Mechanisms of the Augmented Resistance of Trehalose-6,6'-dimycolate(TDM)-Treated Mice to Influenza Virus Infection. Masanobu Azuma, Katsuhiko Sazaki, Tatsuo Suzutani, Takashi Sakuma and Itsurou Yoshida. Department of Microbiology, Asahikawa Medical College, Asahikawa 078, JAPAN.

Mice inoculated intravenously with TDM (in oil-in-water emulsion), a glycolipid component of the cell wall of Mycobacterium, acquired a high resistance to intranasal infection by influenza virus. The augmented antiviral resistance of TDM-treated mice was diminished by inoculation of anti-Thy-1 monoclonal antibody or anti-interferon α/β antibody before virus infection, and also diminished by prior inoculation of silica particle suspension. Athymic nude mice inoculated with TDM could not acquire such an augmented resistance to influenza virus infection. Humoral antibody production after influenza virus infection and activity of natural killer cells were not augmented in the TDM-treated mice. In vitro experiments showed that macrophage cultures treated with TDM released an activator(s) of Lyt-1^+ and Lyt-2^+ T lymphocytes, which activates the T lymphocytes without costimulation with Con A or PHA. These results suggest that an acquired antiviral resistance of TDM-treated mice was caused by elicitation of macrophages with TDM, then an activation of T lymphocytes, and an amplified earlier interferon production from activated T lymphocytes in response to influenza virus infection.

Efficacy of a novel orally active immunomodulator, S-26308 against arbovirus infections. M. Kende, W.L. Rill, M.J. Contos, and P.G. Canonico. United States Army Medical Research Institute of Infectious Diseases, Fort Detrick, Frederick, Maryland, U.S.A.

S-26308 (3M-Riker Laboratories) was reported to be highly effective against herpes simplex types 1 and 2 and cytomegalovirus infections. As an immunomodulator, it may have a broad spectrum of antiviral efficacy; therefore, it was used to treat viral infections representing 4 families of viruses. On prophylactic schedules, 12-25 mg/Kg of orally administered compound protected 85-90% of CD-1 mice which were challenged with Rift Valley fever (RVF) or Banzi viruses, representing bunya- and flavivirus families, respectively. When administered 24 hr after a lethal challenge with RVFV, 85% of the treated mice survived. Maximum therapeutic efficacy was elicited with 3-4 doses of the compound administered at 3-4 day intervals. High interferon levels are induced 2-4 hr after injection. This regimen decreased viral titers in the serum, liver, brain, and spleen by 2-5 logs and reduced to normal values the liver function enzymes which were increased by the RVFV infection. The LD_{50} of a single, oral dose was 500 mg/Kg. Against Venezuelan equine encephalomyelitis (alpha) and Pichinde (arena) viruses, the drug was marginally effective, if at all. These studies demonstrate the therapeutic efficacy of S-26308 against several viral infections including both DNA and RNA viruses. The therapeutic efficacy is presumed to be exerted via induction of a rapid interferon response. The high safety margin between the toxic and therapeutic doses renders it an attractive candidate for oral treatment of broad viral infections.