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Prediction and characterization of helper T cell epitopes from pneumococcal surface adhesin A (PsaA)

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Despite several recent advances, Streptococcus pneumoniae is still a leading cause of morbidity and mortality among very young, elderly and immunocompromised individuals all over the world. Pneumococcal surface adhesin A (PsaA) is a multifunctional lipoprotein present on all known serotypes of S. pneumoniae and is significantly involved in bacterial adherence and virulence. Mutations in PsaA reduce growth, virulence, and adherence of pathogen. Moreover, this protein inhibits complements activation, binds lactoferrin, and elicits protective systemic immunity against pneumococcal infection. Identification of PsaA peptides that optimally bind human leukocyte antigen (HLA) would greatly contribute to global vaccine efforts, but this is hindered by the multitude of HLA polymorphisms. We used an experimental data set of 28 PsaA synthetic peptides and in silico methods to predict peptide binding to HLA and murine major histocompatibility complex (MHC) class II. We also characterized spleen- and cervical lymph node (CLN)-derived helper T lymphocyte cytokine responses to these peptides after S. pneumoniae strain EF3030-challenge in mice. Individual, yet overlapping peptides, 15 amino acids in length revealed residues 231 to 268 of PsaA consistently caused the highest IFN-γ, IL-2, IL-5, IL-17 responses and proliferation as well as moderate IL-10 and IL-4 responses by ex vivo stimulated splenic and CLN $CD4^+$ T cells isolated from S. pneumoniae strain EF3030-challenged F_1 (B6 x BALB/c) mice. IEDB, RANKPEP, SVMHC, MHCPred, and SYFPEITHI in silico analysis tools revealed that peptides PsaA231-268 also interact with a broad range of HLA-DP, -DQ, and -DR alleles. These data suggest that predicted MHC class II-peptide binding affinities not only correlate with T helper (Th) cytokine and proliferative responses to PsaA peptides, but when used together with in vivo validation can be a useful tool to choose candidate pneumococcal HTL epitopes.

Biography

Dr. Pranav Gupta completed his PhD in Viral Immunology from All India Institute of Medical Sciences, India in 2012. Currently, he is working as a postdoctoral fellow at the Morehouse School of Medicine in Atlanta. He has published four peer-reviewed papers and a chapter in book. Dr. Gupta is working on the development of a peptide-based vaccine capable of inducing broad and protective immune responses against Streptococcus pneumoniae, a microbial pathogen of global importance.

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