Wednesday April 13

Poster Session II
Antiviral Agent Evaluation:
Immunotherapy, Animal Models and Clinical Trials

II-1

Brain-enhanced Delivery of Antiviral Agents by **M. E. Brewster, R. Little, V. Venkatraghavan and N. Bodor, Center for Drug Design and Delivery, University of Florida, Gainesville, FL 32610 and Pharmatec, Inc., Alachua, FL 32615.**

Brain-targeted and enhanced delivery of the anti-herpetic agents trifluorothymidine (TFT) and acyclovir (ACV) and the anti-retroviral agent azidothymidine (AZT) was accomplished by using a dihydropyridine ‡ pyridinium salt type chemical delivery system (CDS). The first CDS made in each case was the 1-methyl-1,4-dihydronicotinate covalently attached to the 5' position of AZT (AZT-CDS), the 3' position of TFT (TFT-CDS) and the hydroxyethyl function of ACV (ACV-CDS). In all three instances, systemic administration of the CDS's led to increased brain levels of the antiviral agents compared with administration of the parent drug. At 1 hour post-treatment for example, no AZT was detected after AZT administration in the rat CNS while levels of 500 ng/g were detected after an equimolar dose of the AZT-CDS (64 μ mol/kg). Similarly, no ACV could be detected in rat treated with the parent compound but levels of approximately 150 ng/g were found after ACV-CDS treatment. In addition these levels were sustained through at least 2 days while peripheral tissue levels dropped to undetectable concentrations by 4 hours. In the case of the TFT-CDS, not only were detectable levels of TFT generated in the CNS but the compound was also found to significantly reduce viral titres in the brain of rats inoculated with herpes simplex virus 1 (HSV-1). These data suggest that the CDS is a relatively general method for brain-delivery of antiviral drugs.