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Research paper

Human herpesvirus 6 (HHV-6)-associated dysfunction of blood monocytes

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Abstract

HHV-6 is a recently described member of the herpesvirus family. HHV-6-associated marrow failure and interstitial pneumonitis where macrophages are the primary infected cell type have been described in marrow transplant patients (Carrigan, 1991; Drobyski et al., 1993). In recent studies we have shown that exposure of normal human marrow to HHV-6_{GS} (a type A strain) or several type B strains resulted in suppression of growth factor induced outgrowth of macrophages by > 90% (Burd and Carrigan, 1993). Additional experiments using HHV-6_{GS} to characterize the effects of the virus on peripheral blood monocytes showed that the respiratory burst capacity of these cells as determined by luminol-enhanced chemiluminescence using phorbol myristate acetate as a trigger was decreased by 83% $\hat{\pm}$ 13% in a series of 5 experiments. The decreased respiratory burst was evident as early as 15 min after exposure to virus. Experiments in

which cells were separated on a fluorescence activated cell sorter prior to respiratory burst assay showed that the response was mediated solely by peripheral blood monocytes. The respiratory burst response of virus-exposed cells to opsonized zymosan was not affected, indicating that the virus may selectively interfere with the protein kinase C pathway of cellular activation. Ultracentrifugation of stock material to remove infectious virus showed that the suppressive factor was associated with the supernatant fraction. These findings suggest that HHV-6 infection may be associated with a defect in one of the major monocyte activation pathways, and this could be of importance with respect to persistent infection by HHV-6 in immune compromised patients.



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Keywords

Human herpesvirus 6; Respiratory burst; Monocyte; Signal transduction; Immune suppression

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