THE BUILDING BLOCKS OF PROTEINS:
AMINO ACIDS, PEPTIDES, AND POLYPEPTIDES (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Draw the basic chemical structure of an amino acid.
2. Identify each common amino acid (name and three letter abbreviation) when its side chain structure is provided.
3. Describe the physical and chemical properties of the common amino acids.
4. Draw the reaction for the formation of a peptide bond between two amino acids.
5. Define the N-terminal and C-terminal ends of a polypeptide chain.
6. Demonstrate how cystine is formed from two cysteine residues.
7. Apply the Henderson-Hasselbach equation to determine the acid/conjugate base ratio, pH, or pK_a of a weak acid when the other two parameters are given.
8. Describe the range of pK_a values for the acid/base groups on amino acids.
9. Draw the titration curves for leucine, lysine, histidine, and aspartate.
10. Describe how the amino acid composition of a protein can determine its electrophoretic and isoelectric focusing patterns.
11. Describe the separation of cellular proteins by two-dimensional electrophoresis and its use in diagnosis of disease.

Key Words:

Amino acids [D12.125]
Peptides [D12.644]
Proteins [D12.776]
Acid-base equilibrium [G02.300.176]
Isoelectric point [G02.300.500]

THE BUILDING BLOCKS OF PROTEINS:
AMINO ACIDS, PEPTIDES, AND POLYPEPTIDES (Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Determine the pK_a's and pI of histidine from its titration curve.
2. Calculate the effect of pH on the activity of an enzyme when the pK_a of a key active site residue is given.
3. Describe the effect of acetylation of vasopressin (produced in lung carcinomas) on its electrophoretic migration.
4. Interpret electrophoresis and isoelectric focusing patterns to identify hemoglobin mutants.
5. Describe how the amino acid composition of a protein can determine its electrophoretic and isoelectric focusing patterns.
6. Interpret two-dimensional electrophoresis data to determine the relative pI's, sizes, and identity of proteins expressed in a breast cancer patient specimen.

Key Words:

Amino acids [D12.125]
Peptides [D12.644]
Proteins [D12.776]
Acid-base equilibrium [G02.300.176]
Isoelectric point [G02.300.500]
Hemoglobins [D12.776.124.400]
Anemia, sickle cell [C16.320.365.155]
Hemoglobin C disease [C16.320.365.463]

THE THREE DIMENSIONAL STRUCTURE OF PROTEINS (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Describe the properties of the peptide bond.
2. Describe the role of the *phi* and *psi* angles of the peptide backbone in determining secondary structure in a protein.
3. Explain how the covalent bonds in a polypeptide chain can generate regular secondary structure.
4. Compare the structural characteristics of the α-helix, β-structure, and the collagen polyproline helix.
5. Define the terms motif, fold, and domain as used by protein chemists.
6. Explain the concepts of secondary, tertiary, and quaternary structure with respect to the generation of the final folded structure of a native protein.
7. Predict the placement of hydrophobic and charged amino acids in a folded protein.
8. Explain protein dynamics, using cytochrome c as an example.

Key Word:

Molecular structure [G02. 111.570]
Protein conformation [G02.111.570.790.709]

THE THREE DIMENSIONAL STRUCTURE OF PROTEINS (Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Predict the structure of a leucine zipper motif based of the placement of leucine residues, and the mechanism by which this structure leads to dimer formation.
2. Explain the structural features of immunoglobulin domains and the forces that stabilize them.
3. Explain protein dynamics, using hemoglobin as an example.
4. Predict the consequences of various point mutations in hemoglobin on its structure and function.
5. Describe the structural basis for the formation of amyloid-*beta* peptide fibrils in Alzheimer's disease.
6. Explain why the type 1 collagen mutation found in the disease osteogenesis imperfecta causes unstable collagen fibrils.

Key Words:

Molecular structure [D12.111.570]
Protein conformation [G02.111.570.790.709]
Hemoglobins [D12.776.124.400]
Amyloid-beta peptides [D12.776.543.039]
Immunoglobulins [D12.776.124.486.485]
Osteogenesis imperfecta [C16.320.737]

THE FUNCTIONAL DIVERSITY OF PROTEINS: THE EXAMPLE OF HEMOGLOBIN (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Describe the quaternary structure of hemoglobin.
2. Describe the different forms of hemoglobin and when they are expressed.
3. Describe the overall chemical features of heme, including the oxidation state of the iron during oxygen binding.
4. Identify major features of the oxygen-binding site in hemoglobin.
5. Write equilibrium binding equations for oxygen binding.
6. Explain the role of conformation change (allosterism) in hemoglobin function, and the significance of the Hill coefficient.
7. Illustrate O_2 association-dissociation curves, including P_{50} values.
8. Predict changes in the equilibrium O_2 binding equation and the P_{50} constant with changes in pH and DPG binding.
9. Describe the regulation of oxygen delivery to tissues.
10. Describe CO_2 transport to lung by the isohydric and carbamino-hemoglobin mechanisms.

Key Words:

Hemoglobins [D12.776.124.400]
Hemoglobins [D12.776.422.316.762]
Heme [D23.767.727.640.587]
Allosteric regulation [D12.776.422.316.762]

THE FUNCTIONAL DIVERSITY OF PROTEINS: THE EXAMPLE OF HEMOGLOBIN
(Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Discuss the consequences of metabolic acidosis in a patient with sickle cell anemia.
2. Discuss how the increased concentration of blood 2,3-diphosphoglycerate (DPG) at high altitudes will affect a patient with sickle cell anemia.
3. Explain why the inability of fetal hemoglobin (HbF) to bind to DPG enhances the transfer of O_2 from the mother to the fetus.
4. Discuss why a mutant hemoglobin (Hb Rothschild) that has a decreased Hill coefficient will deliver less O_2 to tissues.
5. Explain why increased carbonic acid and lactic acid in the muscles of a person undergoing vigorous exercise enhances the release of O_2 from hemoglobin.
6. Explain the role of hemoglobin as a pH buffer in blood.
7. Determine the consequences of a Leu>Pro mutation in the B helix of hemoglobin Perth-Abraham Lincoln.

