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HIV IMPLICATED IN THE *cis*-ACTIVATION OF *c-fes* IN A SUBSET OF HIV-ASSOCIATED LYMPHOMAS.

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Clonal HIV insertions upstream of the proto-oncogene *c-fes* were identified in a subset of AIDS-associated high-grade non-Hodgkin's lymphomas. These lymphomas included large cell lymphomas interspersed with prominent macrophages and a T-cell lymphoma. In a representative case of these neoplasias, tumor associated macrophages were characterized and found to co-express the proto-oncogene *c-fes* and HIV p24. The *c-fes* gene product, p93-*c-fes* was found in an activated, phosphorylated state in macrophages isolated from this tumor tissue. An HIV promoter insertion model characterized 3'LTR mediated *cis*-activated expression through the *c-fes* upstream genomic region in the human Jurkat T-cell line, K562 myeloid progenitor cell line, and primary cultured human macrophages. The cotransfection of a *c-fes* cDNA enhanced 3'LTR *cis*-activation through the *c-fes* upstream genomic region indicating the possible presence of a positive feedback mechanism that potentiates gene dysregulation. This study presents further evidence for tumor-associated retroviral-mediated insertional mutagenesis at a specific genomic locus in humans that may play a direct role in lymphomagenesis.

Keywords: AEGIS, Proto-Oncogenes, Lymphoma, HIV, Promoter Regions (Genetics), Macrophages, DNA Primers, DNA, Tumor Cells, Cultured, HIV-1, HIV Long Terminal Repeat, Commonwealth of Independent States, Human, genetics, AIDS

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