



AMC 500 / BMS 504A

Biochemistry:

Protein Dynamics, Membranes, and Bioenergetics

Fall 2009

M-W-F, 9:00 – 11:00 AM, MS-316 Albany Medical College

Course Directors

Dr. Janice Pata (Wadsworth Center)

Dr. Katharine Herrick-Davis (Albany Medical College)

Course Philosophy

The faculty from the Department of Biomedical Sciences of the SUNY School of Public Health and from Albany Medical College welcome you to AMC 500/ BMS 504A: *Biochemistry, Protein Dynamics, Membranes and Bioenergetics*. This course is part of the core curriculum requirements for all first year graduate students at Albany Medical College and in the BMS department of the SUNY School of Public Health.

A major challenge to biomedical scientists is to gain a better understanding of the structures and functions of molecular systems used by nature. The elucidation of protein structure, the role of enzymes in metabolic processes and cell signaling and the modeling of life processes in the laboratory provide fundamental insights into normal physiological processes and into pathophysiological conditions. Modern biomedical sciences require the mastery of the methods and techniques of biochemistry to successfully deal with a vast variety of problems.

Biochemistry (AMC500/BMS504A) is designed to provide a thorough understanding of the molecular foundations of biological processes. This course will provide an integrated exposure to the major current concepts in biochemistry, which includes bioenergetics, protein structure, enzymology, membrane structure/function and intermediary metabolism. *This course is designed for graduate students and assumes a fundamental knowledge of basic biochemical structures, biosynthetic pathways, and general concepts normally covered in an introductory biochemistry course or advanced cell biology course.*

This course, along with AMC505/BMS500 (Molecular Cell Biology), serves as the groundwork necessary to meet the standards for the MS and PhD degrees in the molecular biosciences. This includes:

- Providing the fundamentals of cell biology, biochemistry and molecular biology, which are seen as a foundation for more advanced course work in the molecular biosciences (protein biochemistry, structural cell biology, microbiology and infectious disease, intermediary metabolism, neuroscience, enzyme kinetics, toxicology, pharmacology, cardiovascular and renal physiology, cancer biology, immunochemistry, cell biology, molecular genetics and molecular biology) and essential to the chosen area of research.
- Providing a familiarity with the research literature in the molecular biosciences, in order to keep abreast of major developments and to acquire a working background in any area.
- Teaching the skills required to solve meaningful problems and questions for research in the molecular biosciences.

Lectures

All lectures will be given from 9:00 AM to 11:00 AM in MS 316 at Albany Medical College on Monday, Wednesday and Friday.

This course is divided into three central themes common for all advanced courses within the different tracks and training programs: Protein Dynamics and Enzymology, Bioenergetics and Metabolism, and Biological Membranes. Each set of lectures is designed to present our current understanding of these biochemical processes. As such instructors will rely both on the classical and current literature to define and analyze the different topical areas. By using this approach, students will be exposed to a variety of biochemical techniques and how they have been and are applied to address specific questions. Central to this teaching strategy will be the use of primary data from the literature to develop lectures on topics ranging from macromolecular assembly to membrane biogenesis. Instructors may use information from the recommended text to define basic foundation principles and may also use specific literature to expand these principles.

Individual instructors will cover each topic area in historical perspective [what has been done] but will place emphasis on the current experimental research. This is intended to provide the students with essential knowledge to make significant and innovative contributions in the future. Specific research articles and seminal reviews that complement the topical area will be assigned. The materials within the assigned articles will be used within the lectures to impart general information and to illustrate experimental design and methods.

Original research articles will also be used to [1] design homework problems; [2] summarize and interpret the data in an exam; and [3] stimulate discussions. Instructors will provide copies of the assigned article(s) several days before the lecture(s) they are intended to complement.

Several days before a specific topic is to be presented, an additional packet of information will be posted on the *BMS504A/AMC500 Biochemistry web site at the SUNY electronic reserve library*. This package will consist of files (pdf or powerpoint format) that include [1] a more detailed outline (if necessary); [2] copies of each of the powerpoint figures (or pdf) used in the lectures, [3] copies of each of the papers that represent required reading, and [4] homework relevant to the lecture.

Unless the instructor for the day's topic fails to post this package several days in advance, it is the student's responsibility to print a hard copy of the material to bring to the lecture.

BMS504A/AMC500 Biochemistry web site at the SUNY electronic reserve library.

1. Going to SUNY electronic reserves: <http://eres.ulib.albany.edu/>
2. Click on "Electronic Reserves & Reserves Pages"
3. Find the course by selecting "Wagenknecht" from the box labeled "Course Reserves Pages by Instructor" or type BMS504A in the box labeled "Search for Course Reserves Pages"
4. The course will be highlighted. Click on it and you will be asked for a password, which is "biochemistry"
5. The page for the course will appear with a listing of the posted lectures, literature, etc.

Textbook

The recommended text for this course is Biochemistry, sixth edition - Berg, Tymoczko, and Stryer (ISBN 0-7167-8724-5). Many of the lectures will be supplemented with reading assignments from this textbook. This textbook is available for purchase at the Albany Medical College Bookstore. A copy of the textbook will be available at the library front desks at AMC and at the Biggs Laboratory (you may sign out the text for 2 hours at a time). Tutorials and three-dimensional structural information from this textbook are available at <http://www.whfreeman.com/stryer>

Internet Applications

During the course, students are required to attend two Internet Applications classes (September 9th and October 2nd) in the AMC Computer Lab (5th floor, AMC library). The purpose of these classes is to introduce students to biomolecular applications ranging from DNA and protein sequence analysis to methods for predicting protein structure and evaluating components of metabolic systems. Knowledge of the information presented during these classes will be essential in order to complete several homework assignments during the course of this class. The overall goal of this component of the course is to introduce resources on the WWW - free software tools that will be accessible to you throughout your careers here in Albany and elsewhere.

Requirements

Hardware: a PC, Mac or UNIX workstation with Internet access

At AMC: You will have access to the computer laboratory at the AMC Library's Fifth Floor Computer Lab during business hours. Access may be restricted to students without AMC ID during restricted hours.

At Wadsworth: PC's, loaded with Protein Explorer 2.0 and Cn3d, have been reserved at the ESP and DAI Libraries for BMS 504A students

Software

A web browser - either Netscape or Explorer.

<http://www.umass.edu/microbio/chime/registfrm/downloadpew.htm>. Protein Explorer 2.45beta - to view protein structures interactively. The program is supplied as freeware for PC, Mac and UNIX. Before this program can be viewed, computers must have Chime installed. If your computer has not been previously loaded with Chime, click on the link to Chime (next to Protein Explorer) and follow the download directions.

<http://www.ncbi.nlm.nih.gov/Structure/CN3D/cn3d.html>. Cn3d and Tutorial - to view protein structures interactively. The program is supplied as freeware for PC, Mac and UNIX. Change your options or preferences file in your web-browser so that Cn3d is a helper application for chemical/ncbi-asn1-binary files.

<http://pymol.sourceforge.net> . PyMol – to view and manipulate molecular structures interactively. Versions of this program for Mac, Windows and UNIX operating system are freely available.

Important Internet Sites for AMC500/BMS504A

<http://www.ncbi.nlm.nih.gov>. The Entrez site at NCBI site provides an integrated entry to the National Institutes of Health databases, including PubMed (for literature searches), Genomes and Proteins databases. The Advanced Search in PubMed is what you should use to find literature references. The BLAST site allows you to identify genes in different organisms.

<http://www.ncbi.nlm.nih.gov/Education/blasttutorial.html>. The BLAST tutorial with demo and exercises all worked out already is a nice place to go if you have problems or questions.

<http://www.tigr.org/tdb/index.shtml>. The TIGR site allows you to follow progress of sequencing projects and has good links to species-specific information.

<http://www.expasy.ch>. The Swiss EXPASY site has many tools for protein analysis (proteomics), including secondary structure predictions in silico.

<http://web.indstate.edu/thcme/mwking/inborn.html>. An overview of metabolic pathways in biochemistry can be found at Metabolic Pathways (<http://www.media.gwu.edu/~mpb/index.html>). This site on inborn errors in metabolism links metabolic defects to clinical presentation and information via PubMed.

<http://web.indstate.edu/thcme/mwking/home.html>. The Biochemistry Website from the University of Indiana School of **Medicine**.

Exams and Grading

There will be 7 tests given during the course of the semester as indicated in the Lecture Schedule on page 6 of this syllabus. The tests will be held from 9:00 AM to 11:30AM at AMC in J-305 & J-306.

Each student is expected to abide by the Honor Codes from both institutions regarding examinations.

Exam questions will be essay style and will require problem solving. There will be a total of 750 points for the course. Each 2 hr lecture will be worth 30 points, and up to 15 points may be assigned as homework (at the discretion of the faculty). On the test, each instructor will determine the length of an acceptable answer by the space provided on the test - you MUST use only the space provided for the answer. Test questions may be based on the required primary literature reading. Each internet application assignment will be worth 30 points. The points for IN1 will be included in the final mark for test I and the points for IN2 will be included in the final mark for test III.

All students will be provided with a grade range and point distribution following each test. Final grades for the course will be determined by the teaching faculty following the final test.

Evaluation by Students

This course will be formally evaluated by the graduate student organizations at Albany Medical College and in the Department of Biomedical Sciences of the SUNY School of Public Health. The results of these evaluations will be given to [1] the AMC/BMS joint curriculum committee; [2] the course directors; [3] the department chairs; [4] the graduate program directors; and [5] each faculty member involved. Included in this evaluation will be content, flow, lectures, instructors, and exams.

Teaching Faculty

The teaching faculty listed below will be available for student questions either by appointment or during defined office hours (each instructor will define their office hours during their first lecture). If you are experiencing any problems in understanding a lecture or group of lectures, you are encouraged to meet individually with the instructor or one of the Course Directors

Course Directors

Dr. Janice Pata (BMS)

Dr. Katharine Herrick-Davis (AMC)

Teaching Faculty

Dr. N. Banavali	BMS	banavali@wadsworth.org	474-0569
Dr. K. Herrick-Davis	AMC	daviskh@mail.amc.edu	262-6357
Dr. J. Jaeger	BMS	jjjaeger@wadsworth.org	408-2225
Dr. D. Jourdeuil	AMC	jourdhd@mail.amc.edu	262-8104
Dr. A. Laederach	BMS	alain@wadsworth.org	486-4103
Dr. A. Mongin	AMC	MonginA@mail.amc.edu	262-9052
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Dr. M. Tenniswood	BMS	mtenniswood@albany.edu	591-7231
Dr. T. Wagenknecht	BMS	terry@wadsworth.org	474-2450

Biochemistry Lecture Schedule

AMC 500 / BMS 504A – BIOCHEMISTRY -FALL 2009

Date	Day	Lecture	Topic	Professor
Aug 31	Mon	BC 1	Overview & Introductory Material	Pata
Sept 2	Wed	BC 2	Working with Macromolecules	Pata
Sept 4	Fri	BC 3	Structure and Function of Proteins	Banavali
Sept 9	Wed	IN 1	Molecular Graphics Programs	Pata
Sept 14	Mon		Test I BC 1-3	
Sept 16	Wed	BC 4	Structure and Function of Large Protein Assemblies	Banavali
Sept 18	Fri	BC 5	Carbohydrate Structure & Protein-Carbohydrate Interactions	Pata
Sept 21	Mon	BC 6	Nucleic Acid Structure & Protein-Nucleic Acid Interactions	Pata
Sept 23	Wed	BC 7	Protein-Ligand Interactions	Herrick-Davis
Sept 30	Wed		Test II BC 4-7	
Oct 2	Fri	IN 2	Bioinformatics	Schwarz
Oct 5	Mon	BC 8	Enzyme Kinetics	Pata
Oct 9	Fri	BC 9	Enzyme Mechanisms	Jaeger
Oct 12	Mon	BC 10	Enzymes: Structure-Function Relationships	Jaeger
Oct 16	Fri		Test III BC 8-10	
Oct 19	Mon	BC 11	Lipid & Membrane Structure	Wagenknecht
Oct 21	Wed	BC 12	Protein-Membrane Interactions: Transporters and Pumps	Wagenknecht
Oct 26	Mon	BC 13	Protein-Membrane Interactions: Ion Channels	Wagenknecht
Oct 30	Fri		Test IV BC 11-13	
Nov 2	Mon	BC 14	Production & Use of Energy in Cells (Ch 15)	Jourd'heuil
Nov 4	Wed	BC 15	Intro. to Metabolism: Glycolysis and TCA Cycle (Ch 16, 17)	Laederach
Nov 6	Fri	BC 16	Electron Transport (Ch 18)	Wagenknecht
Nov 9	Mon	BC 17	Carbohydrate Metabolism (Ch 20, 21)	Jourd'heuil
Nov 16	Mon		Test V BC 14-17	
Nov 18	Wed	BC 18	Fatty Acid metabolism (Ch 22)	Tenniswood
Nov 20	Fri	BC 19	Synthesis of Membrane Lipids and Steroids (Ch 26)	Tenniswood
Nov 23	Mon	BC 20	Metabolic Diseases I	Tenniswood
Nov 30	Mon		Test VI BC 18-20	
Dec 2	Wed	BC 21	Nitrogen Metabolism (Ch 23, 24)	Mongin
Dec 4	Fri	BC 22	Integrated Metabolism (Ch 27)	Mongin
Dec 7	Mon	BC 23	Metabolic Diseases II (Ch 25)	Mongin
Dec 14	Mon		Test VII BC 21-23	

Lecture Outlines for BC 1-23: Fall 2009

<u>Lecture</u>	<u>Date</u>	<u>Topic</u>	<u>Instructor</u>
BC1	8/31	Introduction	Dr. Pata

OBJECTIVES

Nearly all the science we will be discussing in this course is based on a discrete number of fundamental concepts that are common to most biochemical approaches. A major goal of this lecture is to help you to master these concepts, and enable you to use them to approach both classical and novel biological problems.

The molecules of life:

Proteins, nucleic acids, carbohydrates, lipids; water; other small molecules

Chemistry of biological molecules:

Common atoms in biological macromolecules: C, O, N, H, S, P

Covalent bonds and functional groups common in biological molecules

Amino acids, nucleobases, sugars, fatty acids

Overview of common types of reactions

Non-covalent interactions:

Electrostatic (charge-charge)

Van der Waals

Hydrogen bonds

The hydrophobic effect

Key thermodynamic concepts

Enthalpy, entropy, free energy

The importance of water in biology

pH

Acids, bases, and buffers

From molecules to cells and organisms

Evolution & the domains of life (bacteria, eukaryotes, archaea)

Cell structure, tissues, specialization

In vitro vs. *in vivo* and model systems

LITERATURE ASSIGNMENT: Background reading: Biochemistry (Berg, Tymoczko, and Stryer, sixth edition) Chapter 1.

BC2	9/2	Working with Macromolecules	Dr. Pata
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OBJECTIVES

This lecture will provide an overview of methods used to purify macromolecules, to study their structures and interactions, and to characterize their activities. The main goal is to develop an understanding of how biochemical principles are discovered, to bridge the gap between coursework and research.

Recombinant protein expression

Purification methods

Chromatography (ion exchange, size exclusion, hydrophobic interaction, affinity tag)

Structural methods

X-ray crystallography, electron microscopy, NMR, mass spectrometry

Detecting molecules and characterizing their interactions

Labels, dyes, antibodies

Gel electrophoresis

Spectroscopy & Fluorescence

Assays for catalytic activity

LITERATURE ASSIGNMENT: Background reading: Biochemistry (Berg, Tymoczko, and Stryer, sixth edition) Chapter 3. Additional reading and resources will be posted on the website.

BC3 9/4 Structure and function of proteins Dr. Banavali

OBJECTIVES.

The overall objective of this lecture is to study geometrical and functional aspects of protein structure and protein conformational changes. The specific topics that will be covered are :

1. Historical breakthroughs in protein structure.
2. Primary, secondary, tertiary and quaternary structure of proteins.
3. Protein folding and conserved fold families.
4. Quantifying molecular interactions.
5. Conformational changes.
6. Cooperativity.

LITERATURE ASSIGNMENT: (1) Biochemistry (Berg, Tymoczko, and Stryer, sixth edition) Chapters 2 and 3. (2) Lecture slides which will be posted on the website.

IN I 9/9 Internet Application 1: Molecular Graphics Programs Dr. Pata

The amount of structural information available about biological molecules, especially proteins, is growing at a rapid pace because of major proteomics initiatives around the world. This session is designed to provide students with the tools needed to make use of this vast amount of information by using molecular graphics programs to view structures interactively in three dimensions.

LITERATURE ASSIGNMENT: Biochemistry (Berg, Tymoczko, and Stryer, sixth edition) Appendices to Chapters 1 and 2, Visualizing Molecular Structures I and II. PyMol will be the major program used in this session. Versions of this program for Mac, Windows and UNIX operating system are freely available. More information is available online at <http://pymol.sourceforge.net>.

Test I 9/14 BC 1-3 9AM – 11AM in J305&305 at AMC

BC4 9/16 Structure and function of large protein assemblies Dr. Banavali

OBJECTIVES

The objective of the first part of this lecture is to examine molecular recognition and the coordinated operation of molecular machines and large assemblies involving proteins. The objective of the second part of this lecture is to critically analyze a recently published paper related to the structural aspects of function of protein machinery. The specific topics that will be covered are:

1. Quaternary structure and protein-protein interactions.
2. Molecular recognition.
3. Large macromolecular assemblies.
4. An embellished central dogma and the molecular machinery involved.
5. Molecular motors and cytoskeletal structures.
6. Movie : Inner life of a cell.
7. Analysis of a recently published structural study of protein function.

LITERATURE ASSIGNMENT: (1) Lecture slides which will be posted on the website and (2) Published article to be analyzed, which will be posted on the website and *must* be read prior to this lecture.

BC 5 9/18 Carbohydrate Structure & Protein-Carbohydrate Interactions Dr. Pata

OBJECTIVES

Carbohydrates serve a variety of functions in cells: as energy sources, as the backbone of nucleic acids, as modifiers of proteins and lipids, and as structural molecules in the cell walls of plants and bacteria. In these last two capacities, they influence cellular interactions, recognition in the immune system, and infection by viruses and bacteria. The goal of this lecture is to provide an understanding of how carbohydrate structure influences function.

1. Monosaccharides, polysaccharides
2. Cyclization and conformation of rings
3. Complex carbohydrates and enzymatic synthesis

4. Glycosylation of proteins and lipids
5. Carbohydrate recognition

LITERATURE ASSIGNMENT: Biochemistry (Berg, Tymoczko, and Stryer, sixth edition) Chapter 11.

BC6 9/21 Nucleic Acid Structure & Protein-Nucleic Acid Interactions Dr. Pata

OBJECTIVES

Nucleic acids are the source of genetic information and the interaction of proteins with nucleic acids is essential for all aspects of the replication and use of this information. Important aspects of the structure of both DNA and RNA will be presented. This lecture will also provide an overview of the general principles that govern interactions between proteins and DNA or RNA.

1. Basic building blocks, covalent and non-covalent interactions in nucleic acids
2. Nucleic acid secondary structure motifs. DNA duplex, hairpins, RNA pseudo-knots.
3. Tertiary structure, with tRNA structure as a main example
4. Modifications of nucleic acids
5. Nucleic acids features that can be recognized by proteins:
 geometry, H-bond acceptors & donors, electrostatics
6. Similarities & differences in DNA and RNA recognition
7. Protein structural motifs involved in nucleic acid recognition:
 helix-turn-helix, helix-loop-helix, zinc fingers, homeodomains, etc.
8. Molecular recognition:
 sequence- and/or structure- specific binding
 direct or indirect readout of sequence

LITERATURE ASSIGNMENT: Background reading: Biochemistry (Berg, Tymoczko, and Stryer, sixth edition) Chapters 1 and 4. Additional reading and resources will be posted on the website.

BC 7 9/23 Protein ligand Interactions Dr. Herrick-Davis

Objectives: To introduce the student to 1) the principles by which small molecules (e.g. drugs, hormones) interact with protein receptors; 2) the affinity constant (K_d), which is used to define this interaction; 3) the use of the radioligand binding technique as a biochemical measurement of this interaction.

I Introduction

- Scope of lecture, nature and examples of P-L interactions
- Terminology – small molecule, ligand, drug
- Definition of receptors – (biological responses are next lecture)

II Why study drug-receptor interactions? (drugs, receptors and systems as a triad)

- Development of new drugs
- Characterization of new receptors
- Study of new biological systems

III The central significance of K_d for drug-receptor interactions

- all drugs can bind to many molecules (and thus have side effects)
- drug **selectivity** permits intelligent use of drugs as tools
- definition of K_d
- K_d is an invariant property of individual drug-receptor pairs

IV Drug concentration and receptor occupancy: derivation of K_d

- Assumptions
- Derivation of occupancy equation
- Graphical Forms: hyperbola, double-reciprocal, Scatchard, Hill plots

V Radioligand binding – A tool for measuring drug-receptor interactions

Theory

Determination of K_d and B_{max} – Saturation exp (Scatchard Plot)

Competition Experiments – determination of K_i for a non-labeled drug

New receptors: criteria for radiolabeling a receptor

Test 3 10/16 BC 8-10 9:00AM – 11:00AM in J305&305 at AMC

BC11 10/19 Lipid and Membrane Structure Dr. Wagenknecht

This lecture is designed to define membrane structure and biogenesis thereby laying a foundation to understanding membrane transport systems, oxidative phosphorylation and the chemiosmotic hypothesis. The lecture will cover membrane protein structure and membrane fluidity; specificity of lipid and protein composition; mobility of proteins and lipids in membranes.

Objectives:

1. Membrane composition - not all membranes are alike. Differences in fatty acid composition and differences between the lipid composition between the cytoplasmic and exoplasmic faces of the bilayer.
2. Biochemistry of membrane asymmetry
3. Cell Fractionation and phospholipid compartmentalization
4. Different types of phospholipid phases within biological membranes - bilayer; hexagonal arrays; vesicles
5. Membrane phases - role in membrane fusion
6. Membrane fluidity - biophysical considerations; use of differential scanning calorimetry and the identification of phase transition temperature
7. Membrane fluidity and the role of cholesterol and the balance of saturated and unsaturated fatty acids
8. Lipid rafts
9. Membrane fluidity - role of head group and acyl chain of the phospholipid and how these factors influence phase transition temperature and enthalpy in the gel to liquid crystalline phase transition of phospholipid.
10. Analysis of membrane proteins - detergents and critical micelle concentration
11. Analysis of membrane function - vesicles and black lipid bilayers
12. Membrane proteins are laterally mobile in membranes - importance of this property with respect to membrane specialization and function
13. Classes of membrane proteins
14. General features of a 'typical' membrane-bound protein to define [1] α -helix; [2] salt bridges; [3] protein-PL interaction; and [4] N- and O-linked glycosylation
15. Non typical membrane proteins - from gram-negative bacteria and mitochondrial outer membranes; crystallography, algorithms and artificial neural networks
16. Membrane proteins and covalent modification - general features
17. Different types of membrane anchors - [1] fatty acid; [2] farnesyl; [3] GPI
18. Enzymology of farnesylation and formation of GPI anchors
19. Specialized lipid structures, including lipopolysaccharide

LITERATURE ASSIGNMENT: review lecture BC-2 and Chapter 12 in Berg, Tymoczko and Stryer as a foundation for this lecture.

BC12 10/21 Membrane Transporters and Pumps Dr. Wagenknecht

OBJECTIVES

The concepts of active and passive transport across membrane bilayers will be introduced. The types of proteins involved in membrane transport will be discussed.

1. Passive vs facilitated diffusion: how to differentiate experimentally
2. Facilitated diffusion by ionophores: valinomycin and gramicidin
3. Facilitated diffusion by proteins: channels and carriers
4. Classes of protein transporters
5. Channel proteins: porins and aquaporins
6. Modes of active transport—pumps and cotransporters (symporters, antiporters)
7. Lac permease structure/function
8. P-class ion pumps: calcium ATPase and Na^+K^+ -ATPase as prototypes
9. ABC superfamily of ATPase pumps: structure of MsbA

LITERATURE ASSIGNMENT: will be posted on the website.

BC13 10/26 Ligand-gated and voltage-gated ion channels Dr. Wagenknecht

OBJECTIVES

The function and structure of ion channels will be introduced, as well as their roles in generation of action potentials and in certain human diseases.

1. Ionic composition and distributions in cells,
2. Transmembrane equilibrium potentials
3. Patch clamp and bilayer measurements of ionic currents through single channels
5. Structure of potassium channels
 - a. Structure of KcsA channel
 - b. Mechanism of specificity and high conductance
 - c. Families of potassium channels
6. Control of channel gating
 - a. Ligand-gated channels
 - b. Voltage-regulated channels
 - c. Mechano-sensitive channels
7. Structure of a ligand-gated channel, the nicotinic acetylcholine receptor
8. Coordinated action of ion channels and pumps:
 - a. Action Potentials in neurons.
 - b. Excitation-contraction coupling in muscle

LITERATURE ASSIGNMENT: will be posted on the website.

Test 4 10/30 BC 11-13 9:00AM – 11:00AM in J305&305 at AMC

BC14 11/2 Production and use of energy in cells: Bioenergetics Dr. Jourd'heuil

OBJECTIVES

Bioenergetics is the quantitative analysis of how organisms gain and use energy. The goal of this lecture is to introduce basic aspects of biological thermodynamics, which define the limits under which the energetics of biological processes occur. A central goal of this lecture will define the relationship between free energy and reaction equilibria and the dependence of this relationship on environmental variables.

1. Basic thermodynamic concepts.
2. Energy, heat and work - the first law of thermodynamics.
3. Entropy – the second law of thermodynamics.
4. Free energy.
5. Interplay between entropy and enthalpy.
6. Chemical reactions and chemical equilibria.
7. ATP and energy rich compounds.
8. Chemical potential and electron transfer.

LITERATURE ASSIGNMENT: Biochemistry (Berg, Tymoczko, and Stryer, sixth edition) Chapters 1 and 15. Articles will be handed out in class or posted on the website.

BC 15 11/4 Introduction to Metabolism: Glycolysis and TCA Cycle Dr. Laederach

OBJECTIVES

Students should have an understanding of the following concepts:

- Metabolic pathways are dynamic and adaptive systems
- Simple rates govern metabolic flux
- Glucose Metabolism and uptake
- TCA Cycle

LITERATURE ASSIGNMENT: Biochemistry (Berg, Tymoczko, and Stryer, sixth edition) Chapters 15, 16.

BC16 11/6 Electron Transport Dr. Wagenknecht

OBJECTIVES

The fundamentals of electron and proton transport across the mitochondrial inner membrane will be presented.

1. Overview of bioenergetics of oxidative phosphorylation
2. Mitochondria, the site of ox-phos
3. Review of oxidation-reduction chemistry
4. Electron carriers in mitochondrial ox-phos: NADH, FADH₂, ubiquinone, cytochromes, iron-sulfur centers
5. Electron transport chain
6. F₀F₁-ATPase and chemiosmotic theory
7. Malate-aspartate and glycerol 3-phosphate shuttles

LITERATURE ASSIGNMENT: Biochemistry (Berg, Tymoczko, and Stryer, sixth edition) Chapter 18.

BC17 11/9 Carbohydrate Metabolism David Jourdeuil

OBJECTIVES

The fundamentals of carbohydrate metabolism will be presented and the importance of this topic in modern biochemistry will be illustrated within the context of cancer biology and the Warburg effect.

TOPICS TO BE REVIEWED

1. Overview of carbohydrate metabolism
2. Glycogen metabolism
3. Glycolysis and gluconeogenesis
4. Pentose phosphate pathway
5. Tricarboxylic acid (Krebs, TCA) cycle
6. Tissue specific requirements.