Key Words:

Hemoglobins [D12.776.124.400]
Heme [D23.767.727.640.587]
Allosteric regulation [D12.776.422.316.762]
Anemia, sickle cell [C16.320.365.155]
Hemoglobinopathies [C16.320.365]

ENZYME KINETICS (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Define the parameters that characterize reaction rate expressions.
2. Interpret a free energy vs. reaction coordinate diagram.
3. Discuss the effect of an enzyme on the free energy of activation and free energy of reaction.
4. Draw the Michaelis-Menton equation and define the experimental meaning of K_m, k_{cat}, V_{max}.
5. Calculate the rate of reaction given the substrate concentration and other kinetic parameters.
6. Explain how the equation simplifies under conditions of $[S] << K_m$, $[S] >> K_m$, and $[S] = K_m$.
7. Draw velocity vs. [S] plots for two enzyme reactions with different K_m and V_{max} values.
8. Describe how competitive and non-competitive inhibitors affect K_m and V_{max}.
9. Interpret Lineweaver-Burk plots for enzymes in the absence or presence of various types of inhibitors.
10. Describe the characteristics and regulation of a rate controlling enzyme in a metabolic pathway.

Key Words:

Enzymes [D08.811]
Enzyme kinetics [G02.111.325]
Enzyme inhibitors [D27.505.519.389]
Allosteric regulation [D12.776.422.316.762]

ENZYME KINETICS (Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Predict how the numerical value of an enzyme kinetic parameter will be affected by changes in the values of the other parameters

2. Predict how the presence of a competitive, non-competitive, or mixed inhibitor will affect the enzyme kinetic parameters.

3. Draw velocity vs. [S] curves and Lineweaver-Burke plots for an enzyme assay without or with an added competitive, non-competitive, or mixed inhibitor.

4. Calculate the rate of reaction given the substrate concentration and other kinetic parameters.

5. Predict the effect of a positive allosteric activator on the K_m of a regulatory enzyme.

6. Compare the sensitivity to changes in substrate concentration for two enzymes, one without cooperativity and one with a Hill coefficient of 6.0.

Key Words:

Enzymes [D08.811]
Enzyme kinetics [G02.111.325]
Enzyme inhibitors [D27.505.519.389]
Allosteric regulation [D12.776.422.316.762]

ORGANIZING AND PACKAGING OF CHROMOSOMAL DNA (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Describe the overall structure of DNA at different times in the cell cycle.
2. List the three types of DNA sequences that are required to produce a eukaryotic chromosome that can be replicated and then segregated at mitosis.
3. Describe some characteristics of coding and noncoding DNA.
4. Describe the components and the structural organization of the nucleosome.
5. Compare features of highly condensed and less condensed chromatin.
6. Explain the mechanisms for dynamic changes in chromatin structure including chromatin compaction.
7. Recognize common covalent modifications of histone proteins and their consequences for DNA processes.
8. Describe the function of histone readers and writers.
9. Explain the distinction between genetic and epigenetic regulation.
10. Define heterochromatin and explain how it forms and spreads.
11. Describe unique features of centromeric heterochromatin.
12. Describe the concept of using chromatin-remodeling drugs for treatment of disease.

Key Words:

DNA [D13.444.308]
Chromosome structures [G05.360.160]
Nucleosomes [G05.360.160.180.625]
Histones [D12.776.664.469]

ORGANIZING AND PACKAGING OF CHROMOSOMAL DNA
(Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Predict the consequences if a eukaryotic chromosome had only one origin of replication, or one telomere, or no centromere.

2. Calculate the degree of compaction of a chromosome given the number of base pairs, base pair length, and chromosome length.

3. Analyze data to determine the orientation of DNA around a nucleosome.

4. Analyze data to predict where transposable elements are most likely to be found in DNA.

5. Analyze data to determine whether a family of proteins in heterochromatin can bind to specific N-terminal modifications of histone H3.

6. Compare the N-terminal amino acid sequence of a histone variant with that of H3 to predict if the variant can be modified in the same way as H3, and the consequence if it cannot.

7. Analyze data to determine the effects of an inhibitor of histone deacetylases on the proliferation of acute lymphoblastic leukemia cells with and without resistance to doxorubicin.

8. Analyze data to determine differences in epigenetic histone acetylation in twins at different ages.

Key Words:

DNA [D13.444.308]
Chromosome structures [G05.360.160]
Nucleosomes [G05.360.160.180.625]
Histones [D12.776.664.469]

CHROMOSOMAL DNA REPLICATION (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Describe the mechanism of synthesis of a copy of a pre-existing DNA strand, including the direction of synthesis by the polymerase.
2. Explain the following processes required for DNA replication: initiation, unwinding, priming, unidirectional fork movement, untangling, and termination.
3. Define the differences in the synthesis of the leading and lagging strands, and the role of Okazaki fragments and DNA ligase.
4. Describe the proofreading function of DNA polymerase.
5. Describe the functions of topoisomerase I and II.
6. Describe the use of topoisomerase II inhibitors in the treatment of cancer.
7. Compare chromosomal DNA synthesis in eukaryotes and prokaryotes.
8. Describe the fate of nucleosomes during DNA replication.
9. Explain the function of telomeres.
10. Describe the mechanism for the addition of telomere repeat sequences.
11. Describe the mechanism that ensures that eukaryotic DNA is replicated only once and that all DNA is replicated before the onset of mitosis.
12. Describe features of trinucleotide repeat expansion diseases.

