



MULTIPLE SCLEROSIS NEWS TODAY

Key Pathway in Antibody B-Cell Production Identified, Important to Diseases like MS

By: Patricia Inacio, Ph.D | May 5, 201

Scientists discovered two key players — **TBK1** and **ICOS** — that control the effective production of antibodies and may offer new insights into potential therapies for autoimmune diseases, including multiple sclerosis. The study, “A TRAF-like motif of the inducible costimulator ICOS controls development of germinal center TFH cells via the kinase TBK1,” was published in the journal *Nature Immunology*.

Follicular helper T-cells (Tfh cells) are a rare type of T-cells with key functions in our immune system. Specifically, they promote the proliferation of antibody-producing cells, called B-cells.

A research team at La Jolla Institute for Allergy and Immunology discovered the signal that drives maturation of Tfh cells, from an immature to a mature state in which they are fully functional. The signal is an enzyme called **TANK-binding kinase 1 (TBK1)**, the researchers reported in a study led by La Jolla Institute Professor Shane Crotty, PhD, and Instructor Kok-Fai Kong, PhD. TBK1 controls the maturation of antibodies by associating with a second partner, the **Inducible T cell Co-Stimulator (ICOS)**.

ICOS was previously reported as an essential factor for most Tfh cell functions, but its mechanisms were unknown. A better and deeper understanding of ICOS will allow scientists to manipulate and achieve more specific antibody production. This could lead to more efficient **vaccines** and better treatments for immune disorders like multiple sclerosis.

“Tfh cells have recently been recognized as important players in the immune system, and we now know they are essential for almost all antibody responses. Tfh cells control the whole process of generating high affinity antibodies, and ICOS is a receptor molecule strongly required for Tfh cells to work. Understand ICOS better, and you can make more Tfh when needed, and block it when not needed,” Dr. Crotty said in a press release.

“We were looking to find out a specific signaling pathway that impacted ICOS. There is a family of such checkpoint molecules like ICOS, but ICOS has a capability that is not shared with other checkpoint molecules. Its ability to drive antibody differentiation is found only in ICOS, and not in other family members. The connection between ICOS and TBK1 provides important clues to this mystery,” Dr. Kong added.

Researchers in this study discovered that ICOS recruits the signaling TBK1 enzyme to induce **high-affinity antibody** production. The team was able to identify the region in the ICOS molecule that recruits TBK1, and confirmed it with functional studies — by disrupting this area, scientists prevented the association between ICOS and TBK1, which severely affected Tfh cells and antibody production.

They are now focusing on trying to understand how to diminish ICOS signals as a strategy for autoimmune diseases, and how to increase them to develop more effective vaccines.