Understanding Pluripotency

The physiology of stem cell fate and function

Fall 2018
1. Course Information

Fall Term 2018

The fundamental goal of pluripotent stem cell biology is to understand how the self-renew and differentiation capabilities of these extraordinary cells are regulated to produce cells capable of differentiating into a wide range of functional cell types. This course will examine a variety of current topics within the field of pluripotent stem cell physiology. In particular, we will focus on the basic biology of embryo-derived stem cells and their potency. We will briefly cover pre- and post-implantation embryo development, focusing on cell fate determination and the cell lines derived from these developmental stages. We will discuss how these embryo-derived cell lines are isolated and tested, what factors allow for their expansion, how they can be genetically manipulated and what intrinsic and extrinsic factors regulate their self-renewal and cellular differentiation characteristics. We will also discuss pluripotent stem cells derived by somatic cell nuclear transfer and cellular reprogramming technologies. An understanding of this physiology will enable students a thorough understanding of stem cell function and cell fate determination to assess whether regenerative medicine is feasible with pluripotent cells along with gaining the ability to critically evaluate the ethical issues that surround this field.

Lectures:
2 hr classes (~1 hr didactic lecture, ~1 hr problem-based learning exercises / informal class discussions and exercises)

Thursdays, 2:30-4:20, Western Active Learning Space (WALS, Room 66 UCC)

Requisites:
Suggested Prerequisite(s): Physiology 3120, 3130Y and Physiology 3140A (or equivalent).

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.

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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</thead>
<tbody>
<tr>
<td>Dr. Dean H. Betts</td>
<td><a href="mailto:dean.betts@schulich.uwo.ca">dean.betts@schulich.uwo.ca</a></td>
<td>DSB</td>
<td>After Lectures</td>
</tr>
<tr>
<td>[Course Co-coordinator]</td>
<td></td>
<td>2022</td>
<td></td>
</tr>
<tr>
<td>Dr. Cheryle A. Seguin</td>
<td><a href="mailto:cheryle.seguin@schulich.uwo.ca">cheryle.seguin@schulich.uwo.ca</a></td>
<td>DSB</td>
<td>After Lectures</td>
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<tr>
<td>[Course Co-coordinator]</td>
<td></td>
<td>0035A</td>
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<tr>
<td>Josh Dierolf</td>
<td><a href="mailto:jdierolf@uwo.ca">jdierolf@uwo.ca</a></td>
<td>DSB</td>
<td>After Lectures</td>
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<tr>
<td>[TA*]</td>
<td></td>
<td>2027</td>
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* or by appointment; #TA = teaching assistant

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

3. Course Syllabus

Course Objectives:

The main objective of this course is to introduce students to the basic molecular, biochemical and morphological events that regulate pluripotent stem cell biology. Additional objectives are: to improve the students’ ability to read and understand primary scientific literature, to write about science effectively to a lay audience and to provide students with an opportunity to conceptually translate their knowledge of stem cell biology to solve biological problems by designing novel experiments and stem cell based therapies. The course material will include didactic lecturing, but will also utilized a flipped classroom approach for students to conduct in-class exercises to properly examine primary research journal papers, to learn how to write scientific and lay articles and how to properly design hypothesis driven experiments. Students will be expected to come prepared to discuss the content of research articles in class as well as work independently outside the lectures. The lectures will focus mainly on the factors and signalling pathways that govern development of the early embryo, embryo-derived stem cells concentrating on the physiology, utility and ethical issues that surround pluripotent stem cell technologies.
A student who has met the objectives of the course will be able to:

- Explain the basic concepts of stem cell self-renewal and pluripotency and how these features are evaluated in the stem cell field
- Apply their understanding of the basic concepts and fundamental mechanism that regulate pluripotent stem cells as it relates to developmental biology to solve problems/questions
- Navigate, understand and critically evaluate published stem cell research literature
- Debate current ethical issues that surround pluripotent stem cell biotechnologies
- Explain the basic concepts of stem cell self-renewal and pluripotency and how these features are evaluated in the stem cell field
- Explain the basic concepts of stem cell self-renewal and pluripotency and how these features are evaluated in the stem cell field

Method of Presentation: The material of the course will be presented in the form of didactic lectures and a partial flipped classroom platform that includes problem based learning exercises and informal class discussions, exercises and debates.

Methods of Evaluation (Students will be expected to):

- Actively participate in regular classroom discussions and debates
- Read assigned scientific papers prior to class
- Utilize current scientific literature in preparing assignments
- Prepare a scientific lay article
- Apply their learned basic science knowledge of the stem cell field to propose experiments to solve scientific problems/questions
- Write, in short answer essay format, on quizzes, the mid-term and final examinations
Course Learning Outcomes:

Upon successful completion of this course, students will be able to:

- Demonstrate a detailed knowledge and critical understanding of key concepts and regulatory mechanisms governing pluripotent stem cell function by describing concepts, applying and integrating ones' knowledge, and critically evaluating and reflecting upon major theories, practices and ethical issues in the field.

