PEPTIDE VACCINES AGAINST FUNGI CAUSING SYSTEMIC DISEASE. THE *PARACOCCIDIOIDES BRASILIENSIS* QUEST.

Luiz R. Travassos, Alexandre Marques, Maria A. Juliano, Leo K.Iwai, Carlos P. Taborda

Universidade Federal de São Paulo, INCOR and Universidade de São Paulo

The major antigenic molecule of *Paracoccidioides brasiliensis* eliciting humoral and cellular responses is the 43,000 Da glycoprotein (gp43). While the epitopes of B cells are still under study, the epitope eliciting a T cell response has been mapped to a 15-mer peptide called P10. Both gp43 and P10 induce a CD4+ type 1 T-helper response, producing IFN-□ and IL-2. They also showed a protective effect against intratracheal challenge by virulent yeasts of *P. brasiliensis.* P10, QTLIAIHTLAIRYAN, is presented by IA molecules of three mouse haplotypes, and by 21 of 25 HLA-DR alleles as predicted by Tepitope algorithm. The promiscuous presentation of this peptide made it a good candidate for a peptide vaccine against paracoccidioidomycosis (PCM). We confirmed the protection effect of P10 in experiments where mice were infected i.t. and submitted to chemotherapy, with or without P10 immunization. Chemotherapy alone was effective but elicited a prevailing Th-2 response. P10 immunization potentiated treatment maintaining a prevalent Th-1 response as measured by the production of IFN-γ and IL-12. It also protected against relapsing disease in mice previously treated with sulphamethoxazole. P10 was also effective in reversing a state of deep immunosuppression in mice, induced by prolonged administration of dexamethazone, suggesting that it may be useful even in anergic cases. A comparison of P10 with homologous sequences from beta-1,3-glucanases of *Histoplasma capsulatum*, *Blastomyces dermatitidis* and *Aspergillus nidulans* showed that the corresponding sequences had predicted presentations by HLA-DR alleles of 5/25, 3/25 and 18/25 respectively. Therefore, P10 is still the most promiscuous peptide and a strong candidate for adjuvant vaccination in PCM patients submitted to chemotherapy.

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