Biochemistry 4463B – Biochemistry of Genetic Diseases

2018/2019 Course Outline

1. Course Information

Biochemistry 4463B: Biochemistry of Genetic Diseases
Winter term 2019
The objective of this course is to use selected genetic diseases to illustrate the biochemical principles underlying these disorders. Genetic and molecular basis of neurodegenerative disease, skeletal muscle disorder, familial hypercholesterolemia, and diseases related to defects in DNA repair and telomere maintenance will be discussed. We will also examine the structural, functional, metabolic, and pathophysiological consequences of gene mutations associated with these diseases.

Lectures:
Tuesday, Thursday 11:30am – 12:30pm, MSB-190

Requisites:
Prerequisite(s): Biochemistry 3381A
Co-requisite(s)
Anti-requisite(s) Biology 4560A/B

Senate regulation regarding the student's responsibility regarding requisites:
Unless you have either the requisites for this course or written special permission from your Dean to enroll in it, you may be removed from this course and it will be deleted from your record. This decision may not be appealed. You will receive no adjustment to your fees in the event that you are dropped from a course for failing to have the necessary prerequisites.

Accessibility Statement
Please contact the course instructor if you require material in an alternate format or if you require any other arrangements to make this course more accessible to you. You may also wish to contact Services for Students with Disabilities (SSD) at 661-2111 x 82147 for any specific question regarding an accommodation.
2. Instructor Information

<table>
<thead>
<tr>
<th>Instructors</th>
<th>Email</th>
<th>Office</th>
<th>Office Hours</th>
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<tbody>
<tr>
<td>Dr. James Choy</td>
<td><a href="mailto:jchoy4@uwo.ca">jchoy4@uwo.ca</a></td>
<td>MSB-302</td>
<td>By appointment (email or in-class)</td>
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<tr>
<td>(Course Coordinator)</td>
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<tr>
<td>Dr. Martin Duennwald</td>
<td><a href="mailto:martin.duennwald@schulich.uwo.ca">martin.duennwald@schulich.uwo.ca</a></td>
<td>HSA-408A</td>
<td>By appointment (email or in-class)</td>
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<tr>
<td>Dr. Chris Brandl</td>
<td><a href="mailto:cbrandl@uwo.ca">cbrandl@uwo.ca</a></td>
<td>MBL-C210</td>
<td>By appointment (email or in-class)</td>
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<tr>
<td>Dr. Michael Boffa</td>
<td><a href="mailto:mboffa@uwo.ca">mboffa@uwo.ca</a></td>
<td>Robarts Research Institutes 4525A</td>
<td>By appointment (email or in-class)</td>
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<tr>
<td>Dr. Caroline Schild-Poulter</td>
<td><a href="mailto:cschild-poulter@robarts.ca">cschild-poulter@robarts.ca</a></td>
<td>Robarts Research Institutes 3296B</td>
<td>By appointment (email or in-class)</td>
</tr>
<tr>
<td>Sanna Abbasi</td>
<td><a href="mailto:sabbasi5@uwo.ca">sabbasi5@uwo.ca</a></td>
<td></td>
<td>By appointment (email or in-class)</td>
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<tr>
<td>(Teaching Assistant)</td>
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**OWL:** This course will use OWL for communication and distribution of teaching materials including lecture notes. Students with OWL issues should see: [https://owl.uwo.ca/portal/site/owldocs](https://owl.uwo.ca/portal/site/owldocs)

3. Course Syllabus

**Course Topics:**

I. **Neurodegenerative diseases**

**Section 1:** 4 lectures, January 8 – January 17, Dr. Martin Duennwald  
**Section 2:** 4 lectures, January 22 – January 31, Dr. James Choy

