1. Course Information

Biochemistry 4410A: Molecular Biology of DNA and RNA
Fall Term 2017

Gene expression, DNA replication and DNA repair/recombination are the cornerstones of Molecular Biology. In this course we will use examples from primary research literature to explore recent developments in these areas. In addition to these traditional topics, which are typically studied at a reductionist level to define molecular mechanisms, we will introduce basic concepts in Systems Biology. Here the focus is on interactions between components of biological systems and how these interactions give rise to the function and behavior of the system. Throughout the course there will be an emphasis on the use of model biological systems (primarily yeast, bacteria and HIV) to study complex molecular interactions and cellular processes involving nucleic acids. Overall, there will be a strong focus on experimental design, experimental techniques and interpretation of data.

Lectures:
Tuesday and Thursday 12:30-1:30 pm. MSB282

Requisites:
Prerequisite(s): Biochemistry 3381A and Biochemistry 3382A

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

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<tr>
<th>Instructors</th>
<th>Email</th>
<th>Office</th>
<th>Phone</th>
<th>Office Hours</th>
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<tbody>
<tr>
<td>Dr. David Haniford (Course Coordinator)</td>
<td><a href="mailto:haniford@uwo.ca">haniford@uwo.ca</a></td>
<td>MBL C204</td>
<td>84013</td>
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<td>Dr. Chris Brandl</td>
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<td>MBL C210</td>
<td>82395</td>
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<td>Dr. Murray Junop</td>
<td><a href="mailto:mjunop@uwo.ca">mjunop@uwo.ca</a></td>
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TA’s: TBA

3. Course Web site: OWL: BIOCHEM 4410A 001 FW17

Students with OWL issues should see: https://owl.uwo.ca/portal/site/owldocs

4. Course Syllabus

Course Topics

Section 1: Introduction to Systems Biology - Dr Chris Brandl (September 12 –26) (5 lectures)

- Basic concepts in Systems Biology
- Introduction to yeast 2 hybrid system (defining protein interaction networks)
- Introduction to synthetic genetic array (SGA) technology (defining genetic interaction networks)
- Clustering and network analysis
- Introduction to databases for defining/illustrating interaction networks

Section 2: Post-transcriptional regulation of gene expression by sRNAs in bacteria - Dr David Haniford (September 28 – October 10) (4 lectures)

- Genetic criteria for defining small non-coding RNAs (sRNA) in bacteria
- Introduction to a bacterial toxin-antitoxin system
- Silencing a translational enhancer with an sRNA
- Introduction to Salmonella pathogenicity
- Dual-RNA-seq for identifying regulators of Salmonella infection
Section 3: HIV replication and the ‘molecular arms race’ between HIV and its host - Dr David Haniford (October 12 – October 31) (4 lectures)

Gene expression in HIV
Defining a factor (APOBEC3G) that confers a non-permissive HIV infection phenotype
High throughput screening for small molecules that inhibit HIV Vif

Section 4: Telomere biology - Dr David Haniford (November 2 – 14) (4 lectures)

Overview of telomere replication and telomerase
TERRA and telomerase recruitment
ALT pathway for telomere replication
Links between TERRA and ALT

Section 5: DNA repair: disease, cures and cool new stuff – Dr Murray Junop (November 16 – December 5) (6 lectures)

Introduction to DNA damage/repair mechanisms
Impact of DNA damage on genomes (evolution and disease)
Synthetic lethality in DNA repair for cancer therapy
Exploiting DNA repair for gene therapy and genome assembly

Learning Outcomes – Section Specific

Section 1

After completion of this section students should be able to:
Define the key components of systems biology
Describe how clustering and network analysis is used in systems biology
Describe the theory behind two-hybrid analysis and SGA
Outline a strategy to solve a biological problem using a systems approach

Section 2

After completion of this section students should be able to:
Describe mechanisms of RNA processing in bacteria and explain why RNA processing can be important to sRNA function
Describe methods for characterizing the termini of RNA molecules
Describe how sRNAs influence gene expression in bacteria
Outline a strategy to define the function of a newly discovered bacterial sRNA

Describe how RNA-seq is used to characterize genes involved in Salmonella pathogenesis

**Section 3**

After completion of this section students should be able to:

Describe how HIV replicates its genome

Describe the link between HIV genome replication and the capacity of HIV to develop resistance to anti-HIV drugs

Describe approaches for defining an unknown gene whose expression causes phenotypic changes in a given cell line

Describe how Vif protects HIV from host cell restriction

Describe how APOBEC3 family members inhibit HIV infection

Describe the basics of high throughput screening for small molecule inhibitors

**Section 4:**

By the end of this section the student should be able to:

Describe how telomeres are replicated

Describe how telomere binding proteins influence telomerase function

Describe the role of subtelomeres and TERRA in recruitment of telomerase to short telomeres

Describe how telomeres and telomerase can be visualized in real-time in live cells

Describe the link between telomere length, cell proliferation and cancer

Describe how telomerase-minus cancer cells use the ALT pathway to maintain telomeres

Describe how TERRA is linked to the ALT pathway

**Section 5:**
After engaging material covered in this section, individuals will be able to:

Grasp the breadth of challenges faced by genomes during exposure to DNA damage

Describe the basic mechanisms/pathways available for repair of DNA damage

Understand the concept of synthetic lethality and how it can be used to combat disease

Appreciate (and formulate new) ways of exploiting DNA repair mechanisms for use in gene therapy and other applications such as genome assembly

**Learning Outcomes - General**

After completion of this course students should be able to:

Critically read scientific literature in the disciplines of gene expression, DNA replication and DNA repair

Design research strategies to further our understanding of mechanisms of gene expression, DNA replication and DNA repair

Design high-throughput screens for developing small molecule inhibitors of therapeutically important target molecules

Describe to the lay public how detailed understanding of molecular processes involving DNA and RNA impact on diseases such as cancer and AIDS

Define appropriate information sources for answering questions relating to gene expression, DNA replication and DNA repair

Work in a group to synthesize answers to course assignments

**5. Course Materials**

Research papers provided as PDFs

**6. Evaluation:**

Dr Brandl’s assignment (20%) – due 12:30 pm October 3, 2017.

Dr Haniford’s assignment - 1 (15%) – due 12:30 pm October 17, 2017.
Dr Haniford’s assignment - 2 (35%) – due 12:30 pm Nov 21, 2017.

Dr Junop’s in-class quizzes – (10%)

Dr Junop’s assignment (20%) – due December 19, 2017

SPECIAL EXAMINATIONS
A Special Examination is any examination other than the regular or Supplemental Examinations, and it may be offered only with the permission of the Dean 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.
To provide an opportunity for students to recover from the circumstances resulting in a Special Examination, the University has implemented Special Examinations dates as outlined below:
First Term Half Course: 1st Thursday in January following the beginning of classes.

Special Examinations must be written at the University or recognized exam center or an Affiliated University College, and supersede any lectures, tutorials, laboratories, etc., in which the student is registered. Note that students are responsible for any coursework, etc., missed while writing the Special Examination.

Rounding of marks:

*Final grades in 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, while 74.5 becomes 75). Marks WILL NOT be bumped to the next grade or GPA level (e.g., an 84 will NOT be bumped up to an 85). The mark attained is the mark you achieved and the mark assigned; requests for mark bumping will be denied, in accordance with Bachelor of Medical Science Undergraduate Education policy.*

7. Additional Information/Statements

**Statement on Use of Electronic Devices**
No electronic devices may be used for the final exam in this course.
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/handbook/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 ).”

“Computer-marked multiple-choice tests and/or exams may be subject to submission for similarity review by software that will check for unusual coincidences in answer patterns that may indicate cheating.”

Absence from course commitments

Students must complete all of the course evaluations (3 assignments, 1 exam) – there will be no re-weighting of marks due to a missed evaluation. Assignments (hard copy) are to be handed in at the beginning of class on the due date and an e-copy of the assignment is to be submitted on the course web site any time on the date the assignment is due. For the course assignments you will be lose 10% of the total value of the assignment per day handed in late.

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

The policy is also accessible from the Medical Accommodation Policy link at
https://studentservices.uwo.ca/secure/index.cfm

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. For further information please see:
http://www.uwo.ca/univsec/pdf/academic_policies/appeals/accommodation_medical.pdf

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:
B. Absence for non-medical reasons:
If you have timetable conflicts with the final examination time, contact Melita Hayes (melita.hayes@schulich.uwo.ca), the Biochemistry Undergraduate Co-ordinator in the Biochemistry Office (Rm 342 Medical Sciences Building) at least 2 weeks before the examination date.

Documentation is required to receive accommodation for missing either a course assignment or the final exam for non-medical reasons. Documentation must be submitted by the student directly to the BMSc Dean’s/Academic Counselling Office and not to the instructor. It will subsequently be the Dean’s/Academic Counselling Office that will determine if accommodation is warranted.

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

C. Special Examinations
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
Academic Counselling (Science and Basic Medical Sciences): http://www.uwo.ca/sci/undergrad/academic_counselling/index.html
USC Student Support Services: http://westernusc.ca/services/
Student Development Services:  http://www.sdc.uwo.ca

Student Health Services:  http://www.shs.uwo.ca/

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