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Altered patterns of cellular gene expression by JC virus

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The restricted tropism of the polyomavirus JC virus (JCV) makes pathogenesis-related studies challenging. Because of the difficulties in cultivating JCV, most pathogenesis studies have employed SV40-derived cell lines or JCV/SV40 chimeras that utilize composite enhancer sequences from both viruses. Our objective was to study the early genes expressed by JCV to better understand viral gene regulation. Subconfluent monolayers of primary human fetal glial (PHFG) cells were transfected with ligated full-length JCV DNA and replication was confirmed at days 5 and 10. Total cellular RNA was extracted on day 10 from JCV- and mock-transfected PHFG cells. 20 μg RNA was hybridized to an Affymetrix U133A chip, and the data was analyzed using Microarray Suite 5.0. Of the 400 differentially expressed genes, up-regulated genes clustered into 3 major functional groups: cell proliferation, cell-communication, and IFN-responsive genes. Upregulation of IFN-inducible genes such as, MxA, Stat1, OAS1 and *cig5* was confirmed by real-time PCR. Based on Western blot analysis *cig5* and MxA protein levels were significantly elevated. Correlation of T-antigen and agnoprotein gene expression with both mRNA and protein accumulation of antiviral genes such as, MxA and *cig5* at an early stage of viral replication suggests that induction of IFN-inducible genes constitutes one of the first cellular response to JCV replication and viral transcription, and its regulation is orchestrated via virus-induced binding of transcription factors. The global analysis of changes in mRNA expression levels following viral infection offers a catalog of genes that are modulated as a result of the host-pathogen interaction and provides a new approach for the investigation of PML pathogenesis.