BGGN 283 BIMM 194 ~ Epigenetics in Gene Regulation, Development and Cancer

Winter 2022

Course Organizers:

Kees Murre: (murre@biomail.ucsd.edu)

Diana Hargreaves: (dhargreaves@salk.edu)

Jesse Dixon: jedixon@salk.edu

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: Tuesday 2 PM Center Hall 217A

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 and written work. Evaluations will be based on performance with these requirements:

PRESENTATIONS (50%): Participation and quality of presentation.

WRITTEN REVIEWS (50%): One-page critiques of two articles

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.

<u>There are four major questions should be addressed during the presentation:</u>

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?

<u>Presentation Format</u>

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

<u>Written Reviews</u>

You are expected to read EVERY assigned paper before coming to class. In addition, you are required to write a 1-page maximum review for two of the assigned research articles. The first paragraph should succinctly describe the results of the research (what did they find). This should be followed by details regarding the research with a focus on the assigned paper that was discussed in class (how did they find it). Lastly, attempt to frame the discovery in a broader biomedical context (why was it important and why should you care). You will turn in your review at the beginning of class following the chosen presentation. You will be responsible for three reviews in addition to the oral presentation.

<u>Participation</u>

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 4

Moderator: Kees

Overview of the course.

January 11

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).

January 18

Moderator: Diana

Sabari et al. Co-activator condensation at super-enhancers links phase separation and gene control. Science 361, eaar3958 (2018).

January 25

Moderator: Jesse

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

February 1

Moderator: Kees

Soufli et al. Facilitators and impediments of the pluripotency reprogramming factors initial engagement with the genome. Cell 151, 994-1004 (2012).

February 8

Moderator: Diane

Luk et al. Stepwise histone replacement by SWR1 required dual activation with histone H2A.Z and

canonical nucleosome. Cell 143, 725-736 (2010).

February 15

Moderator: Kees

February 22

Moderator: Jesse

Beguelin et al. EZH2 is required for germinal center formation and somatic EZH2 mutations promote lymphoid transformation. Cancer Cell 23, 677-692 (2013).

March 1

Moderator: Diana

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 8

Moderator: Jesse

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