Birla Institute of Technology and Science, Pilani (Rajasthan)
First semester 2016-17
Introduction to Molecular Biology and Immunology (PHA F215)
Comprehensive Examination

Time: 1.5 hr **Part A (40 marks): Closed book** **Date: 11/04/2017**

Q1. Select the correct answer. Only one answer is correct. **Each wrong answer: -0.5 marks.** **[10×1]**

1. CD8 binds with: a. antigen b. MHC class II molecules c. antibody d. TCR e. MHC class I molecules	2. Proteasomes play a key role in processing a. exogenous antigens b. bacterial antigens c. cell surface antigens d. endogenous antigens e. MHC class II peptides
3. The primary immune response is characterized by a. induction by one dose of antigen b. a long lag period c. low levels of antibody produced d. rapid decline e. all of the above	4. Exogenous antigen processing mainly occurs within a. T lymphocytes b. neutrophils c. plasma cells d. dendritic cells e. none of the above
5. Class II MHC molecules contain a. one gamma chain and one light chain b. one alpha chain and one Beta chain c. two light and two heavy chains d. one epsilon chain e. B2-microglobulin	6. One characteristic that distinguishes the construction of immunoglobulin heavy chains from that of light chains is a. somatic hyper-mutation b. the use of gene segments c. looping out of gene segments d. the use of a D gene segment e. the use of a J gene segment
7. When a IgG antibody combines with an antigen, the Fc region is exposed to react with a. TNF and ILl. b. Macrophages. c. B cells. d. Other antibodies. e. none of these.	8. When a B-cell undergoes immunoglobulin class switching a. the variable region of the light chain changes, but its constant region remains the same b. the variable region of the heavy chain remains the same but its constant region changes c. the variable region of the heavy chain changes but its constant region remains the same d. both the variable and constant regions change
9. Which immunoglobulin is the principal one found in secretions such as milk? a. IgG b. IgM c. IgA d. IgD e. IgE	10. Individuals unable to make the J protein found in certain immunoglobulins would be expected to have frequent infections of the a. brain. b. blood. c. liver. d. pancreas. e. intestinal tract.

Q2. Cytotoxic T cells (CTL) play an important role in cellular defense. Against which type of infection CTL activity is most important? What is the major function of CTL? How CTL show its function? **[1+1+3]**

Q3. What is immunoglobulin class switching? Write short notes on the T-dependent and T-independent antibody responses. **[1+2+2]**

Q4. This cell works as a bridge between innate and adaptive immune system. Somehow it lost the gene of B7 from its genome. i) What is the name of this cell? ii) Which cell is directly activated by this cell? iii) How loss of B7 will affect the immune system in case of an infection? **[1+1+3]**

Q5. An 11-year-old boy, AB, presented with a history of recurrent bacterial infection. His IgM levels were very high but serum IgA, IgG, and IgE were barely detectable. Upon close examination, it was found that a critical cell surface protein, X, is not expressed on AB's activated Th cells. The T cell receptor on the Th cell was found to be normal. Can you make an educated guess about the identity of the protein X? Why it's absence resulted in high IgM but low other antibodies? **[1+3]**

Q6. There are mainly two pathways through which intracellular pathogens can be killed: one is a component of **(a)** innate immune system and the other is **(b)** adaptive immune system. Name them. **[1]**

Two examples of viral immune evasion strategies are described below. For each of the three strategies, please state whether virally-infected cells would be killed by **(a)** and/or **(b)**, and explain how the target cell killing will occur.

i. Human cytomegalovirus (HCMV) encodes a protein called US3 that binds to MHC Class I molecules and retains them in the ER, so that they never get presented on the cell surface. **[2]**

ii. Poxviruses encode a protein called crmA, which can inhibit caspases, which are proteins in the apoptosis cascade downstream of granzymes and Fas. **[2]**

Q7. Epstein-Barr virus proteins contain an internal repeat exclusively composed of glycines and alanines that inhibits proteasomal degradation. Among cell mediated and humoral immune system, which one would be the most effective against this virus? Explain. How will it inhibit the viral infection? **[3]**

Q8. Why polysaccharide antigens do not produce any memory B cell response? Why attaching a protein toxoid with the polysaccharide antigen lead to production of memory B cells? **[1+2]**

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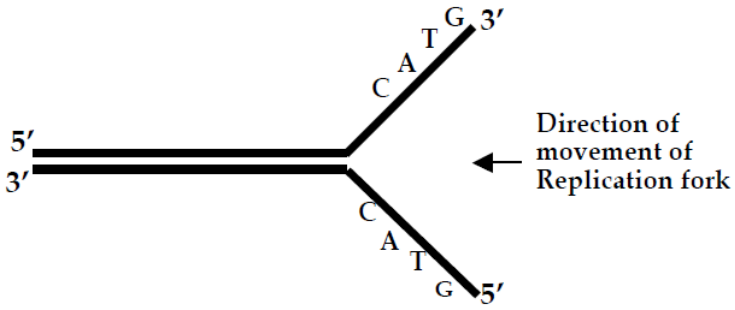
Time: 1.5 hr **Part B (40 marks): Open book** **Date: 11/04/2017**

Q1. Shown below is a segment of replicating DNA in the epidermal cells of the mice.



