### Course Description

Selected topics in cell biology, such as membrane dynamics, cell cycle control, apoptosis, signal transduction and cellular rhythmicity. Presentation and critical discussion of recent research papers, emphasizing current methods and experimental design. Three lecture hours. One term. Three credits.

### Prerequisites

Prerequisite: SC/BIOL 3130 3.00

Students without prerequisite must request permission from the instructor. Permission will only be granted if the student has adequate background knowledge.

### Course Instructors and Contact Information

Dr. Patricia Lakin-Thomas (Dr. Pat)

005 Farquharson, x33461

Office hours: Tues & Thurs 11:30 – 1:00 or by appointment

E-mail: clocklab@yorku.ca I will try to respond within one working day, or answer your question at the next class meeting if appropriate.

### Evaluation

Presentation 30%, quizzes 20% (best 15 out of 19), midterm 20%, final exam 30%

Presentation topics and dates will be assigned on the first two days of class, first come/first served, or assigned at random by the instructor. If there are more presentation dates than students, there will be an opportunity for students to volunteer to give a second presentation and use the better grade.

**NOTE:** Final course grades may be adjusted to conform to Program or Faculty grade distribution profiles.

### Important Dates

**First and Last Class Meetings:** Sept 6 – Dec 4

**Fall Reading Days (no classes, University open):** Oct. 6-12

**Midterm date:** Oct 18 in class

**Drop Deadline:** Fri. Nov. 9, 2018 (last day to drop without course on transcript)

**Course Withdrawal:** Sat. Nov. 10 to Dec. 4, 2018 (course still appears on transcript with “W”)

**NOTE:** for additional important dates such as holidays, refer to the “Important Dates” section of the Registrar’s Website at http://www.yorku.ca/yorkweb/cs.htm
**Resources**

Website: Moodle

Recommended text (not required):
Gillen, C.M. (2007) Reading Primary Literature, Pearson Benjamin Cummings.
This short pamphlet is an excellent introduction to critical reading and experimental design (and how science works). Copies are for sale in the bookstore and also on reserve at Steacie.

**Learning Outcomes**

On completing this course, students should be able to:
1. describe recent developments in a selected set of topics at the frontiers of cell biology research.
2. suggest appropriate methods for answering questions about cells and evaluate the pros and cons of current methodologies for investigating cell structure and function.
3. suggest and evaluate experimental designs in cell biology research.
4. critically read original research papers in cell biology.
5. deliver a presentation of recent research at a professional level.

**Course Content**

Five current topics will be covered. Each will be introduced by a recent review followed by several original papers relevant to the topic. Students will give presentations summarizing the papers and the course director will lead critical discussions on aspects of the papers.

See detailed course schedule for the list of papers.

**Experiential Education and E-Learning**

EE: Students will practice professional presentation skills.

E-learning: The Moodle website will be used for posting presentations and course information.

**Other Information**

**Exam format:** Short answers and a choice of paragraph-length essay answers. The exams are open-book and open-note: You may bring the papers and your notes to the exam. You may not use computers during the exam. It is therefore essential for you to have printed copies of the papers.

**Sample exam questions:**
1. What is the experimental evidence to support a particular conclusion?
2. Given a particular experimental approach, suggest some controls that should be included in the experimental design and explain why they are useful.
3. What techniques would be appropriate to investigate a particular question, and what information would these techniques provide?
4. For a particular figure from a paper, explain the experimental design and explain what information was gained from the results.
5. From a particular review, what did the authors suggest are the most important unanswered questions on this topic?

**Course Policies**

**Late policy**
Presentations will not be accepted after the assigned date unless you have a well-documented excuse, in which case the presentation will be given at the first opportunity.

**Missing the midterm**
If the midterm is missed due to a documented excuse, the weight will be assigned to the final exam.

**Missing a quiz**
There will be one quiz per paper, for a total of 19. The grade will be based on the best 15. If you miss a quiz for any reason, including illness or religious accommodation, it will come out of the 4 dropped quiz grades. There will be no make-up quizzes.
Academic Honesty and Integrity
York students are required to maintain the highest standards of academic honesty and they are subject to the Senate Policy on Academic Honesty (http://secretariat-policies.info.yorku.ca/policies/academic-honesty-senate-policy-on/). The Policy affirms the responsibility of faculty members to foster acceptable standards of academic conduct and of the student to abide by such standards.

