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Crystal Structure of m157, A Viral Antigen that Directly Engages Ly49 Natural Killer (NK) Cell Receptors. Z.S. Juo, E. J. Adams, L.L. Lanier & K.C. Garcia; HHMI/Stanford Univ., Stanford, CA 94305.

NK cells provide a first line of defense against infections. They display both activating and inhibitory receptors on their surface to survey the expression level of major histocompatibility complex (MHC) class I molecules and other antigens of the target cells. Persistent viruses, such as cytomegalovirus (CMV), have developed specific mechanisms to evade immune response by the NK cells. We report here the 2.0Å crystal structure of m157, a decoy protein produced by mouse CMV that is currently the only known viral antigen that directly engages both activating and inhibitory Ly49 receptors of murine NK cells. Although morphologically resembling the canonical MHC class I molecule, m157 deviates from the MHC structures more than other known homologues. One striking feature of m157 is that the helices on the top of platform are positioned closely to each other, leaving no room for peptide presentation. One section of a helix is unwound in a manner strikingly similar to the murine non-classical MHC T22. Since m157 lacks beta-2 microglobulin, which normally associates with mammalian MHC, m157 relies on an extended helix bridging the alpha1/alpha2 platform and the alpha3 stem in order to enforce a tight packing that results in an overall more compact molecule. We predict that m157 will engage with the Ly49 NK cell receptors in a manner different from that by canonical MHC molecules, and discuss companion cellular and functional data probing this interaction.