2011

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Retrovirology, London, v.8 (Suppl 1), p. A114, 2011
http://www.producao.usp.br/handle/BDPI/34836

RETROVIROLOGY

MEETING ABSTRACT Open Access

HTLV-1 Tax Specific CD8+ T cells express low levels of Tim-3 in HTLV-1 infection: implications for progression to neurological complications

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From 15th International Conference on Human Retroviruses: HTLV and Related Viruses
Leuven and Gembloux, Belgium. 5-8 June 2011

Background

Most patients with HTLV-1 infection are asymptomatic, however 3% of individuals develop a progressive neurological disorder, HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP). Factors leading to this complication are not well defined, but are associated with high levels of pro-virus and cytolytic T cells. During chronic viral infections, virus-specific CD8+ T cells undergo altered patterns of differentiation and can become restrained from effector activity. We hypothesized that suppression of immune receptors T cell immunoglobulin and mucin domain-containing protein 3 (Tim-3) and PD-1 would result in partial reversal of a T cell restraint profile. In turn this increased cytolytic activity may mediate neuro-immunopathology of HAM/TSP.

Methods

We investigated the expression of Tim-3 and PD-1 on T cells in 22 serially recruited HTLV-1 asymptomatic and HAM/TSP patients and 7 HTLV-1-seronegative matched controls, their distribution on HTLV-1-specific T cells and the relationship with T cell function.

Results

Using flow cytometry, we found that patients with HAM/TSP had significantly lower levels of Tim-3+ PD-1- expressing CD8+ (p=0.002) and CD4+ (p=0.004) T cells compared to healthy uninfected controls. HTLV-1 Tax11-19, HLA-A*02 restricted CD8+ T cells among HAM/TSP individuals expressed markedly lower levels of Tim-3. Furthermore, we found that the frequency of Tim-3 expressing Tax11-19 specific CD8+ T cells inversely correlated with the number of IFN-γ secreting cells in response to the Tax Tax11-19 peptide.

Conclusions

We propose that this low expression of Tim-3 on HTLV-1 Tax-specific T cells may lead to persistent and deleterious effector T cell pool, resulting in more inflammation and disease progression.

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Published: 6 June 2011

doi:10.1186/1742-4690-8-S1-A94
Cite this article as: Leal *et al.*: HTLV-1 Tax Specific CD8+ T cells express low levels of Tim-3 in HTLV-1 infection: implications for progression to neurological complications. *Retrovirology* 2011 **8**(Suppl 1):A94.

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