

Spring 2008

Pin # KEY

Multiple choice (33 questions, 3 points each, 1 point for proper personal identifier)

1) Initial binding and fusion of HIV with T cells involves

- A) **gp41**
- B) Nef
- C) 5'LTR
- D) p24 capsid protein
- E) A and D above

2) Three of the HIV regulatory proteins are NOT included in the viral particles. What allows the virus to reproduce despite their absence?

- A) they are normally found in T cells that are not infected
- B) they are expressed following incorporation of the viral genome into the host cell**
- C) they are not important for replication of new HIV viral particles
- D) they all function at the RNA level via interaction with normal cellular proteins
- E) none of the above

3) Which of the following directly contribute to the “5 levels of attack” by HIV?

- A) 3'LTR
- B) DNA synthesis
- C) viral budding
- D) frame shifting**
- E) C and D above

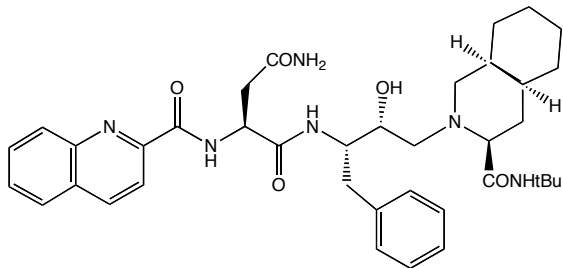
4) Individuals with HIV infection but who do not progress to AIDS are known as “elite controllers” or “long-term nonprogressors.” What is the molecular reason for this class of infected individuals?

- A) carbohydrates on gp120
- B) the high mutation rate of reverse transcriptase
- C) a mutation in CCR5**
- D) a mutation in HIV protease
- E) none of the above

5) Efavirenz is a member of which class of HIV therapeutic agents?

- A) non-nucleoside Nef inhibitors
- B) transition state based protease inhibitors
- C) entry inhibitors
- D) nucleoside RT inhibitors
- E) non-nucleoside RT inhibitors**

6) The R chirality about the carbon to which the hydroxyl group is attached in the following compound (Saquinavir) is important for?



- A) **its function as a transition state analog**
 B) lowering the molecular weight
 C) increasing the K_D
 D) making synthesis easier
 E) all of the above

7) Which lead optimization method was used in the design of Saquinavir?

- A) combinatorial chemistry
 B) **bioisosteric replacement**
 C) homologation
 D) random screening
 E) none of the above

8) Total elimination of HIV from the human body (e.g. a cure for AIDS) is most hindered by:

- A) the use of combination therapy
 B) glycosylation of the gp120 protein
 C) the high rate of mutation by reverse transcriptase
 D) **permanent incorporation of the HIV genome into host cell DNA**
 E) none of the above

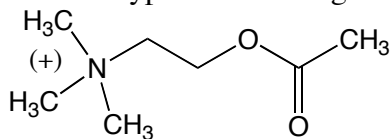
9) Which is part of the Pol polyprotein?

- A) **RNase H**
 B) 3'LTR
 C) RNA polymerase
 D) p17 Matrix protein
 E) chymotrypsin

10) The therapeutic index is

- A) the ratio of EC_{50}/IC_{50}
 B) **the ratio of LD_{50}/IC_{50}**
 C) the ratio of EC_{50}/TD_{50}
 D) the ratio of EC_{50}/EC_{50}
 E) none of the above

11) Acetylcholine binds to both muscarinic and nicotinic receptors. What characteristic of this molecule is essential to allow it to bind to both of these types of cholinergic receptors?



- A) it contains both a positively charged group and a hydrogen bond acceptor
 B) the hydrogen bond acceptor to positively charged group distance is fixed
 C) the conformational flexibility of the molecule
 D) A and B above
 E) **A and C above**

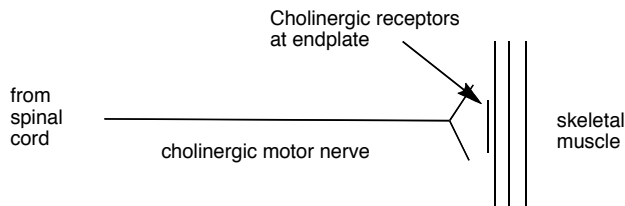
12) A receptor classified based on its ligand being serotonin is classified based on which of the following schemes?