There is also an academic integrity website with comprehensive information about academic honesty and how to find resources at York to help improve students’ research and writing skills, and cope with University life. Students are expected to review the materials on the Academic Integrity website at - http://www.yorku.ca/academicintegrity/

Access/Disability
York University is committed to principles of respect, inclusion and equality of all persons with disabilities across campus. The University provides services for students with disabilities (including physical, medical, learning and psychiatric disabilities) needing accommodation related to teaching and evaluation methods/materials. These services are made available to students in all Faculties and programs at York University.

Students in need of these services are asked to register with disability services as early as possible to ensure that appropriate academic accommodation can be provided with advance notice. You are encouraged to schedule a time early in the term to meet with each professor to discuss your accommodation needs. Please note that registering with disabilities services and discussing your needs with your professors is necessary to avoid any impediment to receiving the necessary academic accommodations to meet your needs.

Additional information is available at the following websites:
Counselling & Disability Services - http://cds.info.yorku.ca/
Counselling & Disability Services at Glendon – https://www.glendon.yorku.ca/counselling/
York Accessibility Hub - http://accessibilityhub.info.yorku.ca/

Religious Observance Accommodation
York University is committed to respecting the religious beliefs and practices of all members of the community, and making accommodations for observances of special significance to adherents. Should any of the dates specified in this syllabus for an in-class test or examination pose such a conflict for you, contact the Course Director within the first three weeks of class. Similarly, should an assignment to be completed in a lab, practicum placement, workshop, etc., scheduled later in the term pose such a conflict, contact the Course director immediately. Please note that to arrange an alternative date or time for an examination scheduled in the formal examination periods (December and April/May), students must complete an Examination Accommodation Form, which can be obtained from Student Client Services, Student Services Centre or online at http://www.registrar.yorku.ca/pdf/exam_accommodation.pdf

Student Conduct in Academic Situations
Students and instructors are expected to maintain a professional relationship characterized by courtesy and mutual respect. Moreover, it is the responsibility of the instructor to maintain an appropriate academic atmosphere in the classroom and other academic settings, and the responsibility of the student to cooperate in that endeavour. Further, the instructor is the best person to decide, in the first instance, whether such an atmosphere is present in the class. The policy and procedures governing disruptive and/or harassing behaviour by students in academic situations is available at - http://secretariat-policies.info.yorku.ca/policies/disruptive-andor-harassing-behaviour-in-academic-situations-senate-policy/
Methods: The listed methods are not the only methods in these papers. They are the methods that are important to the paper or are listed because the paper is the first time we will see those methods in this course. You should concentrate on the listed methods in your presentation but also mention the other important methods.

**Sept 6, 11:** Introduction, methods review

**Golgi Review:**

**Sept 13**

  Methods: Purification of Golgi membranes from rat liver, in vitro vesicle formation and purification, tethering of vesicles to glass, immunogold labeling for EM, immunoprecipitation, confocal microscopy of YFP-fusion proteins in live cells, microinjection, VSV-G transport assay, Sar-1\textsuperscript{DN} inhibition of ER export.

**Sept 18**

  Methods: yeast as model system, 4-D confocal microscopy, Golgi marker proteins with fluorescent tags, alpha-factor, radioactive pulse-chase

**Sept 20**

  Methods: Polymerizable Golgi proteins, HeLa cells, sedimentation assay, nocodazole, CHX, brefeldin A, immunogold labeling for EM, immunofluorescence and confocal microscopy, EM tomography, radioactive labeling

**Sept 25**

  Methods: *Drosophila* neurons as model system, GAL4-UAS system for gene expression, EB1-GFP for microtubule dynamics, ManII-mCherry as a Golgi marker, purification of Golgi vesicles, immunostaining, inhibition of microtubule nucleation with a blocking antibody

**Cell Migration**

**Review:**
Sept 27
   Methods: Dictyostelium as a model organism, time-lapse microscopy and image processing, chemotaxis assay, ACA mutants, Celltracker cytosol dye, chemotaxis index

Oct 2
   Methods: Xenopus embryo as a model system, neural crest cell culture, chemotaxis assays, time lapse microscopy, photobleaching FRET analysis, morpholinos, dominant negative mutants, cell transplantation and mosaic analysis, immunostaining and in situ hybridization

