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Mechanisms of Augmented Resistance of Cyclosporin A-treated mice to Influenza Virus Infection by Trehalose-6,6'-dimycolate. Masanobu Azuma, Katsuhiko Sazaki and Tatsuo Suzutani. Department of Microbiology, Asahikawa Medical College, Asahikawa 078, Japan

Cyclosporin A (CsA), which is suppressive drug of helper T lymphocytes, diminished a resistance of mice to influenza virus infection. Mice inoculated intravenously with trehalose-6,6'-dimycolate (TDM), a glycolipid component of the cell wall of Mycobacterium, recovered the resistance to influenza virus infection impaired by CsA. Numbers of antibody producing cells were markedly reduced in CsA and/or TDM-treated mice. Activity of cytotoxic T lymphocytes was activated in TDM-treated mice and also in CsA- and TDM-treated mice. Interferon production in lung of TDM-treated mice was augmented, however, extremely reduced not only in CsA-treated mice, but also in CsA- and TDM-treated mice. Natural killer cell activity of CsA- and/or TDM-treated mice was not different from that of control mice. In vitro experiments showed that macrophage cultures treated with TDM produced an activator(s) of Lyt-1$^+$ lymphocytes and also Lyt-2$^+$ lymphocytes.

These results suggest that the recovered resistance of CsA-treated mice by TDM treatment was caused by elicitation of macrophages with TDM, then by an activation of cytotoxic T lymphocytes by activator(s) produced from the macrophages elicited with TDM.

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THE LIPOPHILIC MURAMYL PEPTIDE MTP-PE IS A POTENT INHIBITOR OF HIV REPLICATION IN MACROPHAGES, by J.K.Lazdins, K.A.Woods-Cook and M.R. Walker CIBA-GEIGY Ldt, Pharma Research Laboratories, CH-4002 Basle, Switzerland.

The lipophilic muramyl peptide MTP-PE is an immunomodulator with well defined properties as antitumor and antiviral agent in-vivo. In-vitro it has been shown to have marked effects on human blood monocyte and macrophage functions i.e.: induction of tumoricidal activity, induction of cytokine release (TNF,CSF,IL-1) and a regulatory effect on the ability of monocytes to produce $H_2O_2$. The present study was designed to address the question of what are the effects of MTP-PE on the replication of HIV in human in-vitro differentiated blood monocytes. Cultured monocyte-derived macrophages were productively infected with a monocytotropic strain (ADA) of the Human Immunodeficiency Virus in-vitro. Treatment of these cells shortly after infection and several times thereafter with the free form of MTP-PE had an inhibitory effect on virus replication as measured by Reverse Transcriptase and p24Ag levels.When MTP-PE encapsulated in multilamellar liposomes was used, higher levels of protection were achieved and only one treatment following infection was required. During these studies it was noted that the placebo liposomes had some effect in reducing the Reverse Transcriptase levels found in the supernatants of infected cells. This reduction could not be explained by direct cytotoxic effect. Both free and liposomal MTP-PE significantly prevented formation of giant cells during the course of infection as well as reduced the cell associated viral antigen expression. Based on these observations, the therapeutic properties of MTP-PE as an anti-HIV drug should be further investigated.