Key Words:

DNA replication [G02.111.087.222]
Topoisomerase [G02.811.399.403]
Telomere [G05.360.160.845]
Trinucleotide repeats [G05.360.340.024.850.500.850]

CHROMOSOMAL DNA REPLICATION
(Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Discuss basic concepts of DNA replication.
2. Analyze data that demonstrate semiconservative replication.
3. Analyze data on expression of telomerase in normal and cancer cells.
4. Analyze data showing the effect of a telomerase inhibitor on glioblastoma multiforme tumor cells and a mouse xenograft model.
5. Analyze clinical data on trinucleotide repeat expansion in Friedreich's ataxia.

Key Words:

DNA replication [G02.111.087.222]
Topoisomerase [G02.811.399.403]
Telomere [G05.360.160.845]
Trinucleotide repeats [G05.360.340.024.850.500.850]

TOOLS FOR MOLECULAR BIOLOGY (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Describe how restriction enzymes can be used to create recombinant DNA.
2. Explain how gel electrophoresis and hybridization can be used to identify specific pieces of DNA or RNA, and define Southern blotting and Northern blotting.
3. Define the term "restriction fragment length polymorphism" (RFLP) and indicate how RFLP analysis can be used to detect a disease-causing gene.
4. Discuss how *in situ* hybridization can be used in the diagnosis of disease.
5. Explain the polymerase chain reaction technique and its use in diagnosing disease.
6. Explain the technique of multiplex PCR and its use in diagnosing Duchenne muscular dystrophy.
7. Describe microsatellite analysis and its use in forensic science.
8. Describe the technique of reverse transcriptase-PCR and why it is used.
9. Describe real-time (or quantitative) PCR.
10. Describe the dideoxy method for sequencing DNA.
11. Describe the technique of DNA microarray analysis and its use in studying disease processes.

Key Words:

DNA restriction enzymes [D08.811.150.280]
DNA, recombinant [D13.444.308.460]
Blotting, Southern [E05.601.150]
Blotting, Northern [E05.601.140]
Polymorphism, restriction fragment length [G05.365.795.595]
In situ hybridization [E05.393.661.495]
Polymerase chain reaction [E05.393.620.500]
Reverse transcriptase polymerase chain reaction [E05.393.620.500.725]
Real-time polymerase chain reaction [E05.393.620.500.706]
Multiplex polymerase chain reaction [E05.393.620.500.487]
Microarray analysis [E05.196.630.570]

TOOLS FOR MOLECULAR BIOLOGY
(Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Perform a pedigree analysis for cystic fibrosis using PCR data.
2. Perform a pedigree analysis for Duchenne muscular dystrophy using multiplex PCR data.
3. Perform a pedigree analysis for sickle-cell anemia using a RFLP technique.
4. Design a PCR procedure based on microsatellite markers for determining whether a DNA sample came from a specific individual.

Key Words:

DNA restriction enzymes [D08.811.150.280]
Polymorphism, restriction fragment length [G05.365.795.595]
Polymerase chain reaction [E05.393.620.500]
Multiplex polymerase chain reaction [E05.393.620.500.487]

GENOME MAINTENANCE AND DIVERSITY:
DNA REPAIR AND RECOMBINATION (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. List the different small-scale and large-scale DNA mutations.
2. Distinguish between somatic and germline mutations.
3. Define loss of heterozygosity.
4. Describe some consequences of unrepaired DNA damage.
5. Describe the mechanism of direct DNA repair.
6. Describe the mechanism of base excision repair.
7. Describe the mechanism of nucleotide excision repair.
8. Describe the mechanism of strand-directed mismatch repair during DNA replication.
9. Explain transcription coupled repair.
10. Describe how DNA double-strand breaks are repaired by nonhomologous end joining and homologous recombination.
11. Describe the process of general recombination in meiosis.
12. Describe the process and consequences of gene conversion.

Key Words:

Mutation [G05.365.590]
DNA repair [G02.111.087.219]
Loss of heterozygosity [G05.365.590.029.530]
Recombination, genetic [G05.355.760]
Meiosis [G05.355.105.220.687]
Gene conversion [G05.355.760.615.475]

GENOME MAINTENANCE AND DIVERSITY:
DNA REPAIR AND RECOMBINATION
(Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Draw the major steps of nucleotide excision repair.
2. Predict the success of cisplatin therapy for different cancers based on data of the cellular levels of nucleotide excision repair proteins.
3. Analyze data on the effect of mismatch repair proteins on cisplatin-induced tumor cell death.
4. Analyze data on cisplatin-induced enrichment of mismatch repair deficient cells in tumors.

Key Words:

Mutation [G05.365.590]
DNA repair [G02.111.087.219]
DNA mismatch repair [G05.355.195.220]
Cisplatin [D01.210.375]

RNA SYNTHESIS AND PROCESSING (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. List the different types of RNA and describe their functions.
2. List the different eukaryotic RNA polymerases and the types of genes they transcribe.
3. Describe the function of the promoter in gene transcription.
4. Describe transcription initiation from a gene transcribed by RNA polymerase II.
5. Describe the features of RNA polymerase II transcripts that direct their maturation to a functional mRNA.
6. Diagram the pre-mRNA splicing reaction.
7. Discuss how mutations in splicing can give rise to human disease.
8. Describe the mRNA capping and cleavage / polyadenylation processes and explain their functions.
9. Describe transcription initiation for genes transcribed by RNA polymerase I and RNA polymerase III.
10. Describe maturation of a pre-rRNA to a mature rRNA
11. Describe maturation of a pre-tRNA to a mature tRNA

Key Words:

RNA SYNTHESIS AND PROCESSING
(Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Analyze data on inhibition of RNA synthesis after DNA damage.
2. Diagram the major steps in assembly of the basal transcription machinery for a typical eukaryotic gene transcribed by RNA polymerase II.
3. Analyze data of splice site mutations and predict the effect on mRNA products.
4. Analyze data on altered transcription initiation of genes in Huntington's disease.

