MCB 493: Epigenetics Fall 2023

Time and Place: Mondays, Wednesdays, Fridays, 2-2:50 PM, Lincoln Hall 1057

Policy for Zoom broadcasting and recording: We will again wait and see how the COVID situation plays out this semester. For now, I will by default NOT live-broadcast the class lecture but will try to record it and post the recorded lectures. However, if anyone has COVID or COVID-like symptoms **let me know ahead of class** and I can broadcast the lecture so that you can participate if you are quarantining at home.

Zoom link for those occasions: MCB 493 Epigenetics
https://illinois.zoom.us/j/87827766288?pwd=ZnFyRVJCNVBKeHF2bTdLRFlwKzFSUT09

Meeting ID: 878 2776 6288
Password: Epigenetic

Instructor:
Dr. Andrew Belmont
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Office Hours: (via Zoom) 9-10 am, Thursdays
Zoom Link for Office Hours: MCB493 OFFICE HOURS
https://illinois.zoom.us/j/83664723495?pwd=RDRiNEhqNTROcUhabzRRZnltVFJsZz09

Moodle Shortname: MCB 493 EPI FA23
Moodle Access URL: https://learn.illinois.edu/course/view.php?id=74465

Course Goals and Philosophy: Science instruction is typically torn between conveying scientific knowledge versus conveying actually how we go about acquiring that knowledge- i.e. the actual "art of science" as a natural philosophy. My goal for this course is to shift the balance from primarily conveying information, which is characteristic especially of many lower-level undergraduate courses, to an equal weight on conveying where the field is in terms of acquiring this information- what we really know, what we think we may know, what we definitely don't know, and what we'd like to know. In other words, I'd like to give you a taste of "real" science- not just the summary of what we think we know about a scientific topic that you will find in a textbook. At the same time, I will try to describe the tools the field has developed to address these questions, and recent progress the field has made using these tools.

Most importantly, my goal this semester is to design the course in such a way that its emphasis is on teaching you how to independently learn about new findings in the field of epigenetics. Without doubt, these new findings will have impact in future medical care for you and your family. At the very least, you should learn how to read about new discoveries in epigenetics both in the lay and scientific literature and to judge how these new discoveries may impact future health care practices.

With this goal in mind, basic concepts will be presented with a focus on contemporary methods and observations as well as seminal experiments. We often will give a historical perspective as well before leading into contemporary methods and research. This is important because science is a human process that can be flawed. Current researchers often "rediscover" previous discoveries that a generation of previous investigators had ignored or failed to appreciate. Conversely, in some cases researchers often wear "blinders", based on prevailing but wrong theories, whereby they misinterpret the significance of new experimental results. Providing a historical perspective can help understand the long-term trajectory of a field.

Where possible we will also cover applications of epigenetics to contemporary topics in both basic and translational sciences. Lectures will be supplemented with problem set assignments; these questions will address interpreting and explaining experimental results and may be distilled directly from original experiments described in the primary literature.

Occasionally, I will include lectures focused on an in-class discussion of primary research papers that you will read ahead of class. In one of the early lectures, I will introduce how to approach reading a scientific paper, recognizing that this may be new to many or you.

Then in the last several lectures of the class, we will focus on a contemporary topic in epigenetics, including more primary papers we will read and discuss as a class.

This year the scientific focus will be on the relationship of epigenetics to the study of cell reprogramming and human aging.

Course Style:

As much as I am able to, I will teach this class as a "flipped course".

There will be a required pre-class assignment that will cover background material that you will need to cover before coming to class. In class we will build on this background material to further cover the topic(s) for that day. Then we will have weekly Problem Set that is meant to reinforce concepts through active problem-solving using the assigned material. As much as possible, these Problem Set questions will be designed to also prepare you for the exam questions that you will experience in two mid-term exams and one final exam.

For many, if not most, lecture topics, I will try to convey appropriate background material via assignments- reading assignments and/or review of slides and/or online video explanations of the material- that you will do PRIOR to class. Then we will use the class time for higher level exploration of the lecture topic. This might be class discussion of key points from the assignment. Or, if the assignment covered historical background on the topic, we might use the class time to cover where the field has advanced in more recent years. Or we might discuss related material, such as newer experimental approaches that are being applied to this topic and/or the newer experimental methods used in these new experimental approaches. Or we might work through problems related to the topic material, including from the near weekly Problem Sets.

