Oral Session III: Respiratory Virus Infections I

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NMSO3, a potent inhibitor of Respiratory Syncytial virus (RSV) infection in vitro and in vivo. S Shigeta, S Mori, K Kimura, M Terada, Fukushima Medical University and Nissui Food Product Co. Japan

NMSO3, a tetra-sulfated sialic acid which is conjugated with 2,2-bis(docosyl)propyl chain has a molecular weight of 1480 and showed potent anti-RSV activity in vitro and in vivo. NMSO3 inhibited replication of RSV in HEp-2 cells at EC50 of 0.23 μM (an average of 7 strains) which was 53 times less that of ribavirin. NMSO3 exhibited minimal cytotoxicity for HEp-2, MDCK and Vero cells and its selectivity index for RSV (CC50 for HEp-2/EC50) exceeded 2980. From the temperature shift experiment during the period of contact between virus and cells, NMSO3 inhibited both the binding of RSV to the cell membrane and its penetration into cell membrane. Intraperitoneal administration of 100 mg/kg/day of NMSO3 to cotton rats from the 1 st day to 3 days after the intranasal inoculation of RSV, every day, decreased RSV titer in lungs to $10^{-4.4}$ (-96%) on the 5th day of infection. Histopathological feature the lungs of infected rats which was evidenced by interstitiale pneumonia was markedly reduced in the lungs of NMSO3 treated rats. NMSO3 is a potent and safe anti-RSV compound.

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VP14637: A Sub-nanomolar Inhibitor of Respiratory Syncytial Virus.

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RSV is a major viral respiratory tract pathogen that often causes pneumonia and bronchiolitis. RSV is responsible for an estimated 90,000 hospitalizations and approximately 4,000 deaths among hospitalized infants annually in the U.S. RSV is also a major cause of morbidity and mortality in the elderly. An effective antiviral drug with therapeutic activity is needed for individuals with RSV disease. We report here on the discovery of a novel low molecular weight inhibitor of RSV replication in cell culture. The compound, VP14637, exhibits potent and specific activity against members of the pneumovirus genus of the Paramyxoviridae family in both viral cytopathic effect (syncytia formation) and antigen detection assays at drug concentrations that are non-toxic to cells. Time of drug addition experiments indicate that VP14637 acts on an early event in the virus replication cycle. In virus yield assays, the compound completely inhibits RSV production during multiple rounds of replication. Moreover, VP14637 blocks virus spread from infected cells. Collectively, these features suggest that VP14637 acts by inhibiting viral fusion activity. VP14637 represents an exciting new antiviral development candidate for the treatment of RSV disease.