Midsem: Fundamentals of Biology II by Dr. Gaurav Ahuja Date: 25/09/2025

Max Marks 50
Multiple Choice Question (Attempt any 5, 5 marks each, -1 negative)

1. b) G protein will remain inactive
2. b) Convergent signaling
3. a) Uncontrolled protein activation leading to cancer-like growth
4. b) Differences in epigenetic modifications
5. b) Genetic instability
6. b) Frameshift mutation due to insertion or deletion
7. a) Base-excision repair

Short Answer Questions (Attempt any 3, 5 marks each)

1. Compare and contrast autocrine, paracrine, and endocrine signaling with one biological example each.

Ans: Cells communicate through different modes of signaling depending on the distance between the signal-producing and target cells. Autocrine signaling occurs when a cell releases a signal that acts back on itself, allowing self-regulation; for example, T lymphocytes secrete IL-2 to stimulate their own proliferation during an immune response. Paracrine signaling acts locally on neighboring cells, often through diffusion of molecules in the extracellular space; a classic example is neurotransmitters like acetylcholine released from a nerve terminal to act on adjacent muscle cells. Endocrine signaling is long-range communication in which hormones are secreted into the bloodstream and act on distant organs, such as insulin released from pancreatic β-cells regulating glucose uptake in muscle and liver. Thus, the major difference lies in the range of action—autocrine is self-directed, paracrine is local, and endocrine is systemic.

2. Explain the process of GPCR desensitization. Why is this mechanism important for cells?

Ans: G protein-coupled receptors (GPCRs) are key mediators of cellular signaling, but persistent stimulation can be harmful. To prevent overstimulation, cells employ a process called desensitization. Upon repeated activation, GPCRs are phosphorylated by GPCR kinases (GRKs), which creates binding sites for the regulatory protein arrestin. Arrestin binding blocks further interaction between the receptor and G proteins, effectively shutting down the signaling cascade. In some cases, the receptor is also internalized into endosomes and either recycled back to the membrane or degraded. This mechanism is crucial because it prevents continuous signaling that could lead to cellular damage, exhaustion of second messengers like cAMP, or uncontrolled processes such as abnormal cell growth. GPCR desensitization therefore acts as a feedback safeguard to maintain cellular homeostasis.

3. How can two genetically identical organisms (such as identical twins) show different traits? Explain with reference to epigenetics.

Ans: Although identical twins share the same DNA sequence, they can display differences in traits and disease susceptibility due to epigenetic modifications. Epigenetics refers to heritable changes in gene expression that do not alter the underlying DNA sequence. These modifications include DNA methylation, histone modifications, and the action of non-coding RNAs, all of which regulate which genes are turned on or off. Environmental factors such as diet, stress, toxins, or lifestyle can influence these marks, leading to differences in gene expression patterns between twins. For example, variations in DNA methylation may cause one twin to be more susceptible to a disease such as cancer, while the other remains healthy. Thus, epigenetics provides a molecular explanation for how genetically identical individuals can develop distinct phenotypes.

4. What is the difference between a mutation and a polymorphism? Give one example of each.

Ans: A mutation is a rare and permanent change in the DNA sequence, usually harmful and occurring at a very low frequency in the population (<1%). For example, a point mutation in the β-globin gene causes sickle-cell anemia by substituting glutamic acid with valine. In contrast, polymorphism is a DNA variation that occurs more frequently (>1%) and generally contributes to normal genetic diversity rather than disease. The most common type of polymorphism is the Single Nucleotide Polymorphism (SNP), which represents a single base change in the genome that is shared by a significant portion of the population. SNPs often underlie natural variation in traits such as eye color, height, or drug metabolism, without necessarily being harmful. For example, SNPs in the ABO gene determine human blood groups, while certain SNPs in metabolic genes influence individual responses to alcohol or medication. Thus, mutations are usually rare and disease-associated, whereas SNPs are common polymorphisms that contribute to normal human diversity.

