



ORAL PRESENTATION

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In vivo immunogenicity of Tax (11-19) epitope in HLA-A2/DTR transgenic mice: implication for dendritic cell-based anti-HTLV-1 vaccine.

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Viral oncoprotein Tax plays key roles in transformation of human T-cell leukemia virus (HTLV-1)-infected T cells leading to adult T-cell leukemia (ATL), and is the key antigen recognized during HTLV-associated myelopathy (HAM). In HLA-A2+ asymptomatic carriers as well as ATL and HAM patients, Tax (11-19) epitope exhibits immunodominance. Here, we evaluate CD8 T-cell immune response against this epitope in the presence and absence of dendritic cells (DCs) given the recent encouraging observations made with Phase 1 DC-based vaccine trial for ATL. To facilitate these studies, we first generated an HLA-A2/DTR hybrid mouse strain carrying the HLA-A2.1 and CD11c-DTR genes. We then studied CD8 T-cell immune response against Tax (11-19) epitope delivered in the absence or presence of Freund's adjuvant and/or DCs. Overall results demonstrate that naturally presented Tax epitope could initiate an antigen-specific CD8T cell response in vivo but failed to do so upon DC depletion. Presence of adjuvant potentiated Tax (11-19)-specific response. Elevated serum IL-6 levels coincided with depletion of DCs whereas decreased TGF- β was associated with adjuvant use. Thus, Tax (11-19) epitope is a potential candidate for the DC-based anti-HTLV-1 vaccine and the newly hybrid mouse strain could be used for investigating DC involvement in human class-I-restricted immune responses.

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