The interplay of sequence conservation and T cell immune recognition

Predicting which peptides can elicit a T cell response (i.e. are immunogenic) is of great importance for many immunological studies. While it is clear that MHC binding is a necessary requirement for peptide immunogenicity, other variables exist that are incompletely understood. In this study we examined the hypothesis that conservation of a peptide in bacteria that are part of the healthy human microbiome leads to a reduced level of immunogenicity due to tolerization of T cells to the commensal bacteria. This was done by comparing experimentally characterized T cell epitope recognition data from the Immune Epitope Database with their conservation in the human microbiome. Indeed, we did see a lower immunogenicity for conserved peptides conserved. While many aspects how this conservation comparison is done require further optimization, this is a first step towards a better understanding T cell recognition of peptides in bacterial pathogens is influenced by their conservation in commensal bacteria. If the further work proves that this approach is successful, the degree of overlap of a peptide with the human proteome or microbiome could be added to the arsenal of tools available to assess peptide immunogenicity.

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