



POSTER PRESENTATION

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Ubiquitination-dependent, proteasomal degradation of the retroviral oncoprotein Tax by niclosamide, an anti-helminthic molecule

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Adult T cell leukemia and lymphoma (ATL) is a highly aggressive form of hematological malignancies, which is caused by chronic infection of human T cell leukemia virus type 1 (HTLV-1). The viral genome encodes an oncogenic protein Tax that plays a key role in transactivating viral gene transcription and in deregulating cellular oncogenic signaling to promote survival and proliferation of virally infected T cells. Hence, Tax is a desirable therapeutic target, particularly at early stage of HTLV-1-mediated oncogenesis. We here show that niclosamide, an anti-helminthic molecule, induced apoptosis of HTLV-1-transformed T cells. Niclosamide promoted formation of polyubiquitinated Tax protein aggregate, facilitating its subsequent degradation in proteasome. Consistent with niclosamide-mediated Tax degradation, the transcription of HTLV-1 viral genes is suppressed. Furthermore, niclosamide inhibited the activities of MAPK/ERK and Stat3, and down regulated pro-survival Bcl-2 family members such as Mcl-1. Since Tax, Stat3 and Mcl-1 are growth-promoting molecules in HTLV-1-transformed T cells, our data demonstrated a novel mechanism of niclosamide in inducing polyubiquitination-dependent degradation of Tax and certain cellular pro-survival molecules, thereby promoting apoptosis of HTLV-1-associated leukemia.

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