HTLV ANTISENSE PROTEINS ROLE IN THE NF-κB MODULATION.

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The retrovirus HTLV-1 is the causative agent of adult T-cell leukemia, whereas the genetically related sierotype 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 imparing cell signaling pathways involved in the mechanisms of survival, and proliferation, including the NF-κB 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-κB activation. We demonstrated that HBZ and APH-2 differ in the NF-κB 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 IκB, 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-κB 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-κB cell signaling. This study may provide insight into the effect of host-viral interactions in human viral oncogenesis.