LS 3202 Mid-semester Examination 2019

Time: 1.5 h 30 marks

I. Write down the letter corresponding to the correct answer for the following questions.
Correct answer: +1. Wrong answer: -0.5 8x1 = 8

1. Which of the following processes in a signal transduction pathway of a cytokine can BOTH be a cytoplasmic and nuclear event?
A. Receptor ligand interaction
B. Transcription activation
C. kinase cascade activation
D. Transcription factor activation

2. In a patient, a signal transduction protein that is a part of a kinase cascade is found to be constitutively activated because of a single mutated amino acid. Which of the following is the most probable mutation?
A. Serine to threonine.
B. Serine to alanine.
C. Serine to tyrosine.
D. Serine to glutamate.

3. Which of the following will act as an amplification step in a GPCR signalling pathway?
A. GPCR-ligand interaction
B. G protein-adenylate cyclase interaction
C. adenylate cyclase-ATP reaction
D. Receptor desensitization

4. In a protein-protein interaction network with 8 proteins, number of possible interactions is?
A. 16
B. 28
C. 56
D. 64

5. A negatively autoregulated gene product (mRNA or protein) has an activated synthesis rate 0.65 ng/min and a degradation rate of 0.4 ng/min. After an initial activation, the gene product reaches a steady state concentration of 100 ng. How long will it approximately take to reach half the steady state concentration?
A. 27 min
B. 1 h 17 min
C. 2 h 37 min
D. 247 sec

6. Cells treated with *Pertussis* toxin, the toxin produced by the bacterium that causes whooping cough, are found to have inactive $G\alpha_i$ protein in a GDP-bound condition. What would be the probable result of this phenomenon?
A. The Gα protein does not dissociate from the βγ complex.
B. The Gα protein does not interact with the receptor.
C. The Gα protein does not interact with the GTPase activating proteins.
D. The Gα protein does not interact with adenylyl cyclase.

7. In a patient with a cancer, genome analysis showed the presence of a mutation in a receptor tyrosine kinase which was making it constitutively active. Where in the receptor is the mutation most likely to be present?
A. Extracellular domain
B. Cytoplasmic domain
C. Ligand binding pocket
D. Transmembrane domain

8. Which of the following is a cis-acting element of a gene?
A. Promoter
B. Transcription factor
C. Mediator
D. Chromatin remodelling complex

II. Answer the following questions briefly. (In one or two sentences) 4 X 3= 12

1. While studying the regulation of two genes A and B, a scientist finds the production rate of B to be much more susceptible to fluctuations compared to A? Why do you think this is the case?

2. Although all SH2 domain containing proteins bind to phosphotyrosines, specific SH2 domain containing proteins recognize and bind to specific activated receptors with phosphorylated tyrosines. How is this possible?

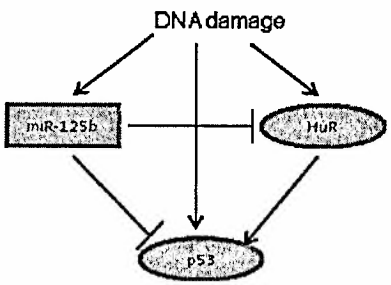
3. The rate of transcription of a gene Y was found to be reduced in a mutant cell line. However while mapping the mutation, it was found to be present not in gene Y but in gene X, which is a transcriptional activator of gene Y. Write down three possible effects that the mutation might be having on X, so as to reduce the transcription of Y.

4. Continuous exposure of a GPCR to its ligand results in the signaling pathway becoming unable to transduce the signal. Suggest three possible mechanisms by which such desensitization of the receptor might happen.

III. Answer ANY 2 of the following questions concisely. (In a few sentences) 2 X 5= 10

1.(a) The dissociation constant for the binding of the ligand to a GPCR is 10^{-10} M. It was found that ligand binding to only 10% of the around 1000 GPCRs on the cell is required for the maximal activation of the G protein. Calculate what is the ligand concentration required to bring about the maximal activation.
(b)Now you mutate the G-protein α_s subunit to increase its affinity to GTP. What will be the effect on ligand binding to the receptor and why? If these mutant G-proteins are now treated with a non-hydrolyzable analog of GTP, what is going to happen to the ligand binding and why?

2.



a) In the above simplified network diagram of the regulation of p53 expression in response to DNA damage, identify the network motifs which will act as 1) Pulse generators 2) Persistence detectors. Write what type of network motif each is.
b) p53 is a tumor suppressor protein which causes cell cycle arrest in response to DNA damage and repairs the damage, but causes apoptosis if the damage is extensive and cannot be repaired. Why do you think p53 expression network both requires a pulse generator and persistence detector?

3. a) Design an experiment to find out whether a protein X, which you suspect is a transcription factor, binds to an enhancer element of a gene and also interacts with the RNA transcription machinery to activate transcription. You have done a structural analysis of X and have found that it is predicted to have a domain that binds to DNA and another domain which binds to protein.
b) How can you find out other cellular proteins which might interact with protein X?