LITERATURE ASSIGNMENT:

- 1) Biochemistry (Berg, Tymoczko, and Stryer, sixth edition): Relevant topics in chapters 16, 17, 20, and 21.
- 2) The Biology of Cancer: Metabolic Reprogramming Fuels Cell Growth and Proliferation. DeBerardinis, RJ, Lum JJ, Hatzivassiliou G., and Thompson CB. Cell Metabolism 7, January 2008, page 11-20

Test 5 11/16 BC 14-17 9:00AM – 11:30AM in J305&305 at AMC

BC 18 11/18 Fatty Acid Metabolism Dr. Tenniswood

This lecture is split into two parts A and B. The first hour will be spent on fatty acid synthesis and the second on fatty acid degradation. Each is an essential process and is integral to understanding energy production and utilization as well as regulation dependent upon the polyunsaturated fatty acids, particularly eicosanoids.

OBJECTIVES

- Know fatty acid structures and properties
- Understand the biochemical pathways of fatty acid synthesis
- Compare the structures of ACC and FAS

7. Nitrogen fixation and synthesis of essential amino acids as origin of all nitrogen-containing biomolecules.
8. Synthesis of non-essential amino acids: link to glycolysis and the TCA cycle.
9. "One-carbon" metabolism; folic acid, B12 and SAM.
10. Synthesis of sulfur containing amino acids: methionine, cysteine and taurine.

LITERATURE ASSIGNMENT: Berg, Timoczko, & Stryer. Biochemistry (6th Ed.) Chapters 23 & 24.

BC 22 12/4 Integrated Metabolism Dr. Mongin

This lecture will be divided into two parts. The first half of the lecture will discuss the link between the metabolism of amino acids and other biologically active substances that also contain nitrogen. During the second half of the lecture we will evaluate the connections between metabolism of amino acids, carbohydrates and lipids. We will also talk about unique biochemical profile of human organs as specialized metabolic compartments.

OBJECTIVES:

After this lecture students are expected:

- (1) to recognize major classes of organic molecules that are derived from amino acids and know underlying biosynthetic pathways;
- (2) to know the "crossroads" of major metabolic pathways as well as the key molecules that are common in metabolism of amino acids, carbohydrates, and lipids;
- (3) to appreciate the complexity and coordination of metabolic regulation and its dependence on the needs of human organism.

SPECIFIC TOPICS OF DISCUSSION:

1. Creatine and its physiological roles.
2. Neurotransmitters and hormones derived from amino acids, biological amines and their inactivation.
3. Melanin synthesis and albinism.
4. Nitric oxide and its biological actions.
5. Glutathione and antioxidant defense.
6. NAD and carnitine.
7. Overview of heme biosynthesis.
8. Overview of nucleotide biosynthesis and degradation.
9. Crosstalk between different metabolic pathways and key junctions in metabolism.
10. Biochemical sub-specialization of human organs, and metabolic adaptations in health and disease.

LITERATURE ASSIGNMENT: Berg, Timoczko, and Stryer. Biochemistry (6th Ed.) Chapter 24.4, 25, & 27.

BC23 12/7 Metabolic Diseases II Dr. Mongin

This lecture is designed to apply biochemical knowledge gained during lectures BC21 and BC22 to major metabolic diseases.

OBJECTIVES:

After this lecture students are expected:

- (1) to utilize the preceding material for explaining the biochemical basis of human inborn and acquired metabolic disorders;
- (2) to be able to use major biochemical web-sites for studying metabolic diseases.

SPECIFIC TOPICS OF DISCUSSION:

1. Ammonia toxicity. Hyperammonemia, and its underlying mechanisms.
2. Human disorders linked to tyrosine metabolism: PKU, alkaptonuria, and others.
3. Maple syrup urine disease.
4. Disorders linked to nucleotide metabolism: gout and Lesch-Nyham syndrome.
5. Porphyrins and porphyrias.
6. Metabolic derangements in obesity and diabetes.
7. Useful web sites for studying human metabolic disorders.

LITERATURE ASSIGNMENT: Berg, Timoczko, and Stryer. Biochemistry (6th Ed.). Review disease-related material in Chapters 23, 24, 25, & 27. **Additional materials will be provided before the lecture.**

Test 7 12/14 BC 21-23 9:00AM – 11:00AM in J305&305 at AMC