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Feline Immunodeficiency Virus: A Lentivirus Model for Chemotherapy of AIDS and Drug-Resistance. Thomas W. North, Richard C. Cronn, Kathryn M. Remington, Jeff D. Whitmer and Judy M. Gobert, Division of Biological Sciences, University of Montana, Missoula, MT 59812.

We have purified the reverse transcriptase (RT) from feline immunodeficiency virus (FIV) and have previously shown that it is similar to the RT from human immunodeficiency virus type 1 (HIV) in physical properties, catalytic activities, and sensitivities to the active forms of several antivirals. The RNase H activity associated with the FIV RT is also very similar to that of the HIV RT. The FIV and HIV RNase H activities have a preference for poly(dC)-poly(rG) rather than poly(dT)-poly(rA) as substrate. In contrast, the RNase H activity of the RT from avian myeloblastosis virus prefers poly(dT)-poly(rA). In addition, the FIV and HIV RNase H activities are similar in their sensitivities to polyanionic inhibitors (heparin and dextran sulfate).

We have also developed conditions for in vitro selection of drug-resistant mutants of FIV. We have isolated several mutants of FIV that are resistant to 3'-azido-3'-deoxythymidine (AZT). One of those mutants is similar to AZT-resistant clinical isolates of HIV in that it is resistant to 3'-azidonucleosides but remains sensitive to other RT-targeted antivirals. We have also isolated FIV mutants that are resistant to 2',3'-dideoxyinosine (ddI). Properties of these mutants will be discussed. In vivo systems are available for studies of FIV and these are being used to determine whether the drug-resistant mutants of FIV are different from wild-type FIV in infectivity or pathogenesis. (This work was supported by Public Health Service grant AI 28189 from the National Institute of Allergy and Infectious Diseases.)

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Utilization of Pulse Oximetry for Study of Potential Anti-Influenza Virus Compounds in Mice. R.W. Sidwell, J.H. Huffman, J. Gilbert, R. Burger, and R.P. Warren. Antiviral Research Program, Utah State University, Logan, UT USA.

It has been found that pulmonary disease in BALB/c mice induced by intranasal instillation of influenza virus can be monitored by measurement of blood oxygen saturation (SaO_2%). This measurement can be readily determined by placing the mouse in a standard finger probe of an Ohmeda Pulse Oximeter 3740. Such instruments are routinely used in hospitals to monitor patients in potential respiratory distress, with the SaO_2% determined based on computer-interpreted pulsatile absorbance of light. Mice were assayed for SaO_2% using pulse oximetry, then immediately killed and heparinized arterial blood which was taken anaerobically immediately analyzed using a Radiometer OSM-3 Hemoximeter and ABL-2 Blood Gas Analyzer. The SaO_2% values matched closely using all methods. Mice infected with varying concentrations of influenza virus were assayed for SaO_2% daily for 7 days; pneumonia-associated deaths were noted as they occurred. The SaO_2% values declined in inverse proportion to the viral inoculum; when they dropped to approximately 70%, the animal usually died. Ribavirin and its 3-carboxamidine derivative, ribamidine, were evaluated using twice daily intraperitoneal treatments against influenza A (H1N1) virus infections in mice, with SaO_2% values used as one measure of their disease-inhibiting efficacy. Both compounds significantly inhibited the usual SaO_2% decline, prevented death, lowered lung consolidation and reduced infectious virus recoverable from the lung. Effects of therapy were also monitored using immunologic parameters in infected and uninfected mice. These parameters included phytohemagglutinin-induced blastogenesis, splenic cell populations, natural killer cell activity and virus-specific cytotoxic T lymphocyte response. Essentially no inhibition of these immunologic responses was seen at disease-inhibitory drug concentrations. Pulse oximetry appears to be practical, reliable and sensitive, and, coupled with the other more commonly used measures of influenza disease, is an additional means of monitoring the anti-influenzal disease efficacy of potential antiviral drugs.