Structures of MHC-I/Tapasin and MHC-I/TAPBPR Describe the Mechanism of Peptide Loading Antigen Presentation

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MHC molecules of the class I type (MHC-I) bind to endogenous peptides in the endoplasmic reticulum and the peptide-loaded MHC-I molecules are subsequently transported to the cell surface where they serve as indispensable ligands for T cell and NK cell development and function. Peptide loading occurs in the ER within the peptide loading complex (PLC) in which critical aspects of MHC-I stabilization and peptide loading are dependent on the chaperone, tapasin. However, MHC-I molecules can also be loaded independently of the PLC by a tapasin homolog designated TAPBPR. To elucidate mechanistic aspects of PLC-dependent and independent peptide loading we have determined the X-ray crystal structures of MHC-I with tapasin and compare that with previously reported the structure of a MHC-I/TAPBPR complex (Jiang, et al., Science 2017, 358, 1064-68). These structures capture distinct chaperone-stabilized MHC-I conformation, and provide insight into the mechanism of PLC-dependent and PLC-independent MHC-I peptide loading. (Supported by the Intramural research program of the NIAID, NIH)