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COMPARISON OF ANTIVIRAL EFFICACY AND MECHANISM OF ACTION OF IMMUNOMODULATORS AGAINST EXOTIC RNA VIRUSES. A.J. Pinto[+], D. Stewart[+], P.S. Morahan[+], and M. Brinton[*]. [+]The Medical College of Pennsylvania, and [*]The Wistar Institute, Philadelphia, PA., USA.

We demonstrate that several immunomodulators protect mice against challenge with Semliki forest alphatogavirus (SFV), Banzi flavivirus (BV), Caraparu bunyavirus (CV), and herpes simplex virus (HSV-2). Prophylactic treatment with maleic anhydride divinyl ether copolymer, C. parvum, CL246,738 (an orally active small molecular weight agent), Ampligen (a mismatched polyribonucleotide), recombinant murine gamma interferon (rMuIFN-G), and recombinant human alpha A/D interferon (MuIFN-A) reduced mortality and increased survival time significantly. In addition, early therapeutic treatment with the IFNs, ampligen and CL246,738 was also effective. Although broad spectrum antiviral activity was observed, there were differences in virus sensitivity with SFV and BV being the most sensitive and CV being the least sensitive to immunomodulator treatment. In contrast, CV was the most sensitive to treatment with the synthetic nucleoside ribavirin. No unified immunomodulatory antiviral mechanism was identified although most of the compounds induced IFN and activated macrophage and natural killer cell function.

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Late intervention therapy using immunomodulators and antiserum in a of model Flavivirus infection. D. H. Coppenhaver, I. P. Singh, J. Poast, P. Sriyuktasuth, M. Sarzotti, S. Baron. Dept. of Microbiology, University of Texas Medical Branch, Galveston, Texas, USA 77550.

Many antiviral agents which are efficacious in vivo prove to be effective only prophyatically. Hence, in order to explore possibilities for late therapy, we developed a system to evaluate candidate antiviral therapies in vivo after infected animals show clinically demonstrable correlates of infection. Our studies show that the earliest gross manifestation of Banzi virus (BZ) infection in mice is a rise in core body temperature on day 3 postinfection (p.i.). Weanling mice challenged with BZ were monitored, and those animals with elevated body temperatures (>99.5°F) on day 3 p.i. were given a maximum tolerated dose of poly I:CLC (80 µg/mouse, intraperitoneally) in combination with anti-BZ antiserum. Mice receiving the combination therapy showed significantly enhanced survival compared to single drug and virus control groups. Similar observations were made in repeat experiments when therapeutic intervention was provided on day 4 p.i. The results show that mice can be rescued after the clinical onset of a Flavivirus infection. They also show exogenously administered antibodies and immunomodulators can be an effective combination antiviral therapy. Supported by USAMRIID contract #DAMD17-86-C-6119.