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Immunomodulatory functions of defensins, innate molecules, as mucosal adjuvant with the peptide antigens of HIV-1 at the mucosal surfaces

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Introduction: The mechanisms of resistance to HIV infection in the human oral cavity are incompletely understood while salivary components have been implicated in protection. There are growing evidences that human defensin peptides originating in the oral epithelial cells may be playing an important role in the prevention of HIV infection.

Methodology: We have synthesized HIV and Defensin peptides and their corresponding analogues by making some modifications in the natural sequence. We have done Anti HIV, Anti-microbial and other characteristic study of defensins to prove them active. Then, immunized theses formulations in Outbred and Two different Inbred mice (H^{2b}, H^{2d}) through IN route using Microsphere as delivery vehicle. We have studied Humoral Response of HIV peptides with and without Defensins by estimating antibody levels (IgG/IgA) in the serum as well as in lung, intestinal, vaginal and rectal washes till day 120. For cell mediated immune response, peptide specific T cell proliferation and cytokine/chemokine levels were studied in the cells isolated from the three different mucosal sites i.e. spleen, lamina propria and peyer's patches of the primed mice. Simultaneously, we have done Cytolytic activity analysis, by estimating IFN-γ/Perforin secretion by CD4+ also through FACS, which was checked by IFN- γ/Perforin secretion.

Result & Discussion: The HIV peptides alone in microsphere showed low peptide specific response of peak titre in sera and different washes while the presence of defensins increased significantly this titre both in sera (1,02,400-4,09,600) as well as in washes (800-12,800) ($p<0.05$) Very interestingly, we have found that the cellular immunogenicity of all the HIV peptides with defensin peptides in different formulations showed a significantly higher (upto 2 fold ranging from 10-50 stimulation index) ($p<0.001$) proliferation response as compared to HIV peptide alone. The cytokine measurement profile showed mixed Th1 and Th2 type of immune response. The FACS analysis data revealed that $CD8^+$/ $CD4^+$ T cells showed significantly higher Cytolytic activity in the HIV with Defensin peptide formulations. Surprisingly, $CD4^+$ T-cells were also showing Cytolytic property.

Conclusion: We have shown from the present study that these defensin peptides and their analogues are markedly enhanced the antigen specific immune response even at very low concentration. Thus, the results reported here demonstrate the effectiveness of synthetic defensin peptide analogues to induce strong and long lasting humoral and cellular immune response through intranasal route using PLG- microsphere as a delivery vehicle. Our findings may have implications in the development of new antiviral agent for AIDS therapy.

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