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Aurélien Riquet, Sébastien Chevalier, Julien Villaudy, Louis Gazzolo, Jean Pierre Vartanian, et al.. Human T-cell leukemia virus type 1 (HTLV-1) Tax oncoprotein induces DNA damages through Activation-Induced cytidine Deaminase (AID). 16th International Conference on Human Retroviruses: HTLV and Related Viruses, Jun 2013, Montreal, Canada. pp.045, 10.1186/1742-4690-11-S1-O45 . inserm-00924959

HAL Id: inserm-00924959

<https://inserm.hal.science/inserm-00924959v1>

Submitted on 7 Jan 2014

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ORAL PRESENTATION

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Human T-cell leukemia virus type 1 (HTLV-1) Tax oncoprotein induces DNA damages through Activation-Induced cytidine Deaminase (AID)

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From 16th International Conference on Human Retroviruses: HTLV and Related Viruses
Montreal, Canada. 26-30 June 2013

How T cells are transformed by HTLV-1 is still unclear, but it is well accepted that the viral oncoprotein Tax is associated with genomic instability of infected cells. Tax has recently been shown to directly induce, in T cells, the expression of AID (Ishikawa *C et al.*, *Carcinogenesis*, 2011), a cytidine deaminase whose physiologic expression is usually restricted to B cells, in which it initiates class-switch recombination and somatic hypermutations to reshape the primary antibody repertoire after antigen encounter. It is also well established that AID-mediated mutations outside of immunoglobulin gene locus are involved in the oncogenic transformation of B lymphocytes. Besides its role in B cell lymphomagenesis, AID was recently proposed to play a key role in different human cancers linked to chronic inflammation, or in cancers associated with infectious agents. We first confirmed that both Tax⁺ and HTLV-1-infected T-cell lines, but not uninfected T cells expressed *aid* mRNA as well as AID protein. We further demonstrated that, primary CD4⁺ T cells and MOLT-4 T-cell line transduced with lentiviral vector expressing Tax expressed high level of AID. More importantly, we also observed a high level of *aid* in splenic T lymphoma cells obtained from HTLV-1-infected humanized Rag2^{-/-}gamma c^{-/-} mice that have developed lymphomas. We demonstrate that AID up-regulation in T cells is associated with DNA damage accumulation. Finally, inhibiting AID expression by small hairpin RNA strategy strongly decreases Tax-induced DNA damages. Altogether our data strongly

suggest that AID is involved in DNA damages and genomic instability of HTLV-1-infected T-cells.

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Published: 7 January 2014

doi:10.1186/1742-4690-11-S1-O45

Cite this article as: Riquet et al.: Human T-cell leukemia virus type 1 (HTLV-1) Tax oncoprotein induces DNA damages through Activation-Induced cytidine Deaminase (AID). *Retrovirology* 2014 11(Suppl 1):O45.

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