Biochemistry Cumulative – March, 2010

Nucleic Acids: DNA Damage Response

Answer **any four** of the following questions.

1. (WC) Briefly describe at least three different mechanisms by which two kinases, ATM and ATR, mediate DDR induced signaling in mammalian cells.

2. (LF) Jackson and Bartek suggest that DDR knowledge can be harnessed for disease treatment.
(a) Name four drugs used as DNA-damaging drugs to treat cancer and briefly discuss the types of DNA lesions induced by each. (12 pts)
(b) Gene therapy is a long-sought-after treatment for many human maladies. How will DDR knowledge provide advances in gene therapy? (8 pts)

3. (RJK) DNA damage response events operate in diverse biological settings including the generation of immune-receptor diversity, the production of gametes for sexual reproduction, telomere homeostasis and aging, the physiological control, and the life cycles of pathogens. Describe the DDR for two of these settings.

4. (LM) Answer ONE (1) of the following questions:

i) Explain how DNA damage accumulation in neurons leads to neurodegenerative disorders.
ii) Explain the relationship between cancer and DNA damage.

In your answer, please give reasons why the diseased cells might have an increased rate of DNA damage. Also, please note the mechanism(s) by which the DNA damage response is altered or suppressed in diseased cells.

5. (JHM) Based on each of the following key protein components, (1) name the DNA damage response mechanism (Repair pathway), (2) the lesions that are acted upon and (3) the sources that give rise to those lesions.

a) Rad51, BRCA2
b) DNA glycosylases
c) Ku, DNA-PK, Aprataxin
d) Polymerase h,i,k, REV3, REV1
e) XPC, DDB1/2, CSA, CSB
f) MSH2-MSH6, MLH1-PMS2
g) CHK1 and CHK2