Oct 4
   Methods: human mammary epithelial cells, MDCK cells, human epidermal carcinoma cells, micropatterning of cells on gel, durotaxis assay, fluorescent time-lapse imaging, kymographs, traction force microscopy, monolayer stress microscopy, siRNA knockdown

Oct 9, 11: No class (reading days)

Oct 16: Midterm Review
Oct 18: Midterm

Apoptosis and Cancer
Reviews:

Oct 23
   Methods: human colon cancer cells, overexpression and knockout cell lines, apoptosis assays, GFP fusion proteins, immunofluorescence, immunoprecipitation, subcellular fractionation, caspase inhibitors

Oct 25
   Methods: HeLa cells, human glioblastoma cells, synthetic chemistry, fluorescence polarization assay for molecular binding, GST-tagged proteins and biotin tags for protein-protein interaction assays, native PAGE for protein complex formation, assays for apoptosis and caspase activation
Oct 30

Methods: cancer cell lines, DNA fingerprinting to identify cell lines, small molecule Smac mimetic, luminescent cell survival assay, siRNA knockdown, immunoprecipitation, chemical inhibitors of signaling pathways

Nov 1

Methods: multiple commercial and patient-derived cancer cell lines, apoptosis-inducing drugs and chemotherapy drugs, Western blotting of apoptosis proteins, flow cytometry and Hoechst staining for cell death assays, orthotopic xenografts of luciferase-expressing cells in mice and in vivo bioluminescence imaging

Stem Cells
Reviews:

Nov 6

Methods: isolation of mouse embryonic and adult fibroblasts, embryonic cell culture on feeder cells, retroviral transduction, selection for pluripotency using Fbx15 gene, chromatin immunoprecipitation assays, karyotyping, genetic fingerprinting, promoter methylation assay by bisulfite sequencing, teratomas and embryoid bodies, chimeric mice, other assays for pluripotency

Nov 8

Methods: production and characterization of human iPSCs, neuronal differentiation, rabies virus tracing, neurite and synaptic counting, electrophysiology, calcium dye for spontaneous transients, antipsychotic drugs

Nov 9: Drop Deadline

Nov 13
Methods: human oocyte donation, cell synchronization, enucleation and nuclear transfer, embryo culture, microsatellite genotyping, karyotyping, mtDNA genotyping, cardiac differentiation, teratoma assay, ARMS-qPCR assay for mtDNA

Nov 15
Methods: iPS cells from human skin using a kit, SCNT, oxygen consumption for mitochondrial activity, ECAR for glycolysis rate, in vitro differentiation methods, FACS cell sorting of differentiated cells, ARMS-qPCR for mutational analysis, mtDNA sequencing, RNA-seq for gene expression analysis

3D Cell Culture and Bioprinting
Review:

Nov 20
Methods: Human iPS neural stem cells, artificial ECM, hydrogels, 3D cell culture, rat model of stroke, immunohistochemistry.

Nov 22
Methods: Colorectal cancer cells, endothelial cells, fibroblasts, hydrogels, 3D cell culture using RAFT system.

Nov 27
Methods: Endothelial progenitor cells, vascular endothelial growth factor, gelatin microparticles, hydrogel, 3D bioprinting, flow cytometry, cell migration assays, immunocytochemistry and histology.

Nov 29
Methods: immortalized kidney tubule cells, 3D culture, bioprinting, organ-on-a-chip, engineered ECM, hydrogel, flow cytometry, immunofluorescence, drug toxicity testing.

Dec 4: Final Exam Review
Biology 4141 – Current Topics and Methods in Cell Biology
Additional Course Information, Fall 2018

Finding Papers

All papers for this course are available to download from the journals’ own websites. You do not need to photocopy paper journals, and there are no copies of the papers on reserve. Papers are not posted on the course website, for two reasons: 1) Posting may violate copyright laws. 2) You need to practice how to find papers online.

Go first to York Library eResources and find by periodical title, then find the paper by volume and page number. (You need to be connected via a York computer, or know how to get access from off-campus using Passport York.) If not listed in York’s holdings, then go directly to the journal’s own website for access. (Google the name of the journal in quotes.)

Another way to access a paper is to go to York’s library website and search for Scopus, then search for the name of the paper in Scopus using “Article Title”. From the citation in Scopus you can find the paper through “View at publisher.”

