Name_____KEY_____ UT EID_____

BIO 330
Quiz 5
April 15, 2014

1. Influenza virus replication is inhibited by Actinomycin D, whereas rhabdovirus replication is not. Why? (5 points)

Actinomycin D blocks DNA-dependent RNA synthesis, including synthesis of capped cellular mRNAs. Influenza virus uses newly synthesized capped mRNAs to obtain primers for viral mRNA synthesis. The viral polymerase cleaves the first 10-13 bases from cell mRNAs to use as a primer. Therefore, influenza virus replication is blocked at the stage of mRNA synthesis in the presence of Actinomycin D. Unlike the influenza viruses, rhabdoviruses replicate in the cytoplasm, and their mRNA synthesis is not blocked by Actinomycin D. The rhabdovirus RNA-dependent RNA-polymerase does not need a primer for mRNA synthesis, but the viral polymerase provides its own capping activity.

2. Name two influenza viral proteins that are current drug targets. How do these drugs work? (5 points)

NA (neuraminidase) is the target of Relenza and Tamiflu. These small molecule inhibitors bind to the active site of the enzyme and prevent its enzymatic activity (cleavage of the sialic receptors). In the presence of the inhibitors, spread of the flu virus is inhibited.

M2 – This protein is a tetramer that forms an ion channel in the envelope of influenza virus. Amantadine can block this ion channel, preventing protons from entering the interior of the virus. Without the drop in pH, the M1 matrix protein cannot be removed, uncoating cannot be completed, and the nuclear localization signal (NLS) on the NP protein is not exposed. The RNPs cannot be directed across the nuclear pores and cannot start transcription. Amantadine also can affect a late stage of virus replication by allowing premature exposure of the HA fusion peptide in the Golgi.

3. How does influenza virus regulate the levels of M1 relative to M2 protein? (5 points)

The levels of M1 compared to M2 are controlled by differential splicing. The M1 protein is translated from the unspliced mRNA whereas the M2 protein is translated from spliced mRNA from segment #7. More unspliced mRNA is produced than spliced mRNA (ratio of ~9:1).

4. What is the major difference between innate immunity to viruses in worms and mammals? (5 points)

Innate immunity to viruses in worms is RNA-based and is controlled by cleavage of viral RNAs by Dicer and loading into the RISC complex. Innate immunity to viruses in mammals is protein-based and is more complex, involving multiple signaling pathways through Toll-like receptors (TLRs) and the interferons.