Scientists find a key to immune system's ability to remember

October 23 2006

The human immune system is a peerless memory bank. Its ability to accurately catalog and recall long past encounters with viruses, bacteria and other pathogens is why we only get the measles or chicken pox once, and is why exposure to deactivated virus particles in vaccines confers protection from disease.

But how that memory system works -- how it acts at the finest level of detail to thwart the pathogens that invade our bodies -- is not well understood. Now, however, an international team of scientists has ferreted out an important clue to how the key cells of the immune system are able to remember old foes and quickly mount a response to hold them at bay.

Writing this week (Oct. 23, 2006) in the *Proceedings of the National Academy of Sciences* (PNAS), a team of researchers led by University of Wisconsin-Madison researcher Marulasiddappa Suresh identify the role of a protein that is important in stimulating the cells of the immune system, whose role is to take quick and effective action when agents of disease reinvade the body.

"We have found at least a part of how the immune system remembers its encounters," says Suresh, a professor of pathobiological sciences in the UW-Madison School of Veterinary Medicine. "We now know one of the reasons why we get such a quick (immune) response" when we are exposed to pathogens we've experienced before.

The new insight is important not only because it sheds light on the biochemical intricacies of immune system memory, but also because it may one day aid in the development of vaccines against infections like AIDS, and help victims of autoimmune diseases and transplant patients whose immune systems reject donor organs.

The protein, which scientists call Lck, is essential for immune system T cells -- white blood cells that attack virus-infected cells, foreign cells and cancer cells -- to cement the memory induced by cell surface sensors known as antigen receptors that act to identify the signatures of pathogens like measles virus and HIV, agents that hide inside cells.

Lck is important in helping "naive" T cells -- those cells that have never been exposed to a particular pathogen -- capture the receptor template of the invading agent and store it for future reference. Among the millions of naïve T cells, there are a few that are primed for active duty against an individual infectious agent. Following infection or vaccination, Lck initiates a biochemical chain of events that vastly increases the number of T cells that march off to combat the invader.

After the infection subsides, the number of T cells marshaled to fight that agent decreases dramatically. But a smaller subset, known as "memory" cells, retains the imprint of its previous encounter should the pathogen make a return appearance.

According to the study, while Lck primes naïve cells to fight a pathogen, it is not required by memory cells, which initiate the fast and furious response when that same pathogen comes calling again years later. Unlike naïve T cells, which are confined to the lymphatic system, memory T cells are found everywhere in the body, enabling them to sense and react more quickly when an infectious agent is reencountered.

"Now we know one of the reasons we get such a quick response and

clearance (of the pathogen) with reinfection," Suresh explains. "If you increase the size of your army, you can clear your enemies faster. The memory T cells are greater in number and they are more potent."

The new insight could help refine therapeutic targets to treat autoimmune diseases and may inform new strategies for suppressing T cell response after transplantation. Now, transplant patients require life-long regimens of drugs to suppress immune response to the foreign cells in the donated organ.

Source: University of Wisconsin-Madison