

## **SYLLABUS**

COURSE: DENF 1521 Biochemistry  
SEMESTER: Fall  
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COURSE DIRECTOR: Alan E. Levine, Ph.D., M.Ed.

## GOAL

The goal of this course is to help students acquire a basic knowledge of the biochemistry of the human body for use as an aid in the diagnosis, prevention and treatment of oral disease. Some of the material will be of immediate value as students encounter forthcoming studies in histology, microbiology, nutrition, oral medicine, pathology, pharmacology and physiology. Most of it will contribute to a conceptual discipline based on the structure and function of components of living tissues in health and in disease.

The relevance of biochemistry to dentistry will be described to a limited degree at appropriate places as the course progresses. The students will appreciate the value of a good biochemical background only as they progress throughout the 4 years of dental school and into a dental practice. Biochemistry provides a vocabulary of the broadest applicability in the clinical world as well as in the scientific literature of modern dentistry.

The material is organized in the same fashion as found in biochemistry courses in most American dental school curricula. The first section explores the molecular design of life through a focus on molecular biology and the genetic process. The second section considers some properties related to cells and tissues which are attributable to the structure and function of protein molecules and includes enzyme catalysis. The biochemistry of the extracellular matrix, particularly as it pertains to the mineralized tissues, bones and teeth will be covered in the third section. The fourth section describes the processes of metabolism whereby energy is generated and stored followed with how building blocks are synthesized and broken down.

Since you have all had a biochemistry course in order to be admitted to Dental School, you will be expected to utilize this knowledge in this course. The course will review some principles and will build on these principles to allow students to acquire a growing capability to make valid clinical judgments based upon scientific knowledge gained from basic sciences courses including biochemistry.

## OBJECTIVES

The following concepts should be familiar to you from your undergraduate Biochemistry course. The instructors will assume that you are knowledgeable in the following areas. Please contact the course director early in the course if you do not feel comfortable with these topics.

1. Structure and classification of the nucleotides found in DNA and RNA.
2. Structure of the DNA double helix.
3. Structure of RNA.
4. Structure of chromatin
5. The “Central Dogma” of molecular biology
6. Replication and transcription of DNA
7. Translation of RNA into protein
8. The genetic code and the concept of mutations
9. The structure and classification of the 20 amino acids
10. Basic protein structure
11. Enzyme structure and function
12. Basic metabolic pathways (glycolysis, citric acid cycle, gluconeogenesis, pentose phosphate pathway)

### I. FLOW OF GENETIC INFORMATION

1. Review the bases found in DNA and the properties of DNA and the double helix.
2. Review the bases found in RNA and the types of RNA found in cells.
3. Compare and contrast the structure and composition of cellular DNA and RNA.
4. Review the flow of genetic information as outlined by the Central Dogma.
5. Review the structure of the eukaryotic chromosome including the organization of the human genome

### II. DNA SYNTHESIS (REPLICATION)

1. Identify the steps required for the replication of DNA.
2. Distinguish between the different activities of DNA polymerase.
3. List the respective functions of the proteins involved in DNA replication.
4. Summarize the features of the “sliding clamp” model of DNA replication.
5. Compare and contrast eukaryote and prokaryote DNA replication.
6. Describe the telomeres found in eukaryotic chromosomes and summarize the evidence for altered telomerase function in aging and disease.
7. Describe the function of reverse transcriptase and describe its role in retroviral replication.

### III. RNA SYNTHESIS (TRANSCRIPTION)

1. Identify the steps in the process of RNA transcription and the proteins required for each step.
2. Compare and contrast the structure and function of *E. coli* RNA polymerase and the eukaryotic RNA polymerases.
3. Describe the structure of a typical eukaryotic gene.
4. Explain the steps involved in the maturation of the RNA transcript derived from a eukaryotic gene.
5. Review the processes of transcription initiation, elongation and termination in prokaryotes.
6. Compare and contrast the inhibitors of prokaryote and eukaryote transcription and their mechanisms of action.
7. Describe the structure of a prokaryote promoter and the function of promoter sequences.
8. Describe the structure of eukaryote promoters and compare them to prokaryotic promoters.

### IV. PROTEIN SYNTHESIS (TRANSLATION)

1. Explain the basis for the genetic code and the concept of colinearity of the gene and protein.
2. Define the cellular components required for translation and summarize the evidence that shows that mRNA, and not ribosomes, indicate which proteins are synthesized.
3. Explain the importance of amino acyl-tRNA synthetase enzymes to translation.
4. Review the basic steps involved in initiation, elongation, and termination of protein translation.
5. Explain the role of rRNA in protein translation.
6. Describe how antibiotics disrupt protein synthesis.
7. Compare and contrast the spatial and temporal differences in prokaryotic and eukaryotic transcription and translation.

### V. GENE EXPRESSION IN PROKARYOTES

1. State the main level at which gene expression is controlled.
2. Define the terms: gene, operon, inducer, operator and polycistronic transcript.
3. Describe how the expression of the lac operon is regulated in *E. coli*.
4. Describe the molecular basis of catabolite repression.
5. Describe the structure of the trp operon and explain how this structure plays a role in expression of the gene.

6. Describe the regulation of the tryptophan operon by its repressor and tryptophan.
7. Explain how an attenuator regulates expression of the tryptophan operon.

