S49-6 CTL-based influenza vaccine

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The current vaccination strategy against influenza is to induce the production of antibodies directed against surface antigens of viruses. However, the frequent changes in the surface antigens of influenza viruses allow the viruses to avoid antibody-mediated immunity. On the other hand, it is known that cytotoxic T-lymphocyte (CTL) populations directed against internal antigens of influenza A virus are broadly cross-reactive to influenza virus subtypes. In the present study, CTL epitope peptides derived from internal antigens of influenza viruses were coupled to liposomes and induction of protection against infection with influenza viruses was investigated using HLA-transgenic mice. HLA-A*0201-binding CTL epitopes predicted among amino-acid sequences of six coding regions—M1, NP, PA, PB1, PB2, and NS—in influenza viruses were coupled to liposomes. Immunization with liposomal conjugates of the CTL epitope peptides in HLA-A*0201 transgenic mice induced significant antigen-specific $CD8^+$ T-cells and CTLs and successfully suppressed replication of both H1N1 and H3N2 influenza viruses in the lung in the mice. The CTL epitopes employed in the present study are contained not only in the seasonal influenza viruses but also in the currently emerging swine-origin influenza A (H1N1) virus. These results suggest that liposome-coupled CTL epitope peptides derived from highly conserved internal antigens of influenza viruses might be applicable for the development of broadly protective influenza vaccines.