RETROVIROLOGY

MEETING ABSTRACT Open Access

NFkB activation promotes immune activation in HTLV-I-associated myelopathy / tropical spastic paraparesis

Matthew McCormick[1], Unsong Oh[1], Dibyadeep Datta[1], Richard Turner[1], Kathryn Bobb[2], Dileep Monie[2], Drago R Sliskovic[3], Jie Zhang[2], Jeffrey Meshulam[2], Steven Jacobson[1*]

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

Evidence suggests that HTLV-I-induced immune activation plays a key role in the pathogenesis of HAM/TSP. The HTLV-I-encoded transactivating protein Tax is known to activate nuclear factor kappa B (NFkB), a key host signaling pathway regulating immune response, but the contribution of the NFkB pathway to the immune activation associated with HAM/TSP has yet to be fully defined. We examined NFkB activation in peripheral-blood mononuclear cells (PBMC) from subjects with HAM/TSP, and tested the effect of NFkB inhibition on key ex vivo correlates of immune activation in HAM/TSP.

We examined the role of NFkB activation during immune activation associated with HAM/TSP by using small molecule NFkB inhibitors, including a newly developed selective inhibitor of NFkB, PBS-1086.

NFkB activation was assessed in peripheral-blood mononuclear cells (PBMC) from subjects with HAM/TSP and in healthy donors (HD). Nuclear translocation of the NFkB RelA was significantly higher in PBMC from subjects with HAM/TSP compared to HD ($p=0.032$) following short-term (20 h) culture, indicating increased activation of the NFkB pathway in HAM/TSP. Treatment with the small molecule inhibitor PBS-1086 reduced NFkB activation ($p<0.01$). PBS-1086 reduced expression of CD25 and CD69 in HAM/TSP PBMC as well as phosphorylation of STAT5 in a dose-dependent manner ($p<0.01$ for all). PBS-1086 also inhibited spontaneous lymphoproliferation of HAM/TSP PBMC in a dose-dependent manner ($p=0.0286$). PBS-1086 treatment resulted in a mean proviral load reduction of 20% compared to untreated PBMC in a 72 h culture

These results indicate that NFkB activation plays a critical upstream role in the immune activation associated with HAM/TSP, and identify the NFkB pathway as a potential therapeutic target for immune modulation in HAM/TSP.

Author details
[1]Neuroimmunology Branch, National Institute of Neurological Diseases and Stroke, National Institutes of Health, Bethesda, MD, USA. [2]Profectus Biosciences, Inc., Baltimore, MD, USA. [3]IDSC, Chelsea, MI, 48118, USA.

Published: 6 June 2011

doi:10.1186/1742-4690-8-S1-A117
Cite this article as: McCormick *et al.*: NFkB activation promotes immune activation in HTLV-I-associated myelopathy / tropical spastic paraparesis. *Retrovirology* 2011 **8**(Suppl 1):A117.

Submit your next manuscript to BioMed Central and take full advantage of:

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at
www.biomedcentral.com/submit

BioMed Central

* Correspondence: jacobsons@ninds.nih.gov
[1]Neuroimmunology Branch, National Institute of Neurological Diseases and Stroke, National Institutes of Health, Bethesda, MD, USA
Full list of author information is available at the end of the article

BioMed Central

© 2011 McCormick et al; licensee BioMed Central Ltd. This is an open access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/2.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.