Key Words:

PROTEIN SYNTHESIS (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. List key features of the Genetic Code.
2. Explain the Wobble phenomenon and explain its relationship to degeneracy in the genetic code.
3. Diagram the steps involved in production of an aminoacylated tRNA molecule.
4. Describe how an aminoacyl-tRNA synthetase contributes to the accuracy of protein synthesis (e.g. ensures the correct amino acid is loaded on the correct tRNA).
5. Describe the major steps in protein synthesis (initiation, elongation and termination).
6. Identify the specific steps in protein synthesis where GTP hydrolysis occurs.
7. Describe the cellular mechanisms that ensure the accuracy of protein synthesis.
8. Compare transcription and translation in prokaryotic and eukaryotic cells.

Key Words:

PROTEIN SYNTHESIS (Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Describe the contributions of the aminoacyl-tRNA synthetase and ribosomes to the accuracy of protein synthesis.
2. Explain the effect common mutations have on protein synthesis and the protein product.
3. Analyze data on a new inhibitor of protein synthesis.
4. Discuss the major differences in transcription and translation between prokaryotic and eukaryotic cells.

Key Words:

GENE EXPRESSION I:
GENERAL MECHANISMS AND THE PROPERTIES OF TRANSCRIPT FACTORS (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Discuss how gene expression helps to determine the properties and functions of different types of cells.

2. Diagram the regulatory elements involved in eukaryotic transcription initiation (promoter, enhancer, insulator).

3. Define heterochromatin and euchromatin and describe the role of histone acetylation / deacetylation in their generation.

4. Describe the role of histone methylation in gene expression / repression.

4. Explain the role of activation domains, DNA binding domains, and dimerization domains in transcription factors.

5. Describe transcription factor dimerization and the role of a palindrome sequence in promoting dimer binding.

6. Recognize a leucine zipper, bZIP, helix-loop-helix, helix-turn-helix, and a zinc finger domain and describe how each binds to DNA.

Key Words:

GENE EXPRESSION I:
GENERAL MECHANISMS AND THE PROPERTIES OF TRANSCRIPT FACTORS
(Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Describe the properties and functions of common protein motifs (leucine zipper, bZIP, zinc finger) found in transcription factors
2. Analyze data from a DNAse footprinting experiment.
3. Analyze data from a mobility shift assay (gel retardation assay).
4. Analyze data from a reporter gene experiment demonstrating enhancer activity
5. Analyze data from a DNA-protein precipitation assay.

Key Words:

GENE EXPRESSION II:
MECHANISMS FOR REGULATING TRANSCRIPTION; EPIGENETIC REGULATION OF CELLULAR INHERITANCE AND DIFFERENTIATION (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Describe how eukaryotic cells regulate gene transcription through the binding of multiple transcription factors.
2. Describe how chromatin structure can regulate cell phenotype.
3. Explain how the X-chromosome is inactivated in female cells.
4. Define epigenetics.
5. Explain how DNA methylation affects gene expression and how a pattern of DNA methylation is passed from parental to progeny cells.
6. Explain how CG islands function in maintaining expression of housekeeping genes.
7. Explain how histone acetylated regions of the genome can be passed from parental to progeny cells.
8. Explain how genomic imprinting occurs in a sex dependent manner

Key Words:

GENE EXPRESSION II:
MECHANISMS FOR REGULATING TRANSCRIPTION; EPIGENETIC REGULATION OF CELLULAR INHERITANCE AND DIFFERENTIATION (Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Identify a positive feedback loop of a transcription factor.
2. Identify sites of DNA methylation and describe the effects of DNA methylation on regulation of gene transcription.
3. Explain the role of histone acetylation and deacetylation in regulation of gene transcription.
4. Analyze data on the effects of Myc, Max, and Mad transcription factor regulation.
5. Analyze data from a gene transfection experiment.
6. Analyze data from a Western blot experiment.

Key Words:

GENE EXPRESSION III:
EUKARYOTIC POST-TRANSCRIPTIONAL REGULATION (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Identify steps in post-transcriptional gene expression that can be regulated.
2. Describe how a single gene can give rise to alternative protein products through regulation of alternative promoters, polyadenylation sites, or splicing.
3. Explain how eIF2 phosphorylation regulates global protein synthesis.
4. Explain how phosphorylation of eIF4E binding protein regulates translation initiation.
5. Compare cap-dependent and cap-independent (IRES-mediated) translation initiation.
6.. Explain the advantage to cells of unstable, rapidly degraded mRNAs and proteins.
7. Describe how mRNAs are degraded.
8. Describe the relationship between synthesis and degradation of a protein or mRNA with respect to steady state expression levels.
9. Describe how miRNAs regulate the level of a given mRNA.
10. Describe the ubiquitin conjugation system and the role of ubiquitin in protein degradation by the proteasome.

Key Words:

GENE EXPRESSION III:
EUKARYOTIC POST-TRANSCRIPTIONAL REGULATION (Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Describe how a single gene can give rise to alternative protein products.
2. Describe how splicing enhancer and repressor proteins act to regulate constitutive and alternative splicing of an mRNA.
3. Describe how global protein synthesis is regulated in response to cellular stress, viral infection and in reticulocytes by the level of heme.
4. Explain the role of ubiquitin and the proteasome in degradation of abnormal proteins and important regulatory proteins (such as those involved in cell growth and survival).
5. Describe how miRNAs can regulate gene expression and how measurements of miRNA levels can be used in disease diagnosis.

