VAC_10 - Peptides for a polyeptide anti-leishmanial vaccine

Prisciliana Jesus de Oliveira[2]; Paloma Napoleão Pêgo[1]; David William Provance Junior[1]; Salvatore Giovanni de Simone[1]; Eduardo Fonseca Pinto[2]; Adriano Gomes da Silva[2].
[1]Fiocruz/CDTS
[2]Fiocruz/IOC

Introduction: About 20 species of Leishmania cause different forms of leishmaniasis: cutaneous, mucosal, diffuse and visceral. Leishmaniasis can be fatal and affects neglected populations in at least 4 endemic regions worldwide. Although this fact, there is currently no vaccine available for human use. Peptide or subunit vaccines have been widely investigated as anti-leishmanial vaccine candidates. In addition to several advantages such as industrial scale production, this platform allows the combination of the most appropriate epitopes to design a pan- specific vaccine. The cross-protection against different clinical forms of leishmaniasis sought by this type of vaccine may be beneficial from an economic, health system, manufacturing and epidemiological perspective. In a previous reverse vaccinology analysis, we selected two Leishmania cysteine proteins with vaccine target properties.

Objectives: The aim of this work is to select epitopes from these proteins to construct a pan-specific leishmaniasis vaccine prototype.

Methodology: We used the following criteria for epitope mining: antigenicity, predicted immunogenicity, low similarity to human peptide sequences, sequence conservation and homology within the Leishmania genus. The selected peptides comprised a construct based on a TGP protein core whose three-dimensional structure was solved in Alphafold. Our selection methodology consisted of the synthesis of the respective protein epitopes by spot synthesis, immunoblotting with sera from patients cured of cutaneous leishmaniasis, in silico assays: antigenicity, prediction of BCR and HLAII and I binding epitopes and HLA binding diversity, domain and sequence conservation by alignment, and homology.

Results: As result we selected 15 antigenic epitopes that were potentially immunogenic and diverse in terms of HLA binding, with sequences in domains and regions conserved in the genus Leishmania and with low similarity to human sequences. The three-dimensional structure of the polyprotein resulting from the insertion of these peptides into the TGP core was stable, with linear and well-positioned epitopes.

Conclusion: We concluded that these epitopes met all the criteria we had set for the composition of the pan- specific anti-leishmaniasis vaccine approach.

Keywords: Anti-leishmaniasis vaccine; Peptides; Polyprotein