#### VI. GENE EXPRESSION IN EUKARYOTES

1. Describe the points at which gene expression may be regulated in eukaryotes.
2. Explain the role of chromatin structure in gene regulation and describe the modifications of chromatin that occur.
3. Compare and contrast heterochromatin and euchromatin and describe experimental methods to differentiate between the two.
4. State the structure of the upstream regulatory regions of a gene.
5. Define the terms: cis-acting element, enhancer and transcription factor.
6. Compare and contrast the function and structure of promoter and enhancer sequences.
7. Describe the importance of protein-protein interactions in controlling gene expression.
8. Define general transcription factors and give two (2) examples.
9. Define a homeotic gene/protein and explain its role in regulation of gene expression.
10. List four (4) common DNA-binding motifs found in transcription factors.
11. Describe the role of transcription factors in tooth development and how their expression varies with different stages of tooth development.
12. Describe two (2) diseases or abnormalities of tooth development resulting from deficiencies in the expression transcription factors.
13. Explain the role of mRNA stability and alternative splicing in gene expression.
14. Compare and contrast the control of gene expression in prokaryotes and eukaryotes.

#### VII. MUTATIONS

1. Define the following types of site mutations: substitution, transition, transversion, insertion, deletion, tautomer, frameshift and nonsense mutation.
2. State the possible causes of mutations.
3. Describe how the following repair mechanisms: dimer repair, excision repair, mismatch repair, trans-lesion repair, and recombinational repair.
4. Describe the molecular basis of: xeroderma pigmentosum, hereditary nonpolyposis colorectal cancer (HPC), and Fanconi's anemia.

#### VIII. MECHANISMS OF INHERITANCE

1. Define a gene in terms of inheritance.

2. Describe general Mendelian inheritance patterns.
3. Define the terms allele, recessive and dominant.
4. Understand the difference between expressivity and penetrance of phenotypic expression.
5. Understand the genetic mechanisms that are important in the expression of non-Mendelian genetic patterns.

IX. RECOMBINANT DNA TECHNIQUES AND THE STUDY OF DISEASES

1. Define the following terms: vector, insert, chimeric molecule, clone, cloning, molecular cloning, recombinant DNA, library and library screening.
2. Define a restriction endonuclease.
3. Describe how a restriction endonuclease interacts with DNA and the importance of these enzymes to molecular biology.
4. Describe how restriction fragments can be analyzed by gel electrophoresis and southern blotting.
5. State the basic principles of recombinant DNA technology.
6. State the uses of restriction enzymes, DNA ligase, synthetic linkers in cloning.
7. Describe how plasmid and lambda bacteriophage can be used as cloning vectors.
8. Describe how mRNAs can be cloned.
9. Explain how a library can be screened for specific clones using: synthetic oligonucleotide probes, cDNA molecules, and antibodies.
10. State how, starting with one piece of information, genes, protein sequences, proteins, antibodies and vaccines can all be obtained by recombinant DNA technology.
11. Understand the differences between Southern blots, Northern blots, and Western blots.
12. State the basis for mapping genes (mutations) by restriction fragment length polymorphism.
13. Describe the molecular basis for the polymerase chain reaction.
14. State the molecular basis for DNA fingerprinting and its uses in clinical diagnosis and forensics.
15. Compare the hypotheses that are tested by PCR, DNA fingerprinting, RFLP mapping, Northern blots, Southern blots, and Western blots.
16. Understand the techniques and experiments involved in *in vivo* cloning of animals.
17. Understand the techniques and experiments involved in creating transgenic mice.
18. Understand the techniques used in creating homologous recombination knockout mice.

19. Compare the hypotheses that are tested by in vivo cloning, transgenic mice, and homologous recombination mice.
20. Compare how different recombinant DNA techniques were used to elucidate the molecular mechanisms involved in specific diseases such as osteogenesis imperfect and cystic fibrosis.

X. PROTEIN STRUCTURE (Covered in Web modules)

1. Review the structures of the 20 common amino acids and classify them based on their "R" groups.
2. Describe the structure and properties of the peptide bond and explain how the properties of the peptide bond contribute to protein structure.
3. Define primary structure, secondary structure, tertiary structure and quaternary structure of proteins and give an example of each.
4. Describe the structure of the alpha helix, the beta pleated sheet, and the beta turn including the stabilizing forces, relative positions of R groups, and their significance to the overall protein structure.
5. Define a disulfide bond and explain how it stabilizes protein structure.
6. Describe the general orientation of polar and nonpolar (hydrophobic) amino acids in globular proteins and the significance of such orientations.
7. Compare and contrast the effects of conservative and non-conservative mutations on protein structure and function.
8. Define protein domains.
9. Describe the steps involved in protein folding, including additional proteins involved, and how problems in protein folding contribute to human diseases.
10. Explain the role of immunological techniques, X-ray crystallography, isoelectric focusing, and Western blots in studying protein structure/function.

XI. ENZYMES

1. Describe the key characteristics of an enzyme
2. Explain how enzymes function as catalysts.
3. Explain basic concepts of thermodynamics as they apply to chemical reactions.
4. Explain the significance of the enzyme-substrate complex in enzyme catalysis.
5. List the general properties of active sites of enzymes and explain the role of each in catalysis.
6. Define the meaning of  $K_m$  and  $V_{max}$  in the Michaelis-Menten equation.
7. Explain the effects of substrate concentration on reaction velocity.

