A. Answer the following short answer questions. (44 POINTS TOTAL)

1) Draw a schematic of a typical simple retrovirus RNA genome. Be sure to identify all relevant features including coding and non-coding sequences (8 points).

2) Compare and contrast a herpesvirus with a poxvirus and provide an example of each (8 points).

3) Predict the consequence of having an HIV genome that encodes a defective protease. Explain the primary defect (4 pts).
4) Viruses containing a linear DNA genome have a problem in DNA replication. State the problem and explain how adenovirus solves this problem (4 points).

5) In the blanks below, indicate the type and nature of the viral genome for each of the viruses indicated. Be precise in your answer (for example poliovirus: single strand linear, positive sense RNA) (10 pts).

Adenovirus  ____________________________________________________________________

HIV  ____________________________________________________________________

Herpesvirus  ____________________________________________________________________

SV40  ____________________________________________________________________

Rous Sarcoma  ____________________________________________________________________

6) Describe two mechanisms by which a retrovirus gag-pol polyprotein can be expressed and the effect on gene product expression. (4 points).
7) Briefly describe the strategy by which VSV has been modified for gene therapy to control HIV infection (6 points).

B. Answer the following TRUE (T) OR FALSE (F). (2 points each, 20 POINTS TOTAL)

_____ 8. SV40 causes tumors in its natural host.
_____ 9. RNA splicing occurs during the SV40 replication cycle.
_____ 10. Retrovirus transcription occurs prior to integration.
_____ 11. Most retroviruses that carry oncogenes are defective for replication.
_____ 12. AIDS is a syndrome that describes the late stages of HIV infection and is correlated with a drop in the number of CD4+ T cells and an overactive immune response.
_____ 13. Adenovirus RNA splicing occurs in the cytoplasm.
_____ 14. AIDS is a syndrome that describes the late stages of HIV infection and is correlated with a drop in the number of CD4+ T cells and an overactive immune response.
_____ 15. Entry of adenovirus into the host cell requires two cellular receptors for attachment and penetration.
_____ 16. The promoter for retrovirus transcription is present in the Unique 3’ (U3) sequence.
_____ 17. The Large T antigen of SV40 is an oncogene that was acquired by recombination with the host cell genome.
C. **Answer the following problem solving question (24 points).**

18) After your graduation from Purdue, you land a high-paying job working for a major drug company. For your first project, you are asked to design a set of novel compounds that will have antiviral activity against HIV. The company has indicated that it would like you to concentrate on the following targets in the virus life cycle:

   a. Integrase  
   b. SU (gp120)  
   c. TM (gp41)

   i. For each target describe its function in the virus life cycle  
   ii. Describe the mechanism of action for the compound that you will develop  
   iii. Explain your assay for antiviral activity. It should be specific for the step in virus replication that is being inhibited (don’t just say virus infectivity assays).
D. Answer the following thought question (12 points).

The majority of vectors currently in use in clinical gene therapy trials are those derived from viruses. Discuss the pros and cons of this rationale.