

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

Aurélien Riquet, Sébastien Chevalier, Julien Villaudy, Louis Gazzolo, Jean-Pierre Vartanian, Renaud Mahieux, Madeleine Duc-Dodon, Nathalie Bonnefoy

► **To cite this version:**

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. *Retrovirology*, 11 (Suppl 1), pp.O45, 2014, <10.1186/1742-4690-11-S1-O45>. <inserm-00924959>

HAL Id: inserm-00924959

<http://www.hal.inserm.fr/inserm-00924959>

Submitted on 7 Jan 2014

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



ORAL PRESENTATION

Open Access

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

Aurélien Riquet^{1,2*}, Sébastien Chevalier^{1,2}, Julien Villaudy³, Louis Gazzolo³, Jean-Pierre Vartanian⁴, Renaud Mahieux^{1,2†}, Madeleine Duc-Dodon^{3†}, Nathalie Bonnefoy⁵

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.

Authors' details

¹Université de Lyon, Lyon, France. ²Centre International de Recherche en Infectiologie INSERM U1111 - CNRS UMR5308, Université de Lyon, Ecole Normale Supérieure de Lyon, France. ³Laboratoire de Biologie Moléculaire de la Cellule, UMR5239 CNRS, Ecole Normale Supérieure de Lyon, Lyon, France. ⁴Unité de Rétrovirologie Moléculaire, Institut Pasteur, Paris, France. ⁵Institut de Recherche en Cancérologie de Montpellier, Inserm U896 - Université Montpellier 1 - CRLC Val d'Aurelle, Montpellier, France.

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.

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



* Correspondence: aurelien.riquet@inserm.fr

† Contributed equally

¹Université de Lyon, Lyon, France

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