8. Distinguish between reversible (competitive and noncompetitive) and irreversible enzyme inhibition.
9. Interpret the effects of competitive and noncompetitive inhibitors on the  $K_m$  and  $V_{max}$  of the treated enzyme.
10. Define an allosteric enzyme.
11. Compare the kinetics of allosteric enzymes to enzymes observing Michaelis-Menten kinetics.
12. Describe the catalytic strategies used in enzyme reactions.

## XII. MECHANISMS OF ENZYME ACTION

1. Identify the three (3) amino acids involved in the catalytic mechanism of the enzyme chymotrypsin and explain their function in catalysis.
2. Explain how differences in the amino acids in the binding pockets of the serine proteases influence substrate specificity.
3. Compare the catalytic mechanisms of the cysteine and the serine proteases and the analogous role played by the key amino acids in each enzyme.
4. Explain the role of metal ions in the metalloproteases.
5. Describe some uses of protease inhibitors in disease.

## XIII. REGULATORY STRATEGIES FOR CONTROLLING ENZYME ACTIVITY

1. Describe the concept of feedback activation/inhibition using aspartate transcarbamoylase as an example.
2. Distinguish between the catalytic and regulatory subunits of aspartate transcarbamoylase and describe the conditions that induce their dissociation.
3. Explain how changes in quaternary structure mediate allosteric interactions.
4. Define the "T and R" state for allosteric enzymes.
5. Define an isozyme.
6. Define post-translational modification of proteins and explain the role of these modifications in regulating enzyme and protein structure and function..
7. Recognize the structure of  $\gamma$ -carboxyglutamic acid and explain its biological functions.
8. Explain the function of hydroxylysine and hydroxyproline in collagen.
9. Define a zymogen and explain its function in enzyme regulation.
10. Explain how the proteolytic activation of chymotrypsinogen leads to the formation of an active enzyme.
11. Explain how protein/enzyme function can be affected by the binding of regulatory proteins.

12. Explain the “cysteine-switch” mechanism of activation of matrix metalloproteinases
13. Explain how alterations in proteases and protease inhibitors contribute to pathological states.
14. Discuss the role of ubiquitin in protein degradation.
15. Describe the structure of the proteasome and its role in protein degradation.

XIV. STRUCTURE/FUNCTION OF HEMOGLOBIN AND MYOGLOBIN

1. Compare and contrast the physiological functions and three-dimensional structures of myoglobin and hemoglobin.
2. List the atoms that are coordinated to the iron atom in heme in hemoglobin.
3. Define the role of the 5<sup>th</sup> and 6<sup>th</sup> coordinate positions of iron in heme in hemoglobin.
4. Describe how allostery affects the binding of oxygen to hemoglobin.
5. Describe how oxygen binding to hemoglobin alters hemoglobin structure.
6. Explain the role of 2, 3 bisphosphoglycerate, pH, and CO<sub>2</sub> concentration in regulating oxygen binding to hemoglobin.
7. Compare adult and fetal hemoglobin in terms of structure and oxygen binding properties.
8. List three mutations in hemoglobin and explain how the mutations affect hemoglobin function.

XV. BLOOD COAGULATION

1. Describe the role of zymogen activation in blood coagulation.
2. Explain the role of Vitamin K in blood coagulation.
3. Describe the process of activation of prothrombin.
4. List the steps involved in the formation and stabilization of a fibrin clot.
5. Recognize the defects involved in the disease hemophilia.
6. Describe the role of protein-protein interactions in the regulation of blood coagulation.

XVI. MEMBRANES/PROTEIN TARGETING

1. Describe important chemical and physical properties of cell membranes and their major components.
2. Relate the significance of these properties to membrane structure.
3. Summarize the evidence for our current model of membrane structure.
4. Describe the differences between integral and peripheral membrane proteins.
5. Describe the biosynthesis of membrane and secreted proteins

6. Describe the role of specific amino acid sequences in targeting proteins to cell organelles

XVII. MEMBRANE TRANSPORT

1. Describe mechanisms for transport of small molecules across the membrane, including simple diffusion, facilitative diffusion, active transport by  $\text{Ca}^{2+}$  ATPase,  $\text{Na}^+$ ,  $\text{K}^+$ , ATPase, ABC transporters, secondary active transport.

XVIII. INTRACELLULAR SIGNALLING I

1. Define growth, growth factor, growth factor receptor, mitogen.
2. Define the terms receptor, effector, second messenger.
3. Describe the action of hormones and other biologically active agents that act via receptors in the nucleus and/or cytoplasm.
4. Describe the biosynthesis of thyroid hormones.
5. Describe hormones that act by activation of adenylate cyclase, the role of 7-helix receptors coupled to G proteins, the intracellular cascades triggered by hormone binding to these receptors and how the signal is switched off at each stage.
7. Describe the role of cyclic AMP as a second messenger, activation of its synthesis and breakdown, and its activation of protein kinase A.
8. Describe hormonal activation of phospholipase C, the role of 7-helix receptors coupled to G proteins, the action of  $\text{Ca}^{2+}$  and diacylglycerol as second messengers, activation of protein kinase C.
9. Describe the role of calmodulin in signaling processes.

XIX. INTRACELLULAR SIGNALING II/BACTERIAL TOXINS

1. Describe hormone receptors that exhibit hormone-regulated tyrosine kinase activity, the intracellular signaling cascades triggered by hormone binding to these receptors and how the signal is switched off at each stage.
2. Compare the similarities and differences in the actions of insulin, epidermal growth factor and growth hormone.
3. Describe the action of "small G proteins".
4. Describe the mechanism of action of transforming growth factor- $\beta$ .
5. Compare and contrast the signaling mechanisms used by epidermal growth factor and transforming growth factor- $\beta$
6. Compare the actions of cholera toxin, diphtheria toxin and pertussis toxin on cell signaling components.

