

# Biochem 6600 Regulation of Metabolism

2018 Spring B 1.5 credits

Tu/Th 9:30-11:00 AM

HSEB2908

## Course Director

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## Course Objectives

1. To review and integrate the basic metabolic pathways involving primarily carbohydrates and fats.
2. To provide the foundation for students to be able to understand the literature in the broad fields of type 2 diabetes and metabolic regulation.
3. To understand the integration of signaling events that are initiated outside of a cell (such as insulin binding to the insulin receptor) with those initiated within a cell (such as increased AMP levels activating AMP-activated protein kinase).
4. To learn specific cutting-edge topics in metabolic regulation from experts in the field.
5. To demonstrate knowledge in metabolic regulation by teaching a 15 min. session on a relevant topic.

## Course description

This course will be taught by a mixture of discussion, didactic (lecture), readings, on-line quizzes and student presentation modalities. The focus is on the regulation of sugar and fat metabolism in eukaryotes, with an emphasis on mammals. The course will begin with a review of carbohydrate and lipid metabolic pathways, particularly pathway integration and regulation. We will then progress to an in-depth analysis of current research in specific areas of nutritional sensing, signaling and metabolic regulation.

## Course resources

**Required textbook:** Keith Frayn, *Metabolic Regulation: A Human Perspective*, 3<sup>rd</sup> Edition. This is a very readable textbook that covers the basic physiology of how human metabolism is regulated. It does NOT have metabolic pathways, but instead clearly explains the concepts of how we can either feast for days or fast for weeks and still function. It is a very accessible introduction to basic endocrine physiology, with a focus on insulin, glucagon and cortisol. This book is available on-line from the Marriot Library (see:

<http://site.ebrary.com/lib/utah/docDetail.action?docID=10358863> ) You will need to either be on campus or use VPN to access this free electronic book. The paperback version is available from Amazon for ~\$45.

**Basic Metabolism Overview (BMO):** This 66-page pdf divided into 4 chapters reviews the metabolic pathways central to human metabolism. You will be expected to know and use this information, as well as being able to integrate it with the physiology described in the Frayn textbook.

**Pathways of human metabolism map:** We will be referring regularly to this searchable metabolic map. Additionally, it will be provided for your in-class quiz. Therefore, this class is NOT about memorizing metabolic pathways, but you will be expected to be able to read and interpret the map.

For the first part of the course, access to an undergraduate or medical biochemistry textbook may also be useful. For example: Stryer (Berg et al) or Lehninger Biochemistry might be useful. The Medical Biochemistry website may also be helpful: <http://themedicalbiochemistrypage.org/>

**Primary literature** and review articles will be assigned as reading for some sessions.

**Canvas:** A canvas site will be used during this course to post: 1. Learning objectives, 2. Pre-class homework (set up as quizzes), and 3. Reading and lecture materials.

## Student assessment

Grades will be based on the following criteria:

Attendance	7%
Classroom participation	13%
Pre-class homework	20%
In-class Quiz (March 15)	30%
Student presentation	30%

This course is based on active discussion and participation within the classroom. Therefore, attendance and participation are required and graded. You will receive 0.5 pt for each class that you attend. Your classroom participation grade will be based on the following criteria: 1) contributed fully to the class discussion of problems, and 2) behaved in a professional and respectful manner towards classmates and faculty, 3) submitted a thoughtful question as part of the homework posted on Canvas (see below), 4) successfully completed any in-class graded activities. If you are not in class you will not be able to earn classroom participation or attendance points. However, if you notify Dr. Lindsley in advance of your need to miss a class, it may be possible to make up some missed points by completing an alternative assignment.

**On-line homework questions will be posted on Canvas prior to most class sessions. These homework assignments will close at 10:00 PM the night before class.** They are designed to help prepare you to fully participate in the learning activities occurring during class time. There will be two parts to each assignment (each part posted as a quiz). The multiple-choice question part will be set up to allow you two chances to choose the correct response. The second part will be a few short answer/essay questions, including a place for you to submit a question you have relating to the upcoming class discussion. Submission of a question will count towards your class participation grade.

During the final 3 sessions of the course each student will teach a 15-min session on a metabolism topic of interest. All students will provide written feedback to the instructing student; this feedback will also count as part of the participation grade. See appendix B for the student feedback form.