a) On the schematic, draw the elongating DNA strands and label their 5' and 3' ends. **[1]**

b) To which strand (choose from top, bottom or both) can primer 5`-CATG-3` bind during replication? **[1]**

c) Which strand (choose from top or bottom) is the template for lagging strand synthesis? **[1]**

d) Identify the protein/ enzyme that relieves a replicating segment of DNA from super-coiling. **[1]**

e) Which enzyme is responsible for the lagging strand synthesis? **[1]**

Q2. You treat mouse epidermal cells in a plate with the drug, TAT-2. You observe that TAT-2 treated cells show reduced shortening of their chromosomes following each cell division and survive longer than the untreated cells.

i. Name the replication enzyme that serves as the target of TAT-2 and state whether TAT-2 activates or inhibits the function of this enzyme. **[2]**

ii. What would be the effect of reduced shortening of chromosomes following each cell division on the long- term survival of a cell? Explain. **[3]**

Q3. In an experiment, you irradiate the mouse epidermal cells, growing on a plate, with UV light. This treatment results in the formation of a thymine dimer in the DNA segment.

a) Name the repair steps and the enzyme required in the process. **[2.5]**

b) If the treatment resulted in deamination, what type of repair will take place? Name the enzymes. **[2.5]**

Q4. Assume that Protein A is a 5 amino acid protein the sequence of which is indicated below. Each of these amino acids is critical for the proper folding of this protein.

N - pro-asn-ser-met-leu-C

The DNA sequence encoding the above 5 amino acids is included within the sequence below.

5′-AACCGAATTCCATGTTATAGC-3′
3′-TTGGCTTAAGGTACAATATCG-5′

You have been given the following two different mutant alleles of Gene A. Each mutant allele is due to a point mutation that is bold and underlined. Which of these mutants will ALTER the folding of Protein A? Explain. **[5]**

Mutant 1

5′-AACC**A**AATTCCATGTTATAGC-3′
3′-TTGG**T**TTAAGGTACAATATCG-5′

Mutant 2

5′-AACCG**T**ATTCCATGTTATAGC-3′
3′-TTGGC**A**TAAGGTACAATATCG-5′

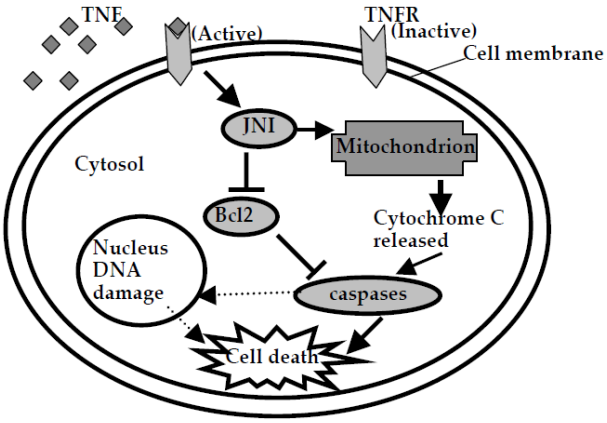
Q5. You observe that some Gene X is transcribed both in epidermal and muscle cells to produce a nascent / primary mRNA transcript. This mRNA directs the synthesis of two different proteins in these two different cell types.

- In the muscle cells Gene X encodes a protein (120 amino acids long) that functions as a cytoplasmic protein
- In epidermal cells, Gene X encodes a protein (100 amino acids long) that functions as a cell membrane protein.

Could Gene A direct the synthesis of two different proteins due to the…

Difference in….	Explain why you selected this option
Splicing? **[1.5]**	
Protein processing? **[1.5]**	
Promoter sequence? **[2]**	

Q6. Consider the following schematic of a signal transduction pathway that results in apoptosis .



i) Tumor necrosis factor (TNF) binds to and activates its specific receptor (TNFR)

ii) The activated TNFR activates JNI.

iii) The activated JNI activates caspases by releasing cytochorome C from mitochondria and also by inhibiting Bcl2. Bcl2, when active, promotes cell survival by inhibiting caspases.

iv) The active caspases result in DNAdamage and cell death.

In the schematic an arrow represents activation and a T represents inhibition.

a) In the schematic above, list the component(s) of signaling pathway that may promote cancer cell growth if they had an oncogenic gain-of-function mutation. **[2.5]**

b) In the schematic above, list the component(s) of signaling pathway that may promote cancer cell growth if they had a loss-of-function mutation. **[2.5]**

Q7. Shown below is the complete DNA sequence of a gene that encodes a short peptide. Also shown is the sequence of the mRNA synthesized from this gene.

Genomic DNA sequence:

```
5'-AGCTCATGTGCGAGTCCTGACGCTGACTAGG-3'
3'-TCGAGTACACGCTCAGGATTGCGACTGATCC-5'
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Mature mRNA sequence (G* = G cap):

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5'-G*UCAUGUGCGAACGCUGACUAGGAAAAAAAA....-3'
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Answer the following questions: **[2×4=8]**

i) In the genomic DNA sequence shown above, draw a box around each of the two exons in the gene.

ii) How many amino acids are there in the peptide encoded by this gene? Name them.

iii) This DNA and RNA are prokaryotic in origin. True or false? Why?

iv) If you want to make this mRNA into double stranded cDNA, what would be the sequence of both the primers (primer length - 4 nt)?

Q8. Indicate whether each of the following statements is true or false. **If false, correct the statement**. **[2×1=2]**

i) Removal of the signal sequence from a protein converts a secretory protein into a cytosolic protein.

ii) During protein folding, chaperones binds with the nascent peptide chain through hydrogen bond.

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