- A) Biochemical
 B) Pharmacologic
 C) Molecular
 D) Anatomic Location
 E) Biophysical

13) Below is a diagram of nictitating innervation. If there is stimulation of the cholinergic motor nerve at the spinal cord following addition of a high concentration of an antagonist at the endplate, which of the following responses would be seen in the skeletal muscle.

Both answers are correct

- A) no response will be observed**
 B) a response of 100% maximal amplitude will be observed
 C) a response of less than 100% maximal amplitude will be observed
 D) the response amplitude will decrease by 100%
 E) the response amplitude will not be affected



14) Essential features of the pharmacophore of all sulfa drugs include

- A) a basic amine nitrogen
 B) a guanine base
 C) a $-SO_2NH_2$ moiety
 D) bromine atoms
 E) 1,3 orientation of hydrogen bond acceptors

15) Grind and find is an example of

- A) combinatorial chemistry
 B) clinical observation
 C) classical isosteres

- D) homologation
 E) **none of the above**

16) An advantage of enzyme-based in vitro assays include

- A) they screen for absorption
 B) **they are quick and inexpensive**
 C) they screen for metabolism
 D) they may be used to determine the LD₅₀
 E) none of the above

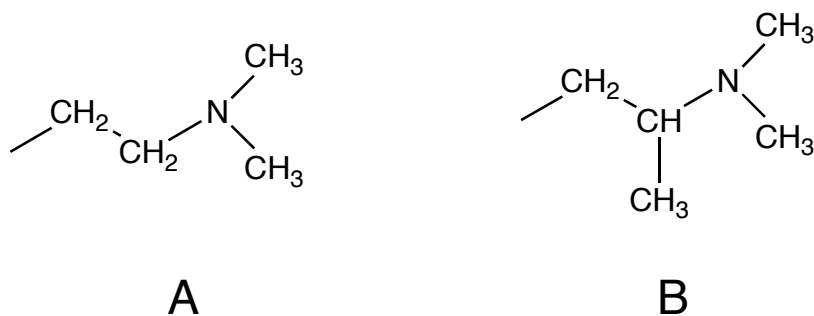
17) Possible outcomes associated with the use of homologation for lead optimization include

- A) micelle formation
 B) identification of the ideal linker length
 C) increased hydrophobicity
 D) A and B above
 E) **A, B and C above**

18) Which of the following may be considered a classical isostere of -N= ?

- A) **-CH=**
 B) -O=
 C) -NH₂
 D) -NH-
 E) -S-

19) Converting from functional group A to B represents



- A) **chain branching**
 B) homologation
 C) ring-chain transformation
 D) drug metabolism
 E) all of the above

20) Experimental studies on 5 compounds, A to E, yielded the following data.

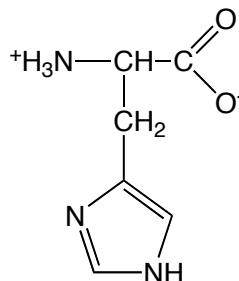
Compound	“learning lecture material”	“missing class”
A	87	4
B	3	2
C	67	100
D	4	45
E	201	67

Biological activities are EC_{50} s in units of nM.

Based in that data, which compound would be the best with respect to successfully completing the Pharm.D. program:

- A)
 B)
 C)
 D)
 E)

21) Which amino acid does the following structure represent?



- A. Tryptophan
 B. Guanine
 C. **Histidine**
 D. Proline
 E. Serine

22) The polarizability in the following equation is important as it

$$E = -\frac{1}{2} \frac{q_1^2 \alpha_2}{r_{1,2}^4}$$

- A. influences the dielectric constant
 B. **relates to the ability to induce a dipole moment**
 C. relates to the ability to form an instantaneous dipole
 D. controls the distance between the functional groups
 E. is not in the above equation

