BICD194 ~ Epigenetics in Gene Regulation, Development and Cancer

Winter 2023

Course Organizers:

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GOALS OF THE COURSE:

The course is focused on epigenetic mechanisms that control gene expression. There will be a heavy emphasis on understanding the basis of design, execution and interpretation of relevant scientific experiments. The goal of the course is to read, critically evaluate and present primary data from research articles.

COURSE WEBSITE: Tritoned

All reading assignments will be posted on the website as well as other notifications. You will be responsible for locating and printing the weekly reading assignments.

TEXT BOOK: No text is required.

CLASS TIME AND PLACE: Monday 4 PM York Hall

PREREQUISITE: BIMM100 (Molecular Biology).

GRADING: There will be no final exam. Your performance in the course will be determined by the quality of oral presentations. Evaluations will be based on performance during the discussions. Grades will be based on participation (50%) and quality (50%).

Each paper will be discussed. Students will be randomly assigned into groups during the day of presentation that will be responsible for presenting the papers. This includes approximately 45 minutes for the presentation and 15 minutes for questions and discussion. All students should be prepared for each session to participate.

Presentations should be thoroughly prepared and clearly delivered. Furthermore, you may need to search additional publications to assist in your understanding and presentation. The aim is to help the class gain a clear understanding of the conceptual context, purpose, approaches taken and significance of each paper. A good understanding of the experimental methods employed is also essential for critical reading of any paper. Leading the group discussion consists of taking the class step-by-step through the rationale, approach and results in each paper. This often requires judicious choices regarding which figures and concepts are central and which are secondary. Several of the manuscripts are complicated but by working together, we will achieve a common level of understanding of the research described in the manuscripts

Presentation Content

In general, each group presentation should include the following information:

Background/Introduction. Offer the necessary background to provide context for the paper. i.e. What are the authors attempting to show? How does this work fit into the broader view of the field? What tools are used to approach the problem?

Discussion of Data/Results. Provide a thorough description of the techniques employed in the paper. Describe the specific experiments, highlighting any controls that are important for the interpretation of the data. Summarize the results of the experiment, including whether what *you* observe within the provided figures actually supports (or not) what the author's write in the text. Discuss any reservations you may have about the data. Figures should be divided between members of the group.

Conclusions and implications. Discuss the major conclusions from the findings presented in the paper. Where possible, include a model (often included at the end of the paper) to provide an overview of the findings. Discuss any caveats to the interpretation, and discuss the long-term implications of the work.

There are four major questions should be addressed during the presentation:

1. What is the most important conclusion and take home message? 2. What is the most critical experiment that supports their main conclusion? 3. Are there major caveats in the study? 4. What are the most important follow up questions that should be addressed?

Presentation Format

All students should be prepared to present and discuss assigned papers for each class.

Participation

Participation during discussions will be a major factor of our evaluation in assigning final grades. It is assumed that each student has read carefully, and is conversant with the contents of each of the papers assigned for a given week. Anyone in the class may (and will) at any time be called upon by the presenters or instructor to discuss a particular figure or finding in the paper under discussion. In addition, it is expected that each student will regularly make spontaneous contributions to the discussion.

SCHEDULE FOR SEMINARS AND READING MATERIAL

January 9

Moderator: Kees

Overview of the course.

January 23

Moderator: Jesse

Fulco et al. Activity-by-contact model of enhancer-promoter regulation from thousands of CRISPR perturbations. Nature Genetics 51, 1664-1669 (2019).

January 30

Moderator: Jesse

Flavahan et al. Insulator dysfunction and oncogene activation in IDH mutant gliomas. Nature 529, 110-114 (2016).

February 6

Moderator: Jesse

Larson et al. Liquid droplet formation by HP1a suggests a role for phase separation in heterochromatin. Nature 547, 236-245 (2017).

February 13

Moderator: Diana

Luk et al. Stepwise histone replacement by SWR1 requires dual activation with histone H2A.Z and canonical nucleosome. Cell 143, 725-736 (2010).

February 20

Moderator: Kees

Takahasi and Yamanaka. Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. Cell 126, 663-676 (2006).

February 27

Moderator: Kees

Wang et al. A prion-like domain in transcription factor EBF1 promotes phase separation and enables B cell programming of progenitor chromatin. Immunity 53, 1-17 (2020).

March 6

Moderator: Kees

Liu et al. WAPL maintains a cohesin loading cycle to preserve cell-type-specific distal gene regulation. Nature Genetics 53, 100-109 (2021).

March 13

Moderator: Kees

Boija et al. Transcription factors activate genes through the phase-separation capacity of their activation domains. Cell 175, 1842-1855 (2018).