Neurodegenerative diseases, such as Alzheimer’s disease, Parkinson’s disease, amyotrophic lateral sclerosis (ALS), and Huntington’s disease, are a rapidly growing public health problem in our aging population. Research in past few decades has provided insights into basic common mechanisms underlying most neurodegenerative disease. Yet there is still not cure for neurodegenerative diseases. Protein misfolding and the failure of cellular protein quality control systems are key factors in the pathogenesis of most neurodegenerative diseases. This section will focus on how specific disease-associated proteins misfold, will review biochemical and cellular aspects of protein misfolding and protein aggregation, and will discuss how protein misfolding leads to neurodegeneration in different diseases. We will also study how cellular protein quality control systems normally protect from protein misfolding and how these protective mechanisms may fail in neurodegenerative disease.
II. **Skeletal muscle disorder**  
**Section 3:** 4 lectures, February 5 – February 14, Dr. Chris Brandl  
In this section, we will explore the molecular mechanisms and cell biology that enable the contraction of skeletal muscle. Topics covered will include: the actin-myosin ATPase and its regulation by tropomyosin and troponin in skeletal muscle and calcium flow during contraction and relaxation -- ryanodine receptor, sarcoplasmic reticulum and the Ca\(^{2+}\)-Mg\(^{2+}\) ATPase. We will then examine the genetic and molecular basis of diseases that disrupt the function of skeletal muscle.

III. **Familial hypercholesterolemia**  
**Section 4:** 4 lectures, February 26 – March 7, Dr. Michael Boffa  
In this section, we shall be focusing on familial hypercholesterolemia (FH). This common, autosomal dominant, genetic disorder features grossly elevated plasma concentrations of low density lipoprotein (LDL, the “bad cholesterol”) and carries with it an extremely high risk for premature coronary artery disease and other atherothrombotic disorders. FH is linked to mutations in one of three genes, LDLR, APOB, or PCSK9. Accordingly, we shall examine the structural, functional, metabolic, and pathophysiological consequences of FH mutations. Other topics in FH that we shall cover are mutation discovery and annotation by next-generation sequencing and bioinformatic analysis, and the recent development of PCSK9 inhibitors as cholesterol-lowering drugs. Finally, we shall learn about a variant of LDL known as lipoprotein(a) (Lp(a); the “really bad cholesterol”) which constitutes a fourth – and underappreciated – form of FH. Our discussion of Lp(a) will allow us to consider the intersection between genetics and epidemiology.

IV. **Defects in DNA repair and telomere maintenance**  
**Section 5:** 4 lectures, March 12 – March 21, Dr. Caroline Schild-Poulter  
In this section, we will discuss the molecular basis of several diseases that occur due to defects in DNA repair and telomere maintenance processes. The pathways and factors involved in DNA repair and telomere maintenance are closely linked and globally contribute to maintaining genomic integrity. Defects in DNA repair and in telomere maintenance have been shown to result in diseases characterized by premature aging, neurodegeneration and cancer. This section will give an overview of the molecular pathways involved in DNA repair and telomere regulation and focus on specific examples of genetic diseases caused by mutations in factors regulating these processes.

4. **Learning Outcomes**  
After completing this course, students should be able to:

1. Demonstrate understanding of the molecular mechanisms and basic biochemical principles underlying certain genetic diseases.

2. Extract and critically evaluate information about the genetic and molecular basis of human diseases from literature and digital data repositories.
3. Communicate technical concepts in disease research to general audiences both orally and in writing, in a professional manner.

5. Course Materials

There is no required textbook for the course. All the lecture notes and additional reading materials specified by the instructors will be made available through the Biochemistry 4463B OWL site.

Copyright Statement:
Course material produced by faculty is copyrighted and to reproduce this material for any purposes other than your own educational use contravenes Canadian Copyright Laws.

6. Evaluation:

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<tr>
<th>Component</th>
<th>Date</th>
<th>% of Final Mark</th>
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<tr>
<td>Quizzes (in class)</td>
<td>January 17</td>
<td>40 (4 x 10%)</td>
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<td>January 31</td>
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<td>February 14</td>
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<td>March 7</td>
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<td>March 21</td>
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<td>Essay (Outline)</td>
<td>Due February 25 by 5 pm</td>
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<td>Essay (Final version)</td>
<td>Due March 15 by 5 pm</td>
<td>30</td>
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<td>Group presentation</td>
<td>March 26, 28</td>
<td>20</td>
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<td>April 2, 4, 9</td>
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<tr>
<td>Participation in the presentations</td>
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Important Details:

Quizzes
There will be 5 in-class quizzes and each is worth 10% of your final mark. Since the lowest score quiz will be dropped, the quizzes together is worth 40% of your final mark (4 x 10% = 40%). For instance, if you receive scores of 9%, 7%, 8%, 10%, and 6% in your 5 quizzes, the total marks of quizzes that count towards your final mark will be 34 (9 + 7 + 8 + 10 = 34). Since one quiz will be dropped, no excuses will be accepted for missed quizzes.

