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Secretion of the Human T Cell Leukemia Virus Type I Transactivator Protein Tax

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The HTLV-1 Tax protein is well known as a transcriptional transactivator and inducer of cellular transformation. However, it is also known that extracellular Tax induces the production and release of cytokines, such as TNF-a and IL-6, which have adverse effects on cells of the central nervous system. The cellular process by which Tax exits the cell into the extracellular environmment is currently unknown. This study characterizes the process of Tax secretion from the cell. Specifically, cytoplasmic Tax was demonstrated to localize to organelles associated with the cellular secretory process including the endoplasmic reticulum and Golgi complex. Additionally, it was demonstrated that full-length Tax was secreted from both baby hamster kidney cells and a human kidney tumor cell line. Tax secretion was partially inhibited by brefeldin A, suggesting that Tax migrated from ER to Golgi complex. The combined treatment of Tax-transfected cells with PMA and ionomycin resulted in a small increase in the amount of Tax secreted suggesting that a fraction of cytoplasmic Tax was present in the regulated secretory pathway. These studies provide a link between Tax accumulation in the cytoplasm, the detection of Tax in the extracellular environment.