven weeks. In the control group, however, calmodulin activity stopped at seven weeks, allowing PDE to switch from its activator-dependent fetal form to an activator-independent adult form—that responsible for regulating cyclic GMP levels.

The researchers aren't sure what the initial cause of decreased calmodulin production is, but hypothesize that perhaps the autosomal recessive, autosomal dominant or sex-linked gene known to transmit retinitis pigmentosa might code for defective calmodulin. They plan to begin injecting calmodulin into the vitreous humor (fluid part of the eye in front of the retina) of dogs with rod-cone dysplasia in hopes that calmodulin will increase PDE activity, lower levels of cyclic GMP and delay retinal cell damage and vision loss. If calmodulin does counter rod-cone dysplasia, the researchers will then attempt to determine whether it can delay vision loss in retinitis pigmentosa patients. "If it works," says Chader, "super, wonderful. If it doesn't, we go on to something else." □



Cyclic GMP-PDE enzyme switches from activator-dependent to independent type in controls but not in diseased retinas, where calmodulin is decreased.

Irradiated mice — no changes

Twenty-one years ago, Jake Spalding began dosing 26-day-old mice with 200 rads of X-ray radiation (2,000 times more than the average tooth X-ray) and mating the male to his sister. Eighty-two successive generations of irradiated and sibling-mated mice later, Spalding still claims to have found no significant effects in the mice's ability to reproduce or in their susceptibility to mutation, compared with a control group. By the 75th generation, the irradiated mice actually showed a 33 percent increase in the number of animals contributing to the next generation, Spalding said. He found only two mutations: a hairless strain in the control group at the 31st generation, and a spastic mouse in the irradiated group after 23 generations. Spalding's work, conducted at the Los Alamos Scientific Laboratory's "Mouse House" in New Mexico, with grants from the Atomic Energy Commission, is the longest-running of its type.

But Earl L. Green, former director of the Jackson Laboratory in Bar Harbor, Maine, said that "if deleterious mutations are induced by radiation, they would be eliminated under a system of brother-sister mating." Green tried a similar experiment without inbreeding. After about 20 generations, he said, "We were not able to find evidence to support what we believe is true — that radiation produces mutations." □

Electrons get a kick out of laser light

The invention of the laser totally changed the science of optics. Some say it rescued optics in the nick of time, preventing it from becoming a closed science in which there was nothing left to be found, only technological applications to be sought. Since 1960 the thin red line of laser light (it now comes in other colors, too) has penetrated a large and varied number of the nooks and crannies of physics, chemistry and biology. The latest suggestion for laser applications, one of the largest nooks in physics and hardly a cranny, is particle acceleration.

In the July 23 PHYSICAL REVIEW LETTERS, T. Tajima and J. M. Dawson of the University of California at Los Angeles outline a means by which laser light could be used to impart great energy to electrons in a small space. Particle acceleration, the energizing of electrons, protons or ions to use as experimental probes, is basic to particle physics, nuclear physics and many investigations in solid-state and fluid physics. Getting it done in a short space would be a fundamental technical advance.

The standard method now used is to energize the particles with radio waves broadcast in special waveguides. To get an electron from very low energy (it's never a standing start) to 20 billion to 30 billion electron-volts requires a flight path measured in kilometers through a series of such accelerating sections. (The raw total length of the actual accelerating sections is less than the over-all two miles of the installation. There has to be room for magnets, etc.) Depending on electron conditions at the start, Tajima and Dawson suggest that their method could give a billion electron-volts in a centimeter of length or maybe 30 centimeters.

The method will work, they calculate — or rather their computer simulates — by shining light from one or possibly two lasers into a plasma of electrons. If there is a particular relationship between the frequency of the laser light (or the beat frequency of two crossed laser beams) and the plasma frequency of the electrons (the frequency at which they would normally oscillate in the plasma), the passage of the light leaves behind a "wake" in the plasma, a wave that traps electrons and carries them with it, imparting great energy to them as it goes forward. With current high power lasers (10^{18} watts per square centimeter) and a plasma density of 10^{18} particles per cubic centimeter, Tajima and Dawson say a billion volts in a centimeter could be achieved. A somewhat rarer plasma (10^{17}) would require 30 centimeters for a billion volts. Either would gladden the hearts of accelerator specialists if it is ever translated into a practical device. □