Be sure to download the pdf version (not full text/html) for printing. Use the html version for high-resolution figures (to use in your presentation) and to see colour figures. Also be sure to check for and download any supplemental files: most papers have additional information that is not included in the printed version and is only available online. (You may need to go to the journal’s own website to get the supplements, not through an intermediary like Scholar’s Portal.) Many papers require color for some of the figures; if you don’t print in color, you may need to look at the figures in the electronic version to understand them.

Reading Papers

The Gillen pamphlet is a very good basic introduction to reading scientific papers. It is short enough for you to read it on reserve in the library. An abbreviated version of the main points can be found in a simple tutorial posted on the author’s website:

http://biology.kenyon.edu/Bio_InfoLit/index.html

Finding information on methods

(Include your sources in your presentation, at the bottom of the slide and/or a final references slide.)

1) For basic methods, go first to your cell biology textbook (Alberts), and the index. Try other textbooks such as molecular biology or genetics texts.
2) Look in Green & Sambrook for basic molecular methods (reference listed below).
3) Try Current Protocols Online: Access through the library’s website. Select “Current Protocols in Cell Biology” (or another topic) and use the search function with a keyword.
4) For methods specific to your paper, go to the earlier papers that are referenced as sources for the methods. This may send you on a long chain of references to earlier and earlier papers.
5) Try websites of companies named in the paper that manufacture kits or supply reagents. This is a good source for proprietary (patented) kits and methods.
6) Wikipedia is surprisingly good for background information but don’t use it as a primary reference—look at the bibliography at the bottom of the Wikipedia page and find those references. There is a Wiki project for molecular and cell biology: http://en.wikipedia.org/wiki/Portal:MCB
7) I do not recommend Googling the name of the method; this is inefficient and often unreliable. Often the websites you find will not be primary (reliable) sources, but rather someone’s lecture notes. This is not an acceptable source of information.
General References
   Very useful for background information and basic methods. Website has good figures to use in presentations: http://www.garlandscience.com/
   The standard reference for molecular biology methods.
Model Organisms and Cell Lines
For model organisms, the best strategy is to look for the species name in Wikipedia and look at the External Links to get to the databases specific for each species.
For cell lines and information about them, go to:
www.atcc.org/

Presentation of Papers

Time limit: Approx. 20-30 min plus questions. Practice and time your talk.
Evaluation: Your grade will be based on the criteria listed on the evaluation form. Students will provide evaluations of their peers to be taken into consideration by the professor, but the final evaluation will be the professor’s subjective judgment.
Organization: Start with a brief summary of the introduction: Why was this research done? Why is it important? How does it fit into the general topic we are studying? Next summarize the methods, then the results, and the final conclusions from the work as stated in the discussion.
Methods: Present a detailed description of methods, with appropriate diagrams to illustrate techniques. Explain how the method works and what information it provides. Concentrate on the methods unique to your paper but mention other important methods used in the paper. Most of these are listed for each paper on the course outline, but don’t limit yourself to that list if you believe other methods should also be discussed.
Results: Present and explain the most significant results from the paper (using figures from the paper). You don’t need to cover all the figures if there are too many. Summarize the conclusions and explain how the results lead to those conclusions. Briefly summarize the major points in the discussion section of the paper. Don’t critique the paper- leave that for class discussion.
Questions: Be prepared to answer questions about the subject of your presentation.
Visual Aids: Use PowerPoint slides, and/or document camera for hard copy, and/or chalkboard. Use supplemental movies from the paper where useful. WARNING: Bring your presentation on a USB drive and come early to class to get it loaded onto the computer. You will not be allowed to plug in your own computer. If your presentation fails to run for technical reasons you will NOT be allowed to postpone it, so test it beforehand AND have a backup plan (email your presentation to yourself, or bring hard copy of your slides to show on the document camera in case your presentation fails to run). I will edit presentations for accuracy and length and post them on Moodle after the presentation. If you use online slide presentation software, you MUST provide me with an EDITABLE copy to post on the course website.
Handouts: Handouts can sometimes be useful, but are not required. A handout could be a summary of the main points in the paper, a diagram or additional data/figures not in the paper. Please limit the length to one page. Do not bring copies of all of your slides to distribute.
**Biology 4141- Fall 2018  Presentation Evaluation**

Speaker:  Date:  
Paper:  

