Expression Of Rb2/p130 Tumor-suppressor Gene In Aids-related Non-hodgkin's Lymphomas: Implications For Disease Pathogenesis.

Abstract:

In this study we examined 21 cases of AIDS-related lymphomas for genomic organization and expression of RB2/p130 oncosuppressor gene and compared the results with the proliferative features of these neoplasms. We found no mutations in the RB2/p130 gene and unusually high percentages of cells expressing nuclear pRb2/p130 in tumors with a high proliferative activity, such as AIDS-related lymphomas. These findings might suggest that a molecular mechanism usually observed in viral-linked oncogenesis could be involved. We performed in vitro and in vivo binding assays to investigate whether the human immunodeficiency virus (HIV) gene product Tat and Rb2/p130 could interact. The results of these assays revealed that the HIV-1 Tat protein binds specifically to pRb2/p130. This may result in the inactivation of its oncosuppressive properties and the induction of genes needed to proceed through the cell cycle including p107, cyclin A, and cyclin B. Using single-cell polymerase chain reaction (PCR) assay, we found HIV-1 DNA in the neoplastic cells of only 2 of the 21 cases examined, whereas PCR on whole tissue revealed HIV-1 DNA in all of the cases. Furthermore, a diffuse and nuclear stain was observed in tissue sections with anti-Tat monoclonal antibody. These findings are in accordance with the notion that soluble Tat protein could function as a biologically active extracellular protein released by infected cells and taken up readily by uninfected B cells. In conclusion, our results seem to suggest that pRb2/p130 oncosuppressor protein may be a target in the interaction between the HIV-1 gene products and host proteins.