



POSTER PRESENTATION

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The MHC Class II transactivator CIITA inhibits the persistent activation of NF- κ B by Tax-1

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Human T-cell Lymphotropic Virus type-1 (HTLV-1) is the causative agent of an aggressive malignancy of CD4+ T lymphocytes. Many studies have shown that the constitutive activation of NF- κ B pathway by the viral transactivator Tax-1 is crucial for T-cell transformation. We previously identified the cellular factor Class II transactivator (CIITA), the master regulator of Major Histo compatibility Complex Class II gene transcription, as a restriction factor inhibiting HTLV-1 replication by blocking Tax-1-mediated activation of the viral LTR promoter (1). Here we show that CIITA suppresses also the activation of the canonical NF- κ B pathway by Tax-1 and mapped the region of CIITA mediating this effect. CIITA affects the subcellular localization of Tax-1, which is mostly retained in the cytoplasm and this correlates with an impaired migration of Rel A in to the nucleus. By using nuclear and cytoplasmic deletion mutants of CIITA, we demonstrate that CIITA suppresses the activation of NF- κ B by Tax-1 in both the subcellular compartments. Interestingly, CIITA binds to Tax-1 in vivo without preventing the binding of Tax-1 to both IKK γ and RelA. Nevertheless, Tax-1-induced IKK kinase activity is affected in the presence of CIITA as demonstrated by impaired phosphorylation of I κ B inhibitor, which is responsible for the impaired migration of RelA into the nucleus. Thus, the inactive p50/RelA heterodimer is trapped in the cytoplasm and this results in the suppression of the activation of NF- κ B responsive genes by Tax-1. Overall, these findings indicate that CIITA has evolved as a versatile molecule that, besides inhibiting viral gene expression promoted by Tax-1, it might counteract also Tax-1 transforming activity. Thus, unveiling the molecular basis of CIITA-mediated Tax-1

inhibition may be important in defining new strategies to control HTLV-1 spreading and on cogenic potential.

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