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Advancing MHC-Peptide Binding Prediction with Two-Dimensional Interaction Maps and Vision Transformer

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The binding of short peptides derived from antigenic pathogens to major histocompatibility complex (MHC) is a fundamental and highly selective mechanism in adaptive immunity. By binding peptide fragments to its groove, MHC enables T cells to recognize the source pathogens, thereby initiating the adaptive immune response. Accurate prediction of the binding affinity between MHC-peptide pairs is crucial for understanding the mechanism of immune response. Furthermore, it can contribute to the identification of novel immunogenic epitopes, which can serve as potential targets for immunotherapy.

Most existing computational tools are trained on one-dimensional sequential inputs to predict binding specificity of peptide-MHC pairs. However, these approaches do not adequately capture the high-order interactions between sequences. To address this limitation, our model employs a two-dimensional modeling to create interaction maps, representing the complex spatial interactions patterns between amino acids from the peptide and MHC. The generated interaction maps are subsequently used to predict the binding between MHC class Ⅰ/Ⅱ and peptides through Vision Transformer (ViT) model.

In addition, we constructed three distinct types of interaction maps of each binding pair based on BLOSUM62 substitution matrix, amino acid interaction frequencies, and pre-trained embeddings from ESM2 model. These different kinds of maps were used as inputs to a three-channel ViT model. By applying the self-attention mechanism to these diverse interaction representations, our model can detect the core binding spot involved in MHC-peptide binding from various perspectives. This multi-view approach offers significant insights into the interpretability of our model.

In conclusion, we predicted the binding specificity between MHC class Ⅰ/Ⅱ molecules and peptides, and highlighted the model's interpretability across various interaction representations. Our research has the potential to aid the discovery of immunogenic biomarkers and contribute to the development of immunotherapies.