Key Words:

PRINCIPLES OF CLINICAL CYTOGENETICS (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. List the techniques used to detect abnormalities of chromosome number and structure.
2. Define the terms metacentric, submetacentric and acrocentric and identify chromosomes by their appearance in a chromosomal spread or ideogram
3. Explain the numbering system used to identify specific chromosome bands
4. Describe the outcomes of nondisjunction occurring during either meiosis I or meiosis II during gametogenesis and indicate how they may be distinguished.
5. Analyze karyotypes to identify common genetic diseases caused by aneuploidy
6. Describe how common chromosomal abnormalities such as insertions, deletions, isochromosomes, dicentric chromosomes and ring chromosomes occur.
7. Define balanced and unbalanced chromosomal rearrangements and compare the resulting phenotype of an individual expressing one or the other.
8. Compare the cytogenetic features of reciprocal and Robertsonian translocations.
9. Diagram how a carrier of a balanced translocation can give rise to an unbalanced offspring
10. Describe how microdeletions and duplications are formed.
11. Compare the genetic and phenotypic consequences of chromosome microdeletions and duplications.
12. Explain uniparental disomy and its relationship to Prader-Willi and Angelman syndromes.

Key Words:

PRINCIPLES OF CLINICAL CYTOGENETICS (Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Calculate the risk of an abnormal pregnancy involving a carrier of a balanced translocation.
2. Calculate the risk of an abnormal pregnancy in matings involving aneuploidy
3. Describe the type of information provided by FISH and by DNA methylation analysis, and identify the conditions that dictate when each is appropriate.

Key Words:

PATTERNS OF SINGLE GENE INHERITANCE (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Recognize symbols and terminology often used in pedigree analysis.
2. Recognize recessive, dominant, X-linked recessive, and X-linked dominant inheritance patterns from a pedigree.
3. Define co-dominant and haploinsufficiency.
4. Describe how inbreeding and consanguinity affect the risk of recessive genetic diseases.
5. Explain how sex-linked diseases differently affect males and females.
6. Describe genomic imprinting and inheritance of Prader-Willi and Angelman syndromes.
7. Explain how triplet repeat disorders, dynamic mutations, and anticipation are related.
8. Explain mitochondrial inheritance.

Key Words:

PATTERNS OF SINGLE GENE INHERITANCE (Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Analyze pedigree patterns and predict genotypes and modes of inheritance.
2. Calculate possible genotypes and phenotypes of children of parents expressing complex traits using the Punnett Square.
3. Analyze data to calculate the coefficient of inbreeding

Key Words:

GENETIC VARIATION IN INDIVIDUALS AND POPULATIONS (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Use formal notation for describing genetic mutations
2. Describe paternal and maternal contributions to de novo mutations rates in progeny
3. Define haplotype
4. Explain how disease susceptibility varies among ethnic groups with respect to ABO, Rh and MHC classifications.
5. Explain the Hardy-Weinberg principle
6. Describe how concepts such as gene flow, founder effect and balanced polymorphism influence allele and genotype frequencies in a population.

Key Words:

GENETIC VARIATION IN INDIVIDUALS AND POPULATIONS (Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Calculate disease frequency and carrier frequency within a population
2. Use formal notation to express genetic mutations.
3. Calculate risk of genetic disease for progeny within a particular ethnic populations.

Key Words:

GENETICS OF COMMON DISORDERS WITH COMPLEX INHERITANCE (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Define the terms qualitative (dichotomous) trait and quantitative (continuous) trait and explain how they differ.
2. Explain how the multigenic theory of quantitative traits can be modified to account for the existence of qualitative (dichotomous) traits that are inherited in a complex manner.
3. Explain relative risk and how it is calculated.
4. Define the terms concordance and discordance.
5. Explain how concordance rates between monozygotic and dizygotic twins are used to evaluate relative contribution of genes and environment to a complex disorder.
6. Describe a Gaussian distribution and explain its relevance to quantitative traits in a human population.
7. Explain the relationship between variance and the contributions of genes and environment to quantitative traits.
8. Explain how a modifier gene can account for variable expressivity and incomplete penetrance.
9. Determine the recurrence risk for relatives of a proband diagnosed with a multigenic disorder from the known population risk for the disorder.

Key Words:

GENETICS OF COMMON DISORDERS WITH COMPLEX INHERITANCE
(Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Use empirical risk tables to predict recurrence rates for complex diseases.
2. Calculate relative risk ratio for a complex disease.
3. Describe factors that may decrease the recurrence risk for neural tube defects.
4. Describe the genetic and environmental factors that contribute to thrombosis in young adult women taking birth control pills

Key Words:

MEMBRANE STRUCTURE AND FUNCTION (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Describe the major molecules that form biological membranes.
2. Describe the physical forces that underlie the stability of biological membranes.
3. Define membrane fluidity and explain the molecular characteristics of lipids that determine this property.
4. Define transition temperature in biological membranes and explain what properties are responsible for it.
5. Describe the effects of cholesterol on biological membranes.
6. Describe the structure of sphingolipids and glycolipids.
7. Describe lipid raft formation and cell signaling via phosphatidylinositol.
8. Describe the distinct associations of proteins with lipid membranes.
9. Explain the functional significance of the hydropathy index.

Key Words:

MEMBRANE STRUCTURE AND FUNCTION (Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Analyze data on membrane cholesterol to phospholipid ratios to estimate erythrocyte deformation
2. Describe how phospholipase A2 in snake venom promotes erythrocyte hemolysis.
3. Describe how phospholipase C secreted by some bacteria facilitates tissue invasion.
4. Explain the structural differences between ceramides and diacylglycerols.

