

Biochemistry and Cell Biology of Lipids and Membranes Syllabus

Department of Biochemistry & Molecular Biology

BIOC4302 Fall 2024

Dalhousie University acknowledges that we are in Mi'kma'ki, the ancestral and unceded territory of the Mi'kmaq People and pays respect to the Indigenous knowledges held by the Mi'kmaq People, and to the wisdom of their Elders past and present. The Mi'kmaq People signed Peace and Friendship Treaties with the Crown, and section 35 of the Constitution Act, 1982 recognizes and affirms Aboriginal and Treaty rights. We are all Treaty people.

Dalhousie University also acknowledges the histories, contributions, and legacies of African Nova Scotians, who have been here for over 400 years.

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Lectures: Tupper BLDG 14B02, Weds and Fri 11:35-12:55 am

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 the intra- and extra-cellular transport for lipids. The biophysical properties of lipids are explored, as are biomembranes and the interaction of lipids with proteins and enzymes.

Course Prerequisites: BIOC3300

Course Delivery: In-person

Course Objectives/Learning outcomes

- Recognize how the structure of lipids influences the physical and biological properties of membranes.
- Describe where and how lipids are made in cells, and their contribution to organelle structure and function.
- Describe the role of lipids in signal transduction pathways.
- Summarize the techniques for lipid isolation, analysis and quantitation.
- Summarize the mechanisms for regulation of lipid synthesis.
- Identify how defects in lipid metabolism can affect organism function and viability.
- Describe the lipid transport pathways in and between cells.
- Describe and interpret scientific data figures from primary research articles.
- Identify the rationale and key points of a primary research article
- Summarize and present a research study to an audience of peers in written and oral form.

Biochemistry is an experimental science that constantly evolves with the publication of scientific results. As such, lecture material will reflect this approach by inclusion of data and models derived from scientific research articles. As well, research articles provided by instructors will be discussed during selected classes (see schedule) to introduce students to the critical evaluation and interpretation of scientific literature that contributes to our understanding of lipid metabolism and cell biology. Students are expected to contribute

to focused discussions on these articles, including the 1) research hypothesis/objectives, 2) types of methods and techniques used, 3) discoveries (results), 4) conclusions and impact and 5) limitations of the study.

Course materials: The textbook recommended for this course is the 7th edition (2021) of *Biochemistry of Lipids, Lipoproteins and Membranes* (eds. ND Ridgway and RS McLeod, Elsevier, New York). The text is available from the library as an eBook or from the instructors. Instructors will provide relevant journal articles and reviews to augment the lecture topics. Course material will be posted on Brightspace.

Course Assessments

Exams—Two in-class tests will be held on Oct. 4 and Nov. 29. A midterm test (75 min) on Oct. 4 will cover material in Lectures 1-9. There will be a final in-class exam (75 min) on Dec. 1 that covers material in lectures 10-18. Both exams will consist of short answer and data interpretation questions.

Essay--Students will choose an essay topic from the list of journal articles (see attached) that describe recent studies on lipid metabolism, regulation, signaling and associated diseases. 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 with respect to its hypothesis/objectives, methods/techniques, results, and the relevance and impact of the findings. The essay should be 10 pages in length (double spaced). Figures and tables are not necessary and will not contribute to the page total. The essay is due Dec.6 (5:00 pm). Unless you have an accommodation from the instructor, 5% will be taken from the grade for each day after the due date.

Student presentations—Students will deliver a 10-minute journal club-style presentation during the Nov. 8, 20 and 22 lecture periods (Nov. 27 is available if extra time is required). Journal articles can be chosen from a list provided (see attached) or students can choose an article from the literature (with approval of Dr. Ridgway). 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.

Class participation--Students will be graded on their participation in the discussion of papers during class and student presentations.

