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Novel strategy for generation of mucosal immune responses against HIV-1 following systemic vaccination

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from 2006 International Meeting of The Institute of Human Virology
Baltimore, USA. 17–21 November, 2006

Published: 21 December 2006

Retrovirology 2006, **3**(Suppl 1):S30 doi:10.1186/1742-4690-3-S1-S30

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A significant hurdle in effective vaccine design for infectious pathogens is the ability to mount immune responses at the portal of entry, namely mucosal sites. The development of a systemic-delivered vaccine approach driving secretory IgA and mucosal T cell immune responses against pathogens would fundamentally change many vaccine strategies. Using mucosal pathogens HIV-1 and Influenza A as models, we demonstrate that a novel systemic administered DNA vaccination strategy utilizing co-delivery of specific mucosal-derived chemokine adjuvants, can produce distal mucosal immune responses. This strategy resulted in redirection of α4β7 and CCR9 or CCR10 positive immune cells to the site of immunization with mucosal re trafficking phenotype. The immune phenotype included enhanced cytokine and cytolytic markers expressed by antigen-specific T cells from the spleen, lung and lamina propria, as well as elevated IgG and secretory IgA responses in secondary lymphoid organs, B cells from the gut, peripheral blood and fecal extracts. Systemic immunization controls, as expected, failed to induce mucosal immunity. These studies have great significance for basic understanding of gut lymphocyte homing, mucosal phenotype commitment and development of vaccine strategies for mucosal pathogens. This work is supported by F32AI054152 to MAK, and N01-A1-15429, NIAID-HVDDT to DBW.