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Effect of immunotherapy on UV induced recurrent herpes simplex virus infections. C.J. Harrison, D.I. Bernstein, L.R. Stanberry. Children's Hospital Research Foundation, Cincinnati, Ohio, U.S.A.

An alternative to antiviral therapy to prevent recurrent herpes simplex virus (HSV) disease is the use of immunotherapy. Here we report the effects of R837 (3M Riker), a potent immune modulator that significantly reduces acute HSV-2 genital lesions in guinea pigs, IL-2 (Cetus), and also interferon alpha (Roche) as preventive therapy for UV induced recurrent HSV-2 genital lesions in the guinea pig model. Guinea pigs that had recovered from acute HSV-2 genital disease were irradiated 80-100 days after initial HSV inoculation, a time when spontaneous recurrences are minimal. Following UV exposure, 75% of placebo animals (N=20) developed a mean of 1.4 recurrent lesion days/animal over the next 7d. Four day regimens of intraperitoneal (IP) interferon or IP IL-2 were begun 24 hours prior to UV irradiation, and topical R837 was begun immediately after UV. Topical R837 therapy (n=20) reduced the number of animals developing recurrences to 45% and the mean recurrent lesion days to 0.6 days/animal ($p<.02$). Both IL-2 ($n=20$) and interferon (n=20) reduced the number of animals developing recurrences to 40% ($p<.05$) and the mean number of recurrent lesion days to 0.7 days/animal ($p<.02$). This guinea pig model of UV induced genital HSV-2 recurrent disease permitted rapid evaluation of immunotherapeutic agents, each of which effectively reduced recurrent HSV-2 disease.

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QUANTITATIVELY DIFFERENT EFFECTS OF CYTOKINES ON CHRONIC HIV-1 INFECTION

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Activation of latent or chronic virus infection in cell lines may mimic events that occur during progression to AIDS in vivo. Therefore, it is of considerable interest to study the mechanisms of HIV gene induction in vitro. Cellular activation signals such as mitogens, antigens, and agents inducing stress responses have been shown to activate HIV-gene expression in chronically infected cells. Cytokines are physiological signals known to activate cells and to induce the production of cellular factors which may be involved in HIV-gene expression. We investigated the influence of a series of cytokines on HIV-1 gene expression in the chronically infected monocytic cell line U1, isolated by A. Fauci and collaborators (1). P24 antigen production was measured quantitatively by ELISA. PMA, GM-CSF, and IL-6 were found to increase significantly p24 expression in U1 cells, whereas IL-3 and IL-8 showed no effect. IL-4 enhanced p24 levels reproducibly by a factor of two. The amount of p24 antigen increased with the cytokine concentration up to a certain maximum concentration which was found to be 0.3 ng/ml for GM-CSF and 3 ng/ml for IL-6. Higher cytokine concentrations up to 1000 ng/ml did not further increase p24 production. Remarkably, the level of maximum p24 expression was characteristic for the cytokine used: GM-CSF stimulated about 10fold and IL-6 75fold as compared to PMA which increased the basal expression of p24 500fold. Combination of GM-CSF with IL-6 induced p24 production in a super additive way.

Experiments are ongoing to investigate in more details the molecular mechanisms of these effects and of cytokine interactions.

(1) T.M. Folks et al. (1988), J. Immunol. 140, 1117-1122.