Essay
Each student will write an essay on a genetic disease of his/her choice. The essay is expected to be a concise literature review of the selected disease. It should provide an overview of the disease, summaries of the molecular mechanism underlying this disorder, the current treatments, and latest research in this area.
The outline and the final version of the essay worth 5% and 25% of the final mark, respectively. The outline of your essay is due on February 25 by 5 pm, whereas the final version is due on March 15 by 5 pm. Both the outline and final version of the essay must be submitted electronically to the OWL site for this course. The submissions may be inspected by Turnitin, a plagiarism checking software.

In the one-page outline, student should give a brief description of the selected disease and outline the structure of the essay. You may also list some of the key references you have found.

The final version of the essay should be a maximum of 4 pages (US letter size), single-line spaced. Use 12-point Times New Roman font and insert a margin of minimum 2 cm around the page. Two additional pages of references and/or figures may be attached to the end of the essay.

**Group Presentation**
Each group of students (2 students per group) will deliver a presentation on an assigned topic. The presentation will be 15-20 minutes, followed by a 5-minute Q&A period. All the group members are responsible for the presentation and answering questions. Marks will be given based on the content, organization, and delivery of the presentation, and the presenters’ response to questions.

**Participation in the group presentations**
Students are required to attend all the group presentations. Students can choose to ask or submit a question after each presentation. 5% of the final mark is assigned to your participation in the presentation discussions.

_A detailed and comprehensive set of regulations concerning the scheduling of tests, assignments, etc. is available at:_

[http://www.uwo.ca/univsec/academic_policies/examinations.html](http://www.uwo.ca/univsec/academic_policies/examinations.html)

**15% Assessment Rule:**
At least three days prior to the deadline for withdrawal from a course without academic penalty, students will receive assessment of work accounting for at least 15% of their final grade. For more details, refer to the link below:

[http://www.uwo.ca/univsec/pdf/academic_policies/exam/evaluation_undergrad.pdf](http://www.uwo.ca/univsec/pdf/academic_policies/exam/evaluation_undergrad.pdf)

**Policy on the Rounding and Bumping of Marks:**
Across the Basic Medical Sciences Undergraduate Education programs and within the department of Biochemistry we strive to maintain high standards that reflect the effort that both students and faculty put into the teaching and learning experience during this course. All students will be treated equally and evaluated based only on their actual achievement. **Final grades** on this course, irrespective of the number of decimal places used in marking individual assignments and tests, will be calculated to one decimal place and rounded to the
nearest integer, e.g., 74.4 becomes 74, and 74.5 becomes 75. Marks WILL NOT be bumped to the next grade or GPA, e.g. a 79 will NOT be bumped up to an 80, an 84 WILL NOT be bumped up to an 85, etc. The mark attained is the mark you achieved and the mark assigned; requests for mark “bumping” will be denied.

7. Additional Information/Statements

Statement on Use of Electronic Devices
No electronic devices, including mobile phone and calculator, will be allowed during quizzes.

Statement on Academic Offences
“Scholastic offences are taken seriously and students are directed to read the appropriate policy, specifically, the definition of what constitutes a Scholastic Offence, at the following website:

http://www.uwo.ca/univsec/pdf/academic_policies/appeals/scholastic_discipline_undergrad.pdf

All required papers may be subject to submission for textual similarity review to the commercial plagiarism detection software under license to the University for the detection of plagiarism. All papers submitted for such checking will be included as source documents in the reference database for the purpose of detecting plagiarism of papers subsequently submitted to the system. Use of the service is subject to the licensing agreement, currently between The University of Western Ontario and Turnitin.com (http://www.turnitin.com).

Absence from course commitments
Medical/Compassionate Relief Program Policy
It is current policy that students who are unable to write a test or examination or other form of course evaluation are required to obtain a medical certificate that is taken to the Academic Counseling Office, WSC140 (for Science and Basic Medical Science students) or to your appropriate Home Faculty Counseling Office. In the case of an unexpected absence on compassionate grounds, documentation is also requested. Such documentation must be submitted by the student directly to the Academic Counseling office and not to the instructor. An academic counselor in that office will review and either approve or deny the accommodation request. It will be the Academic Counseling office that will determine if accommodation is warranted. This policy applies to all forms of assessment, including evaluations that are less than 10%.