Key Words:

ELECTRICAL PROPERTIES OF MEMBRANES (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. List the extracellular and intracellular concentrations of major ions.
2. Describe the major differences between active and passive transport of a molecule or ion across the membrane
3. Describe the distinct types of active transport in membranes.
4. Define uniport, symport, and antiport transporters.
5. List the three types of ATP-driven pumps.
6. Describe the sequence of events in one functional cycle of the Na+/K+ ATPase
7. Explain the difference between primary and secondary active transport
8. Explain the involvement of ABC transporters in disease
9. Explain the origin of resting potentials in cells and describe the roles for Na+/K+ ATPases and K+ channels.
10. Explain the concept of the Nernst Potential (Equilibrium Electrochemical Potential) for an ion.
11. Define the directions of positive and negative currents in relation to ions moving across a cell membrane.
12. Explain what determines a negative or positive current in relation to the Nernst Potential of a given ion.

Key Words:

ELECTRICAL PROPERTIES OF MEMBRANES (Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Explain the role of the Na+/K+ pump in the generation and maintenance of the membrane resting potential

3. Explain the physical forces involve in the determination of the Nernst potential of K+ across the cell membrane

4. Describe the distinct categories of ion channels based on their activation (channel opening) or deactivation (channel closing).

Key Words:

INTRACELLULAR COMPARTMENTS AND VESICULAR TRANSPORT (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Describe how coat proteins on the cytosolic surfaces of membranes mediate vesicle budding and the selective transfer of materials between compartments.

2. Describe the structure and assembly of the clathrin coat and explain its role in vesicle formation.

3. Describe the function of adaptor proteins in concentrating receptors and their cargos in clathrin coated membrane domains and membrane vesicles.

4. Describe the role of dynamin in the formation of clathrin-coated vesicles.

5. Describe the role of COPI in retrograde transport and COPII in anterograde transport between the ER and the Golgi.

6. Describe the role of SAR GTP binding protein in membrane trafficking and assembly of protein coats.

7. Describe the function of the auxiliary proteins guanine nucleotide exchange factor (GEF) and GTPase activating protein (GAP) in coatomer coat assembly and disassembly.

8. Describe the role of the Golgi apparatus in the retention of ER resident proteins.

9. Describe the role of phosphoinositides and Rab proteins in ensuring that newly formed transport vesicles dock to and fuse with the correct membrane.

10. Describe the contribution of v-SNAREs and t-SNAREs to the specificity of vesicle targeting and vesicle membrane fusion

11. Compare membrane–vesicle fusion to the fusion of membrane encapsulated viruses with eukaryotic cells.

12. Identify the various compartments of the Golgi apparatus and explain the relation between Golgi compartmentalization and oligosaccharide processing.

13. Compare constitutive and regulated exocytosis

14. Explain how bidirectional vesicular transport can concentrate cargo into secretory vesicles

Key Words:

INTRACELLULAR COMPARTMENTS AND VESICULAR TRANSPORT
(Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Describe how coat proteins promote vesicle formation and influence vesicle contents.
2. Explain how Rab proteins contribute to specificity in vesicle formation, transport, and fusion with target membranes
3. Describe the role of SNAREs and soluble accessory proteins in vesicle-membrane fusion.

Key Words:

INTRACELLULAR COMPARTMENTS AND PROTEIN SORTING (Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Describe how proteins synthesized in the cytosol are sorted into the nucleus, mitochondria, peroxisomes, and endoplasmic reticulum.
2. Analyze data on how defects in intracellular protein trafficking result in human disease.
3. Analyze data on how mutations in the cystic fibrosis transmembrane regulator result in disease.

Key Words:

LYSOSOMES AND LYSOSOMAL STORAGE DISEASES (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. List the major characteristics of lysosomes and how they differ from early endosomes and pre-lysosomal compartments.
2. Describe the role of lysosomes in maintaining the structural and functional integrity of cells.
3. Describe how lysosomes remodel and maintain extracellular components comprising the connective tissue matrix.
4. Explain how lysosomal enzymes are sorted in the trans-Golgi network and collected for transport to the lysosomes.
5. Explain the biological significant of proteolytic processing of lysosomal enzymes and secretory proteins after leaving the trans-Golgi network.
6. Identify the source and kinds of cellular proteins and non-proteinaceous materials degraded in lysosomes.
7. Describe how these proteins and non-proteinaceous substrates are delivered to the lysosome.
8. Define and compare phagocytosis, endocytosis, transcytosis, and polarizes protein sorting
9. Describe the basic phenotypes and clinical presentations that characterized some relatively common lysosomal storage diseases.
10. Explain how enzyme replacement therapy may be useful in treating some lysosomal storage diseases.

Key Words:

LYSOSOMES AND LYSOSOMAL STORAGE DISEASES (Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Describe the role of the Golgi in protein sorting during their transport through the endomembrane system.
2. Describe how lysosomal proteins are directed to lysosomes during their biogenesis and explain the function of endosomes in lysosomal biogenesis.
3. Describe receptor-mediated endocytosis in mammalian cells and the recycling of membrane and receptors during this process.
4. Explain where secretory proteins are processed and describe the role of convertases in the proteolytic processing of secreted proteins.
5. Compare proteolytic processing of secreted proteins to the proteolytic processing (activation) of lysosomal enzymes with respect to where and how they are processed.
6. Analyze data to identify distinctive lysosomal storage diseases

Key Words:

THE CYTOSKELETON (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Describe the morphology, cellular location, and function of the three major cytoskeletal elements (actin filaments, microtubules and intermediate filaments).
2. Describe the subunits that make up the actin filaments and the kinetics by which they assemble.
3. Describe the importance of ATP hydrolysis in actin filament dynamics and treadmilling.
4. Describe the global cytoskeletal rearrangements regulated by Rho family proteins.
5. Describe the characteristics of actin-based molecular motors.
6. Describe the overall structure of myosin II in the bipolar thick filament found in muscle.
7. Describe the subunits that make up microtubule filaments and the kinetics of their assembly.
8. Describe the importance of GTP hydrolysis in microtubule filament dynamics and dynamic instability.
9. Describe the structural composition and function of microtubule-based astral arrays, cilia and flagella.
10. Describe the characteristics of microtubule-based molecular motors.
11. Compare the functions of actin and microtubule motor proteins.
12. Describe the subunits that make up intermediate filaments and how the structure of intermediate filaments provides high tensile strength.