- Demonstrate a strong understanding of the scientific methodologies behind pluripotent stem cells by formulating hypotheses, designing experiments, analyzing and interpreting data and making reasoned conclusions and improvements in experimental design in light of published work.

- Interpret figures and proper figure descriptions along with identifying the strengths and weaknesses of information and the various research techniques used.

- Perform literature searches and be able to evaluate and critique current literature in pluripotent stem cell physiology to generate a clear and concise written layperson article.

- Explain and apply different stem cell models and technologies (e.g. knockout vs. knock-in, genome editing approaches etc.) with varying experimental procedures (Western vs. real time RT-qPCR etc.) to interpret the scientific literature encompassing the pluripotent stem cell field.

- Demonstrate the ability to critically evaluate, manage, reflect on, integrate and apply their pluripotent stem cell knowledge in solving problem based learning exercises and examination questions.

- Develop convincing arguments to effectively debate complex ideas and relevant scientific and/or ethical issues to be made aware of that scientific knowledge changes, has different interpretations and that ethical issues are not always simple choices between two differing views.
Physiology 4510
Understanding pluripotency: The physiology of stem cell fate and function

Lecture Schedule*
Thursdays, 2:30-4:20 Western Active Learning Space (WALS, Room 66 UCC)

<table>
<thead>
<tr>
<th>DATE</th>
<th>TOPIC (Instructor)</th>
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<tbody>
<tr>
<td>6 Sept.</td>
<td>Course Introduction; Fundamental principles of “stemness”; pre- and post-implantation embryo development as it relates to embryo-derived stem cells and cell fate determination (Betts)</td>
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<tr>
<td>13 Sept.</td>
<td>Cell Differentiation/Lineage Restriction (Séguin)</td>
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<tr>
<td>20 Sept.</td>
<td>Embryonic Stem Cells and Pluripotency (Séguin)</td>
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<td>27 Sept.</td>
<td>Extracellular Signals to Direct Stem Cell Differentiation (Séguin)</td>
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<tr>
<td>4 Oct.</td>
<td>Intracellular Signals to Direct Stem Cell Differentiation (Séguin)</td>
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<tr>
<td>18 Oct.</td>
<td>Somatic Cloning and Epigenetic Reprogramming in Mammals (Betts)</td>
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<tr>
<td>25 Oct.</td>
<td>Induced Pluripotent Stem Cells (Betts)</td>
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<tr>
<td>1 Nov.</td>
<td><strong>In class mid-term test (questions based on first 7 lectures)</strong></td>
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<tr>
<td>8 Nov.</td>
<td>Systems Biology Approaches (e.g. RNA-seq; ChIP; microarray; proteomic)/Genetic manipulation of pluripotent stem cells (e.g. genome editing, knockdown, transgenic approaches) (Betts/Tobias)</td>
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<td>15 Nov.</td>
<td>“Jigsaw” readings and presentations of important pluripotent stem cell papers (Betts and Séguin)</td>
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<td>22 Nov.</td>
<td>Ethical Issues Surrounding Pluripotent Stem Cells (Betts), In class activity to play “decide” ethics kit on stem cells</td>
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<td>29 Nov.</td>
<td>Cell-Based Therapies from Pluripotent Stem Cells (Betts)</td>
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<tr>
<td>6 Dec.</td>
<td>Design your own pluripotent stem cell based therapy (Betts) and Course Review (Betts and Séguin)</td>
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* Select journal papers and study notes for these lectures will be made available on the course OWL site at least the week prior to each lecture
4. Course Materials

Textbook: None required

Suggested Textbooks:


Supplemental Information: Published journal articles will be provided for downloading from OWL as required reading for lectures. Students are encouraged to peruse the scientific literature and read review and/or primary research articles in the stem cell biology field. Examples of such journals: Cell Stem Cells, Cellular Reprogramming, Current Stem Cell Research, Development, Journal of Cell Science, Journal of Biological Chemistry, Nature journals, Proc Natl Acad Sci U S A, Science, Stem Cells, Stem Cell Reports, Stem Cells and Development.

