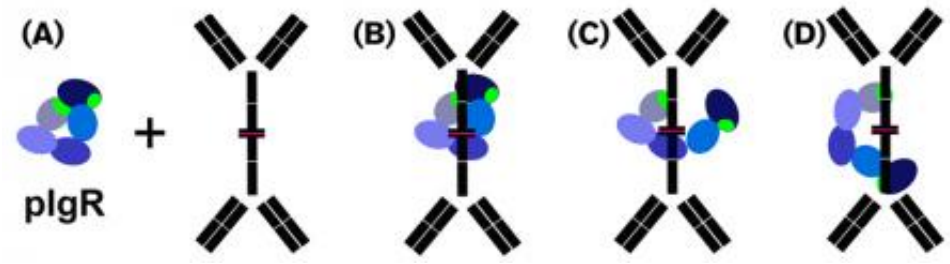
Multitasking protein keeps immune system healthy

September 2 2016, by Lori Dajose



Simplified diagram of pIgR binding to an antibody. A) pIgR and an antibody. B) Recognition binding. pIgR chemically recognizes an antibody. C) Conformational change. The pIgR protein opens up. D) The bound state of pIgR and an antibody. Credit: B. Stadtmueller

The polymeric immunoglobulin receptor, or pIgR, is a multitasking protein produced in the lining of mucosal surfaces, such as the intestines. It plays a pivotal role in the body's immune functions by sequestering bacteria and by assisting antibodies—large proteins that can identify and neutralize specific bacteria and viruses. Now, scientists at Caltech have determined the three-dimensional structure of pIgR, providing important insights into how the protein keeps the immune system running smoothly.

Beth Stadtmueller, a postdoctoral scholar in the laboratory of Centennial Professor of Biology Pamela Björkman, is the first author on two recent papers describing the findings.

"Proteins such as pIgR are folded into complicated shapes," says Stadtmueller. "Having a complete model of a protein is analogous to an architectural model of a building showing scaled dimensions of walls, the locations of windows and doors, angles of the roof, and so on. Understanding the structure of this protein provides information on how it carries out normal functions while also providing a basis to rationally engineer modified proteins with enhanced functions, which could be used as therapeutics."

The pIgR protein is best known for attaching to antibodies and ferrying them from the bloodstream to the interior of the intestines, where the antibodies can neutralize pathogens. In mammals such as humans, the group discovered that pIgR looks like five round beads—biologists call these regions "domains"—that are connected to form a tightly closed, triangle-shaped loop. The group also showed that upon encountering an antibody, the pIgR molecule opens up—like changing from a fist to an open hand—to enclose around the antibody and to transport it into the intestines.

While pIgR is crucial for helping antibodies to function, the protein also has disease-fighting abilities of its own. For example, some molecules of pIgR are released into the intestines where they alone engage bacteria, such as pneumonia-causing Streptococcus pneumoniae.

The group also studied the structures of pIgR from fish and birds, to see how the protein has changed as vertebrates evolved. In fish, pIgR has only two domains and forms a straight line. In birds, an evolutionary intermediary between fish and humans, the protein has four domains. The group was surprised to find that the shape of the bird pIgR is not fixed in a closed loop or a straight line—it can change freely between closed and open configurations, and can grasp antibodies much like the human protein.

"The human pIgR is like a door that has to be unlocked to open, whereas the bird pIgR is constantly opening and closing like a revolving door," Stadtmueller says. "These are very different structures, which are likely to support functions unique to each protein."

"The immune system has changed considerably as vertebrates have evolved," she adds. "Studying pIgR in a spectrum of vertebrates illustrates how the protein architecture has changed to support species-specific defense systems. It helps us to understand why certain immune system functions have evolved and provides a foundation to test their contributions to specific states of health and disease."

More information: Beth M Stadtmueller et al. The structure and dynamics of secretory component and its interactions with polymeric immunoglobulins, *eLife* (2016). DOI: 10.7554/eLife.10640

B. M. Stadtmueller et al. Biophysical and Biochemical Characterization of Avian Secretory Component Provides Structural Insights into the Evolution of the Polymeric Ig Receptor, *The Journal of Immunology* (2016). DOI: 10.4049/jimmunol.1600463

Provided by California Institute of Technology