



ORAL PRESENTATION

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A transgenic *Drosophila melanogaster* model to study HTLV-I oncoprotein Tax-driven leukemogenesis in vivo

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Adult T-cell Leukemia/Lymphoma is an aggressive malignancy caused by HTLV-1 infection. HTLV-2 is genetically related to HTLV-1, but does not cause a malignant disease. The HTLV-1 Tax (Tax-1) viral transactivator is required for HTLV-1 expression and modulates the classical and non-canonical NF- κ B pathways. Interaction of Tax-1 with IKK γ /NEMO results in constitutive activation of NF- κ B in HTLV-1 infected cells, and contributes to HTLV-1-driven leukemogenesis. Tax-1 transgenic mice develop leukemia, lymphomas or spontaneous osteolytic bone metastases demonstrating Tax-1 oncogenic properties in vivo. However, the cellular pathways and the partners involved in vivo have not been described. HTLV-2 Tax (Tax-2) has properties different from Tax-1, including different post-translational modifications and different intracellular localization. Thanks to the availability of collection of mutants and RNAi lines, *Drosophila melanogaster* allows simple and exhaustive genetic screens. We generated transgenic *Drosophila* models expressing either Tax-1 or Tax-2 in the compound eye and plasmacytes (leukocyte-like cell). We demonstrate that Tax-1 but not Tax-2 induces a perturbation of the crystalline array of the ommatidia and increase in plasmacyte proliferation indicating that Tax-1 but not Tax-2 has transforming potential in *Drosophila*. We further show that induction of the eye phenotype is primarily dependent on Kenny, the *Drosophila* homolog of IKK γ /NEMO, upstream of Relish (NF- κ B) activation. Using this model we were able to identify a novel

post-translational modification which Tax-1 undergoes in addition to the well-known ubiquitylation and SUMOylation. This novel Tax post-translational modification was confirmed in HTLV-I transformed cell lines. Altogether, these results show that the *Drosophila* system is useful for dissecting the molecular mechanisms of HTLV-1-induced cell transformation in vivo.

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