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

Mid-term exam	22.5%
In-class final exam	22.5%
Essay	25%
Presentation	25%
Class participation	5%

Conversion of numerical grades to final letter grades follows the [Dalhousie Grade Scale](#)

A+ (90-100)

B+ (77-79)

C+ (65-69)

D (50-54)

LECTURE SCHEDULE (2024)

Tupper BLDG 14B02, Weds and Fri 11:35-12:55 am

Date	LECTURE TOPIC	INSTRUCTOR
Sept. 4	1. Introduction to lipids and membranes	Ridgway
Sept. 6	2. Organization and structure of membranes	Ridgway
Sept. 11	3. Lipid synthesis in yeast and prokaryotes	Ridgway
Sept. 13	4. Regulation of mammalian phospholipid synthesis	Ridgway
Sept. 18	5. Phospholipid degradation by phospholipases	Ridgway
Sept. 20	6. Cancer and other diseases phospholipid metabolism	Ridgway
Sept. 25	7. Techniques for lipid separation and analysis	Ridgway
Sept. 27	8. Fatty acid metabolism and triglyceride storage	Ridgway
Oct. 2	9. Triglyceride metabolism in the liver	Ridgway
Oct. 4	Mid-term 1 (Lectures 1-9)	Ridgway
Oct. 9	10. Biosynthesis and degradation of sphingolipids	van der Spoel
Oct. 11	11. Biological roles of sphingolipids	van der Spoel
Oct. 16	12. Lysosomal glycosphingolipid storage diseases	van der Spoel
Oct. 18	13. Cholesterol biosynthesis and regulation by sterol sensing	Ridgway
Oct. 23	14. The LDL receptor family and cholesterol homeostasis	Ridgway
Oct. 25	15. Mechanisms for cholesterol disposal and homeostasis	Ridgway
Oct. 30	16. Endomembrane system I — the secretory pathway	Fairn
Nov. 1	17. Endomembrane system II — the endo-lysosomal pathway	Fairn
Nov. 6	18. Endomembrane system III — organelle crosstalk	Fairn
Nov. 8	Student seminars	
Fall study break Nov. 11-15		
Nov. 20	Student seminars	
Nov. 22	Student seminars	
Nov. 27	Student seminars/review	
Nov. 29	In-class final exam (lectures 11-19)	
Dec. 4	Classes end	

Course content

Lecture 1. Introduction: Cellular and molecular biology of lipids

Structure and organization of biological membranes; Structure of glycerolipids, sterols, sphingolipids; Macro- and micro-structure of membranes; Lipid distribution in membranes; 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 and membrane structure; Role in pathogenesis and infection.
Discussion of journal article (TBA).

Lecture 4. Regulation of mammalian phospholipid synthesis

Biosynthesis and regulation of other major phospholipids; Intracellular sites of phospholipid synthesis; Mechanisms of phospholipid transport; Phospholipid transport proteins.

Lecture 5. Phospholipid degradation by phospholipases

Enzymology of phospholipases; Integration of phospholipid synthesis and degradation by lipases; Roles for lipases in cell signaling; **Discussion of journal article (TBA).**

Lecture 6. Cancer and other diseases phospholipid metabolism

Lipid dysregulation and cancer; Genetic disorders of phospholipid metabolism in peroxisomes.

Lecture 7. Lipid separation and analysis

Quantitative and semi-quantitative methods; Mass spectrometry/lipidomics.

Lecture 8. Fatty acid metabolism and triglyceride storage

Fatty acid utilization and storage in triglyceride; Triglyceride biosynthesis and mobilization in adipose tissue; Development and roles of adipose tissues.

Lecture 9. Transport of triglyceride in lipoproteins

Regulation of hepatic triglyceride synthesis and storage; Assembly and secretion of triglyceride-rich lipoproteins; **Discussion of journal article (TBA).**

Lecture 10. Biosynthesis and degradation of sphingolipids

Structural variation among sphingolipids; Biosynthetic and degradative pathways of simple and complex sphingolipids.

Lecture 11. 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 12. Lysosomal glycosphingolipid storage diseases

Gaucher disease: a prototypical genetic disorder of GSL degradation; Pharmacological treatment for Gaucher disease: why does it work?

Lecture 13. Cholesterol biosynthesis and regulation by sterol sensing

The cholesterol biosynthetic pathway/regulatory junctions; Mechanisms of transcriptional and post-translational regulation; Sterol-sensing in the endoplasmic reticulum/SREBPs; Lipid modification of proteins.

Lecture 14. The LDL receptor family and cholesterol homeostasis

The LDL receptor pathway; LDL receptor related proteins; Signaling activity of the LDL receptor family; **Discussion of journal article (TBA).**

Lecture 15. Mechanisms for cholesterol disposal

Intestinal and hepatic integration of cholesterol homeostasis; Reverse cholesterol transport and atherosclerosis; Bile acid synthesis.