XX. CELL CYCLE/ONCOGENES/APOPTOSIS

1. Describe the stages of the cell cycle and the events associated with each stage.

2. Describe the control of the cell cycle and the proteins involved
3. Compare the roles of cyclins, cyclin-dependent kinases, and cyclin-dependent kinase inhibitors in the cell cycle checkpoints.
4. Define oncogene, proto-oncogene, and tumor suppressor.
5. Describe examples of cellular or viral oncogenes that alter cellular signaling pathways.
6. Describe apoptosis, the apoptosome, caspases, the role of cytochrome c, Bcl2 and IAP proteins

#### XXI. INTRODUCTION TO EXTRACELLULAR MATRIX

1. Name the types of biochemical constituents which make up the extracellular matrix of connective tissues.
2. Define the term extracellular matrix.

#### XXII. COLLAGEN/MATRIX METALLOPROTEINASES

1. Describe the molecular structure of collagen including its assembly from collagen monomer to collagen fiber.
2. Explain the importance of glycine, proline and hydroxyproline in the formation of the collagen triple helix.
3. List two properties conferred on collagen by the triple helix.
4. Describe the telopeptides of collagen and their importance.
5. Describe the occurrence and significance of collagen types.
6. Describe two general classes of collagen that differ in having continuous or interrupted triple helices: fibril and FACIT.
7. Name the major type of collagen in most connective tissues in basement membranes, bone and in oral tissues such as dentin and enamel.
8. Compare the biosynthesis of collagen to the process in other proteins emphasizing the steps unique to collagen.
9. Compare the structure of a procollagen molecule to that of a collagen molecule.
10. List the types of post-translational modifications of procollagen that take place in the rough endoplasmic reticulum of cells.
11. Describe the relationship (packing) of collagen molecules (monomers) in formation of collagen fibrils.
12. Define the terms hole zone and overlap zone used to describe collagen fibrils.
13. Describe the importance of cross-links to collagen.
14. Understand how collagen is regulated by tissue-specific transcriptional control

15. Describe the role of matrix metalloproteinases in collagen and ECM protein processing.

### XXIII. ELASTIN

1. Describe the nature of elastic fibers and list the two components found in elastic fibers.
2. Define the term tropoelastin.
3. Describe the two types of structures found in elastin.
4. Compare the cross-linking of elastin with that of collagen.
5. Explain how the molecular structure of elastin gives rise to its resilience.

### XXIV. ADDITIONAL EXTRACELLULAR MATRIX PROTEINS

1. Describe the structure and function of laminin.
2. Describe the structure and function of fibronectin.
3. Describe the RGD sequence and its biological function

### XXV. INTEGRINS AND INTEGRIN RECEPTORS

1. Describe the structure and function of integrins.
2. Describe how integrins interact with the integrin receptors.
3. Describe two types of integrin mediated adhesion.
4. Define the difference between avidity and affinity with respect to integrin receptor function.

### XXVI. PROTEOGLYCANS

1. Describe the general features and composition of proteoglycans.
2. Describe the composition, structure and properties of glycosaminoglycan (GAG) chains.
3. Explain how the type of structure formed by proteoglycans is related to the chemical nature of the GAG chains.
4. Explain how the function of proteoglycans is related to their chemical structure.
5. Describe the "bottle brush" model for proteoglycan structure.
6. Describe the overall composition and properties of Aggrecan and explain how these properties give rise to function.
7. Describe the proteoglycans versican, decorin and biglycan and indicate in which tissues they are found.
8. Explain how the breakdown of proteoglycans begins outside cells in the extracellular matrix.
9. Describe the overall process of synthesis and breakdown of GAG chains.

10. Define the term mucopolysaccharidosis and know the diseases associated with it.

#### XXVII. COMPOSITION OF MINERALIZED TISSUES

1. Name the major organic constituent of bone, dentin and cementum.
2. Define the terms osteogenesis, dentinogenesis and amelogenesis.
3. Name the principal inorganic component of the mineral phase of bones and teeth and the ions from which it is formed.
4. Compare and contrast the relative amounts of organic components, inorganic components and water in dentin, bone and enamel.
5. Contrast the apatite crystals of enamel with those in bone and dentin.

#### XXVIII. DENTIN

1. Name the classes of organic components in dentin.
2. Describe the properties of dentin collagen that show how it is different from collagen in non-mineralizing tissues.
3. Describe the properties of dentin phosphophoryn and how these properties relate to its function in dentinogenesis.
4. Describe the structure of osteocalcin and name a unique acid in this protein.
5. Describe how the proteoglycans of bone and dentin are unique (i.e., different from those in cartilage and other tissues).
6. List two possible ways that proteoglycans could inhibit mineralization of bone and dentin.
7. Describe the potential function of proteoglycans in the process of dentinogenesis.
8. Summarize the possible steps that take place in dentinogenesis.

#### XXIX. ENAMEL

1. List ways that enamel is unique among the mineralized tissues of vertebrates.
2. Describe amelogenins and their fate during amelogenesis.
3. Describe enamelins and their fate during amelogenesis.
4. Contrast the apatite crystals in the early phase of amelogenesis (i.e., in immature enamel) with apatite crystals in mature enamel.
5. Explain how the removal of proteins in amelogenesis can bring about growth of apatite crystals.

#### XXX. THE MINERAL PHASE OF BONES AND TEETH

1. Explain the difference between the organic and inorganic constituents in bones and teeth.
2. List three major elements in the inorganic constituents.

3. Name the crystalline material that makes up the mineral phase.
4. Specify the unit cell formula for hydroxyapatite.
5. Compare the size of hydroxyapatite crystals in bones and dentin with those in enamel.
6. Compare the inorganic composition of human bone, dentin and enamel as given in the table.
7. Know the approximate amounts of calcium and phosphorus in bones and teeth.
8. Name at least three minor or trace elements in bone.

XXXI. MECHANISMS OF MINERALIZATION

1. Define the terms mineralization and calcification.
2. List the general solubility products for hydroxyapatite and bone mineral.
3. Define metastability of serum and extracellular fluids with respect to hydroxyapatite.
4. Understand the effect of solution pH on mineral solubility.
5. Compare homogeneous and heterogeneous nucleation.
6. List the sequence of reactions which can allow apatite crystals to form with a lower energy expenditure.
7. Define the terms nucleator
8. Describe matrix vesicles and their role in mineralization.
9. Name two enzymes associated with matrix vesicles.
10. Contrast mineralization associated with matrix vesicles with that involving collagen fibrils.

XXXII. INTRODUCTION TO METABOLISM

1. Explain the significance of free energy in biochemical reactions.
2. Discuss how an energetically unfavorable reaction can be driven by coupling with an energetically favorable reaction.
3. Describe the central role of ATP in biochemical reactions.
4. List the major vitamin-derived coenzyme carrier molecules and explain their role in metabolic pathways.
5. List the major control mechanisms used by cells to regulate their metabolism.
6. Describe how energy charge can be used to predict whether the cellular environment favors catabolic or anabolic reactions.

XXXIII. CARBOHYDRATES

1. Describe the chemical structures of common monosaccharides, disaccharides and carbohydrate polymers.
2. Describe how oligosaccharides are attached to proteins.
3. Discuss the roles of glycoproteins in the following processes: protein turnover, bacterial cell adherence, cell:cell interactions.

XXXIV. OXIDATIVE PHOSPHORYLATION

1. Describe the structure and organization of mitochondrial oxidative phosphorylation and identify sites of ATP formation.
2. Review mitochondrial structure and compartmentalization and relate this to electron transport, proton pumping, and ATP synthesis
3. Describe the structure of ATP Synthase and explain how this enzyme uses the proton gradient to synthesize ATP.
4. Explain how oxidative phosphorylation is regulated.
5. Compare the effects of uncouplers and inhibitors on electron transport and ATP synthesis.
6. Explain the significance of “respiratory coupling” to overall cellular metabolism.
7. Describe the importance of shuttles and transport systems in providing intermediates for oxidative phosphorylation.
8. Summarize the relationship between mitochondrial defects between and disease.

XXXV. GLYCOGEN METABOLISM

1. Describe the structure of glycogen and relate its importance to the metabolism of glycogen.
2. Compare the enzymes and pathways involved in the synthesis and degradation of glycogen.
3. Describe the reaction cascade controlling glycogen synthesis and degradation.
4. Describe the role of the hormones epinephrine, glucagon, and insulin in the control of glycogen metabolism
5. Compare and contrast the effects of phosphorylation and dephosphorylation on the key enzymes of glycogen metabolism.

XXXVI. GLYCOLYSIS

*(NOTE: The basics of Glycolysis, Citric Acid Cycle, Gluconeogenesis, and the Pentose Phosphate Pathway will be covered in web-based lessons.)*

1. Describe the main function of the glycolytic pathway and identify the function of each of the three stages of the pathway.

2. Explain how the metabolic fate of pyruvate depends on the metabolic conditions present in the cell.
3. Identify the net number of ATP's produced by glycolysis and where each ATP is produced.
4. Define substrate-level phosphorylation and identify where it occurs in glycolysis.

#### XXXVII. CITRIC ACID CYCLE

1. Understand the enzymatic reaction converting pyruvate to acetyl CoA and its entry into the citric acid cycle.
2. List the reactions which result in the formation of GTP, NADH, FADH<sub>2</sub>, and CO<sub>2</sub> in the citric acid cycle.
3. Discuss how the metabolic intermediates of this cycle interact with other anabolic and catabolic pathways.
4. Describe how the coenzyme forms of thiamine, niacin, riboflavin, lipoic acid and coenzyme A participate in reactions of the pyruvate dehydrogenase complex and alpha-ketoglutarate dehydrogenase complex.

#### XXXVIII. GLUCONEOGENESIS

1. Compare the reactions in gluconeogenesis and glycolysis and explain why gluconeogenesis does not involve the reversal of all of the glycolysis reactions.
2. Discuss the role of biotin in the enzymatic conversion of pyruvate to oxaloacetate.
3. Discuss how oxaloacetate is shuttled from mitochondrion to cytosol.
4. List the "bypass reactions" unique to gluconeogenesis.
5. Summarize the reactions and the importance of the Cori cycle to glucose metabolism.
6. Compare the role of lactate dehydrogenase in the liver and muscle.

#### XXXIX. PENTOSE PHOSPHATE PATHWAY

1. Describe the oxidative and non-oxidative branches of the pentose phosphate pathway with emphasis on their major metabolic functions.
2. Describe how transketolases and transaldolases link the pentose phosphate pathway to glycolysis.
3. Identify the vitamin-derived cofactor in transketolases.
4. Describe two diseases caused by abnormalities in transketolase and glucose-6-phosphate dehydrogenase.

