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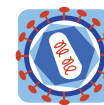
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HTLV-1 Tax Specific CD8+ T cells express low levels of Tim-3 in HTLV-1 infection: implications for progression to neurological complications

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MEETING ABSTRACT

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

Fabio E Leal^{1,2*}, Lishomwa C Ndhlovu³, Aaron M Hasenkrug³, Aashish R Jha³, Karina I Carvalho¹, Ijeoma G Eccles-James³, Fernanda R Bruno¹, Raphaella G Vieira³, Vanessa A York³, R Brad Jones⁴, Yuetsu Tanaka⁵, Walter K Neto⁶, Sabri S Sanabani⁶, Mario A Ostrowski⁴, Aluisio C Segurado², Douglas F Nixon³, Esper G Kallas^{1,2}

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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.

Author details

¹Division of Clinical Immunology and Allergy School of Medicine, Universidade de Sao Paulo, Brazil. ²Department of Infectious Diseases School of Medicine Universidade de Sao Paulo, Sao Paulo, Brazil. ³Division of Experimental Medicine, Department of Medicine, University of California, San Francisco, CA, 94110, USA. ⁴Department of Immunology, University of Toronto, Medical Sciences Building, King's College Circle, Toronto, ON M5S 1A8, Canada. ⁵Department of Immunology, University of the Ryukyus, Okinawa, 903-0215, Japan. ⁶Molecular Biology Laboratory, Fundação Pro-Sangue, Hemocentro de Sao Paulo, Sao Paulo, Brazil.

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* Correspondence: fabioit@meridionalrd.com

¹Division of Clinical Immunology and Allergy School of Medicine, Universidade de Sao Paulo, Brazil

Full list of author information is available at the end of the article