Key Words:

CELL JUNCTIONS, CELL ADHESION & EXTRACELLULAR MATRIX (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Describe the function of tight (occluding) junctions in blood vessels and epithelial cells.
2. Explain the importance of transcellular transport of nutrients across sheets of epithelial cells that are linked by tight junctions.
3. Explain the process of paracellular transport.
4.. List the different types of anchoring junctions and their functions.
5. For each type of anchoring junction, identify the class of transmembrane adhesive proteins and cytoskeletal proteins to which the adhesive protein attach.
6. Explain the role of selectins in the interaction of white blood cells and endothelial cells.
7. Describe the function of gap (communicating) junctions.
8. Identify the transmembrane proteins that form gap junctions and the types of molecules that can / cannot pass through them.
9. List the major components of the extracellular matrix and identify the cells that secrete them.
10. Identify the characteristics of glycosaminoglycans.
11. Explain the relationship between glycosaminoglycans and proteoglycans.
12. Identify the three principal types of collagen.
13. List the structural features of collagen that provide strength to the extracellular matrix.
14. Identify the characteristics of elastin fibers that gives them their elasticity.
15. List the adhesive glycoproteins that bind cells to the matrix.
16. Describe the function of the basal lamina.
17. Identify the major glycoprotein and proteoglycan components of the basal lamina.
18. Describe the basic structure of integrins and their function in binding cells to the matrix.

Key Words:

CELL JUNCTIONS, CELL ADHESION & EXTRACELLULAR MATRIX
(Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Explain how changes in cell adhesion or cell junctions relate to cancer metastasis.
2. Analyze data on the components of epidermal cell junctions to which autoantibodies are directed in Pemphigus patients.
3. Explain how genetic mutations in collagen alter its strength and give rise to Osteogenesis Imperfecta.
4. Describe how cell type specific intermediate filament proteins can be used for identification of stem cell subsets for use in regenerative medicine.
5. Explain the role of actin mutations in myopathies.
6. Explain the role of microtubule-associated protein disruption in neurological degenerative diseases.

Key Words:

CELL SIGNALING I (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. List the two required components for cell-cell signaling to occur.
2. Define contact-dependent, autocrine/paracrine, synaptic, and endocrine forms of intercellular signaling.
3. Explain how a cell can respond in a specific way in an environment containing a variety of signaling molecules.
4. Explain how a single signaling molecule can have different effects on different target cells.
5. Recognize examples of hormones that have intracellular receptors.
6. Describe the early primary and delayed secondary responses induced by activation of nuclear hormone receptors.
7. Describe how hydrophilic signaling molecules active protein receptors on the surface of a target cell.
8. Describe how a G-protein coupled receptor activates a G-protein and how the G-protein inactivates itself.
9. Describe how some cell surface receptors increase intracellular cyclic AMP by activating adenylyl cyclase via the alpha subunit of a stimulatory G protein (G_S).
10. Describe the steps involved in the activation of adenylyl cyclist by a G_S-coupled receptor.
11. Explain how adenylyl cyclase returns to an inactive state.
12. Diagram how cyclic AMP activates cyclic AMP-dependent protein kinase A (PKA).
13. Describe how PKA recognizes and alters the function of specific cellular proteins.
14. Explain how different hormones can activate cyclic AMP formation yet lead to different effects in different cells.
15. Describe how the effects of PKA are rapidly reversed.
16. Describe how G-protein coupled receptors can be desensitized following ligand binding.
17. Describe the cellular signaling mechanisms that occur when a signaling molecule binds to a receptor that activates the inhibitory G (Gi) protein.

Key Words:

CELL SIGNALING II (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Describe the activation of phospholipase C-β by a Gq-coupled cell surface receptor
2. Explain how phosphatidylinositol-4,5-biphosphate is hydrolyzed by phospholipase C-β and name the resulting products.
3. Describe how diacylglycerol participates in signal transduction through activation of protein kinase C.
4. Describe the role of Inositol 1,4,5-triphosphate (IP3) in signal transduction via Ca2+ release from the endoplasmic reticulum.
5. Describe how Ca2+ release in the form of waves or oscillatory spikes can be modulated by hormone concentration.
6. Describe how the Ca2+-calmodulin complex activates Ca2+/calmodulin dependent protein kinases (CAM-kinase).
7. Explain how CAM-kinase activity can be maintained even when Ca2+ levels decrease and how its activity is turned off.
8. Describe how activation of the inositol phospholipid pathway can have different effects in different cell types.
9. Explain how a single signaling molecule can have multiple receptor subtypes resulting in agonistic or antagonistic signaling.
10. Describe how nitric oxide mediates cGMP production and activation of protein kinase G.

Key Words:

CELL SIGNALING I AND II (Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. List the events in Gs mediated activation of adenylyl cyclase by a hormone.

2. List eight natural cellular mechanisms used to turn off the signal elicited by a hormone using the cyclic AMP signaling pathway.

3. Describe the inositol-phospholipid pathway mediated by Gq.

4. List eight cellular mechanisms that are used to turn off the signal elicited by a hormone using the inositol phospholipid signaling pathway.

5. Explain the biochemical effects of specific drug compounds (phenylephrine, Albuterol, Tamsulosin, Atenolol) on cell signaling systems.

Key Words:

CELL CYCLE I (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Diagram the cell cycle and explain the major event that occur at each stage.