Lecture 16. Endomembrane system I — the secretory pathway

Membrane protein biogenesis; mechanisms of cargo selection and membrane carrier formation within the secretory pathway; membrane carrier transport, tethering and fusion

Lecture 17. Endomembrane system II — the endo-lysosomal pathway

Mechanisms of cargo selection and membrane carrier formation at the plasma membrane (e.g., endocytosis); endosome maturation, recycling and fusion with lysosomes; mechanisms of lysosomal degradation

Lecture 18. Endomembrane system III — organelle crosstalk

Mechanisms of inter-organelle crosstalk within cells; inter-organelle vesicular trafficking pathways, membrane contact sites, lipid transfer proteins; **Discussion of journal article (TBA)**

ESSAY TOPICS

(Due Friday Dec.6th at 5:00 pm)

Non-lethal inhibition of gut microbial trimethylamine production for the treatment of atherosclerosis (2015) *Cell* 163 (7):1585-1595.

Lupus-like autoimmune disease caused by a lack of Xkr8, a caspase-dependent phospholipid scramblase (2018) *Proceedings of the National Academy of Sciences USA* 115 (9): 2132-2137.

Last step in the pathway of LDL cholesterol from lysosome to plasma membrane to ER is governed by phosphatidylserine (2020) *Cell* 117 (31): 18521-18529.

SLC25A48 controls mitochondrial choline import and metabolism (2024) *Cell Metabolism* 36, 1-11.

Mitochondria bound to lipid droplets have unique bioenergetics, composition, and dynamics that support lipid droplet expansion (2018) *Cell Metabolism* 27: 869-885.

Cardiolipin synthesis in brown and beige fat mitochondria is essential for systemic energy homeostasis (2018) *Cell* 174:159-174.

Structural basis of substrate recognition and translocation by human ABCA4 (2021) *Nature Communications* 12(1): 3853. doi: 10.1038/s41467-021-24194-6.

Gaucher disease glucocerebrosidase and α -synuclein form a bidirectional pathogenic loop in synucleinopathies (2011) *Cell* 146 :37-52.

Loss of the sphingomyelin-degrading enzyme SMPD4 causes a developmental disorder characterized by microcephaly and congenital arthrogryposis (2019) *The American Journal of Human Genetics* 105; 689-705. <https://doi.org/10.1016/j.ajhg.2019.08.006>.

A semi-invariant V α 10+ T cell antigen receptor defines a population of natural killer T cells with distinct glycolipid antigen-recognition properties. (2011) *Nature Immunology* 12: 616-23.

Dietary sphinganine is selectively assimilated by members of the mammalian gut microbiome (2021) *Journal of Lipid Research* 62: 100034. <https://doi.org/10.1194/jlr.RA120000950>.

NPC1 enables cholesterol mobilization during long-term potentiation that can be restored in Niemann-Pick Type C by CYP46A1 activation. (2019) *EMBO Reports* 20: e48143

Protein crowding mediates membrane remodelling in upstream ESCRT-induced formation of intraluminal vesicles. (2020) *Proceedings of the National Academy of Science USA* 117: 28614-24

Protrudin-mediated ER-endosome contact sites promote MT1-MMP exocytosis and cell invasion. (2020) *Journal of Cell Biology* 219: e202003063

Retrofusion of intraluminal MVB membranes parallels viral infection and coexists with exosome release. (2021) *Current Biology* 31: 1-10

Nutrient-regulated control of lysosome function by signaling lipid conversion (2023) *Cell* 186, 5328-5346

An ATG12-ATG5-TECPR1 E3-like complex regulates unconventional LC3 lipidation at damaged lysosomes (2023) e56841

ORAL PRESENTATION TOPICS

Caffeine blocks SREBP2-induced hepatic PCSK9 expression to enhance LDLR-mediated cholesterol clearance (2022) *Nature Communications*. 13; 770. doi: 10.1038/s41467-022-28240-9

Genetic Dissection of the Impact of miR-33a and miR-33b during the Progression of Atherosclerosis (2017) *Cell Reports* 21; 1317-1330.

Feedback modulation of cholesterol metabolism by the lipid-responsive non-coding RNA LeXis (2016) *Nature* 534: 124-128.

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

TMEM41B acts as an ER scramblase required for lipoprotein biogenesis and lipid homeostasis (2021) *Cell Metabolism* 33:1-16.

Cholesterol and fatty acids regulate cysteine ubiquitylation of ACAT2 through competitive oxidation (2017) *Nature Cell Biology* 19; 808-819.

Sphingosine-1-phosphate receptor 1 activation in astrocytes contributes to neuropathic pain (2019) *Proceedings of the National Academy of Sciences* 116 (21): 10557-10562. doi: 10.1073/pnas.1820466116.

Cellular stress promotes NOD1/2-dependent inflammation via the endogenous metabolite sphingosine-1-phosphate (2021) *EMBO Journal* 40(13):e106272. doi: 10.15252/emj.2020106272.

LDAF1 and Seipin Form a Lipid Droplet Assembly Complex (2019) *Developmental Cell* 51(5): 551-563.

Phagolysosome resolution requires contacts with the endoplasmic reticulum and phosphatidylinositol-4-phosphate signalling (2019) *Nature Cell Biology* 21; 1234-1247

Filoviruses Use the HOPS Complex and UVRAG To Traffic to Niemann-Pick C1 Compartments during Viral Entry. (2020) *Journal of Virology* 94: e01002-20.

LDL delivery of microbial small RNAs drives atherosclerosis through macrophage TLR8 (2022) Nature Cell Biology. <https://www.nature.com/articles/s41556-022-01030-7>

A concerted mechanism involving ACAT and SREBPs by which oxysterols deplete accessible cholesterol to restrict microbial infection (2023) eLife. <https://elifesciences.org/articles/83534>

DGAT2 inhibition blocks SREBP-1 cleavage and improves hepatic steatosis by increasing phosphatidylethanolamine in the ER (2024) 36, 1-13.

A gut-derived hormone regulates cholesterol metabolism (2024) Cell 187, 1685-1700

Phosphatidylserine enrichment in the nuclear membrane regulates key enzymes of phosphatidylcholine synthesis (2024) EMBO Journal 43: 3414 - 34

University Policies and Statements

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 or e-mail the Indigenous Student Centre at 1321 Edward St or elders@dal.ca. Additional information regarding the Indigenous Student Centre can be found at:

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

Internationalization

At Dalhousie, 'thinking and acting globally' enhances the quality and impact of education, supporting learning that is "interdisciplinary, cross-cultural, global in reach, and orientated toward solving problems that extend across national borders." Additional internationalization information can be found at:

<https://www.dal.ca/about-dal/internationalization.html>

Academic Integrity

At Dalhousie University, we are guided in all our work by the values of academic integrity: honesty, trust, fairness, responsibility, and respect. As a student, you are required to demonstrate these values in all 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. Additional academic integrity information can be found at:

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

Accessibility

The Student Accessibility Centre is Dalhousie's centre of expertise for matters related to student accessibility and accommodation. If there are aspects of the design, instruction, and/or experiences within this course (online or in-person) that result in barriers to your inclusion, please contact the Student Accessibility Centre (https://www.dal.ca/campus_life/academic-support/accessibility.html) for all courses offered by Dalhousie with the exception of Truro. For courses offered by the Faculty of Agriculture, please contact the Student Success Centre in Truro (<https://www.dal.ca/about-dal/agricultural-campus/student-success-centre.html>)

Conduct in the Classroom – Culture of Respect

Substantial and constructive dialogue on challenging issues is an important part of academic inquiry and exchange. It requires willingness to listen and tolerance of opposing points of view. Consideration of individual differences and alternative viewpoints is required of all class members, towards each other, towards instructors, and towards guest speakers. While expressions of differing perspectives are welcome and encouraged, the words and language used should remain within acceptable bounds of civility and respect.