Pre-class Assignments and CPAs:

What is this pre-class assignment? Most often it will be a traditional, straightforward review of the topic that will be the focus of the class so that our in-person class time can be spent more productively in either active learning or covering more challenging material.

For each class topic, I will have a study guide that will list the concepts and/or questions that will guide you with regard to the key information I want you to extract from this pre-class assignment.

Each of these study guides will have a small number of questions. These questions will constitute a **"CLASS PARTICIPATION ASSIGNMENT" or CPA that you will bring to each class** (see below, **CPAs, Problem Sets, Exams, Course Grading**). These will be scored Pass/Fail with Pass representing being in class and turning in a CPA at the end of class that represents a good faith effort in both preparing for class and participating during class.

Recognizing that each student will have one or more preferred learning styles, depending on the type of material, you will have more than one option for learning the material of each assignment. For a typical class topic, there often will be an assigned review book chapter or contemporary journal review article. Additionally, I will have a Powerpoint slide presentation. Finally, I will have an online video presentation that talks through the Powerpoint slide presentation. The Powerpoint presentation frequently will be designed as a more concise and directed summary of the assigned reading material, summarizing, and covering the key points of this reading material as far as the learning goals of this class. Typically, the assigned reading material is designed for practicing scientists and advanced graduate students in that research field. Therefore, focus on the Powerpoint slides and online video presentation of these slides, together with the study guide, to extract the subset of information that I am choosing to cover. But feel free to use the assigned reading to clarify points from the Powerpoint slides and or video presentation of these slides or for your own deeper exploration of these topics.

For most students, I imagine reviewing the slides carefully would be the best starting point. This can then be followed by selective scanning of the assigned reading or online video presentation to understand and/or further explore the key points summarized in each slide and to extract the information you need to answer the CPA questions and to cover the key points for each topic stressed in the Study Guide.

Class Participation Assignments (CPAs)

Before each class, you will briefly answer several questions and/or write notes or an outline of your answer that you can lean on if asked to discuss the answer in class. These questions will be from the Study Guide. Your answers to these questions as described above is your CPA.

You will bring in two copies of your CPA- one to turn in at the start of class and one to refer to and possibly write notes on during class.

You will not be graded on your answers other than a Pass for a sincere effort and a Fail for not turning in of the CPA or what is judged as an inadequate CPA. If for some reason you are not able to attend class, you can email me and explain the circumstances and see if you can be excused and/or turn in the CPA through another means- hard copy or electronic version.

You will require a certain percentage of Passes for these CPAs to earn certain grades in the class (See below- CPAs, Problem Sets, Exams, Grading).

Problem Sets

To reinforce lecture topics and also our emphasis on experimental science, we will have weekly problem sets. We may cover some of these problems in class- either before or after the Problem Sets are due. After you turn in these problems sets, answers will be posted. Office hours will provide you with an opportunity to receive additional explanation as needed.

Problem Sets will be designed to help you take the facts and knowledge that you learn in the class and to apply them to thinking about and solving problems. You will not be graded on each problem set, but I will keep track on your participation- namely what effort you have applied to these problems sets. This will be Pass, Fail, with a Pass based on showing a good faith effort at working through the problems.

Like with the CPAs, a certain percentage of Pass on these Problem Sets will be required to earn certain grades for the class.

These problem sets are meant to prepare you for the exams. Exams will be in a similar style to problem set questions and will focus on your conceptual understanding of the material rather than memorization of facts. You will need to know some facts but then apply them to interpret experimental data, demonstrate your conceptual knowledge of the field, and to solve problems.

Course Mechanics:

All reading assignments, slides, and online video presentations that prepare you for in-class lectures and discussion will be posted on the class Moodle site. The Study Guides and CPAs will be posted together with these reading assignments, Slides, and online video summaries. I will try to post these assignments several days or more before the in-person class.

