Scientists discover how common vaccine booster works

May 21 2008

In an online paper in the journal *Nature*, Yale University researchers funded by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, explain how a common ingredient in many vaccines stimulates and interacts with the immune system to help provide protection against infectious diseases.

Vaccines must possess not only the bacterial or viral components that serve as targets of protective immune responses, but also ingredients to kick start those immune responses. In many vaccines, the bacterial or viral components themselves have this capability. For other vaccines, the immune system requires an added boost. Adjuvants are those substances added to a vaccine to help stimulate the immune system and make the vaccine more effective.

Currently the only vaccine adjuvants licensed for general use in the United States are aluminum hydroxide/phosphate formulations, known as alum. Although alum has been used to boost the immune responses to vaccines for decades, no one has known how it worked.

In this paper, the Yale team, led by Richard Flavell, M.D., Ph.D., and Stephanie Eisenbarth, M.D., Ph.D., examined the immune system pathway and cell receptors used by alum. Many microbial compounds function as adjuvants by stimulating Toll-like receptors. These receptors identify microbial invaders and alert the body to the presence of a disease-causing agent, or pathogen. Alum, however, does not stimulate Toll-like receptors.

The Yale team found that alum stimulates clusters of proteins called inflammasomes, found inside certain cells. Inflammasomes respond to stresses such as infection or injury by releasing immune cell signaling proteins called cytokines. Inflammasomes are a component of the innate immune system that operates in parallel with, but separate from, Toll-like receptors, also part of the innate immune system.

To make this determination, Dr. Eisenbarth and her coworkers used mice that had been genetically engineered to be deficient in various components of a specific type of inflammasome, characterized by the presence of the protein termed Nalp3. The team demonstrated that an immune response did not occur in those animals with the deficient Nalp3 inflammasomes, despite the inclusion of alum, while it did occur in normal mice. The team's findings provide the first convincing evidence that the Nalp3 inflammasome forms the basis for alum's adjuvant action.

According to the study authors, several unanswered questions remain regarding how activation of this pathway controls a highly specific and long-lasting immune response generated by a vaccine. But this new information on the molecules that alum uses to activate the innate immune system should provide the keys to better understanding adjuvant function and should facilitate the design of new vaccine adjuvants.

Source: National Institute of Allergy and Infectious Diseases