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IN SILICO PREDICTION OF IMMUNOGENIC T CELL EPITOPES OF LEISHMANIA DONOVANI GP63 PROTEIN: AN ALTERNATIVE APPROACH FOR ANTI-PARASITE VACCINE DEVELOPMENT

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Visceral leishmaniasis (VL) is a major parasitic childhood disease in sub-Saharan Africa. Expensive and toxic anti-leishmanial drugs are current control methods. Safe, effective and cheap vaccines are potentially powerful strategies to control VL. Traditional vaccine development techniques have failed to deliver an effective vaccine. *Leishmania* vaccine development may benefit from immunoinformatics tools. This paper describes an improved in silico prediction method for immunogenic *Leishmania donovani GP63* protein t cell epitopes as VL candidate vaccines. Using the EpiMatrix algorithm, the amino acid sequence of *Leishmania donovani GP63* protein (GenBank accession: ACT31401) was screened for putative t cell cluster epitopes that would bind to the most common HLA (human leukocyte antigen) class II alleles among at-risk populations. Nine epitopes were initially identified using EpiMatrix. Based on cluster score, number of EpiMatrix hits, hydrophobicity, and number of EpiBars (an EpiBar is a 9 amino acid frame predicted to bind at least 4 different HLA molecules), four peptides (P1-P4) were selected for synthesis. In a proof of concept study, blood samples from consenting healthy, leishmanin skin test (LST) reactive and non-reactive volunteers were stimulated and IFN-γ, (Interferon gamma) IL-4 (Interleukin 4), and IL-10 were measured. IFN-γ and IL-4 levels were similar in both groups. However, mean IL-10 levels were significantly reduced in LST reactive individuals. To evaluate whether cross-reactivity with the human genome (HG), the human gut microbiome (HM) and common human pathogens (HP) was responsible for these differences, the sequences of the evaluated peptides were screened using JanusMatrix. One of the peptides (P1), which increased IL-10 in the LST reactive volunteers, showed high cross-reactivity with HG, suggesting that P1 might induce a regulatory immune response in humans. In conclusion, immunoinformatics tools provide a promising alternative approach for anti-parasite vaccine development. Data obtained can be used in the development of epitope-based *Leishmania* vaccine.

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