Name: ______KEY____________________________

MCB 100A/ChemC130 Midterm 1 2008

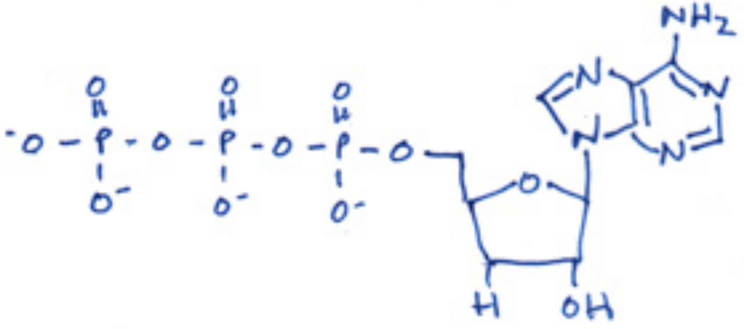
Please write your name on the first page.

1. Find the letter below that best matches the following statements. Use a letter only once. **(20 pts.)**

A. A-minor motif
B. R value
C. rmsd
D. net result of the exchange of interactions in folded and unfolded states
E. Ramachandran plot
F. van der Waals contact
G. rotamer
H. covalent bond
I. cross-strand purine stack
J. protein denaturation
K. AUG
L. C3’ endo sugar pucker
M. tetraloop
N. X-ray crystallography
O. major groove
P. sensitive to base hydrolysis
Q. accessible surface area
R. ionic interaction

i) __M__ commonly occurs at the end of RNA stems
ii) __C__ reflects the overall quality of a NMR structure
iii) __E__ determined by van der Waals contacts in a tripeptide
iv) __R__ long-range noncovalent interaction
v) __H__ closest favorable interaction
vi) __A__ commonly occurs where three RNA strands come together
vii) _L/P_ RNA
viii) __O__ each base pair displays a unique pattern of H-bond donors and acceptors
ix) __Q__ used to define atoms on the “inside” and “outside” proteins
x) __G__ combination of low-energy side-chain dihedral angles

2a. Draw the structure of 3’-deoxyadenosine 5’-triphosphate **(6 pts.)**



2b. This molecule is the triphosphate form of a drug, cordycepin, which is an inhibitor of poly-A synthesis at the 3’ end of mRNA. At high concentrations it affects all RNA synthesis. What is the basis of inhibition? **(3 pts.)**

When it gets incorporated into RNA, the chain can’t be elongated because there is no 3’ nucleophile.

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2c. Why does this molecule (cordycepin triphosphate) fail to inhibit DNA synthesis? **(3 pts.)**

The molecule is rejected by DNA polymerase because of the 2' OH group.

3a. For transcription and translation, list 1. the information–containing template, 2. the "monomer" substrate and 3. the "polymerase" that catalyzes polymer synthesis. **(12 pts.)**

	Transcription	**Translation**
Template	DNA	mRNA
Monomers	rNTPs	Amino-acyl tRNAs
Polymerase	RNA polymerase	ribosome

3b. What is the common metabolite whose hydrolysis is coupled to all the reactions involving nucleotides in DNA replication, transcription and translation? **(4 pts.)**

inorganic pyrophosphate or PPi

4. Match the amino acids to their common reactions. Use each letter only once. **(8 pts.)**

Asp-Pro	D	A. Deamidation
Gln	A	B. Oxidation
Asn-Gly	C	C. Isomerization
Cys	B	D. Cleavage

5. Which physical force or effect provides the dominant driving force for each of these structural patterns **(12 pts.)**:

a. The tendency of RNA stems to line up with the helix axes aligned.
 Stacking

b. The A-minor motif and ribose zipper.
 H-bonds

c. The occurrence of 20 or more consecutive nonpolar amino acids in transmembrane helices.
 Hydrophobic effect

d. The tendency of charged groups in proteins to be surrounded by groups of opposite charge.
 Ionic interactions

e. The requirement for positively charged ions to stabilize nucleic acid structures.
 Ionic interactions

f. Intercalation of bases in the structure of tRNA.
 Stacking

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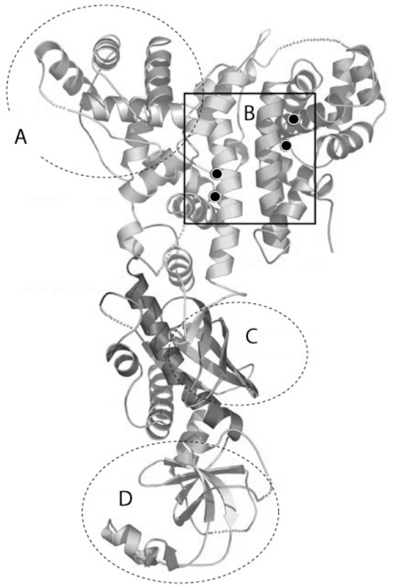
6. Which of the following amino acid sequences is most likely to form an amphipathic α-helix? Briefly explain two different reasons for your choice **(12 pts.)**.

a. `NPEALKDAFKQVAHRMKQLARG` **a.**
b. `KPKKIQVDASFSVRLDVDIRRQ`
c. `PRWILVAVLFFCTMILVIAVRG`

1. **The 3-4-residue periodicity of hydrophobic side chains matches the 3.6-residue periodicity of the alpha helix.**
2. **N @ N-terminus-1, P @ N terminus or G @ C-terminus.**
3. **E near N-terminus and R near C-terminus complement the helix dipole.**
4. **b looks like an antiparallel beta strand (alternating hydrophobic and polar residues).**
5. **c looks like a transmembrane helix (>= 20 consecutive hydrophobic residues).**

7. The ribbon diagram of the ~750-amino-acid, RNA-cutting enzyme "dicer" from *Giardia* is shown on the right.



7a. The dicer sequence has two separate segments that show 29/103 and 36/139 sequence identities to a bacterial enzyme called ribonuclease (RNase) III. What two additional pieces of information from sequence analysis would you use to evaluate whether or not these segments of dicer contain the RNase active sites? **(8 pts.)**

1. **E-value < 0.001**
2. **Active-site motifs for RNase III**
3. **Structure match to RNse III by threading**
4. **Motif sequences match each other. Since two cleavages take place, dicer might contain a gene duplication.**

7b. This dicer cuts double-stranded RNA into pieces that are 25 base pairs long. The distance from region A to region D is ~100 Å. If the active site of dicer is in region B, which additional region of the protein do you think is required to measure the precise length of RNA for cleavage and why did you pick this region? **(6 pts.)**

Region D. It's the only region far enough away from the active site in region B to measure te length of a 25 base pair piece of RNA. The distance should be:
25/11 turns x 34 Å/turn = 77.3 Å or

25 bp x 2.9 Å/bp = 72.5 Å.

7c. List two other enzymes (in addition to dicer) that form large or elongated structures that also recognize or act on distant parts of a RNA molecule. **(6 pts.)**

Amino-acyl tRNA synthetases, RNA polymerase or ribosome.