Pulling together a cluster theory of immune response

When stimulated by foreign material, immune system cells called B cells switch into action. They begin growing, dividing and developing specialized internal structures to produce antibodies to fight the invading substance. A team of Johns Hopkins School of Medicine scientists now offers a mathematical description of the mechanism they believe underlies this switch. They propose that the triggering signal results from the clumping of approximately 20 specialized molecules on the surface of the B cells.

This model, if proved correct, could help clinicians enhance or inhibit patients' immune responses. "Within 2 to 3 years, we should know if it will be useful," researcher Howard Dintzis predicts. The model might lead to prevention of autoimmune disease or of allergic reactions or stimulation of anticancer activity.

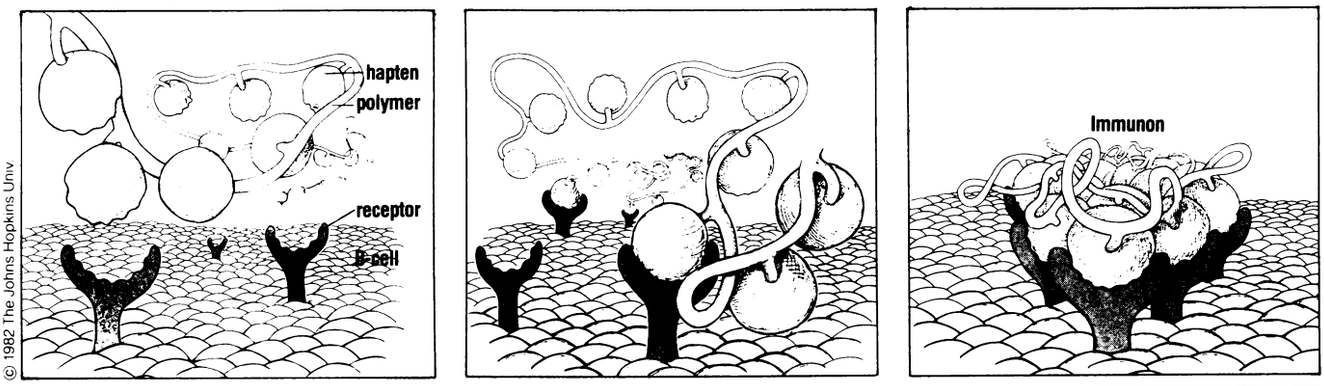
Dintzis and colleagues Renee Dintzis and Bert Vogelstein designed simple, synthetic molecules to investigate the trigger response. They linked together on a polymer small molecules, called haptens, which elicit antibody production only when attached to a larger carrier molecule. They expected to need a few haptens per molecule for a response, but 15 to 20 haptens per molecule were required. "It was a big surprise," Howard Dintzis told reporters in Baltimore.

According to the model, a foreign molecule, called an antigen, binds to receptors on the B cell surface. It then pulls the receptors into a continuous cluster, which the Hopkins scientists have named an "immunon." This model can explain what has been a puzzling aspect of immunology. High levels of antigen trigger less response than do more moderate amounts. Howard Dintzis explains that an overabundance of antigen would allow each receptor to bind to a separate antigen molecule, rather than to different sites on the same molecule. Under this condition the receptors would not be linked nor drawn together into an immunon.

In two papers to be published in the PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, the scientists described the theory and supporting evidence from experiments with living mice and samples of mouse spleen. "There is a remarkable correlation between our theory and experimental results," Howard Dintzis says.

The response of immunologists to their model has been bimodal, Howard Dintzis says. Those interested in molecular level biology are encouraging, while those who concentrate on more complex cellular phenomena are not. Dintzis and colleagues expect their model, if correct, to apply to the differentiation of other cells. "It is highly unlikely that nature has devised a special cell differentiation mechanism for the immune response," Howard Dintzis says. —*J. A. Miller*

As the first step in triggering antibody production, a synthetic molecule approaches receptors on the B cell surface, the hapten portions bind to the receptors and the molecule pulls about 20 receptors into a cluster.



Plasmaphoresis against lupus

Plasmaphoresis, a technique that allows plasma to be separated from red and white blood cells and discarded so that the patient can receive plasma from a donor, has been used experimentally against a number of autoimmune diseases. In these diseases, which range from myasthenia gravis (SN: 12/10/77, p. 391) to multiple sclerosis (SN: 1/30/82, p. 76), it is thought that antibodies in the plasma react against the body. At the American Heart Association's Ninth Science Writers Forum in Charleston, S.C., last week, Edmund J. Lewis of Rush-Presbyterian-St. Luke's Medical Center in Chicago reported that plasmaphoresis now looks promising as a treatment for systemic lupus erythematosus.

Lupus is an autoimmune disease in which antibodies form against a patient's DNA, and the antibody-DNA complexes then inflame the brain, heart, kidneys and other organs. Lupus is not a common disease, striking only 50 out of 100,000 people in the United States. But it is a disorder that afflicts young victims (mostly young women) and that causes significant morbidity and mortality in spite of anti-inflammatory drug treatment. Fifty percent of patients with severe lupus die within three years.

Lewis and his colleagues conducted a pilot study to determine whether plasmaphoresis could help 18 lupus patients over the short term and they found that it could. The treatment removed a large amount of damaging antibody-DNA complexes from the patients' blood and reduced their disease, especially in the kidneys.

Still to be determined are the long-term effects of plasmaphoresis on lupus and how they compare to those of standard anti-inflammatory drug treatment for the condition. Lewis and his colleagues, along with scientists at 11 other centers, will be conducting a seven-year trial on 200 lupus patients to answer these questions.

—*J. A. Treichel*

Robert Silberglied dies

Robert Silberglied, an entomologist with the Smithsonian's Tropical Research Institute in Balboa, Panama, died in the Jan. 13 crash of a jetliner in Washington, D.C. He was returning to Panama after participating in the annual meeting of the American Association for the Advancement of Science.

Before joining the Institute full time last year, Silberglied was a professor of biology at Harvard University and an associate curator at its Museum of Comparative Zoology. Silberglied, 35, had published 24 papers, mostly on the evolution of insect behavior, mimicry, and the relationship between insects and plants. His recent research on male butterfly color patterns resulted in a new hypothesis of butterfly courtship behavior, presented at the AAAS meeting (SN: 1/16/82, p. 38). In his memory, the Smithsonian is creating, through private contributions, a Robert Silberglied Memorial Fund "for research in tropical entomology." □