All Problem Sets and Problem Set answers will be posted on the Moodle site and you will use the Moodle site to turn in your assignments.

CPAs will be turned in at the beginning of class. I suggest bringing in two copies. One to turn in and one to keep and refer to during class and possibly to add notes to.

Problem sets will be posted on Fridays and due the following Friday. After this, I will post an answer key to the problem set. **You should carefully examine the posted answers to these problem sets and to make sure that you understand the solutions. These problem sets are meant to help prepare you for the exams.** The problem set questions are often made more

difficult than the exam questions. You will have more time and they are meant as a learning exercise that will prepare you for the exam questions.

CPAs, Problem Sets, Exams, Grading:

Your final grade in the course will reflect a combination of two inputs. First, are the midterms and final exam grades. Second is your participation in the class as judged by your completion of CPAs and Problem Sets and your participation in discussion during class.

The key issue with a flipped class, or even just making the most of a traditional class, is how to keep up regularly with the assigned material. I realize all of you are busy with other competing classes, activities, and interests.

The CPAs are meant to encourage you to keep up on a regular basis without being too onerous. They replace the surprise quizzes from previous years, and I hope you will view them as less onerous that such surprise quizzes. We will reassess as we move forward with the class this year.

You will need to complete a certain percentage of both CPAs and Problem Sets to earn certain grades in the class. This is a new grading scheme I am trying out this year and we will reassess as we progress during the course.

Right now, I am proposing the following:

a) "A+" will require BOTH Pass completion of 85% or more of CPAs and Problem Sets AND an appropriate score on Exams.

b) Borderline grades (e.g. A versus A-, A- versus B+, B+ versus B, B versus B-) will be boosted to the higher grade with completion of 75% or more of CPAs and Problem Sets

c) Letter grades will drop by one level (e.g. A to A-, B+ to B, B to B-) with completion of less than 50% of CPAs or 50% of Problem Sets

Midterm and Final Exams will be evening exams to ensure that you are not limited by time constraints. They will be designed to be completed within 1 hour if you know the material well. However, you will be given 3 hours to complete the exam. Both the two midterms and the final will mostly cover the content of the preceding ~1/3 of the lectures. However, exam questions may build on concepts and knowledge from earlier parts of the course. Each exam will count equally towards your grade.

Exceptional participation in class- answering certain difficult questions for example- will earn bonus points added to your exam total. If I perceive that overall your participation in class is high throughout most of the course, then this will also be a factor in shifting your grade upwards in borderline grade decisions- e.g. between A versus A-, A- versus B+, B+ versus B, etc.

Expectations will be different for Undergrads versus Grad students and separate grade curves will be applied

Recommended Texts:

I will assume you all have a good reference textbook for molecular and cellular biology from previous courses. I understand that the MCB undergraduate core uses the Lodish textbook. Many of you may have the Alberts textbook. You will be able to cover valuable review by referring to one or the other of these textbooks. I may refer you to specific pages of these textbooks.

1. Molecular Cell Biology, 8thth edition, Lodish, et al
OR
2. Molecular Biology of the Cell, 6th or 7th edition, Alberts, et al

Reference Text:

A reference textbook for many lectures will be the Epigenetics book listed below. However, I have listed this as a reference because nearly all chapters are available online in the public domain through PubMed, the edition is somewhat outdate, and I will be posting copies on the website.

This book is "dense" even for researchers in the field. I will be summarizing key points in the online video summaries, and using this as a launching point for the lecture and discussions.

Epigenetics, 2nd edition, David Allis et al, Cold Spring Harbor Laboratory Press

Literature: Where appropriate we also will cover material from the scientific published literature. In some cases, I will simply summarize key results into my lecture and discussion material but post the original articles for anyone interested in reading further. In other cases, papers may be assigned reading for the course.