2. Define the classes of cyclins and the checkpoints they act on.

3. Explain how cyclin concentrations vary and regulate cdk activity in a cell cycle dependent manner.

4. Explain the role of Cdk regulatory kinases (CAKs and Wee1) and cdc25 phosphatases in regulating Cdk-cyclin activities

5. Explain the function of the ubiquitination complexes SCF and APC in the regulation of the cell cycle.

6. Explain the role of CKIs (p27, p21) in regulation of the cell cycle.

7. Diagram the retinoblastoma protein (Rb) – E2F pathway and explain the role of phosphorylation / dephosphorylation in relation to the cell cycle.

8. Explain how a DNA virus can regulate the mammalian cell cycle.

9. Describe the role of p53 in regulation of Rb phosphorylation.

10. Describe the role of mdm2 in p53 regulation.

11. Diagram the pathway for regulation of the cell cycle by p53 and Rb proteins.

Key Words:

CELL CYCLE II: MECHANISMS OF CELL DIVISION-MITOSIS (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Describe the major events in each of the subphases of the M phase of the cell cycle.
2. Describe the two major regulators of the M-phase and their substrates.
3. Describe the changes in the nuclear membrane during cell division and what phase of the cell cycle they occur in.
4. Describe how M-Cdk activity regulates nuclear membrane disappearance.
5. Describe the centromeres, centrioles and microtubules and how they participate in cell division.
6. Discuss the mechanisms of microtubule growth and shrinkage.
7. Discuss the role of microtubule associated proteins (MAPs) and catastrophins and their regulation of M-Cdk.
8. Describe the function of cohesin proteins and condensin proteins and how they are regulated.
9. Describe the important anaphase checkpoint prior to the initiation of anaphase.
10. Describe how the anaphase protein complex (APC) is regulated by Cdc20.
11. List the major proteins that mediate cytokinesis.
12. List the important substrates of M-Cdk and APC in regulating the different subphases of the M phase.

Key Words:

CELL CYCLE I AND II (Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Describe the steps of the cell cycle and the mechanisms of regulation.

2. Explain the function of the phosphorylated and unphosphorylated conformations of Rb proteins.

3. Diagram the pathway of p53 regulation of Rb phosphorylation and explain the role of p53 in cancer and drug resistance.

4. Explain the effect of loss of one or both alleles of a tumor suppressor protein.

5. Describe the mechanisms of cell cycle checkpoint regulation.

6. Explain how aberrations in regulation of the anaphase checkpoint lead to genetic instability and cancer.

Key Words:

CELL CYCLE III (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Explain the mechanism by which tyrosine kinase growth factor receptors transmit growth factor signals.
2. Describe the function of SH2 and SH3 domains.
3. Explain the role of GRB2 and the guanine nucleotide exchange factor SOS in RAS activation by tyrosine kinase receptors (RTK).
4. Explain the purpose and properties of the MAPK (mitogen activated protein kinase) cascade by activated Ras.
5. Explain how the activation of Myc by the Ras pathway leads to cell division.
6. Compare apoptotic and necrotic cell death
7. Explain how inhibition of apoptosis can promote cancer.
8. Explain how inhibition of apoptosis can lead to drug resistance.
9. Explain the involvement of apoptotic pathways in autoimmune disease, neurodegenerative disorders and ischemic diseases.

Key Words:

CELL CYCLE III (Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Describe the major components and their functions in the Ras-MAPK signaling pathway.
2. Describe the components and their functions in the apoptotic pathway/
3. Explain how increased apoptosis or decreased apoptosis can lead to disease.

Key Words:

MOLECULAR GENETICS AND CELL BIOLOGY OF CANCER I (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Define the terms proto-oncogene, oncogene, and tumor suppressor protein.

2. Explain how oncogenes act in a dominant fashion and tumor suppressor genes in a recessive fashion.

3. Describe the steps leading to activation of the caspase cascade in intrinsic (mitochondrial) apoptosis and extrinsic (death receptor) apopotosis.

4. Explain a mechanism by which Bcl-2 and Bak/Bax regulate cytochrome C release from the mitochondria.

5. Describe how the Ras – MAPK pathway can regulate apoptosis by modifying the activity of Bcl-2-like pro- and anti-apoptotic factors, regulating p53 levels, and regulating transcription factors like NF-kB.

6. Explain epithelial to mesenchymal transition (EMT) and its reversal (MET) in metastasis.

7. Describe the steps and barriers to the metastatic process.

8. Explain the role of type IV collagenase and urokinase plasminogen activator in metastasis.

9. Explain the role of laminin receptors in the three-step mechanism for basement membrane invasion by tumor cells.

10. List the major inducers of blood vessel growth (angiogenesis).

11. Explain how invasion in angiogenesis by non-transformed endothelial cells is mechanistically similar to invasion by metastatic cells

12. Explain the origins of the anti-angiogenic factors angiostatin and endostatin.

Key Words:

MOLECULAR GENETICS AND CELL BIOLOGY OF CANCER I (Small Group Problems)

Learning Objectives

At the end of the small group session, the learner will be able to:

1. Identify the major components and their functions in the apoptotic pathway.
2. Analyze data on tumor regression following treatment with angiogenesis inhibitors.
3. Analyze data on BRCA1 mutations and altered cell cycle regulation in breast cancer.

Key Words:

MOLECULAR GENETICS AND CELL BIOLOGY OF CANCER I (lecture)

Learning Objectives

At the end of the lecture, the learner will be able to:

1. Define the terms proto-oncogene, oncogene, and tumor suppressor protein.

2. Explain how oncogenes act in a dominant fashion and tumor suppressor genes in a recessive fashion.

3. Describe the steps leading to activation of the caspase cascade in intrinsic (mitochondrial) apoptosis and extrinsic (death receptor) apopotosis.

4. Explain a mechanism by which Bcl-2 and Bak/Bax regulate cytochrome C release from the mitochondria.

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11. Explain how invasion in angiogenesis by non-transformed endothelial cells is mechanistically similar to invasion by metastatic cells

12. Explain the origins of the anti-angiogenic factors angiostatin and endostatin.

Key Words: