Course Description

The course focuses on the biochemistry, cell biology and metabolism of glycerolipids, sphingolipids and cholesterol. Course content emphasizes the physiological and second messenger functions of lipids, regulatory pathways that control lipid metabolism, and intracellular and inter-tissue transport pathways for lipids. The chemistry and physics of lipids in an aqueous environment are explored, as is the interaction of lipids with proteins and enzymes. Students should have a basic understanding of lipid biochemistry at least equivalent to that provided in the prerequisite classes (BIOC3300 and 3700). Those with limited prior exposure to lipid biochemistry or who have forgotten basic concepts are urged to review appropriate sections of *Biochemistry* (4th Edition) D. Voet and J.G. Voet, 2010 or *Principles of Biochemistry* (6th Edition) Lehninger, 2012.

Course materials

The textbook recommended for this course is the 6th edition (2016) of *Biochemistry of Lipids, Lipoproteins and Membranes* (eds. ND Ridgway and RS McLeod, Elsevier, New York). The textbook can be purchased at the medical school bookstore, but is also available on short-term loan from instructors or from the library as eBook and full text (search the book title). In addition to the recommended text, instructors will provide relevant journal articles to augment the lecture topics. Course material (lecture PDFs, papers, course syllabus) will be posted at [http://www3.biochem.dal.ca](http://www3.biochem.dal.ca).

Course Objectives/Learning outcomes

The objectives of this course are to provide students with an advanced understanding of (1) the physiochemical properties of lipids and sterols, and how these properties affect the form and function of membranes, 2) lipid and sterol metabolism and regulation by transcriptional and post-transcriptional mechanisms, (3) how lipids are transported in the cellular and extracellular environment, (4) lipid and sterol metabolism in normal and disease states and (5) the roles of lipids in cellular communication.

Because biochemistry is an experimental science, course material will focus on design and interpretation of studies that address current topics in the cellular and biochemical function of lipids. Lectures will reflect this approach to the subject by 1) including material derived from scientific research articles, 2) incorporating experimental details and 3) integrating the discussion of research articles into the lecture subject.

Course Assessment

*Essay*

Students will choose an essay topic from the list of journal articles (see attached) that describe recent
studies on lipid metabolism, regulation and signaling. The essay should include a review of the subject area of the journal article (approx. 4-5 pages), with the remainder of the essay summarizing the research article and its relevance and potential impact. The essay should be 10 pages in length (double spaced). The inclusion of figures and tables is not necessary and will not contribute to the page total. The essay is due Oct. 23 (5:00 pm). Unless you have a deferral from the instructor, 5% will be taken from the grade for each day after the due date.

**Student presentation**

A 10-12 minute journal club-style presentation will delivered by each student during the Nov. 6 and 8 lecture period. Journal articles will be chosen from a list provided (see attached). The presentation should be in PowerPoint format, and include 1) background on the research area covered by the journal article and 2) a summary of the research findings and conclusions presented in the article. A short discussion period (3-5 min) will follow each presentation. Students are expected to read each journal article and participate in the discussion. Evaluation will be based on visual and oral components of the presentation, as well as ability to discuss and answer questions concerning the subject matter.

**Midterm and final exam**

One midterm test will be held during class on Oct. 9. The midterm test (80 min) will cover material presented in Lectures 1-9, and will consist of short answer and data interpretation questions. The final examination (3 hours) in December (scheduled by the instructors) will cover all lecture material, but weighted more on material after the midterm exam (lectures 10-21).

The final grade for this course will be determined based on the following:

<table>
<thead>
<tr>
<th>Component</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Mid-term exam</td>
<td>25%</td>
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<tr>
<td>Essay</td>
<td>20%</td>
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<tr>
<td>Presentation</td>
<td>20%</td>
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<tr>
<td>Final exam</td>
<td>35%</td>
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**Conversion of numerical grades to Final Letter Grades follows the Dalhousie Common Grade Scale**

<table>
<thead>
<tr>
<th>Numerical Grade</th>
<th>Letter Grade</th>
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<tbody>
<tr>
<td>A+ (90-100)</td>
<td>A (85-89)</td>
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<tr>
<td>B+ (77-79)</td>
<td>B (73-76)</td>
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<tr>
<td>C+ (65-69)</td>
<td>C (60-64)</td>
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<td>D (50-54)</td>
<td>F (&lt;50)</td>
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<tr>
<td>A- (80-84)</td>
<td>B- (70-72)</td>
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<td>B- (70-72)</td>
<td>C- (55-59)</td>
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# LECTURE SCHEDULE (2018)

Tupper BLDG 14B02, 8:35-9:55 am (Tues and Thurs)

<table>
<thead>
<tr>
<th>Date</th>
<th>LECTURE TOPIC</th>
<th>INSTRUCTOR</th>
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<tbody>
<tr>
<td>Sept. 4</td>
<td>1. Introduction: cellular and molecular biology of lipids</td>
<td>N Ridgway</td>
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<tr>
<td>Sept. 6</td>
<td>2. Structure and function of lipids/membranes</td>
<td>N Ridgway</td>
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<tr>
<td>Sept. 11</td>
<td>3. Lipid synthesis in yeast and prokaryotes</td>
<td>N Ridgway</td>
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<tr>
<td>Sept. 12</td>
<td>4. Mammalian phospholipid synthesis I</td>
<td>N Ridgway</td>
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<td>Sept. 18</td>
<td>5. Mammalian phospholipid synthesis II</td>
<td>N Ridgway</td>
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<tr>
<td>Sept. 20</td>
<td>6. Phospholipid transport</td>
<td>N Ridgway</td>
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<tr>
<td>Sept. 25</td>
<td>7. Phospholipases</td>
<td>N Ridgway</td>
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<tr>
<td>Sept. 27</td>
<td>8 Phospholipids in disease</td>
<td>N Ridgway</td>
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<td>Oct. 2</td>
<td>9. Lipid separation and analysis</td>
<td>N Ridgway</td>
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<td></td>
<td><strong>Limit of material for mid-term test</strong></td>
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<tr>
<td>Oct. 4</td>
<td>10. Triglyceride synthesis/storage I</td>
<td>N Ridgway</td>
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<tr>
<td>Oct. 9</td>
<td><strong>Mid-term Test</strong></td>
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<tr>
<td>Oct. 11</td>
<td>11. Triglyceride synthesis/storage II</td>
<td>N Ridgway</td>
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<tr>
<td>Oct. 16</td>
<td>12 Biosynthesis and degradation of sphingolipids</td>
<td>A van der Spoel</td>
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<tr>
<td>Oct. 18</td>
<td>13. Biological roles of sphingolipids</td>
<td>A van der Spoel</td>
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<tr>
<td>Oct. 23</td>
<td>14. Lysosomal glycosphingolipid storage diseases</td>
<td>A van der Spoel</td>
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<tr>
<td>Oct. 25</td>
<td>15. Cholesterol biosynthesis and metabolism I</td>
<td>N Ridgway</td>
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<tr>
<td>Oct. 30</td>
<td>16. Cholesterol biosynthesis and metabolism II</td>
<td>N Ridgway</td>
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<tr>
<td>Nov. 1</td>
<td>17. Cholesterol biosynthesis and metabolism III</td>
<td>N Ridgway</td>
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<tr>
<td>Nov. 6</td>
<td><strong>Student seminars</strong></td>
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<tr>
<td>Nov. 8</td>
<td><strong>Student seminars</strong></td>
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<td></td>
<td><strong>Fall study break Nov. 12-16</strong></td>
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<tr>
<td>Nov. 20</td>
<td>18. Integration of cholesterol and lipid metabolism</td>
<td>N Ridgway</td>
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<td>Nov. 22</td>
<td>19. Intracellular cholesterol trafficking</td>
<td>B Karten</td>
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<td>Nov. 27</td>
<td>20. Endosomes, Lysosomes</td>
<td>B Karten</td>
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<tr>
<td>Nov. 29</td>
<td>21. Cholesterol homeostasis in the brain</td>
<td>B Karten</td>
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<tr>
<td>Dec. 4</td>
<td><strong>Classes end</strong></td>
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Details of Lecture Topics

**Lecture 1. Introduction: cellular and molecular biology of lipids**
- Structure and organization of biological membranes
- Structure of glycerolipids, sterols, sphingolipids
- Transporters that affect membrane structure/function

**Lecture 2. Structure and physical properties of lipids/membranes**
- How lipids and proteins affect membrane structure/function
- Physical variables that affect membrane structure/function

**Lecture 3. Lipid synthesis in yeast and prokaryotes**
- Lipid metabolic pathways/comparison to mammals
- Role in pathogenesis and infection

**Lecture 4. Mammalian phospholipid synthesis I**
- Biosynthetic pathways for phospholipid synthesis
- Regulation of phosphatidylcholine synthesis
- Maintenance of membrane lipid composition

**Lecture 5. Mammalian phospholipid synthesis II**
- Biosynthesis and regulation of other major phospholipids
- Interconversion of phospholipids
  *Discussion of journal article (TBA)*

**Lecture 6. Phospholipid transport**
- Intracellular sites of phospholipid synthesis
- Mechanisms of phospholipid transport
- Phospholipid transport proteins

**Lecture 7. Phospholipid degradation/cell signaling**
- Enzymology of phospholipases
- Integration of phospholipid synthesis and degradation by lipases
  *Discussion of journal article (TBA)*

**Lecture 8. Glycerolipid metabolism in disease**
- Glycerolipids and cancer
- Barth syndrome/cardiolipin metabolism
- PC and choline synthesis

**Lecture 9. Lipid separation and analysis**
- Quantitative and semi-quantitative methods
- Mass spectrometry/lipidomics

**Lecture 10. Triglyceride metabolism in adipose tissue**
- Development and roles of adipose tissues
- Triglyceride biosynthesis and mobilization in adipose tissue
- Role of leptin and adiponectin in tissue TG metabolism
- Pharmacologic and dietary strategies for adipose maintenance/reduction
Lecture 1. Triglyceride metabolism in the liver
Regulation of hepatic triglyceride synthesis and storage
Assembly and secretion of triglyceride-rich lipoproteins
Pathologies associated with altered TAG synthesis/secretion

Lecture 2. Biosynthesis and degradation of sphingolipids
Structural variation among sphingolipids
Biosynthetic and degradative pathways of simple and complex sphingolipids

Lecture 3. Biological roles of sphingolipids
Cell biology of sphingolipids: intracellular transport
Regulation of sphingolipid metabolism
Glycosphingolipids and the central nervous system
Glycosphingolipids and insulin signaling

Lecture 4. Lysosomal glycosphingolipid storage diseases
Gaucher disease: a prototypical genetic disorder of GSL degradation
Pharmacological treatment for Gaucher disease: why does it work?

Lecture 5. Cholesterol biosynthesis and metabolism I
The cholesterol biosynthetic pathway/regulatory junctions
Mechanisms of transcriptional and post-translational regulation
Sterol-sensing in the endoplasmic reticulum/SREBP

Lecture 6. Cholesterol biosynthesis and metabolism II
Synthesis and secretion of lipoproteins
Lipoprotein receptors: the LDL receptor pathway
Discussion of journal article (TBA)

Lecture 7. Cholesterol biosynthesis and metabolism III
Pathways for cholesterol disposal
Reverse cholesterol transport
Bile acid synthesis/intestinal and hepatic integration

Lecture 8. Integration of cholesterol and lipid metabolism
Mechanism for co-regulation of cholesterol and lipid metabolism
Cholesterol homeostasis in the secretory pathway
Lipid raft assembly

Lecture 9. Intracellular cholesterol trafficking
Cholesterol in membranes
Sterol transfer proteins
Membrane contact sites
Measurement of cholesterol trafficking

Lecture 10. Endosomes, lysosomes
Endocytosis, maturation of endosomes, lysosomes
Autophagy
Cholesterol in the endocytic pathway
Lecture 21. Cholesterol homeostasis in the brain

- Cholesterol homeostasis during brain development and in mature brain
- Myelin, glial lipoproteins, apoE
- Niemann-Pick Type C Disease
- Cholesterol in Alzheimer Disease
- Hedgehog signaling
ESSAY TOPICS

(Due Tues Oct. 23rd at 5:00 pm)


Phospholipid synthesis fueled by lipid droplets drives the structural development of poliovirus replication organelles (2018) PPLOs Pathogens https://doi.org/10.1371/journal.ppat.1007280


Polyunsaturated phospholipids facilitate membrane deformation and fission by endocytic proteins (2014) Science 345:693-697.


ORAL PRESENTATION TOPICS

The lamin B receptor is essential for cholesterol synthesis and perturbed by disease causing mutations (2016) eLife 5:e16011


Lysosomal cholesterol activates mTORC1 via an SLC38A9-Niemann-Pick C1 signaling complex (2017) Science 355; 1306-1311.

Continuous transport of a small fraction of plasma membrane cholesterol to endoplasmic reticulum regulates total cellular cholesterol (2017) eLife 6:e25466.


Impaired autophagy in the lipid storage disorder Niemann-Pick C1 disease (2013) Cell Reports 5: 1302-1315.


Faculty of Science Course Syllabus (Section B)

BIOC4302

Please ensure that the following information on University Policies and Student Resources is available to all students in your course. This document may be posted on your Brightspace course site, or elements may be copied into your Course Syllabus, Section A.

University Policies and Statements

This course is governed by the academic rules and regulations set forth in the University Calendar and by Senate.

Academic Integrity

At Dalhousie University, we are guided in all of our work by the values of academic integrity: honesty, trust, fairness, responsibility and respect (The Center for Academic Integrity, Duke University, 1999). As a student, you are required to demonstrate these values in all of the work you do. The University provides policies and procedures that every member of the university community is required to follow to ensure academic integrity.

Information: https://www.dal.ca/dept/university_secretariat/academic-integrity.html

Accessibility

The Advising and Access Services Centre is Dalhousie's centre of expertise for student accessibility and accommodation. The advising team works with students who request accommodation as a result of a disability, religious obligation, or any barrier related to any other characteristic protected under Human Rights legislation (Canada and Nova Scotia).

Information: https://www.dal.ca/campus_life/academic-support/accessibility.html

Student Code of Conduct

Everyone at Dalhousie is expected to treat others with dignity and respect. The Code of Student Conduct allows Dalhousie to take disciplinary action if students don’t follow this community expectation. When appropriate, violations of the code can be resolved in a reasonable and informal manner—perhaps through a restorative justice process. If an informal resolution can’t be reached, or would be inappropriate, procedures exist for formal dispute resolution.


Diversity and Inclusion – Culture of Respect

Every person at Dalhousie has a right to be respected and safe. We believe inclusiveness is fundamental to education. We stand for equality. Dalhousie is strengthened in our diversity. We are a respectful and inclusive community. We are committed to being a place where everyone feels welcome and supported, which is why our Strategic Direction prioritizes fostering a culture of diversity and inclusiveness.

Statement: http://www.dal.ca/cultureofrespect.html

Recognition of Mi’kmaq Territory

Dalhousie University would like to acknowledge that the University is on Traditional Mi’kmaq Territory. The Elders in Residence program provides students with access to First Nations elders for guidance, counsel and support. Visit the office (Rm 3037, McCain Building), e-mail (elders@dal.ca) or leave message (902-494-6803).

Information: https://www.dal.ca/campus_life/communities/indigenous.html

Important Dates in the Academic Year (including add/drop dates)

https://www.dal.ca/academics/important_dates.html

University Grading Practices

https://www.dal.ca/dept/university_secretariat/policies/academic/grading-practices-policy.html
Student Resources and Support

Advising

General Advising: https://www.dal.ca/campus_life/academic-support/advising.html
Science Program Advisors: https://www.dal.ca/faculty/science/current-students/academic-advising.html
Indigenous Student Centre: https://www.dal.ca/campus_life/communities/indigenous.html
Black Advising Centre: https://www.dal.ca/campus_life/communities/black-student-advising.html
International Centre: https://www.dal.ca/campus_life/international-centre/current-students.html

Academic supports

Library: https://libraries.dal.ca/
Writing Centre: https://www.dal.ca/campus_life/academic-support/writing-and-study-skills.html
Studying for Success: https://www.dal.ca/campus_life/academic-support/study-skills-and-tutoring.html
Copyright Office: https://libraries.dal.ca/services/copyright-office.html
Fair Dealing Guidelines: https://libraries.dal.ca/services/copyright-office/fair-dealing.html

Other supports and services

Student Health Services: https://www.dal.ca/campus_life/health-and-wellness/health-services/services.html
Counselling: https://www.dal.ca/campus_life/health-and-wellness/counselling.html
Student Advocacy: https://www.dsu.ca/dsas

Safety

Biosafety: https://www.dal.ca/dept/safety/programs-services/biosafety.html
Chemical Safety: https://www.dal.ca/dept/safety/programs-services/chemical-safety.html
Radiation Safety: https://www.dal.ca/dept/safety/programs-services/radiation-safety.html

Scent-Free Program: https://www.dal.ca/dept/safety/programs-services/occupational-safety/scent-free.html