#### XL. REGULATION OF GLYCOLYSIS, CITRIC ACID CYCLE, GLUCONEOGENESIS, AND GLYCOGEN METABOLISM

1. Define reciprocal regulation of metabolic pathways.

2. Compare the three (3) levels of regulation of the glycolytic pathway.
3. Compare the role of fructose 2,6-bisphosphate in the regulation of glycolysis and gluconeogenesis.
4. Identify the main regulatory step in each of the three (3) pathways.
5. Compare and contrast the regulatory molecules involved in the regulation of glycolysis, the citric acid cycle, and gluconeogenesis.
6. Summarize the effects of regulatory molecules on the regulation of the glycolytic pathway.
7. Describe the effects of blood glucose levels on the [fructose 2,6-bisphosphate].
8. Compare and contrast the role of allosteric and covalent regulation of each pathway.
9. Outline oxaloacetate metabolism and explain why its control is important to the citric acid cycle and gluconeogenesis.
10. Compare the role of phosphorylation in the regulation of the different pathways.
11. Compare and contrast the role of energy charge in the regulation of the different pathways.
12. Describe how glucose acts as an allosteric modifier of phosphorylase to regulate glycogen metabolism.
13. Explain how hormonal control mechanisms allow the liver to regulate blood glucose and allow skeletal muscle to rapidly respond to hormonal stimuli.

#### XLI. FATTY ACID METABOLISM

1. Describe the basic structure of triacylglycerols and fatty acids.
2. Outline the pathways of fatty acid synthesis and compare it to fatty acid degradation.
3. Identify the key regulatory reactions of fatty acid metabolism and their control.
4. Explain the conditions required for ketone body formation.
5. Describe the relationship between carbohydrate and fatty acid oxidation and ketone body formation.
6. List the molecules that can be derived from fatty acids.
7. Describe the mechanism of action of the various non-steroidal anti-inflammatory agents.

#### XLII. STEROL AND LUIPID BIOSYNTHESIS

1. Review the structure of cholesterol and its biosynthesis.
2. Describe the regulation of the enzyme HMG-CoA reductase.
3. Explain the regulation of cholesterol metabolism by cholesterol.
4. Describe the biochemical mechanism of action of the statin-type anti-cholesterol drugs.

5. Describe the biosynthetic pathway of bile salts from cholesterol.
6. Describe the pathway of the biosynthesis of steroid hormones from cholesterol.
7. Explain the basis of the diseases associated with cholesterol and steroid metabolism.
8. Describe the role of serum lipoproteins in cholesterol transport in the body.
9. Explain the relationship of the LDL receptor to hypercholesterolemia and atherosclerosis.
10. Recognize the structure of triacylglycerides.
11. Describe the role of CDP-diacylglycerol in phospholipids biosynthesis.
12. Describe the structure of the gangliosides.
13. Recognize the metabolic defects found in Tay-Sachs disease and respiratory distress syndrome.

XLIII. AMINO ACID METABOLISM; UREA CYCLE; HEME

1. Describe how the alpha-amino group is removed from amino acids and excreted.
2. Describe the involvement of vitamin derivatives such as pyridoxal phosphate in amino acid metabolism.
3. Describe the urea cycle and its regulation.
4. Distinguish between ketogenic and glucogenic amino acids.
5. Describe the strategies used to metabolize the carbon skeletons of amino acids for ATP formation.
6. Summarize how various defects in the metabolism can lead to different disease states.
7. Summarize the strategies used in the biosynthesis of amino acids.
8. Explain the importance of tetrahydrofolate and S-adenosylmethionine as one-carbon unit donors.
9. Describe the pathway for the synthesis of heme from glycine and succinyl coenzyme A.
10. Discuss inherited disorders of porphyrin metabolism.

XLIV. NUCLEOTIDE METABOLISM

1. Review the names and structures of the nitrogenous bases, nucleosides and nucleotides.
2. Explain the role of phosphoribosyl pyrophosphate in the synthesis of nucleotides.
3. State the rate-limiting step in the biosynthesis of purines and explain its regulation.
4. Explain how AMP and GMP are formed from IMP.
5. Explain the regulation of purine biosynthesis

6. State the rate-limiting step in the biosynthesis of pyrimidines and explain its regulation
7. Explain the regulation of pyrimidine biosynthesis
8. Compare and contrast the *de novo* biosynthesis of purines and pyrimidines.
9. Compare and contrast the regulation of the *de novo* biosynthesis of purines and pyrimidines.
10. Outline the steps involved in the degradation of purines and list three metabolic diseases associated with this pathway.
11. Explain how CTP is formed from UTP.
12. Explain how deoxyribonucleotides are synthesized and identify the steps which are targets of anticancer drugs
13. Explain how nucleotide analogues can be used in treating cancer and AIDS.

XLV. INTEGRATION OF METABOLISM

1. Review the coordinate regulation of metabolic pathways which synthesize or utilize ATP.
2. Explain the importance of the compartmentalization of metabolic pathways and metabolic specialization of organs.
3. Explain why glucose-6-phosphate, pyruvate and acetyl CoA are key junction points in metabolism.
4. Compare and contrast major features of metabolism in brain, muscle, adipose tissue and liver.
5. Delineate the role of insulin, glucagon, epinephrine and norepinephrine in the regulation of fuel metabolism.
6. Describe how the liver regulates blood glucose levels.
7. Explain metabolic adaptations to prolonged starvation and how they are designed to minimize protein degradation.
8. Describe the metabolic alterations found in type I and type II diabetes mellitus and relate them to those found in starvation.
9. Describe the regulatory mechanisms occurring during different levels of exercise.