5. Describe the Holliday model of homologous recombination and its significance in DNA repair.

Ans: The Holliday model explains how homologous recombination occurs between DNA molecules. The process begins when two homologous DNA duplexes align, and single-strand nicks allow the exchange of strands between the two molecules. This crossover forms a structure called a Holliday junction, where strands from different DNA molecules are covalently linked. The junction can undergo branch migration, extending the heteroduplex region of base-pairing. Eventually, the junction is resolved by specific nucleases that cut and rejoin the DNA, resulting in either crossover or non-crossover products. The significance of this model lies in its dual role: during meiosis, it creates genetic diversity by shuffling alleles between homologous chromosomes, and during DNA repair, it helps fix double-strand breaks, ensuring genome stability. Without homologous recombination, cells would accumulate severe DNA damage, leading to mutations or cell death.

Long answer question (10 marks)

1. Explain the concepts of DNA mutations and polymorphisms, including the different types of each and how they are distinguished from one another. (3 Marks)

   Ans: A mutation is a rare and permanent change in the DNA sequence, usually harmful and occurring at a very low frequency in the population (<1%). Mutations can disrupt normal gene function and may cause genetic disorders; for example, a point mutation in the β-globin gene causes sickle-cell anemia. In contrast, a polymorphism is a DNA variation that occurs more commonly in the population (>1%) and contributes to normal genetic diversity without necessarily being harmful. The most common type of polymorphism is the Single Nucleotide Polymorphism (SNP), which represents a single base change present in many individuals. SNPs underlie natural variation in traits such as eye color, height, or drug response. Thus, mutations and polymorphisms are distinguished by their frequency in the population and their functional consequences—mutations are rare and often pathogenic, while polymorphisms are common and usually neutral or beneficial.

   b)Describe the various types of mutations, including point mutations and expanding nucleotide repeats. (2 Marks)

   Ans: Mutations can be of several types. Point mutations involve a single nucleotide change and are classified as:

- Silent mutations – do not change the amino acid sequence.
- Missense mutations – change one amino acid to another, possibly altering protein function.
- Nonsense mutations – convert a codon into a stop codon, leading to premature termination.

  Other types include insertions and deletions (indels), which may cause frameshift mutations, altering the reading frame of the gene. A special class of mutations is expanding nucleotide repeats, in which short DNA sequences (e.g., CAG, CGG) undergo abnormal repeat expansion during DNA replication. These are linked to diseases such as Huntington's disease (CAG repeat expansion) and Fragile X syndrome (CGG repeat expansion).

   c) Discuss at least three factors that can influence mutation rates. (2 Marks)

Ans: Several factors affect the rate at which mutations occur:

1. DNA replication errors – although DNA polymerase has proofreading activity, mistakes such as base misincorporation or strand slippage can introduce mutations.

2. Exposure to mutagens – physical agents like UV radiation and X-rays, or chemical mutagens such as alkylating agents, can directly damage DNA.

3. Inefficient DNA repair – defects in repair pathways (e.g., mismatch repair deficiency) lead to accumulation of mutations.
   Other influences include oxidative stress, age of the organism, and environmental toxins.

d)Detail at least three DNA repair mechanisms, explaining the specific types of DNA damage each system is designed to correct. (3 Marks)

Ans: Cells have evolved multiple repair systems to maintain genome stability:

- Base Excision Repair (BER): corrects small, non-helix-distorting lesions such as oxidized bases (e.g., 8-oxo-guanine) or deaminated cytosine. DNA glycosylases recognize and remove damaged bases, followed by repair synthesis.

- Nucleotide Excision Repair (NER): removes bulky, helix-distorting lesions such as UV-induced thymine dimers or chemical adducts. A stretch of nucleotides surrounding the damage is excised and resynthesized.

- Mismatch Repair (MMR): corrects errors that escape DNA polymerase proofreading, such as base mismatches and small insertion/deletion loops. Defects in this pathway are linked to hereditary nonpolyposis colorectal cancer (HNPCC).

- Homologous Recombination (HR) and Non-Homologous End Joining (NHEJ): specialized mechanisms for repairing dangerous double-strand breaks, with HR being error-free and NHEJ more error-prone.