

HTLV ANTISENSE PROTEINS ROLE IN THE NF- κ B MODULATION.

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The retrovirus HTLV-1 is the causative agent of adult T-cell leukemia, whereas the genetically related serotype HTLV-2 is sporadically associated with neurological diseases. The HTLV-1 genome encodes regulatory proteins, such as the oncoprotein Tax and the antisense proteins HBZ, involved into T-cells proliferation and transformation. Tax-1, HBZ, and the HTLV-2 homologs, Tax-2 and APH-2 interact with many host cell factors impairing cell signaling pathways involved in the mechanisms of survival, and proliferation, including the NF- κ B pathway.

The aim of this study is to investigate the involvement of the regulatory proteins HBZ and APH-2 in the constitutively Tax-mediated NF- κ B activation. We demonstrated that HBZ and APH-2 differ in the NF- κ B promoter suppression. The APH-2 protein, differently from HBZ, localizes into the cytoplasm in presence of Tax, where it prevents the degradation of the inhibitor I κ B, hindering the nuclear translocation of p65. Unlike HBZ, we found that APH-2 interacts with the E3 ubiquitin ligase TRAF3, an upstream inhibitor of the alternative NF- κ B pathway. By generating a TRAF3-KO cell line applying the CRISPR/Cas9 technique, we are investigating the HBZ and APH-2 activity on the alternative NF- κ B cell signaling. This study may provide insight into the effect of host-viral interactions in human viral oncogenesis.