The Length Distribution of Class I-Restricted T Cell Epitopes Is Determined by Both Peptide Supply and MHC Allele-Specific Binding Preference - DTU Orbit (08/11/2017)

The Length Distribution of Class I-Restricted T Cell Epitopes Is Determined by Both Peptide Supply and MHC Allele-Specific Binding Preference

HLA class I-binding predictions are widely used to identify candidate peptide targets of human $CD8^+$ T cell responses. Many such approaches focus exclusively on a limited range of peptide lengths, typically 9 aa and sometimes 9-10 aa, despite multiple examples of dominant epitopes of other lengths. In this study, we examined whether epitope predictions can be improved by incorporating the natural length distribution of HLA class I ligands. We found that, although different HLA alleles have diverse length-binding preferences, the length profiles of ligands that are naturally presented by these alleles are much more homogeneous. We hypothesized that this is due to a defined length profile of peptides available for HLA binding in the endoplasmic reticulum. Based on this, we created a model of HLA allele-specific ligand length profiles and demonstrate how this model, in combination with HLA-binding predictions, greatly improves comprehensive identification of $CD8^+$ T cell epitopes.

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