VAC_08 - Identification of Core Immunogenic Peptides of *Shigella sonnei* for a Peptide-Based Vaccine

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Introduction: Shigella figures among the top five genera associated with gut infections, with four species causing 165 million cases and 1 million associated deaths worldwide. *S. flexneri* used to be of major concern in Latin America (LA) and Asia, but *S. sonnei* isolates are steadily more common and less susceptible to antibiotics in LA. There are no licensed vaccines for *Shigella*, but 11 are under clinical trials. A peptide-based vaccine would reduce the potential for reactogenicity and a quadrivalent chimera could provide protection against all serotypes.

Objective: Identify and evaluate surface peptides common to *S. sonnei* strains according to their localization, immunogenicity, promiscuity using the EpitoCore pipeline.

Methodology: With EpitoCore Docker (github.com/fiuzatayna/epitocore) we located S. sonnei Complete Genomes in NCBI's Genome Assembly Summary and extracted the available proteomes. We then used a subcellular localization predictor (PsortB) and transmembrane domain (TM) predictor (TMHMM) to look for proteins with Outer Membrane localization and either valid TMs or predicted to be outside of the cell. CMG Biotools clustered these proteins and IEDB's MHC Class II binding predictor estimated their binding affinities to 27 HLA alleles. EpitoCore picked the strongest HLA binders (top 0.02% peptides in the Consensus Percentile Rank) to select the remaining clusters and provided a minimal set of TM or external high-affinity binder promiscuous peptides by crossing the outputs of the aforementioned softwares. Subsequently, we compared the minimal peptide set to other *Shigella* proteomes as well as to Homo sapiens proteins.

Results: We located five valid S. sonnei proteomes. PsortB and TMHMM identified 348 outside or external proteins (~70 from each proteome) from the 21539 proteins (~4.2k each proteome). CMG Biotools produced 85 clusters and EpitoCore worked with 21 of those based on the HLA binding affinity. Within this set of 262 peptides, EpitoCore pointed to a minimal set of seven external or outside peptides that strongly bind to at least 10 HLA alleles besides being found in all five strains. *Shigella* species contain four of the seven peptides, with *S. dysenteriae* being the least represented and absent for three peptides. Human proteins contain partial matches to four peptides (<= 60% coverage).

Conclusion: We identified a set of seven highly immunogenic external promiscuous *S. sonnei* core peptides using EpitoCore scripts. These peptides may not be restricted to the 10 HLA alleles, since they bind with moderate to high strength to other MHCs, potentially triggering immune responses in a greater number of individuals. Not only are they core S. sonnei peptides, but are also found in other *Shigella* species, which indicates a prospect for cross protection. We want to further assess cross-reactivity to human proteins due to the partial matches identified as well as perform allergenicity evaluations.

Keywords: *Shigella sonnei*; Reverse Vaccinology; Panproteomics