Transcriptional analysis of the role of CD8+ T lymphocytes in acute neural herpes simplex virus infection

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Abstract

CD8+ T cells have a crucial role in clearance of herpes simplex virus (HSV) from the peripheral nervous systems of infected mice, but the mechanism of this protection is not known. To approach this problem, comparative transcriptional analyses of sensory ganglia from (i) HSV infected immunocompetent mice and (ii) HSV infected mice depleted of CD8+ cells were done. Two types of analysis were undertaken. The first was directed at mRNAs encoding molecules of known importance in immunity and the second utilized mRNA differential display, a non-directed method for identifying differentially expressed genes. The directed analyses examined the effect of CD8+ cell depletion on IL-2, IL-4, IL-6, IL-10 and IFN-γ mRNA levels in ganglia of mice at the peak (day five) or the recovery phase (day seven) of HSV infection. Transcription of each cytokine tested was upregulated in sensory ganglia in response to HSV infection. IL-4 mRNA levels were increased by the depletion of CD8+ cells both at day five and day seven, raising the possibility that overexpression of IL-4 may be detrimental to clearance of HSV. IL-2 and IL-6 mRNAs were more abundant in the CD8+ cell depleted mice at day five and day seven, respectively. The remaining cytokine transcripts were not significantly affected by CD8+ cell depletion. Notably, mRNA for IFN-γ, a candidate effector of CD8+ T cell function, was not altered.

An mRNA differential display based analysis was developed, with the aim of detecting transcripts whose abundance in HSV infected sensory ganglia is dependent on the presence (or absence) of CD8+ T lymphocytes. Nine such mRNAs were found and partial cDNAs of five of these were cloned. Northern blotting confirmed that two of the differential display clones, designated CC28 and CT03, represented mRNAs that were more abundant in HSV infected ganglia of immunocompetent mice compared with CD8+ cell depleted mice. Nucleic acid sequence analyses disclosed that CC28 contains an as yet unreported sequence and CT03 is likely to represent mRNA for the α subunit of Galpha, a heterotrimeric G protein, not found before in sensory nerve ganglia.