T-cell recognition is shaped by epitope sequence conservation in the host proteome and microbiome - DTU Orbit (08/11/2017)

T-cell recognition is shaped by epitope sequence conservation in the host proteome and microbiome

Several mechanisms exist to avoid or suppress inflammatory T-cell immune responses that could prove harmful to the host due to targeting self-antigens or commensal microbes. We hypothesized that these mechanisms could become evident when comparing the immunogenicity of a peptide from a pathogen or allergen with the conservation of its sequence in the human proteome or the healthy human microbiome. Indeed, performing such comparisons on large sets of validated T-cell epitopes, we found that epitopes that are similar with self-antigens above a certain threshold showed lower immunogenicity, presumably as a result of negative selection of T cells capable of recognizing such peptides. Moreover, we also found a reduced level of immune recognition for epitopes conserved in the commensal microbiome, presumably as a result of peripheral tolerance. These findings indicate that the existence (and potentially the polarization) of T-cell responses to a given epitope is influenced and to some extent predictable based on its similarity to self-antigens and commensal antigens.

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