## RESOURCES

### I. Media Resources

#### A. Printed media

##### 1. Required textbooks

M. Lieberman and A. D. Marks  
*Marks' Basic Medical Biochemistry: A Clinical Approach*  
Lippincott Williams & Wilkins, 3<sup>rd</sup> edition, 2008

A.E. Levine  
Web-based Biochemistry Lessons  
Available on Blackboard (<https://bb.uth.tmc.edu/>)

Specific assignments will be given by each instructor.

##### 2. Recommended textbooks

J.M. Berg, J.L. Tymoczko, L. Stryer  
*Biochemistry*  
W.H. Freeman & Co., 5<sup>th</sup> edition, 2001

D.L. Hartl, E.W. Jones  
*Essential Genetics, A Genomic Perspective*  
Jones and Bartlett, 3<sup>rd</sup> ed., 2002

##### 3. Handouts

PowerPoint slides used by each instructor may be accessed on the course site on Blackboard. You are responsible for printing your own copy of these slides before class. Individual instructors may distribute other printed material at the beginning of each lecture period.

#### B. Multimedia resources

On-line material will be available in Blackboard. This will include PowerPoint slides, World Wide Web based lessons for Dental Biochemistry, and other resources as announced by instructors. You will have a username and password assigned during Orientation.

Web address: <<https://bb.uth.tmc.edu/>>

### II. Faculty

Alan E. Levine, Ph.D., M.Ed.  
Phone: 713-500-4497; Room: DBB 4.127E  
Email: Alan.E.Levine@uth.tmc.edu

*Course Director*

Julia Lever, Ph.D.  
Phone: 713-500-6055; Room MSB-6.200  
Email: Julia.E.Lever@uth.tmc.edu

Amy Ridall, D.D.S., Ph.D.  
Phone: 713-500-4577; Room: DBB 411A  
Email: Amy.Ridall@uth.tmc.edu

III. Administrative Staff

Kandice Kaylor  
Phone: 713-500-4541; Room 4.109A  
Email: Kandice.Kaylor@uth.tmc.edu

Patricia McFarland  
Phone: 713-500-4105; Room 4.109B  
Email: Patricia.Mcfarland@uth.tmc.edu

## STUDY PLAN AND REQUIREMENTS

Each instructor will assume certain knowledge of biochemistry based on the fact that a one-semester biochemistry course was required for admission to the UT Dental Branch program. It is your responsibility to review previous material as needed and to seek additional help from the instructors if necessary. This course seeks to build on your previous knowledge and expand this knowledge to areas particularly relevant to dentistry. If you feel deficient in any area, it is your responsibility to seek additional help from the course director and instructors if necessary.

Biochemistry meets weekly for three hours. Within these scheduled sessions a variety of teaching techniques will be used. These include lecture, small group activities, take-home exercises, and interactive learning using an audience response system ("clickers"). It is very important for you to attend all sessions and have your "clicker" with you. Be prepared for each session by reviewing specific assignments given by each instructor which may include specific reading assignments, web-based lessons, or exercises to be completed before certain sessions.

The scheduled classroom activities are intended to enhance your study of the material - NOT TO COVER IT COMPLETELY. The average student should set aside at least six (6) hours each week for personal study of biochemistry outside of class. One of the most difficult aspects of your study will be to determine the depth of detail and understanding expected or implied by each objective. This can be gathered by attending class and by reviewing instructor handouts.

If you have any difficulty with the material, contact the appropriate faculty member without delay for individualized assistance. You are encouraged to email the instructors with questions or problems as they arise. If necessary you may contact Kandice Kaylor, Health Education Coordinator (713-500-4541 or [Kandice.Kaylor@uth.tmc.edu](mailto:Kandice.Kaylor@uth.tmc.edu)) to set up an appointment with the appropriate faculty member.

**DENF 1521 BIOCHEMISTRY  
2009 Fall Semester Schedule**

August 19 – December 10  
Wednesday and Friday: 10-10:50 am; Thursday, 11-11:50 am.  
See schedule for exceptions. Final exam: December 10

DATE/TIME			SESSION TOPICS	PRESENTER
Aug 19	Wed	10:00	Introduction / Flow of genetic information / Genetic composition and structure	Levine
Aug 20	Thu	11:00	Replication	Levine
Aug 21	Fri	10:00	Transcription	Levine
Aug 26	Wed	10:00	Protein Translation	Levine
Aug 27	Thu	11:00	Prokaryotic Gene Expression/ Eukaryotic Gene Expression I	Levine
Aug 28	Fri	10:00	Eukaryotic Gene Expression II	Levine
Sep 2	Wed	10:00	Mutations	Levine
Sep 3	Thu	11:00	Non-Mendelian Gene Expression	Levine
Sep 4	Fri	10:00	Recombinant DNA-Basic manipulations	Levine
Sep 9	Wed	10:00	Recombinant DNA-In vitro techniques	Levine
Sep 10	Thu	11:00	Recombinant DNA-In vivo techniques	Levine
Sep 11	Fri	10:00	<i>No class</i> Assignment: Protein Structure Web modules	Levine
Sep 16	Wed	<b>10-11:50</b>	<b>EXAM I</b> (two-hour exam) <b>Room 207</b> covers Aug 19 - Sep 11	Levine
Sep 17	Thu	11:00	Enzymes: Kinetics and Mechanisms	
Sep 18	Fri	10:00	Enzymes: Regulation	Levine
Sep 23	Wed	10:00	Enzymes III	Levine
Sep 24	Thu	11:00	Hemoglobin/Blood Coagulation	Levine
Sep 25	Fri	10:00	Membranes/Protein targeting	Lever
Sep 30	Wed	10:00	Membrane Transport	Lever
Oct 1	Thu	11:00	Intracellular Signaling I	Lever
Oct 2	Fri	10:00	Intracellular Signaling II / Bacterial Toxins	Lever
Oct 7	Wed	10:00	Cell Cycle / Oncogenes / Apoptosis	Lever
Oct 8	Thu	11:00	Collagen Structure / MMPs	Levine
Oct 9	Fri	10:00	Non-collagenous extracellular matrix proteins I	Levine