## EVALUATION SCHEME:

Letter Grade	Percentage	Letter Grade	Percentage
A	94-100	C-	70-72
A-	90-93	D+	67-69
B+	86-89	D	64-66
B	82-85	D-	60-63
B-	79-81	E	Below 60
C+	76-78	Scores will be rounded: Example 94.4=94, 94.5=95	
C	73-75		

**Class schedule:** All classes will be in HSEB 2908 from 9:30-11:00 on Tuesdays and Thursdays.

2018 BioC 6600  
Regulation of Metabolism  
9:30 – 11:00 AM in HSEB 2908

Date	Day	Class Title	Reading Assignment	Instructor	
3/1	Th	Introduction to metabolism and its regulation	<b>Frayn Ch 1; BMO Ch 1</b>	Lindsley	1
3/6	Tu	Respiration, TCA cycle, carbohydrate catabolism	<b>Frayn Ch 2; BMO Ch 2</b>	Lindsley	2
3/8	Th	Glycogen, Gluconeogenesis and blood glucose regulation	<b>BMO Ch 3; Frayn Ch 11</b>	Lindsley	3
3/13					
3/15	Th	Integration of Carbohydrate & Fat Metabolism/ In-class Quiz	<b>Frayn Ch 7</b>	Lindsley	5
3/17-3/25			<b>U Spring Break</b>		
3/27	Tu	Adipose biology	TBA	Villanueva	6
3/29	Th	Blood glucose control for diabetics	TBA	Chou	7
4/3	Tu	Lipotoxicity and ceramides	TBA	Summers	8
4/5	Th	Adaptive response to starvation	TBA	Thummel	9
4/10	Tu	Interpreting mitochondrial respiration traces	TBA	Boudina	10
4/12	Th	How the brain regulates metabolism	TBA	Fisher	11
4/17	Tu	Student presentations		Students	12
4/19	Th	Student presentations		Students	13
4/24	Tu	Student presentations		Students	14

### Student presentation

The first step in preparation for your presentation is to choose a goal **for the audience**. In other words, first consider **what is that you want the rest of us to be able to do** after your teaching time. Complete the following sentence: At the end of my presentation, the other students in the class will be able to: \_\_\_\_\_. The verb that you choose should be specific and the outcome measurable (such as describe, explain, differentiate, compare and contrast, interpret, recognize, etc), not generic (understand, know). Your presentation will be evaluated partially based on your accomplishment of this goal. See appendix A for grading rubric and appendix B for evaluation by fellow students.

Potential topics for student presentations (feel free to choose one of these or come up with your own metabolism-related topic):

- Topic of interest from Frayn's Metabolic Regulation Ch. 3-6, 8-9, 12
- Epigenetic regulation of metabolism; metabolic enzymes as transcription factors, etc
- Cellular defenses against reactive oxygen species (ROS)
- Mechanism of thyroid hormone stimulation of metabolism
- Roles of peroxisomes or lysosomes in metabolic regulation
- Metabolite repair enzymes
- Cancer metabolism; TCA cycle enzymes as tumor suppressors or proto-oncogenes
- Hypothalamic control of blood glucose
- Mechanism of proton pumping in the electron transport chain
- Regulation of metabolism by thyroid hormone
- GLP-1 and regulation of blood glucose
- Metabolic flux analysis

**Grading criteria for the student taught session (See appendix A): 30 points total**

Achievement of your chosen goal: **10 pts**

Knowledge of chosen topic: **5 pts**

Presentation organization (including keeping to time limits, referencing primary sources used, appropriate use of technology, correct spelling on slides, etc): **5 pts**

Engaging the audience: (making the lecture interesting, making connections with other parts of the course, encouraging questions and answering them appropriately): **10 pts**

**Extra credit** will be given for use of innovative (not strictly PowerPoint presentation) teaching modalities (use of white board instead of PowerPoint, posing questions to the audience, etc.)

The University of Utah seeks to provide equal access to its programs, services and activities for people with disabilities. If you will need accommodations in the class, reasonable prior notice needs to be given to the Center for Disability Services, 162 Olpin Union Building, 581-5020 (V/TDD). CDS will work with you and the instructor to make arrangements for accommodations. All written information in this course can be made available in alternative format with prior notification to the Center for Disability Services.

Learning Objectives and readings for class sessions:

**Class 1: Introduction to metabolism and its regulation**

**Readings:** Frayn's Metabolic Regulation Ch. 1; Basic Metabolic Overview (BMO) Ch. 1

1. Describe the overall course structure, expectations and modes for assessment/grading.
2. Identify the process of carbon oxidation as the basis of our catabolic metabolism.
3. Sketch an overview of the central metabolic pathways, including connections between them.
4. Explain how indirect calorimetry can be used to determine metabolic rate and estimate the approximate ratios of carbohydrates and fats being oxidized.
5. Diagram the common ways that metabolic pathways are regulated.
6. Predict the overall regulation of metabolism by AMP-activated protein kinase and insulin

**Class 2: Respiration, TCA cycle, carbohydrate catabolism**

**Readings:** Frayn's Metabolic Regulation Ch. 2; Basic Metabolic Overview (BMO) Ch. 2

1. Describe the roles played by the B vitamins niacin, riboflavin, pantothenic acid and thiamine (examples of micronutrients) in the process of carbon oxidation.
2. Explain how the majority of oxygen is used in our bodies.
3. Explain the function of dehydrogenase enzymes in metabolism.
4. Identify amino acids as essential sources of TCA cycle intermediates.
5. Utilize understanding of respiratory control to predict the effects of inhibitors of the electron transport chain.
6. Explain why deleterious mutations of the mitochondrial genome invariably affect cellular respiration.
7. Diagram the process by which brown adipose tissue functions to produce heat.
8. Explain the overall purpose of glycolysis in the context of human physiology.
9. Match the glycolytic enzyme names with the reactions on the metabolic map, based on an understanding of the types of reactions catalyzed by the classes of enzymes.
10. Describe the regulation of the committed step of glycolysis.
11. Predict which situations are likely to result in elevated blood lactate levels.
12. Analyze why 2-deoxyglucose is so effective in labeling tumors.
13. Describe when and why glucose-6-phosphate enters the pentose phosphate pathway.
14. Recognize and explain the effects of glucose 6-phosphate dehydrogenase deficiency.
15. Explain how fructose and galactose are catabolized.

**Class 3: Glycogen, Gluconeogenesis and blood glucose regulation**

**Readings:** Frayn's Metabolic Regulation Ch. 11; Basic Metabolic Overview (BMO) Ch. 3

1. Summarize the metabolic effects of insulin and glucagon on carbohydrate, lipid and protein metabolism.
2. Describe the processes of glycogen synthesis and breakdown.
3. Explain the differing roles of glycogen in the liver and non-liver tissues.
4. Identify the key substrates and enzymes for gluconeogenesis.
5. Describe how insulin and glucagon regulate glycogen synthesis, glycogenolysis and gluconeogenesis.
6. Recognize that a lack of suppression of gluconeogenesis is one of the major causes of hyperglycemia in untreated diabetics.

#### Class 4: Lipid metabolism

**Readings:** Frayn's Metabolic Regulation Ch. 10; Basic Metabolic Overview (BMO) Ch. 4

1. Describe the shared property of all lipids that makes their digestion, absorption and metabolism very different from those of carbohydrates and proteins.
2. Explain when blood levels of chylomicrons are expected to be elevated.
3. Describe the fates of dietary lipids, including conditions that should favor lipid storage or fatty acid oxidation.
4. Describe when, where and how fatty acid oxidation occurs in the body.
5. Explain what ketone bodies are and how their levels are primarily regulated.
6. Identify conditions that promote fatty acid synthesis and outline the process.
7. Explain the transport of lipids through the body.
8. Describe the general features of cholesterol biosynthesis and regulation.
9. Explain the formation, role and fate of chylomicrons, VLDLs, LDL-cholesterol and HDL-cholesterol.
10. Predict how HMG-CoA reductase inhibitors (statins, such as Lipitor), functioning primarily in the liver, lower serum LDL-cholesterol.
11. Hypothesize why people with insulin resistance often have elevated serum triglycerides.

#### Class 5: Integration of Carbohydrate & Fat Metabolism/ In-class Quiz on material from classes 1-5

**Readings:** Frayn's Metabolic Regulation Ch. 7; Basic Metabolic Overview (BMO) review all chapters

1. Diagram the major metabolic processes occurring in liver, adipose, muscle, brain during the feed-fasting cycle and exercise.
2. Explain the major forms of regulation for these metabolic processes.
3. Draw curves showing blood levels of glucose, non-esterified fatty acids, triglycerides, insulin, and glucagon with time following a meal.
4. Describe the differences in the regulation and metabolism that occurs during untreated diabetes.
5. Demonstrate your knowledge of metabolic regulation on an in-class quiz (closed book, but metabolic pathway map will be provided).

Classes 6-14: Objectives to be announced.

Appendix A

Student as teacher:

Faculty Evaluator: **Janet Lindsley**

**Teacher's goal: By the end of this session, students in the course will be able to:**

Possible points	Grading component	Earned points
<b>10</b>	Achievement of your chosen goal: (could students likely now do what you set out to accomplish as your stated goal?)	

Comments:

<b>5</b>	Knowledge of chosen topic: (understanding everything that you present; answered questions appropriately, critically evaluate what's being presented, synthesized well with other material presented during the course)	
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Comments:

<b>5</b>	Presentation organization (including keeping to time limits, referencing primary sources used, appropriate use of technology, correct spelling on slides, etc):	
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Comments:

<b>10</b>	Engaging the audience (making the session interesting, making connections with other parts of the course, encouraging questions and answering them appropriately):	
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Comments:

0-5 extra-credit	Use of innovative (not strictly PowerPoint presentation) teaching modalities (use of white board instead of PowerPoint, posing questions to the audience, etc.)	
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Comments:

Final grade (out of 30 points):

## Appendix B: Student peer feedback form for student-taught sessions

Teacher's Name: \_\_\_\_\_

Evaluator's Name: \_\_\_\_\_

**Teacher's goal: By the end of this session, students in the course will be able to:**

	Strongly agree	Somewhat agree	Neutral	Somewhat disagree	Strongly disagree
Achieved his/her goal					
Speaks clearly					
Materials (PowerPoint, etc) helpful and professional					
No distracting mannerisms					
Pertinent & accurate information; intellectually prepared					
Well organized; appropriate amount of info; summarized					

What worked well in this presentation? List at least one *specific* item.

How could the presenter improve? List at least one *specific* way.