

Combined antiviral action of tumor necrosis factor and interferon in vivo. D.H. Coppenhaver, M. Sarzotti, P. Sriyuktasuth, J. Poast, I.P. Singh, S. Baron. Department of Microbiology, University of Texas Medical Branch, Galveston, Texas, USA. 77550.

Tumor necrosis factor (TNF) is known to be cytotoxic in vitro and to have potent antitumor effects in vivo. It was recently discovered that this cytokine also exhibits a limited antiviral activity in vitro. The mechanism of this antiviral action is unclear at this time. We have investigated the possible antiviral action of TNF in an in vivo model system utilizing outbred weanling mice challenged with Banzai virus, a model Flavivirus. Recombinant TNF was administered daily for 5 days, starting 24 hr before virus challenge. No consistent antiviral action was seen when TNF (0.1-3.0 µg/dose) was administered alone. When TNF was combined with minimally effective doses of natural murine interferon (IFN) α/β a significant enhancement of the antiviral effect was noted compared to single drug controls. This combined antiviral action was consistently seen only at the highest doses of TNF used. Combinations of TNF with natural murine IFN γ did not significantly protect against Banzai virus induced encephalitis when compared to single drug controls. Thus, TNF appears to be a potentially useful antiviral agent which can enhance the efficacy of other antivirals. This is the first demonstration of an antiviral action of TNF in vivo. Supported by USAMRIID contract #DAMD17-86-C-6119.