du Pont de Nemours and Co., for example, plan to set up a small nylon spinning and treatment operation in front of an APS beamline. By lighting up the process with bursts of x-rays, they hope to learn how nylon forms intermingled regions of crystalline and amorphous phases as it is spun—a structure that "has a huge influence on really important properties of the fiber," such as how it takes up dye, says DuPont researcher Randolph Barton Jr.

The narrow range of wavelengths in these bursts—their coherence—should be a boon to biologists and materials scientists who study molecular dynamics with so-called "speckle" measurements. In this technique, researchers train x-ray pulses on a sample and monitor the reflections. Because the x-rays are coherent, the reflections from an irregular sample should interfere with each other: constructively, to produce bright speckles, and destructively, to produce dark regions. Like the dapples on the ceiling of an indoor pool, these speckles contain information about the size and motion of "ripples" in the sample—say, the conformational oscillations of a protein in solution or the topographical fluctuation of a semiconductor's surface as the temperature changes.

Physicists and chemists in other fields also expect their samples to light up with new results, from studies of microscopic magnetic structures, say, or microchemical assays of trace elements. But Arthur Bienenstock, director of the Stanford Synchrotron Radiation Laboratory, cautions against trying to predict everything the APS's bright light will reveal. "All our experience indicates that once you provide a significant [improvement], there will be new science that you just didn't anticipate at all. Creative people will find new uses of the radiation."

–James Glanz

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IMMUNOLOGY

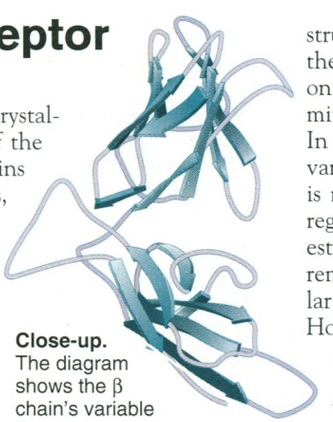
Taking a First Look at a T Cell Receptor

It isn't hard to understand why immunologists place such a high value on understanding the T cell receptor (TCR). Located on the surfaces of the immune system's T cells, this protein complex allows those crucial cells to recognize foreign proteins and initiate immune responses, including the responses needed to fight off pathogenic viruses. But even though researchers cloned the genes for the proteins that make up the T cell receptor in 1983, it has been frustratingly difficult to get a direct look at their three-dimensional structures—until now.

On page 1984, Graham Bentley and Ginette Boulot of the Pasteur Institute in Paris, Klaus Karjalainen at the Basel Institute for Immunology in Switzerland, and Roy Mariuzza at the University of Maryland present the first x-ray crystallographic structure of the β chain, which, along with the α chain, is one of the two proteins that form the site where the TCR recognizes antigens, or pieces of protein. "This is the first breakthrough in hard data on the TCR [structure]," says immunologist John Kappler of the National Jewish Center for Immunology and Respiratory Medicine in Denver.

Kappler cautions, however, that Bentley, Mariuzza, and their colleagues have solved only part of the receptor structure. The β chain, he points out, may look different when found in its normal tight association with the α chain. Still, other researchers will now be able to use the group's results to achieve the next step more quickly: solving the structure of the whole receptor, a feat that will help immunologists understand just how the TCR initiates immune responses. "Finally this problem is yielding to technology," says immunologist Ron Schwartz of the National Institute of Allergy and Infectious Diseases.

Indeed, before the collaborators could determine the β chain structure, they had to apply a technological fix to a problem that has long hindered efforts to obtain crystals of TCR proteins adequate for crystallographic analysis. A few of the amino acids in the proteins carry long chains of sugars, which hinder their ability to form crystals. To get around this problem, Karjalainen used the technique of site-directed mutagenesis to change some amino acids in the β chain into others to which carbohydrates can't be added—and struck lucky with a modified protein that yielded good crystals. This enabled the researchers to obtain the protein structure at a resolution of 1.7 angstroms, good enough to see the positions of all the atoms.



SOURCE: BENTLEY *ET AL.*

Close-up. The diagram shows the β chain's variable *(upper portion)* and constant regions.

The structure confirmed one thing immunologists had already suspected on the basis of the amino acid sequences of the T cell receptor proteins: The β chain's three-dimensional structure resembles that of the immunoglobulins, the proteins that form antibodies and which also bind specific antigens. Both the immunoglobulin and T cell receptor proteins have variable regions, which vary from one molecule to another and form the antigen binding site, plus constant regions, which are the same in all proteins of the same type. Earlier structural studies of the immunoglobulins showed that the sequences that make up each of these regions fold in a characteristic way: The strands weave back and forth, forming a pleated sheet that folds into a sandwichlike structure. The β chain also has this characteristic "immunoglobulin fold." And again as in the immunoglobulins, the amino acids that vary the most—and are thus likely to be involved in antigen binding—form small loops at the edge of the variable domain.

The TCR β chain structure does show some deviations from the immunoglobulin structure, however, and some of these differences may shed light on how the T cell receptor transmits signals to the cell's interior. In the β chain, for example, the variable domain of the molecule is much closer to the constant region. "I'm particularly interested in that elbow ... whether it remains that rigid," says molecular biologist Mark Davis of the Howard Hughes Medical Institute at Stanford University, whose group was among the first to clone a TCR gene. Both Davis and the authors speculate that this rigidity might be involved in telling the T cell that its receptor has bound an antigen.

How the hinge functions, however, is not at all clear. And that's only one of several questions remaining about T cell receptor structure and function. In particular, immunologists want to see the whole structure—β and α chains together—to confirm that the current structure is maintained in the dimer. As Kappler cautions, "Some of the unusual features might disappear when the α chain is there."

But the current work should help in snaring the entire structure. Crystallographer Pamela Bjorkman of the California Institute of Technology, who is also working on the T cell receptor structure, predicts that continuing the team's strategy of reducing carbohydrate binding by T cell receptor proteins "should allow the growth of well-ordered crystals" of the complete two-protein molecule. What's more, Kappler says, obtaining the three-dimensional structure of the β chain should help in solving the structure of the dimer, because knowing half the structure should make it easier to get the rest. And then, at last, immunologists should get a complete view of how the TCR works.

–Claire O'Brien

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