



MEETING ABSTRACT

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# HTLV-1 Tax-induced NF- $\kappa$ B activation is negatively regulated by Ubiquitin-specific peptidase 20 (USP20)

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Human T cell leukemia virus type 1 (HTLV-1) causes a fatal hematopoietic malignancy, adult T cell leukemia (ATL), and a viral oncoprotein Tax is considered to play the important roles in leukemogenesis through its potent activation of NF- $\kappa$ B. Protein ubiquitination is crucial for the proper regulation of NF- $\kappa$ B pathway. It is also known that the function of Tax is modified by ubiquitination, indicating that ubiquitination machineries contribute to the oncogenic mechanisms of ATL. We report that two ubiquitin-specific peptidases, USP20 and USP33, deubiquitinate TRAF6 and suppress IL-1 $\beta$ -induced NF- $\kappa$ B activation. We find that USP20 deubiquitinates Tax and inhibits Tax-induced NF- $\kappa$ B activation, consistent with Tax being a substrate of USP20. In HTLV-1-transformed cells, the transcription of USP20 is reduced compared with HTLV-1-negative T cells, and ectopic USP20 expression was found to inhibit the proliferation of an HTLV-1-transformed cell line, MT4. Our findings suggest USP20 is a key negative regulator of NF- $\kappa$ B signaling and can influence HTLV-1-induced leukemogenesis.

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