Prerequisites: MCB 250 and 252 or equivalent, MCB 354 or equivalent is highly recommended

Tentative Topic Schedule:

WEEK 1:

Lecture 1 (M) (8/21): **Course Introduction and What is Epigenetics**

Before Class Assignment:

a. **Read syllabus and/or view Pre-Lecture 1 Online Video about Course Mechanics**
b. **Search "Epigenetics" in Google News**

In class Lecture 1: Discussion about Epigenetics in the News, What is Epigenetics?
Optional Reading: Reviews or Minireviews discussing Epigenetics field

Lecture 2 (W) (8/23): **Early Cytology and connecting cytology to epigenetic phenomenon**
Before Class Assignment:
Read study points for key points to extract, then review Slides and/or view Pre-Lecture 2 Online Video about Early Cytology
In class Lecture 2: Discussion and three examples connecting cytology to epigenetic phenomenon
Optional and Future Reference Reading: Book Chapter on Nuclear Compartments

Lecture 3 (F) (8/25): Drosophila Position Effect Variegation (PEV) and How to Read a Scientific Paper I
Before Class Assignment:
Read Book Chapter on PEV and/or review slides
and/or view Pre-Lecture 3 Video:
In class Lecture 3: Thinking about Chromosome Position Effects versus Position Effect Variegation, Epigenetic barriers to effective gene Therapy, and How to Read a Scientific Paper

Problem Set #1 released and due Friday, Sept. 1

WEEK 2:

Lecture 4 (M) (8/28): Paper Discussion- Connecting Drosophila PEV with intergenerational inheritance of obesity (1st part of following paper): Paternal diet defines offspring chromatin state and intergenerational obesity, Cell 159: p.1352 (2014
Before Class Assignment:
a. Selected reading of first part of paper as assigned
b. Extract answers from the paper for the questions in the online slides about the problem addressed in the paper, the gap in knowledge, and the approach
c. Review online slides to see what to focus on in first part of Results section
d. Write down at least one question you have about the Intro, Abstract or Results
In class Lecture 4: Discussion of this first part of paper

Lecture 5 (W) (8/30): DNA methylation I: phenomenon, enzymes, how to measure
Before Class Assignment:
Read Book Chapter on DNA methylation and/or review slides
and/or view Pre-Lecture 5 Video:
In class Lecture 5: Discussion and examples

Lecture 6 (F) (9/1): DNA methylation II: Patterns of DNA methylation, changes in with aging, and other biological functional connections

Before Class Assignment:

Review Slides and/or view Pre-Lecture 6 Video:

In class Lecture 6: Discussion and examples

Optional Reading: Research article(s) related to DNA methylation

Problem Set #1 Due F, 9/1, Problem Set #2 Released and due F, 9/8

WEEK 3

Lecture 7 (W) (9/6)- Nucleosome Structure and Positioning I: Discovery and mapping of positions

Before Class Assignment:

Review Slides and/or view Pre-Lecture 7 Video:

In class Lecture 7: Discussion, how to measure nucleosome position in Genomics era

Optional Reading: Articles related to genome-wide mapping of nucleosomes

Lecture 8 (F) (9/8)- Nucleosome Structure and Positioning II: In vitro and in vivo effects of nucleosomes on transcription

Before Class Assignment:

Review Slides and/or view Pre-Lecture 8 Video:

In class Lecture 8: Discussion and examples

Optional Reading:

Problem Set #2 Due F, 9/8, Problem Set #3 Released and due F, 9/15

WEEK 4:

Lecture 9 (M) 9/11 Putting concepts into practice: Do Nucleosome "Clutches" Exist? How to test? In class discussion, debate, and hypothesis testing

Before Class Assignment:

Review Slides and/or view Pre-Lecture 9 Video reviewing the question

In class Lecture 9: Discussion, debate, brain-storming (also problem set discussion)

Optional Reading: Observation and Measurement of nucleosome "clutches"

Lecture 10 (W) (9/13) Review of transcriptional regulation

Before Class Assignment:

Read review chapter and/or Review Slides and/or view Pre-Lecture 10 Video

In class Lecture 10: Discussion of transcriptional regulation- past, present, and future

Optional Reading:

Lecture 11 (F) 9/15: GCN5 is a Histone Acetyltransferase

Before Class Assignment:

Review Slides and/or view Pre-Lecture 11 Video describing in-gel HAT assay

Read Allis research paper: Tetrahymena HAT A: a homolog to yeast GCN5

Optional Reading: Brownell and Allis, In-gel HAT assay

In class Lecture 11: Discussion of Allis Research paper, Tetrahymena HAT A

Problem Set #3 Due F, 9/15, Problem Set #4 Released and due F, 9/22

WEEK 5:

Lecture 12 (M) 9/18: Modified Histones/nucleosomes

Before Class Assignment:

Read review chapter and/or review Slides and/or view Pre-Lecture 12 Video describing Histone modifications

Optional Reading:

In class Lecture 12: Discussion of histone modifications

Lecture 13 (W) 9/20: How to measure histone modifications genome-wide

Before Class Assignment:

Read review article and/or review Slides and/or view Pre-Lecture 13 Video

Optional Reading:

In class Lecture 13: Discussion and more examples of Genome Browser

Lecture 14 (F) 9/22: Optional Review for first midterm

First midterm F, 9/22 evening

Problem Set #4 Due F, 9/22, Problem Set #5 Released and due F, 9/29

WEEK 6

Lecture 15 (M) 9/25 Introduction to Genome Browsers

Before Class Assignment: Review Slides and/or view Pre-Lecture 15 Video

In Class Lecture: Bring your computer or iPad/tablet to class, will demo and show how to navigate UCSC Genome Browser

Lecture 16 (W) 9/27 Nucleosome Variants and Neocentromeres

Before Class Assignment: Read review chapter and/or review Slides and/or view Pre-Lecture 16 Video describing Histone modifications

In Class Lecture: Discussion about nucleosome variants and neocentromeres

Optional Reading:

Lecture 17 (F) 9/29: Nucleosome Variants in Health and Human Disease- assigned paper, in-class discussion

Before Class Assignment: Read Research Paper

In Class Lecture: Discussion of research paper

Optional Reading:

Problem Set #5 Due F, 9/29, Problem Set #6 Released and due F, 10/6

WEEK 7

Lecture 18 (M) 10/2 Nucleosome Dynamics I – Chromatin remodeling complexes I

Before Class Assignment: Read review chapter and/or review Slides and/or view Pre-Lecture 18 Video on Remodeling complexes

In Class Lecture: Discussion

Optional Reading:

Lecture 19 (W) 10/4: Nucleosome Dynamics II

Before Class Assignment: Read review article and/or review Slides and/or view Pre-Lecture 19 Video on Nucleosome Dynamics

In Class Lecture: Discussion

Optional Reading:

Lecture 20 (F) 10/6: Conceptual models of Epigenetic Silencing based on Yeast Epigenetic Silencing

Before Class Assignment: Read review chapter and/or review Slides and/or view Pre-Lecture 20 Video on Yeast Epigenetics

In Class Lecture: Discussion

Optional Reading:

Problem Set #6 Due F, 10/6, Problem Set #7 Released and due F, 10/13

WEEK 8

Lecture 21 (M) 10/9: Small RNAs and RNAi- Part 1

Before Class Assignment: Read review chapter and/or review Slides and/or view Pre-Lecture 21 Video on RNAi discovery
In Class Lecture: Discussion
Optional Reading:

Lecture 22 (W) 10/11: Small RNAs and RNAi- Part 2
Before Class Assignment: Read review chapter and/or review Slides and/or view Pre-Lecture 22 Video on small RNAs
In Class Lecture: Discussion
Optional Reading:

Lecture 23 (F) 10/13: Some things about Transposable Elements, Retrotransposons, and Cell Senescence
Before Class Assignment: review Slides and/or view Pre-Lecture 23 Video
In Class Lecture: Discussion: (this lecture unit and discussion will prepare for reading the assigned research paper for Lecture 24)
Optional Reading:

Problem Set #7 Due F, 10/13, Problem Set #8 Released and due F, 10/20

WEEK 9

Lecture 24 (M) 10/16: L1 Retrotransposons and Aging
Before Class Assignment: read assigned research paper
In Class Lecture: Discussion of Research paper

Lecture 25 (W) 10/18: Cell memory of gene expression by polycomb and trithorax I
Before Class Assignment: Read review article and/or review Slides and/or view Pre-Lecture 25 Video
In Class Lecture: Discussion
Optional Reading:

Lecture 26 (F) 10/20: Cell memory of gene expression by polycomb and trithorax II
Before Class Assignment: Read review article and/or review Slides and/or view Pre-Lecture 26 Video
In Class Lecture: Discussion
Optional Reading:

Problem Set #8 Due F, 10/20, Problem Set #9 Released and due F, 10/27

WEEK 10

Lecture 27 (M) 10/23: Intergenerational inheritance
Before Class Assignment: Read review article and/or review Slides and/or view Pre-Lecture 27 Video
In Class Lecture: Discussion
Optional Reading:

Lecture 28 (W) 10/25: Research paper on Intergenerational inheritance of obesity in flies
Before Class Assignment: read assigned research paper
In Class Lecture: Discussion of Research paper

Lecture 29 (F) 10/27: Optional Review Session (Evening midterm exam 2)

Problem Set #9 Due F, 10/27, Problem Set #10 Released and due F, 11/3

Week 11

Lecture 30 (M) (10/30): Higher-order chromatin folding
Before Class Assignment: Read review article and/or review Slides and/or view Pre-Lecture 30 Video
In Class Lecture: Discussion
Optional Reading:

Lecture 31 (W) (11/1): Enhancers, Boundary Elements/Insulators
Before Class Assignment: Read review article and/or review Slides and/or view Pre-Lecture 31 Video
In Class Lecture: Discussion
Optional Reading:

Lecture 32 (F) (11/3): LCRs/Super-enhancers
Before Class Assignment: Read review article and/or review Slides and/or view Pre-Lecture 32 Video
In Class Lecture: Discussion
Optional Reading:

Problem Set #10 Due F, 11/3, Problem Set #11 Released and due F, 11/10

WEEK 12

Lecture 33 (M) (11/6) Nuclear Compartments mapped by Omic methods

Before Class Assignment: Read review article and/or review Slides and/or view Pre-Lecture 33 Video

In Class Lecture: Discussion

Optional Reading:

Lecture 34 (W) (11/8): 3C methods to map chromosome topology and nuclear genome organization I

Before Class Assignment: Read review article and/or review Slides and/or view Pre-Lecture 34 Video

In Class Lecture: Discussion

Optional Reading:

Lecture 35 (F) (11/10): 3C methods to map chromosome topology and nuclear genome organization II

Before Class Assignment: Read review article and/or review Slides and/or view Pre-Lecture 35 Video

In Class Lecture: Discussion

Optional Reading:

Problem Set #11 Due F, 11/10, Problem Set #12 Released and due F, 11/17

WEEK 13

Lecture 36 (M) (11/13): Ligation-independent methods to measure chromosome topology and nuclear genome organization

Before Class Assignment: Read review article and/or review Slides and/or view Pre-Lecture 36 Video

In Class Lecture: Discussion

Optional Reading:

Lecture 37 (W) (11/15): Condensates: a new paradigm

Before Class Assignment: Read review article and/or review Slides and/or view Pre-Lecture 37 Video

In Class Lecture: Discussion

Optional Reading:

Lecture 38 (F) (11/17): Sex chromosome dosage compensation
Before Class Assignment: Read review article and/or review Slides and/or view Pre-Lecture 38 Video
In Class Lecture: Discussion
Optional Reading:

Problem Set #12 Due F, 11/17, Problem Set #13 Released and due F, 12/1

Week 14

Lecture 39 (M) (11/27): Research paper connecting condensates and X inactivation
Before Class Assignment: read assigned research paper
In Class Lecture: Discussion of Research paper

Lecture 40 (W) (11/29): Aging as an epigenetic disease?
Before Class Assignment: Read review article and/or review Slides and/or view Pre-Lecture 40 Video
In Class Lecture: Discussion
Optional Reading:

Lecture 41 (F) (12/1): Partial rejuvenation of aging by partial reprogramming

Problem Set #13 Due F, 12/1

WEEK 15

Lecture 42 (M) (12/4): Research paper on aging reversal
Before Class Assignment: read assigned research paper
In Class Lecture: Discussion of Research paper

Lecture 43 (W) (12/6) Review Session

Final Exam to be arranged