Scientists find molecular switch that creates long-term immunity

July 13 2015

Australian researchers have identified a protein responsible for preserving the antibody-producing cells that lead to long-term immunity after infection or vaccination.Professor David Tarlinton (left), Dr Kim Good-Jacobson (right) and colleagues from Melbourne's Walter and Eliza Hall Institute discovered the presence of a protein called Myb was essential for antibody-producing plasma cells to migrate into bone marrow, preserving them for many years or even decades. Their findings were published in the *Journal of Experimental Medicine*. Credit: Walter and Eliza Hall Institute

Melbourne researchers have identified a protein responsible for preserving the antibody-producing cells that lead to long-term immunity after infection or vaccination.

Dr Kim Good-Jacobson, Professor David Tarlinton and colleagues from the Walter and Eliza Hall Institute discovered the presence of a protein called Myb was essential for antibody-producing plasma cells to migrate into bone marrow, preserving them for many years or even decades. Their findings were published in the *Journal of Experimental Medicine*.

Dr Good-Jacobson said plasma cells were created when the immune system was exposed to pathogens such as viruses or bacteria. "When our immune system encounters a new pathogen, it can create plasma cells that secrete antibodies to specifically prevent future infections, generating immunity," she said.

"Our bone marrow is like a long-term storage facility for plasma cells, allowing them to continue producing antibodies to protect against future infections. Until now, it was not known why some plasma cells moved into the bone marrow, while others remained in the blood stream and perished after a few days."

The research team discovered that when the gene that produces the protein Myb was removed, plasma cells were no longer able to move into the bone marrow to provide long-term immunity. "Myb is a type of protein called a transcription factor, which binds to DNA and, in effect, switches genes 'on' or 'off'," Dr Good-Jacobson said.

"We found that if a plasma cell produced Myb at some stage during an immune response, then those plasma cells had the ability to migrate into the bone marrow. If we can understand how to flip the molecular switch

in plasma cells and activate Myb production, we might be able to encourage the immune system to create long-term immunity for a range of infections."

Plasma cells are created during an immune response in temporary structures called germinal centres, Dr Good-Jacobson said. "Germinal centres act as a rapid proto-typing facility, improving the design of antibodies to better recognise invading pathogens in the future," she said. "The Myb protein marks the plasma cells that produce high-quality antibodies for preservation."

Professor Tarlinton said the discovery would mean researchers could now search for the trigger of Myb production and find out what genes Myb controls. "Now that we know Myb is critical in creating long-term immunity, we can begin dissecting the pathways it uses to mark plasma cells for storage and the genes involved in migrating to the bone marrow," he said.

"Some pathogens, such as malaria, typically trigger the creation of short-lived plasma cells. If we don't create long-lived plasma cells, we don't develop lasting immunity to the disease. If we can trigger the expression of Myb in plasma cells responding to pathogens - either by infection or by immunisation - we might be able to convince the immune system to store these plasma cells in the bone marrow to offer protection against future infections."

More information: *Journal of Experimental Medicine*, jem.rupress.org/content/212/7/1001.abstract

Provided by Walter and Eliza Hall Institute