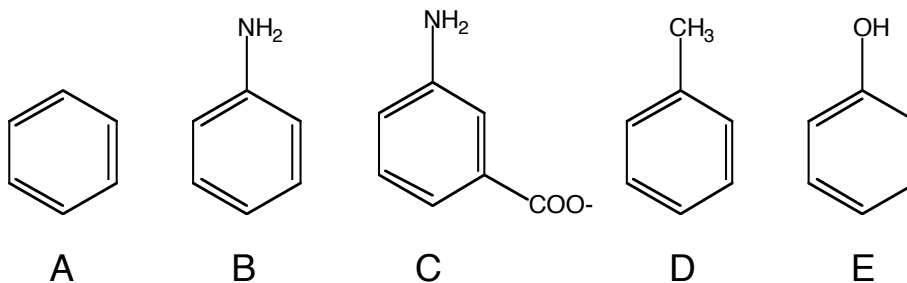
23) Dipole-dipole forces account for _____ kcal/mol per interaction.

- A. -0.5 kcal/mol
 B. -0.7 kcal/mol
 C. **-1 to -5 kcal/mol**
 D. -5 to -7 kcal/mol
 E. -100 kcal/mol

24) The specificity of a drug-receptor interaction is determined by

- A. hydrophobic interactions
 B. Pauli's exclusion principle
 C. covalent bonds
 D. **cooperativity between the types of interactions**
 E. the aqueous solubility

25) If all of the following compounds bind to the same hydrophobic pocket, such that the drug-receptor interactions are identical for all compounds, which one will have the lowest dissociation constant, K_d .



- A)
 B)
 C)
 D)
 E)

26) If a carboxylic acid is placed adjacent to a positive charge its pK_a will:

- A) increase
 B) **decrease**
 C) not change
 D) carboxylic acids are not ionizable
 E) none of the above

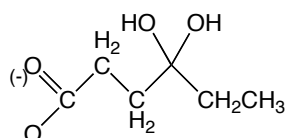
27) Methods of resolving the individual enantiomers from a racemic mixture include

- A) enzymatic transamination
 B) chiral HPLC
 C) reversed phase HPLC
 D) **A and B above**
 E) A, B and C above

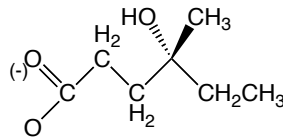
28) cis and trans conformations about a C=C double bond represent

- A) enantiomers
 B) diastereomers
 C) epimers
 D) **geometric isomers**
 E) none of the above

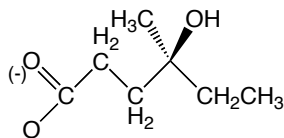
29) Given the following EC_{50} values for the four compounds below, which of the following statements is true?



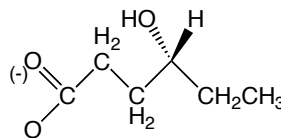
A) 20 nM



B) 6 nM



C) 7 nM



D) 15 nM

- A) **interaction with the receptor occurs via two point binding**
 B) interaction with the receptor occurs via three point binding
 C) compound A has the tightest binding
 D) compound B is the best antagonist
 E) the therapeutic index of compounds A is 20

30. Which of the following would best justify the use of retroviral vectors in gene therapy trials?

- A. They can insert into the host genome and cause insertional mutagenesis of a host gene.
 B. They will readily infect host cells.
 C. They will cause an immune response.
 D. They will readily mutate to become replication competent.
 E. All of the above

31. Which of the following will determine whether a viral gene therapy protocol is successful?

- A. The tissue types targeted.
 B. The inflammatory response.
 C. The expression of desired protein.
 D. All of the above.
 E. None of the above

32. Which of the following is involved in the delivery of a desired gene into a cell using cationic liposomes?

- A. Interactions between positive charges on the liposome and negatively charged DNA**
- B. The production of high titer viral particles from a packaging cell line.
- C. The insertion of the liposome into the host DNA.
- D. The induction of an immune response.
- E. Expression of proteins on the vector

33. Which of the following best highlights the difficulty in using gene therapy approaches to treat diseases that are less than 100% heritable and may be influenced by environmental factors and lifestyle?

- A. These diseases are monogenic and have only one gene that is defective.
- B. These diseases are polygenic and have many genes that may be defective.**
- C. These diseases are monogenic and have many genes that may be defective.
- D. These diseases are polygenic and have only one gene that is defective.
- E. None of the above