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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 Riquet1,2*, Sébastien Chevalier1,2, Julien Villaudy3, Louis Gazzolo3, Jean-Pierre Vartanian4, Renaud Mahieux1,2†, Madeleine Duc-Dodon3†, 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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