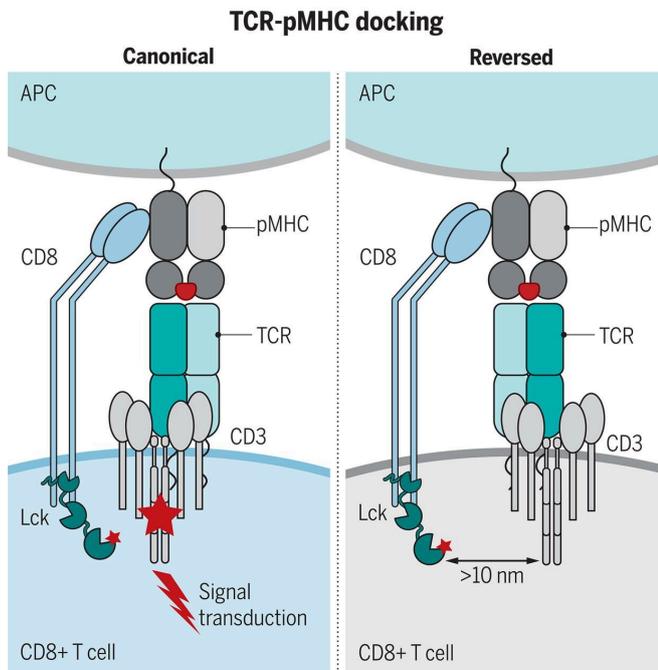


Fundamental advance in understanding T cell immunity

4 June 2021



The canonical polarity of TCR–pMHC docking is essential for colocalization of CD3 and coreceptor-associated Lck and for productive TCR signaling. Schematic shows how canonical TCR–pMHC recognition colocalizes Lck and CD3, driving TCR-mediated signaling. By contrast, a reversed TCR–pMHC recognition polarity mislocalizes Lck and CD3, impeding signaling. Credit: *Science* (2021). DOI: 10.1126/science.abe9124

Monash University researchers have provided a fundamental advance regarding how T cells become activated when encountering pathogens such as viruses.

The recent study, published in *Science*, co-led by Professor Nicole La Gruta, Professor Jamie Rossjohn and Professor Stephanie Gras with first author Dr. Pirooz Zareie from the Monash Biomedicine Discovery Institute, have found that T Cells need to recognize pathogens in a particular

orientation in order to receive a strong activating signal.

T cells play a key role in the immune system by eliminating invading pathogens, such as viruses, and it is crucial to understand the factors that determine how and why T cells become activated after recognizing these pathogens.

T cells express on their surface a T cell receptor (TCR) that recognizes and binds to virus fragments (antigens) presented by infected cells. This recognition event can lead to T cell activation and killing of infected cells.

"The central issue is that there are millions of different T cell receptors (TCRs) in the human body, and a vast array of viruses, making it difficult to understand the rules around how T cell receptor recognition of a virus drives T cell activation. Indeed, it is a problem that has remained contentious for over 25 years," says Professor La Gruta.

"Our study has shown that the orientation in which the T cell receptor binds is a primary factor determining whether the T cell receives an activating signal," Professor La Gruta said.

"This is an advance in our fundamental understanding of how a T cell needs to 'see' pathogenic antigens in order to be activated," she said. "It has clarified a critical mechanism essential for effective T cell immunity. It is also relevant to the ongoing development of immunotherapies that aim to boost the activation of T cells."

Dr. Pirooz Zareie stated: "a combination of technologies, including super-resolution microscopy, X-ray crystallography at the Australian Synchrotron, biochemical assays and using in vitro and in vivo experimental models from a variety of labs led to the findings."

More information: Pirooz Zareie et al, Canonical T cell receptor docking on peptide–MHC is essential for T cell signaling, *Science* (2021). [DOI: 10.1126/science.abe9124](https://doi.org/10.1126/science.abe9124)

Provided by Monash University

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