DATE/TIME			SESSION TOPICS	PRESENTER
Oct 14	Wed	10-11:50	<b>EXAM II</b> (two-hour exam) <b>Room 207</b> covers Sep 17 – Oct 8	Levine / Lever
Oct 15	Thu	11:00	Non-collagenous extracellular matrix proteins II	Levine
Oct 16	Fri	10:00	Integrin Signaling	Levine
Oct 21	Wed	10:00	Mineralized Tissue I	Ridall
Oct 22	Thu	11:00	Mineralized Tissue II	Ridall
Oct 23	Fri	10:00	Mineralized Tissue III	Ridall
Oct 28	Wed	8:00-9:50	Calcium Case with Physiology	Levine/Hutchins
Oct 29	Thu	11:00	ECM-Applications	Levine
Oct 30	Fri	10:00	Introduction to Metabolism/Carbohydrates	Levine
Nov 4	Wed	10-11:50	<b>EXAM III</b> (two-hour exam) <b>Room 207</b> covers Oct 9 - Oct 29	Levine / Ridall
Nov 5	Thu	11:00	<i>No class</i> Assignment: Basic Metabolic Pathways Web modules	Levine
Nov 6	Fri	10:00	Oxidative Phosphorylation	Levine
Nov 11	Wed	10:00	Glycogen Metabolism	Levine
Nov 12	Thu	11:00	Fatty Acid Metabolism	Levine
Nov 13	Fri	9:00-10:50	Regulation of Glycolysis/Citric Acid Cycle/Gluconeogenesis/Glycogen Metabolism (Interactive Learning)	Levine
Nov 18	Wed	8:00-9:50	Hormonal Control of Glucose Case with Physiology	Hutchins/Levine/ Weisbrodt
Nov 19	Thu	11:00	Sterol & Lipid Biosynthesis	Levine
Nov 20	Fri	10:00	Amino acid metabolism/urea cycle <b>Course Evaluation</b>	Levine
Nov 25-27			<i>Thanksgiving Holiday</i>	
Dec 2	Wed	10:00	Nucleotide Metabolism	Levine
Dec 3	Thu	11:00	Integration of Metabolism I	Levine
Dec 4	Fri	10:00	Integration of Metabolism II	Levine
<b>Dec 10</b>	<b>Thu</b>	<b>10-11:50</b>	<b>EXAM IV</b> (two-hour exam) <b>Room 207</b> covers Oct 30 to Dec 4	Levine

## EVALUATION METHODS

The course is divided into four (4) sections with a major examination for each section. Each examination will consist of objective questions (multiple-choice, true-false, and matching) and may also include essay questions. Two hours will be allowed for each of the four (4) of the exams. These examinations are intended not only to help evaluate knowledge but also to further teach biochemical principles. The exams are considered to be an integral part of the learning experience. Your exam papers will be returned within a few days after the exam for comparison with the posted exam key. These exams will require you to apply the knowledge obtained in class to solve problems. Each exam will be based on 100 points. Individual instructors may give exercises within the context of their section of the course which may count for “bonus” points on the exam. Each examination will count 22% of the final grade.

One 15-minute quiz will be given in sections 1, 2, and 3 of the course and two (2) quizzes will be given in section 4 of the course. The purpose of the quiz is to encourage the student to stay up-to-date with reading assignments and lecture material. Quiz questions will come from the lectures, handouts, and assignments covered by the instructor in that section of the course. The instructor will announce the date of the quiz and the exact material to be covered on the quiz. Some quizzes may be given through Blackboard or include questions answered in class with the audience response clicker system. The four (4) BEST quiz grades will be counted towards the final grade. These quizzes comprise 12% of the final grade (3% for each quiz). If you miss 1 quiz for any reason (excused or non-excused absence) this will be the dropped quiz grade. If you miss a second quiz because of an approved excused absence, your quiz average will be determined based on the number of quizzes actually taken. If you miss a second quiz for an unexcused absence you will receive a grade of zero (0) for that quiz. No make-up quizzes will be given.

The material to be covered in each exam and the depth and detail of knowledge expected will be indicated by individual instructors. **All** material presented during lecture or assigned by the instructor (including clinical applications and cases) may be included in the examinations.

### Summary of final grade components

<u>Component</u>	<u>% of final grade</u>
Exam #1	22
Exam #2	22
Exam #3	22
Exam #4	22
4 best quiz grades	12
TOTAL	100