HIGHLY CROSS-CONSERVED BURKHOLDERIA T CELL EPITOPES GENERATE EFFECTOR T CELL RESPONSES *IN VITRO*

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Key Words: Burkholderia, immunoinformatic, T cell epitope, effector immunity, vaccine

Burkholderia pseudomallei and Burkholderia mallei cause glanders and melioidosis, respectively. Both of them are classified as Category B biothreat agents due to their high infectivity and potential use as a bioweapon. The related species Burkholderia cepaciae causes fatal 'cepacia syndrome' in cystic fibrosis patients, which is characterized by rapid deterioration, bacteremia and necrotizing pneumonia. Clinical eradication of Burkholderia infection often fails due to antimicrobial resistance. Effective vaccination against Burkholderia infection is critically important to protect populations living in endemic areas worldwide and against bioterror threats. No vaccines or other prophylactics for these pathogens are available. Vaccines against Burkholderia should target cell-mediated immune response, which is believed to be essential to successfully clear Burkholderia infection. We hypothesize that a single vaccine comprising highly cross-conserved Burkholderia T cell epitopes might generate protective cell-mediated immune response against all the three species. Immunoinformatics tools were used to identify immunogenic consensus sequences (ICS) that are enriched for promiscuous and highly conserved CD4+ T cell epitopes in all three Burkholderia species. The ICS peptides were validated in peripheral blood mononuclear cells (PBMCs) derived from healthy donors [1].

All of the peptides (100%) bound to at least two HLA alleles, 98% bound to at least three HLA alleles, 98% bound to at least four HLA alleles and 92% bound to all seven HLA alleles. The overall predictive accuracy was 81% (both positive and negative) [2]. Significant IFNγ response was induced by all peptides in at least one human donor as measured by IFNγ ELISpot assay. 86% of the peptide-specific IFNγ ELISpot responses were completely inhibited by antibody block of HLA-DR, indicating that these peptides are HLA-DR-restricted. Significant peptide-specific proliferation and Th1 cytokine production (IFNγ, TNFα and IL-2) in CD4+ T cells from healthy donors were observed in flow cytometry analysis. Immunoinformatics predictions, coupled with in vitro validation, can accelerate the selection of highly conserved T cell epitopes from genome sequence databases. The approach can be used for rapid selection of vaccine candidates for a wide array of emerging infectious diseases and biodefense targets.

References:

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