New study focuses on protein dynamics

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A discovery by associate professor of chemistry and biochemistry Brian Baker and his research group at the University of Notre Dame reveals the importance of dynamic motion by proteins involved in the body's immune response. Results of the study were published in *Immunity*, the leading research journal in the field of immunology.

Scientists have long known that receptors on the immune system's T-cells are important for discovering and destroying cells that are infected with viruses or other pathogens. Baker's group studied cross-reactivity, the ability of different T-cell receptors which number perhaps a few hundred million in the body to recognize the vastly larger number of possible antigens produced by other cells. The process is important for dealing with viruses, cancers, autoimmunity, transplant rejection and other issues related to the immune system.

Most past studies considered the receptors on each cell as static components, but in fact the molecules move and adopt multiple structures. Baker's group found that the success or failure of the T-cell receptor to attach to a target cell's antigen involves complex movements in search of a compatible final structure. Different antigens produce different kinds of motion.

"What we're adding to the equation is how motion is involved," Baker said. "It both complicates as well as simplifies how we think about recognition. Different extents of motion can exist when you have different antigens being presented. It complicates our thinking about how diversity is presented to the immune system, yet simplifies our thinking about how diversity is accommodated by the immune system.

"Overall, we've got to consider flexibility when we think about structures in the immune system and structures in biology in general."

The static view long-favored in structural biology is shifting to a greater emphasis on protein dynamics, he says. For example, scientists have discovered that vaccines can help the immune system fight cancer, but vaccines that mimic biological structures can still fail if they do not take into account flexibility and dynamics.

"It probably will be one of the defining areas of biochemistry over the next 10 to 15 years - getting at the role of how biological molecules move and how that movement influences biology," Baker said.

Provided by University of Notre Dame