**Cell Biology of Tissue Development and Function BMS690**

**Spring 2014, 3 credits**

**Course Coordinators:**

Lucy Liaw, Ph.D. (liawl@mmc.org) Calvin Vary, Ph.D. (varyc@mmc.org)

**Meeting time:** Tuesdays and Thursdays 8:00am-­‐9:15am

**Location**: Maine Medical Center Research Institute with videoconference to UMaine, JAX. and MDIBL

**Pre-­requisite:** Passing grade (B-­‐ or better) in BMS690-­‐3, Experimental Methods in Cell and Molecular Biology

**Description:** This course addresses the cellular biology of tissue development in the context of receptorsignaling, cell-­‐cell interactions, and tissue function. Students are expected to have a strong basic understanding of basic cellular and molecular biology. This course will cover major receptor-­‐mediated signaling pathways in the first half. The second half of the course will address how these pathways integrate to control tissue development and function.

**Format:** The course will be a combination of lectures and critique and discussion of primary research

papers. There will also be a mid-­‐term and final exam.

**Grading:** The following will be evaluated for your final course grade: paper, written critiques, and

discussion. In addition, there will be two exams; midterm and final, as well as the weekly assignments. There are 5 paper critiques, and each is worth 10% of your final grade. Remember that your grade for

each paper critique is the combination of your written work AND your participation in class discussion.

We understand that the video-­‐conferencing format has its limitations, especially for those of you at

remote sites. We will elicit responses as much as we can, but the responsibility for participation is yours. The midterm exam and the final exam are each worth 25% of your grade. The weekly assignments will

not receive a grade per se, but will be viewed collectively and have the potential to adjust your grade up

or down if you are on the border between two grades, so take the assignments seriously. Assignments are

also to help you gauge where you may need some extra work or self study.

**Paper critiques:** Primary research papers will be assigned as indicated in the syllabus. Students are

expected to critically read, understand, and be prepared to discuss the work. In addition, a 1-­‐2 page written critique for each assigned paper is due on the day of the paper discussion. Active student participation in the discussion is required and an important part of the grade.

**Faculty:** This is a team-­‐taught course that will be broadcast through the videoconferencing facilities

between MMCRI, UMaine Orono, and the Jackson Laboratory.

**Readings:** Background readings for this course will be primarily recent review articles that will be posted. There is no required textbook for the course, but any of the texts listed below would be useful background or support material.

**Recommended background texts:**

Cell Biology, Pollard and Earnshaw. Updated 1st Edition, 2004

Molecular Biology of the Cell, Alberts, Johnson, Lewis, Raff, Roberts, and Walter. 4th Edition, 2007 Molecular Cell Biology, Lodish, Berk, Zipursky, Matsudaira, Baltimore, and Darnell. 4th Edition, 2000

**Course Syllabus, Spring 2014**

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| Tues 1/14 | overview of course, assignments, reading and reviewing papers, critique writing |
| Thurs 1/16 | Using Excel to perform basic statistical analysis: T test, ANOVA, chi squared tests |
| Tues 1/21 | Basic statistical methods 2 – Sample size and power analysis (demo of recommended internet tool) |
| Thurs 1/23 | Overview of receptor signaling and second messengers – nuclear hormone receptors |
| Tues 1/28 | microRNA regulation and function |
| Thurs 1/30 | TGFbeta/BMP signaling |
| Tues 2/4 | Receptor tyrosine kinase signaling |
| Thurs 2/6 | Paper 1 critique and discussion |
| Tues 2/11 | Wnt/hh pathways |
| Thurs 2/13 | Notch transmembrane receptors and their ligands |
| Tues 2/18 | Signaling from the extracellular matrix |
| Thurs 2/20 | Paper 2 critique and discussion |
| Tues 2/25 | Midterm exam this week |
| Thurs 2/27 |  |
| Spring recess 3/3-­‐3/14 |
| Tues 3/18 | Overview of embryonic development |
| Thurs 3/20 | Overview of signaling in stem cells |
| Tues 3/25 | Signaling in bone and cartilage |
| Thurs 3/27 | Paper 3 critique and discussion |
| Tues 4/1 | Signaling in adipose tissue |
| Thurs 4/3 | Signaling in vascular endothelial cells |
| Tues 4/8 | Signaling in smooth muscle cells |
| Thurs 4/10 | Signaling in cardiac muscle |
| Tues 4/15 | Signaling in skeletal muscle |
| Thurs 4/17 | Paper 4 critique and discussion |
| Tues 4/22 | Signaling in hematopoiesis |
| Thurs 4/24 | Signaling in cancer cells |
| Tues 4/29 | Signaling in cancer stroma (Final exam will be administered) |
| Thurs 5/1 | Paper 5 critique and discussion |
| May 5-­‐9 | Final exam week |

**Assignment Sheet**

Assignments are very short written objectives that direct your studying efforts on a weekly basis. They are expected to be very concise, perhaps a half page description and a diagram if appropriate. Assignments are due on Friday at noon of each class week, and will be used to help gauge your progress in class. These will not be graded individually, but will be used at the end of the semester collectively, along with your participation in class discussion, to help evaluate your overall performance.

Assignments must be submitted to Lucy Liaw (liawl@mmc.org) and Cal Vary (varyc@mmc.org) via email by noon of Friday of the indicated week.

Week of January 13: Make a small capsule describing one category of transcription factors (your choice), providing 1-­‐2 examples of specific proteins in the family and their targets. Examples: basic helix-­‐loop-­‐ helix transcription factors, ets transcription factors, winged-­‐helix/forkhead transcription factors, Hox transcription factors, etc.

