

## **Modulation of Sp1 phosphorylation by human immunodeficiency virus type 1 Tat.**

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We previously reported (K. T. Jeang, R. Chun, N. H. Lin, A. Gatignol, C. G. Glabe, and H. Fan, J. Virol. 67: 6224-6233, 1993) that human immunodeficiency virus type 1 (HIV-1) Tat and Sp1 form a protein-protein complex. Here, we have characterized the physical interaction and a functional consequence of Tat-Sp1 contact. Using in vitro protein chromatography, we mapped the region in Tat that contacts Sp1 to amino acids 30 to 55. We found that in cell-free reactions, Tat augmented double-stranded DNA-dependent protein kinase (DNA-PK)-mediated Sp1 phosphorylation in a contact-dependent manner. Tat mutants that do not bind Sp1 failed to influence phosphorylation of the latter. In complementary experiments, we also found that Tat forms protein-protein contacts with DNA-PK. We confirmed that in HeLa and Jurkat cells, Tat expression indeed increased the intracellular amount of phosphorylated Sp1 in a manner consistent with the results of cell-free assays. Furthermore, using two phosphatase inhibitors and a kinase inhibitor, we demonstrated a modulation of reporter gene expression as a consequence of changes in Sp1 phosphorylation. Taken together, these findings suggest that activity at the HIV-1 promoter is influenced by phosphorylation of Sp1 which is affected by Tat and DNA-PK.

\*Gene Products, tat/METABOLISM \*HIV-1/METABOLISM \*Transcription Factor, Sp1/METABOLISM

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