

VACCINE AND INFECTIOUS DISEASE DIVISION

Crystal structure and functional model of a $\gamma\delta$ T-cell receptor

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A defining characteristic of the immune system's T cells is their ability to recognize fragments of foreign protein, known as antigens, and respond by producing compounds that amplify the immune response or kill infected cells. Most types of T cells rely on other immune cells to process and present the foreign proteins on their surface for the T cells to recognize. However, a rare class of T cells, known as $\gamma\delta$ T cells, behave in a different fashion. These cells are able to recognize antigens directly, and can also recognize and respond to certain proteins made by the body itself. While prior research suggests that the receptors on $\gamma\delta$ T cells are similar in sequence to those found on other T cells, little is known about their precise structure or function, and how they mediate immune responses.

To address these questions, researchers from the laboratory of VIDD member Dr. Roland Strong, in collaboration with the laboratory of CRD member Dr. Thomas Spies, determined the crystal structure of the human $\gamma\delta$ T-cell receptor $\delta 1A/B-3$. They discovered that while the overall structure of this receptor is similar to other known T-cell receptors, its precise conformation in the regions that mediate protein binding had an unusual conformation. They demonstrated that $\delta 1A/B-3$ interacts with the human proteins MICA and MICB, which are expressed in response to cellular stress and in some types of tumors. Interestingly, MIC proteins also interact with the protein NKG2D, another type of immunoreceptor expressed by $\gamma\delta$ T cells. Through analysis of potential models of interaction, the researchers determined that the interactions of MIC proteins with the two $\gamma\delta$ T cell receptor types are mutually exclusive and probably occur sequentially. This work establishes one of the first models of this class of $\gamma\delta$ T cells' interaction with target cells.

Xu B, Pizarro JC, Holmes MA, McBeth C, Groh V, Spies T, Strong RK. **Crystal structure of a $\{\gamma\delta\}$ T-cell receptor specific for the human MHC class I homolog MICA.** *Proc Natl Acad Sci U S A*. 2011 Feb 8;108[6]:2414-9.



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