5. Evaluation

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<tr>
<th>Component</th>
<th>Date</th>
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<tr>
<td>Assignment 1 - Ethics Cartoon</td>
<td>Sept. 20th, 2018</td>
<td>5%</td>
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<tr>
<td>Assignment 2 - Layperson Article</td>
<td>Oct 18th, 2018</td>
<td>10%</td>
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<tr>
<td>Mid-term test (based on first 7 lectures)</td>
<td>Nov. 1st, 2018</td>
<td>30%</td>
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<tr>
<td>Jigsaw Presentations and group work</td>
<td>Nov. 15th, 2018</td>
<td>10%</td>
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<tr>
<td>Design your own therapy (in class)</td>
<td>Dec. 6th, 2018</td>
<td>5%</td>
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<tr>
<td>Final Exam</td>
<td>TBA (Dec. 10th - 21st, 2018)</td>
<td>40%</td>
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<tr>
<td><strong>Total Marks</strong></td>
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<td>100%</td>
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The mid-term (2 hours) and final exam (3 hours) will consist of short answer essay questions developed from lectures, assigned readings/exercises and other presented material. There will be a few practice exam questions provided before the midterm and final exams. The 3 hr final exam will be cumulative, with emphasis on the second half of the course.
6. Additional Information/Statements

Cell Phone and Device Policy

The Department of Physiology and Pharmacology is committed to ensuring that testing and evaluation are undertaken fairly. For all tests and exams, it is the policy of the Department of Physiology and Pharmacology that any devices with a battery (e.g. cell phone, tablet, camera, watch, smart watch, ipod) are strictly prohibited. These devices MUST be left either at home or with the students bag/jacket at the front of the room and MUST not be at the test/exam desk or in the individuals pocket. Any student found with one of these prohibited devices will receive a grade of zero on the test or exam. Non-programmable calculators are only allowed when indicated by the instructor. The Department of Physiology and Pharmacology is not responsible for stolen/lost or broken devices.

Policy on Plagiarism

The Department of Physiology and Pharmacology strongly condemns plagiarism. Plagiarism is the “act or instance of copying or stealing another’s words or ideas and attributing them as ones own.” (Excerpted from Black’s Law Dictionary, West Group, 1999, 7th ed. Pg 1170 and the definition used by Western’s Scholastic Discipline document). Plagiarism can be intentional or unintentional and regardless of intent, is a scholastic offence. It should be noted that self-plagiarism, plagiarizing ones own words for multiple assignments is subjected to the same penalty as plagiarizing another. Courses in Physiology and Pharmacology use turnitin, a similarity checking software embedded within OWL. We encourage all students to run their assignments through turnitin prior to submitting their reports for grading. Any report flagged as yellow (25-49% matching text), orange (50-74% matching text) or red 75-100% matching text) will be considered plagiarism (pending investigation by the instructor). It should be noted that a document could be plagiarized yet still pass the similarity check on turnitin.

The minimum penalty for a first time plagiarism offence of any kind is a grade of zero on the assignment. In addition, details of the offence will be forwarded to Dean’s office and stored. A second offence will carry a much stricter penalty in line with Western’s Scholastic Discipline policies http://www.westerncalendar.uwo.ca/2017/pg113.html

Appeals Policy

The Department of Physiology and Pharmacology follows the Western University student academic appeals policy (http://www.westerncalendar.uwo.ca/PolicyPages.cfm?Command=showCategory&PolicyCategoryID=1&SelectedCalendar=Live&ArchivedID=#SubHeading_181). All appeals to individual graded course components must be submitted to the course instructor within 3 weeks of the grade being released. All final course grade appeals must be received by January 31 (1st term classes) or June 30 (2nd term half classes and full year classes). You must first appeal to the course manager. If this appeal is rejected, then you can appeal to the Undergraduate Chair of the Department of Physiology and Pharmacology (Brad.Urquhart@schulich.uwo.ca). If this appeal is rejected, you may then appeal to the Assistant Dean of the Bachelor of Medical Sciences Undergraduate Education Committee (Candace.Gibson@schulich.uwo.ca).
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

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/arts/counselling/procedures/medical_accomodation.html

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 the student centre website: https://student.uwo.ca/psp/heprdweb/?cmd=login

https://www.uwo.ca/univsec/pdf/academic_policies/appeals/medicalform_15JUN.pdf

B. Absence for non-medical reasons:

Appropriate documentation must be submitted by the student directly to the appropriate Faculty Dean’s Office and not to the instructor for non-medical absences from quizzes, assignments and the final exam is required. It will subsequently be the Dean’s Office that will determine if accommodation is warranted. The accommodation will be in the form of a make-up assignment, make-up quiz, make-up exam or re-weighting, which may involve written exams being replaced by oral exams.

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.

This link [http://www.uwo.ca/univsec/pdf/academic_policies/exam/definitions.pdf](http://www.uwo.ca/univsec/pdf/academic_policies/exam/definitions.pdf) includes a table of the Special Exam dates and clearly indicates that if an exam is missed it is deferred until the scheduled date of the final exam the next time the course is offered.

**Support Services:**

Registrial Services: [http://www.registrar.uwo.ca](http://www.registrar.uwo.ca)

Academic Counselling (Science and Basic Medical Sciences): [http://uwo.ca/sci/counselling/](http://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 Health and Mental Wellbeing: [http://www.uwo.ca/health/mental_wellbeing/index.html](http://www.uwo.ca/health/mental_wellbeing/index.html) for a complete list of options about how to obtain help.