Monoclonal Antibodies Correct Severe Immune Deficiency

Monoclonal antibodies — mass-produced antibodies directed against highly specific targets — have opened radically new approaches toward the diagnosis and treatment of human disease (SN: 8/9/80, p. 85). Now they appear to provide an effective, practical treatment for the most serious of all the immune deficiency diseases — severe combined immunodeficiency (SCID). Ellis L. Reinherz and colleagues of Harvard Medical School report in the October PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES that they have successfully treated a SCID patient with them. This is the first published report of such a successful treatment in humans, according to Reinherz.

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David: Boy in a bubble.

Among the beneficiaries of the technique may be a previously untreatable SCID victim named David, who made international news because he lived in a germ-free bubble (SN: 11/12/77, p. 314). Last month David turned 11 years old. He is still living in a bubble and is the world's oldest uncured SCID patient. His physician and parents are keeping a close watch on the monoclonal antibody technique. If it proves effective in more patients, they may opt to try it on David, Baylor officials told SCIENCE NEWS.

While extremely rare, SCID is the most serious of the immunodeficiency diseases because victims are born lacking all the immune fighters the body needs to counter disease. Also, efforts to treat this swiftly fatal disease with donor bone marrow (a source of the needed immune cells) haven't been very successful because it's hard to find donors whose marrow immunologically matches that of the patient. And if the match isn't exact, immune cells in the donor marrow attack the recipient's cells as foreign objects, resulting in graft-versus-host disease, a killer in its own right. Consequently Reinherz and his colleagues tried a new treatment on a four-month-old female SCID patient with the same problem as David; she had no access to immunologically matched donor marrow.

They treated donor marrow with monoclonal antibodies directed against mature T cells in the marrow. These are the cells that cause mismatched marrow to produce graft-versus-host disease. They also treated the marrow with complement (proteins that help comprise the body's immune system). The antibodies plus complement stripped 99 percent of the culprit cells from the marrow, which was injected into the girl.

Despite elimination of nearly all mature T cells, she developed acute graft-versus-host disease 10 days later. The researchers injected monoclonal antibodies directed against the culprit T cells into her for the next five days; graft-versus-host disease ended. By six weeks after transplantation, precursor immune cells in the marrow had become functioning T and B cells in her body, and the new T cells had become accustomed to her body and did not react against it as the original mature T cells in the marrow had. She was removed from her germ-free environment and discharged from the hospital. She is currently healthy and appears to be cured of her SCID.

If the same technique is found to correct SCID in more patients, Reinherz and his team conclude, it should prove to be an effective, practical treatment for SCID patients who do not have matched donor marrow.

This development is important, says Robert A. Good, a leading immunologist formerly with the Memorial Sloan-Kettering Cancer Center in New York City and now with the Oklahoma Medical Research Foundation in Oklahoma City. Good and his co-workers have successfully treated nine SCID patients with a somewhat similar approach — cleansing mismatched donor marrow of culprit T cells by using plant lectins rather than monoclonal antibodies plus complement. Nonetheless, Good contends that "the monoclonal antibody approach will ultimately be the best one." The reasons, he explains, are that it has worked well in experimental animals, provides a uniform product that can benefit many patients and cleans marrow faster than lectins can.

—*J. A. Treichel*

X-ray flashes that catch surface waves

When a wave skims the surface of a crystal, the rows of atoms oscillate in time with the wave. British researchers, using the Daresbury Synchrotron Radiation Source as a stroboscope, have captured X-ray images of a wave's effect on a crystal's atoms. They also showed that tiny defects in a crystal's structure interact with waves, causing a loss of power. This novel technique, called stroboscopic X-ray topography, "has considerable potential for the study of periodic phenomena in crystals," they report in the Sept. 2 NATURE.

Roger W. Whatmore of Plessey Research Ltd. and Paul A. Goddard, Brian K. Tanner and Graham F. Clark of Durham University studied piezoelectric electronic devices, in which electrical signals excite a crystal's surface layers to move up and down periodically. These surface acoustic waves can be reconverted to electrical signals. Such devices act as high-frequency filters and signal processors in applications like television and radar. Crystal defects reduce the efficiency of these devices.

X-ray topography is a technique for looking at large-scale defects in crystals by examining the scattering pattern. The pattern from imperfect parts of a crystal is different from that due to the perfect parts. In the Daresbury technique, the required X-rays are emitted by high-energy, orbiting electrons as they accelerate in the bending magnets of a storage ring. Because the electrons come in bursts, the researchers can synchronize the generation of the acoustic waves with the illuminating pulses of radiation. Shifts in the normally regular pattern revealed in the X-ray images show the presence of crystal defects and their effect on surface waves. In the photographs, light areas correspond to regions under very small strain, while dark areas arise from planes of atoms where compression or rarefaction has occurred and the strain is high.

"Many of the things being done with synchrotron radiation sources are things that have been done with conventional X-ray sources," says Martin Blume, associate director of the Brookhaven National Laboratory in Upton, N.Y. However, synchrotron sources provide the time structure, extreme brightness and tunability so that many phenomena that can barely be demonstrated with conventional X-ray tubes become accessible, he says.

The British researchers write, "In addition to X-ray topography, several diffraction experiments can now be envisaged to study rapid periodic phenomena in such diverse materials as thin films, ceramics, powders, fibres, polymers or even biological materials." —*I. Peterson*