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<thead>
<tr>
<th>Weight (%)</th>
<th>Mark (0-100)</th>
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<tbody>
<tr>
<td>50%  Did the presentation accurately summarize the important points from the paper, including background information from additional sources if necessary?</td>
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<tr>
<td>25%  Was the material presented clearly and in a well-organized way?</td>
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<tr>
<td>10%  Were the visual aids clear and readable and appropriate?</td>
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<tr>
<td>5%  Was the level of explanation appropriate, not too difficult and not too simple?</td>
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<tr>
<td>5%  Were the timing and pacing right, and was the speaker loud enough and understandable?</td>
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<tr>
<td>5%  Did the speaker project enthusiasm and make the subject interesting?</td>
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Does the speaker have any mannerisms they should try to avoid?

Other comments:
Tips on Presentations

- Make an outline first of the points you want to make and the pictures/graphics you will need to illustrate those points. Try to have an illustration for every important point. A picture is worth a thousand words.

- Start with the title of your presentation and your name.

- Practice and time your presentation. You should try for 25 min, no less than 20 and no more than 30. You will lose points if it’s too short or too long. You might get cut off if you run on too long.

- Speak up and make eye contact with the audience. Don’t talk to the computer or screen.

- Don’t read a script. Use notes if you need them but put only a few words on the notes to remind you what to say. The best technique is to use bullet points on your slides as your speaking notes.

- Acknowledge your sources. Give credit for pictures you download from a website or copy from a published source by putting the reference at the bottom of the slide. Add a final references slide for your sources of information. (A final reference slide is NOT the usual style for scientific seminars, but I am asking for it for this course.)

Tips on visual aids and PowerPoint

- Choose a simple design with high contrast between text and background. Black text on a pale background or white or yellow text on dark blue work well.

- Use large font sizes, at least 24 point. Use 28 or 32 for text and 36 to 44 for titles.

- Choose a clean, standard font like Arial or Times New Roman. Do not use many different fonts, or unusual fonts that might not be found in all standard computer installations.

- Don’t put too much on one slide. Slides don’t cost anything so you don’t have to be frugal with them. One idea per slide is a good rule.

- Don’t write whole sentences on the slide and then read them out word-for-word. Use a few words or a phrase to communicate the key words and ideas.

- Don’t use fancy transitions and moving text. It is not helpful, just distracting. There are rare times when a simple animation can help to make a point, but usually it is a waste of your time and the audience’s patience.

- Put a black slide after your last slide so you don’t drop out of the presentation if you advance after the last slide. Add some extra slides after your last slide with information you might use to answer questions from the audience, such as figures from the paper that you didn’t have time to cover.

- Check your presentation on a computer similar to the one you will be presenting on. This is a warning to Mac users like me: Sometimes Windows versions of PowerPoint don’t display your slides the way you see them on your Mac. Movies are a particular problem: You can’t embed a video file in a presentation made on a Mac if it will be run in Windows.
Topics for Critical Discussion of Papers

We will not cover all these questions for every paper. The questions we will focus on are marked *. Read Gillen for further information about these questions.

Questions you should be able to answer about every paper:

1. Do the title and abstract accurately reflect the contents of the paper?

2. Does the introduction clearly state the question the authors are trying to answer and why it’s important?

3. Are the methods described or referenced in sufficient detail to be able to reproduce the experiments?

4. Are the results presented in a clear and meaningful way? Are figures and tables appropriate and understandable? Are figure legends clear and complete?

*5. Was any evidence presented that the results are reproducible?

*6. Are the experiments causative studies or merely correlational?

7. Does the discussion adequately put the results in the context of other work?

Questions requiring more background or critical analysis:

8. Does the introduction provide adequate background and historical perspective? Have the authors referenced the work of others or do they cite only their own work?

*9. What are the strengths and limitations of the methods? What are the advantages/disadvantages of the choice of organism/cell type?

*10. What controls were run, and why? Were all the appropriate controls included?

11. Were the statistical tests appropriate for the data?

*12. Are the conclusions adequately supported by the data?

*13. Are the results physiologically relevant? (Do they tell us how real live cells behave?)

14. Have the authors discussed the limitations of the methods? Have the authors considered alternative explanations for the results?

15. What questions are left unanswered? What new questions have been raised? Have the authors suggested further experiments?

16. What does the paper tell us that is genuinely novel?

17. Do the authors have any conflicts of interest that might have influenced their work?