Thus the details of the chemical bonds that hold the peptide-MHC-I complexes together remained obscure, recalls Sacchettini, so "we could never figure out how the peptide was bound."

Scientists solved the problem with biotechnology. The researchers at Albert Einstein, for example, harnessed bacteria to mass-produce the two different protein chains that make up a complete MHC-I molecule, then combined the pieces with a peptide made by a virus called VSV. Wilson and his Scripps colleagues used another approach: They coaxed lab-grown fruit fly cells into manufacturing empty MHC-I molecules, which the researchers bound to viral peptides. The Harvard researchers, including Guo, harvested MHC-I molecules from human cells, scrubbed off the mix of peptides present, and paired the molecules with peptides from the influenza virus.

Crystallized and bombarded with X-rays, these materials yielded information that computers translated into several kinds of colorful, three-dimensional structural diagrams. The computer can create "space-filling" diagrams, for example, which show the atoms' intersecting electron clouds. Or it can depict a peptide's main chain and side chains as a network of thin tubes resembling a twisted, Tinker-Toy inchworm. Based on these computer models, the crystallographers can deduce the types of chemical bonds holding the entire structure together.

Previously, low-resolution X-ray studies of MHC-I molecules had suggested the importance of the ends of the peptide main chain, Madden says. Also, a series of biochemical experiments had demonstrated the role of certain amino-acid side chains in strong peptide binding and immune-system response. But the latest round of papers powerfully confirmed the scientists' emerging ideas about the binding mechanisms of MHC-I molecules.

Most intriguing to immunologists is that the colorful computer portraits reveal what MHC-I molecules and their peptides "look like" to the body's T-cells. When MHC-I molecules on a cell display foreign peptides — called antigens — their outward-facing side chains constitute a large part of the cell's distress signal to the immune system. Evidence suggests that buried peptide side chains may warp the MHC-I molecule and that this warping also helps to bind T-cells, the body's first line of defense against nonself cells.

Immunologists would like to know which parts of an MHC-I molecule bound to an antigen activate T-cells, causing them to multiply and attack the infected cell. However, researchers have yet to crystallize and image peptide-MHC-I complexes bound to T-cells.

Such a feat would have important implications for immunology, notes Per A. Peterson, a senior researcher at the Scripps Research Institute. "If you understand the MHC molecule-peptide binding *and* its interaction with the T-cell receptor, you'll be better off in designing improved vaccines," he says.

Researchers offer various examples of how detailed structural knowledge of the MHC-I molecule and its interaction with T-cells might provide practical benefits. Germain, for example, explains that such knowledge might enable immunologists to engineer a vaccine that confers immunity to different strains of the same basic type of virus. Some researchers are now exploring this idea, he notes.

Another, more speculative scenario would require complete understanding of the MHC-I system — including processes that occur long before the MHC molecules reach the cell surface. Based on the way cells chop up and display viral proteins, researchers might predict which peptides MHC-I molecules would most likely display to the immune system. A vaccine based on these peptides, matched to a person's particular complement of MHC-I proteins, might confer immunity to specific viruses.

"That would certainly be quite a goal," says Scripps' Wilson, who remains skeptical of these speculations. He notes that a lot of poorly understood cellular processes work together to break proteins down into peptides and display them to T-cells. The recent structural studies, though impressive on their own, only explain the middle cogs in this machinery.

"Our understanding of the MHC molecule and how it works is really very good now," he says. "But we don't yet understand the presentation to T-cells, and we don't understand the processing of proteins inside the cell and how particular sequences end up being presented."

Despite these important gaps, understanding of the MHC-I molecule has advanced rapidly since 1987, when scientists at Harvard University first glimpsed its convoluted architecture.

"There's really been such an incredible progression from even four years ago to now, where we understand at the atomic level how peptides are presented by the MHC," says Madden. "We're just now seeing what the T-cells have been seeing for all these years."

And although crystallographic pictures of the MHC-I molecule don't lead directly to new vaccines, knowing the basic chemical rules of antigen presentation to the immune system is important.

"If you want to do things on a rational basis, you need the details," Germain maintains. "And the details come from structural studies." □

News of the Week continued from p.71

Life at other stars: A matter of climate

Among the glittering denizens of the heavens, which stars are most likely to support life? Researchers had previously concluded that stars at least 2 billion years old, with a surface temperature and mass similar to those of the sun, might form planets capable of fostering life. A new study suggests that a group of stars with slightly lower mass and surface temperature has an equally good chance of creating life-sustaining planets.

Results of the study, which uses a computer model to determine the climate of planets near a variety of stars, could help guide NASA's Search for Extraterrestrial Life (SETI) (SN: 11/7/92, p.317), says James F. Kasting of Pennsylvania State University in University Park. He and his colleagues, Daniel P. Whitmire of the University of Southwestern Louisiana in Lafayette and Ray T. Reynolds of NASA's Ames Research Center in Mountain View, Calif., report their work in the January ICARUS.

The researchers restricted their study to possible planets that would contain liquid water — an ingredient deemed essential for life — and that would have an atmosphere similar to Earth's. They also assumed that stars capable of forming planets would space those bodies logarithmically, as in the solar system.

In determining the "continuously habitable zone" around a particular star class — the region in which climate is temperate and stable long enough to sustain life — the team took into account the intensity and variation of radiation emitted by different star types. A planet forming too close to a given star loses water due to heating and photodisassociation, while a planet too far away will be frozen. Because more massive stars burn more intensely, their habitable zone begins farther out, notes Kasting.

The study supports previous findings that sun-like stars, classified as G stars, are good candidates for producing life. The team discovered that K stars, which have 70 percent of the sun's mass, may make equally good candidates. The team suggests that it may be wise, as SETI progresses, to look for telltale radio signals among nearby K stars rather than more distant G stars.

David R. Soderblom of the Space Telescope Science Institute in Baltimore says he has included some K stars in a list of stars for the SETI survey. But it is difficult to determine whether a given K star is old enough to have supported the evolution of multicellular organisms. Soderblom says that with improved star-dating techniques on the horizon, the new report may convince him to add more K stars to the SETI survey. — *R. Cowen*