



MEETING ABSTRACT

Open Access

# NF- $\kappa$ B hyper-activation by HTLV-1 Tax induces cellular senescence, but can be alleviated by the viral anti-sense protein HBZ

Huijun Zhi<sup>1</sup>, Liangpeng Yang<sup>1</sup>, Yu-Liang Kuo<sup>1</sup>, Yik-Khuan Ho<sup>1</sup>, Hsiu-Ming Shih<sup>2</sup>, Chou-Zen Giam<sup>1\*</sup>

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

Activation of I- $\kappa$ B kinases (IKKs) and NF- $\kappa$ B by the human T lymphotropic virus type 1

(HTLV-1) trans-activator/oncoprotein, Tax, is thought to promote cell proliferation and transformation. Paradoxically, expression of Tax in most cells leads to drastic up-regulation of cyclin-dependent kinase inhibitors, p21CIP1/WAF1 and p27KIP1, which cause p53-/pRb-independent cellular senescence. Here we demonstrate that p21CIP1/WAF1-/p27KIP1-mediated senescence constitutes a checkpoint against IKK/NF- $\kappa$ B hyper-activation. Senescence induction by Tax is attenuated by mutations in Tax that reduce IKK/NF- $\kappa$ B activation and prevented by blocking NF- $\kappa$ B using a degradation-resistant mutant of I- $\kappa$ B $\alpha$  despite constitutive IKK activation. Small hairpin RNA-mediated knockdown indicates that RelA induces this senescence program by acting upstream of the anaphase promoting complex and RelB to stabilize p27KIP1 protein and p21CIP1/WAF1 mRNA respectively. Finally, we show that downregulation of NF- $\kappa$ B by the HTLV-1 anti-sense protein, HBZ, delay or prevent the onset of Tax-induced senescence. We propose that the balance between Tax and HBZ expression determines the outcome of HTLV-1 infection. Robust HTLV-1 replication and elevated Tax expression drive IKK/NF- $\kappa$ B hyperactivation and trigger senescence. HBZ, however, modulates Tax-mediated viral replication and NF- $\kappa$ B activation, thus allowing HTLV-1-infected cells to proliferate, persist, and evolve. Finally, inactivation of the senescence checkpoint can facilitate persistent NF- $\kappa$ B activation and leukemogenesis.

#### Author details

<sup>1</sup>Department of Microbiology and Immunology Uniformed Services, University of the Health Sciences, Bethesda, MD, 20814, USA. <sup>2</sup>Institute of Biomedical Sciences, Academia Sinica, Taipei, 115, Taiwan.

Published: 6 June 2011

doi:10.1186/1742-4690-8-S1-A200

Cite this article as: Zhi et al.: NF- $\kappa$ B hyper-activation by HTLV-1 Tax induces cellular senescence, but can be alleviated by the viral anti-sense protein HBZ. *Retrovirology* 2011 **8**(Suppl 1):A200.

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](http://www.biomedcentral.com/submit)



\* Correspondence: [cgiam@usuhs.mil](mailto:cgiam@usuhs.mil)

<sup>1</sup>Department of Microbiology and Immunology Uniformed Services, University of the Health Sciences, Bethesda, MD, 20814, USA  
Full list of author information is available at the end of the article