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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)

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

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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.

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* 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