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 (Strategic Priority 5.2). Additional diversity and inclusion information can be found at: <http://www.dal.ca/cultureofrespect.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. The full Code of Student Conduct can be found at:

https://www.dal.ca/dept/university_secretariat/policies/student-life/code-of-student-conduct.html

Fair Dealing Policy

The Dalhousie University Fair Dealing Policy provides guidance for the limited use of copyright protected material without the risk of infringement and without having to seek the permission of copyright owners. It is intended to provide a balance between the rights of creators and the rights of users at Dalhousie. Additional information regarding the Fair Dealing Policy can be found at:

https://www.dal.ca/dept/university_secretariat/policies/academic/fair-dealing-policy-.html

Originality Checking Software

The course instructor may use Dalhousie's approved originality checking software and Google to check the originality of any work submitted for credit, in accordance with the Student Submission of Assignments and Use of Originality Checking Software Policy. Students are free, without penalty of grade, to choose an alternative method of attesting to the authenticity of their work and must inform the instructor no later than the last day to add/drop classes of their intent to choose an alternate method. Additional information regarding Originality Checking Software can be found at: <https://www.dal.ca/about/leadership-governance/academic-integrity/faculty-resources/ouriginal-plagiarism-detection.html>

Student Use of Course Materials

Course materials are designed for use as part of this course at Dalhousie University and are the property of the instructor unless otherwise stated. Third party copyrighted materials (such as books, journal articles, music, videos, etc.) have either been licensed for use in this course or fall under an exception or limitation in Canadian Copyright law. Copying this course material for distribution (e.g. uploading to a commercial third-party website) may lead to a violation of Copyright law.

Student Resources and Support

University Policies and Programs

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

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

Classroom Recording Protocol: https://www.dal.ca/dept/university_secretariat/policies/academic/classroom-recording-protocol.html

Dalhousie Grading Practices Policies:

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

Grade Appeal Process: https://www.dal.ca/campus_life/academic-support/grades-and-student-records/appealing-a-grade.html

Sexualized Violence Policy: https://www.dal.ca/dept/university_secretariat/policies/health-and-safety/sexualized-violence-policy.html

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

Learning and Support Resources

General Academic Support – Advising (Halifax): https://www.dal.ca/campus_life/academic-support/advising.html

General Academic Support – Advising (Truro): <https://www.dal.ca/about-dal/agricultural-campus/ssc/academic-support/advising.html>

Student Health & Wellness Centre: https://www.dal.ca/campus_life/health-and-wellness.html

On Track (helps you transition into university, and supports you through your first year at Dalhousie and beyond): https://www.dal.ca/campus_life/academic-support/On-track.html

Indigenous Student Centre: https://www.dal.ca/campus_life/communities/indigenous.html

Indigenous Connection: <https://www.dal.ca/about-dal/indigenous-connection.html>

Elders-in-Residence (The Elders in Residence program provides students with access to First Nations elders for guidance, counsel, and support. Visit the office in the Indigenous Student Centre or contact the program at elders@dal.ca or 902-494-6803: <https://cdn.dal.ca/content/dam/dalhousie/pdf/academics/UG/indigenous-studies/Elder-Protocol-July2018.pdf>

Black Student Advising Centre: https://www.dal.ca/campus_life/communities/black-student-advising.html

International Centre: https://www.dal.ca/campus_life/international-centre.html

LGBTQ2SIA+ Collaborative: <https://www.dal.ca/dept/vpei/edia/education/community-specific-spaces/LGBTQ2SIA-collaborative.html>

Dalhousie Libraries: <http://libraries.dal.ca/>

Copyright Office: <https://libraries.dal.ca/services/copyright-office.html>

Dalhousie Student Advocacy Services: <https://www.dsu.ca/dsas?rq=student%20advocacy>

Dalhousie Ombudsperson: https://www.dal.ca/campus_life/safety-respect/student-rights-and-responsibilities/where-to-get-help/ombudsperson.html

Human Rights and Equity Services: <https://www.dal.ca/dept/hres.html>

Writing Centre: https://www.dal.ca/campus_life/academic-support/writing-and-study-skills.html

Study Skills/Tutoring: http://www.dal.ca/campus_life/academic-support/study-skills-and-tutoring.html

Faculty of Science Advising Support: <https://www.dal.ca/faculty/science/current-students/undergrad-students/degree-planning.html>

Safety

Biosafety: <http://www.dal.ca/dept/safety/programs-services/biosafety.html>

Chemical Safety: <https://www.dal.ca/dept/safety/programs-services/chemical-safety.html>

Radiation Safety: <http://www.dal.ca/dept/safety/programs-services/radiation-safety.html>

Laser Safety: <https://www.dal.ca/dept/safety/programs-services/radiation-safety/laser-safety.html>