I-36

Inhibition of Epstein-Barr Virus Transformation of B-cells by 3'-Azido-3'-deoxythymidine and Interferon Alpha and Gamma. J.C. Lin, Z.X. Zhang, Ian Sim, and J.S. Pagano. Lineberger Cancer Research Center, Univ. of North Carolina, Chapel Hill, NC 27599 & Hoffman LaRoche, Inc., Nutley, NJ 07110.

The effect of AZT, interferon alpha (IF-α) and gamma (IF-γ) on human umbilical cord lymphocyte (HUCL) transformation by EBV was analyzed. HUCL were infected by B95-8 strain of EBV for 2 h followed by incubation in medium containing various concentrations of drug. B-cell-outgrowth was monitored by focus formation at 4-5 weeks; presence of EBV genomes in transformed foci was confirmed by EBV nuclear antigen. The 50% inhibitory doses for prevention of focus formation were 0.14 μM for AZT, 10 U/ml for IF-α and 1 U/ml for IF-γ. To determine whether inhibition of transformation resulted from cytotoxic effects, non-transformed HUCL were exposed to various concentrations of the drugs for 30 days and viability determined. As compared to the no-drug control, the nontoxic doses were 1 μM for AZT, 30 U/ml for IF-α and 3 U/ml for IF-γ. Combination of either IF-α with AZT or IF-γ with AZT at nontoxic dose ranges indicated that the decreases in the numbers of transformed foci were additive, whereas combination of IF-α and IF-γ showed synergistic effect. Transformation of HUCL by EBV was sensitive to but not abolished by these agents at dosages below those required for cell killing.

I-37

The Folate Antagonist, Methotrexate, Is A Potent Inhibitor of Murine and Human Cytomegalovirus In Vitro.
J.D.Shanley, and R. Debs. VA Medical Center, University of Connecticut, Newington, Ct., and The University of California San Francisco, San Francisco, Calif.

Cytomegalovirus (CMV) is a major source of morbidity for immunocompromised patients, such as AIDS patients. The folic acid antagonists have not been explored as potential antiviral agents against CMV. We examined the effects of methotrexate, compared to acyclovir and ganciclovir, on both murine CMV (MCMV) and human CMV (HCMV) in vitro. Using a plaque reduction assay in mouse embryo fibroblasts or human foreskin fibroblasts for MCMV and HCMV respectively, we found that methotrexate was a potent inhibitor of both viruses in micromolar concentrations.

Drug	50% Plaque Reduction (ug/ml)	
	MCMV	HCMV
Acyclovir	0.20	N.D.
Ganciclovir	0.60	0.35
Methotrexate	0.10	0.025

This effect was due to folic acid antagonism since folinic acid abgated the antiviral effect of methotrexate, but not ganciclovir. The ability of methotrexate to inhibit CMV in vivo is being explored.