Week of January 20: Use a real data set (from your research or if you need one, we will provide one) to perform appropriate statistical test, i.e. t test, ANOVA chi squared test. Justify your choice of statistical analysis method. Perform a power analysis with the data.

Week of January 27: Choose a posttranslational modification that occurs on a protein (for example, glycosylation, phosphorylation, ubiquitylation, acetylation) and outline a short strategy to test whether or not a protein of interest contains that modification.

Week of February 3: Written critique due on Thursday before class – 2 page limit

Week of February 10: Choose any protein coding gene of your interest, and do a search to predict if it is regulated by any microRNAs (for example using miRDB). If you have a long list of potential candidate regulators, identify 1-­‐2 criteria that would help you narrow down this list.

Week of February 17: Written critique due on Thursday before class – 2 page limit

Week of February 24: Midterm examinations due by Friday at noon

Week of March 3: Spring Break

Week of March 10: Spring Break

Week of March 17: Choose a tissue/organ of interest, and identify one living model organism to study the embryonic development of this tissue. Make a list of pros and cons in using this model system to study development of your tissue/organ.

Week of March 24: Written critique due on Thursday before class – 2 page limit

Week of March 31: Choose any cell type and find a good representative picture from the literature that demonstrates the expression of one or more of its differentiation markers. Provide a list of markers that you would use to identify that differentiated cell type.

Week of April 7: Choose a different cell type, and repeat the assignment from last week. Week of April 14: Written critique due on Tuesday before class – 2 page limit

Week of April 21: Describe the Hayflick limit and a strategy to immortalize cells in vitro

Week of April 28: Written critique due on Tuesday before class – 2 page limit

**GUIDELINES FOR WRITING A PAPER**

In science, one of the most basic goals is the development and application of new knowledge. Publishing peer-reviewed papers is the most effective way to share the information with the scientific community. Scientific papers come under great scrutiny as they are reviewed, and then once published, are tested as part of new models and ideas in the field. These published papers will attempt to validate the researcher’s data and interpretations, although new state-of-the-art methods or experimental strategies may later refute previous interpretations. If a paper withstands reproduction, in time the results may become accepted as scientific fact.

Learning to write a good scientific paper is a skill requiring much practice. One must understand the experiment, concepts, and background of the biological question, accurately collect and record data, perform statistical analysis to determine significance of differences, and interpret the results and develop logical conclusions. Further, one must be able to write clearly and concisely to convey ideas and persuade an audience. The ability to write a strong scientific paper is the basis for writing strong grant proposals, as well as developing the ability to critique both papers and grants.

The format of a paper depends on the journal requirements, although typical parts are: Title – accurately descriptive of the study

Abstract or Summary – a concise overview of the biological question, experimental strategy, and results.

Materials and Methods – detailed description (or references) of reagents and protocols used for the study; includes sources of cells, plasmids, antibodies, etc.

Results – Data presentation of the study; includes figures, tables, statistical analysis. Discussion – Interpretation of the data, conclusions, relation of current study to other

work in the field, working models.

References – Literature citations mentioned in the text

Please see the section in this packet with some journal examples of Instructions to Authors. Note that very specific guidelines in the Instructions that deal with more conceptual or experimental items will give you an idea of how the paper will be evaluated by a reviewer and the editor (for example, see the section on (“controls for genetically engineered mice” in the J. Clin. Invest. Instructions). While there are many black and white instructions (word limit, figure limit, reference style, manuscript categories, etc.) there are also subjective criteria that are very important (scientific soundness, novelty, impact to the field, priority level, originality).

**GUIDELINES FOR WRITING PAPER CRITIQUES**

The goal of critiquing a published piece of literature is to evaluate the work in perspective with other work in the field, understand the background of the scientific problem, determine if the conclusions are well supported by the data, and provide your own opinion on the next important experiments.

1. Biological question and hypothesis (Introduction/Background section) – provide a brief description of the biological question being addressed. What is the specific hypothesis (and alternative hypotheses) being presented? Does the hypothesis follow logically from the background material? What is the goal of the series of experiments? What was the background that led the authors to do these experiments? If there are special techniques or novel strategies involved, an introduction to this can be included. Do not write a straight narrative (please see example 1) of every experiment performed and the techniques being used (however, you should be prepared to discuss each experiment and technique during the class discussion period).

2. Experimental strategy (Materials and Methods) – provide an assessment of the strategy that the authors use to address the biological question. Is it appropriate? Are there alternate strategies that may be helpful? For the specific experiments, was there enough detail or references given so that you can reproduce the study?

3. Presentation of the data (Results) – Are the data presented in a clear and understandable manner? One common problem with scientific papers is the lack of controls for confounding variables. With experiments, have the authors conducted the appropriate controls? With comparisons and observations, have the authors used appropriate statistical methods to remove the effects of confounding variables on the "response" variable? The existence of confounding variables means that there may be alternative hypotheses to explain the data.

4. Evaluation of the data – What is the quality of the data? Are the results from the experiments clear and interpretable? Has appropriate statistical analysis been performed to support the significance of differences between groups? Were the results expected, and why?

5. Conclusions (Discussion) – Are the authors conclusions supported by the data? If the original hypothesis was refuted, is there an alternative model proposed? If not, what experiments might be helpful to develop a new model?

6. Future work and significance – What are the next steps for this biological question? How is this work significant?

Be advised that you may want to search the literature or refer to some of the references in the paper(s) to become familiar with the general state of the field and previous studies in the area.