A student requiring academic accommodation due to illness, should use the Student Medical Certificate when visiting an off-campus medical facility or request a Record’s Release Form (located in the Dean’s Office) for visits to Student Health Services. The form can be found at:

http://www.uwo.ca/univsec/pdf/academic_policies/appeals/medicalform.pdf
A. Absence for medical illness:
Students must familiarize themselves with the Policy on Accommodation for Medical Illness for Undergraduate Students, located at:
http://www.uwo.ca/univsec/pdf/academic_policies/appeals/accommodation_medical.pdf

Statement from the Academic Counselling Office, Faculty of Science (for Science and BMSc students)
If you are unable to meet a course requirement due to illness or other serious circumstances, you must provide valid medical or other supporting documentation to the Academic Counselling Office as soon as possible and contact your instructor immediately. It is the student’s responsibility to make alternative arrangements with their instructor once the accommodation has been approved by the Academic Counselling Office and the instructor has been informed. In the event of a missed final exam, a "Recommendation of Special Examination" form must be obtained from the Academic Counselling Office immediately.

A student requiring academic accommodation due to illness, should use the Student Medical Certificate when visiting an off-campus medical facility or request a Record's Release Form (located in the Dean’s Office) for visits to Student Health Services. The form can be found at:
http://www.uwo.ca/univsec/pdf/academic_policies/appeals/medicalform.pdf

B. Absence for non-medical reasons:
If you have course timetable conflicts with the test/examination times, contact the course coordinator at least two weeks before the test/examination. Components of the course evaluation that cannot be completed on the due date because of non-medical reasons must be completed at an alternate date. In the case of assignments, if solutions have already been provided to the class, and therefore the assignment cannot be completed, the other components of the section will be more heavily weighted to absorb the missing evaluation.

Students who are in emotional/mental distress should refer to Mental Health@Western http://www.uwo.ca/uwcom/mentalhealth/ for a complete list of options about how to obtain help.

C. Special Examinations
http://www.uwo.ca/univsec/pdf/academic_policies/exam/definitions.pdf

A Special Examination is any examination other than the regular final examination, and it may be offered only with the permission of the Dean/Academic Counselling Office of the Faculty in which the student is registered, in consultation with the instructor and Department Chair. Permission to write a Special Examination may be given on the basis of compassionate or medical grounds with appropriate supporting documents.
A Special Examination must be written at the University or an Affiliated University College no later than 30 days after the end of the examination period involved. To accommodate unusual circumstances, a date later than this may be arranged at the time permission is first given by the Dean/Academic Counselling Office of the Faculty. The Dean/Academic Counselling Office will consult with the instructor and Department Chair and, if a later date is arranged, will communicate this to the Office of the Registrar.

If a student fails to write a scheduled Special Examination, permission to write another Special Examination will be granted only with the permission of the Dean/Academic Counselling Office in exceptional circumstances and with appropriate supporting documents. In such a case, the date of this Special Examination normally will be the scheduled date for the final exam the next time the course is offered.

When a grade of Special (SPC) or Incomplete (INC) appears on a student's record, the notations will be removed and replaced by a substantive grade as soon as the grade is available.

**Support Services:**
- Registrarial Services: [http://www.registrar.uwo.ca](http://www.registrar.uwo.ca)
- Academic Counselling (Science and Basic Medical Sciences): [http://www.uwo.ca/sci/counselling](http://www.uwo.ca/sci/counselling)
- USC Student Support Services: [http://westernusc.ca/services/](http://westernusc.ca/services/)
- Student Development Services: [http://www.sdc.uwo.ca](http://www.sdc.uwo.ca)
- Student Health Services: [http://www.shs.uwo.ca/](http://www.shs.uwo.ca/)

Students who are in emotional/mental distress should refer to Mental Health@Western [https://www.uwo.ca/health/mental_wellbeing/self/student.html](https://www.uwo.ca/health/mental_wellbeing/self/student.html) for a complete list of options about how to obtain help.