141A

Inhibition of Herpes Simplex Virus Replication by Antisense.

E. M. Cantin, G. Podsakof, R. MacMahon, D. Willey, H. Openshaw. Department of Neurology, City of Hope National Medical Center, Duarte, California, USA.

We have been using antisense DNA and RNA to inhibit expression of the essential HSV-1 IE3 gene by targeting mRNA sequences encompassing the ATG translational initiation codon of IE3. A methyl phosphonate oligodeoxyribonucleotide (OMP, 15mer) inhibited HSV-1, but not vaccinia virus replication in a dose dependant manner in cultured cells. We have also isolated cell lines which express IE3 antisense RNA and shown that while they are capable of supporting vaccinia virus replication, some of them are highly resistant to infection by HSV. We have also designed a ribozyme to cleave the IE3 mRNA at a GUC site 5 nucleotides downstream of the ATG. In an in-vitro reaction under physiological conditions the IE3 ribozyme effected precise cleavage of an in-vitro transcribed IE3 transcript, producing two fragments of the predicted size. In-vitro transcribed, capped ribozymes and also chemically synthesized hybrid (DNA-RNA-DNA) ribozymes have been introduced into tissue culture cells to determine their ability to inhibit HSV-1 replication. Results of these experiments will be reported as well as results of experiments with ribozymes modified to increase their catalytic activity.

Oral Session VI

Animal Models