

PSS6325 – Epigenetic Mechanisms (Fall 2017)

1. Instructor

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Consultation: By appointment

2. Textbook (Recommended but not required; Available at the library on reserve)

Allis CD, Caparros ML, Jenuwein T, Reinberg D (2015) Epigenetics, 2nd Edition, Cold Spring Harbor Laboratory Press, ISBN:978-1-936113-59-0 or newer edition if available.

Lecture hand-outs and power point slides will be accessible to students in electronic or other forms. Supplementary printed reading materials will also be provided as necessary.

3. Course description

Prerequisites: Consent of instructor; 3-credits, lecture

Epigenetics is the study of phenotypic expression that cannot be fully explained by Mendelian principles of heredity, and by DNA sequence variation among individuals. The core of this science is rooted from intrinsically and extrinsically determined processes that lead to dynamic changes in chromatin structure, DNA methylation, RNA-directed gene regulation and genome modification, and how these processes bring about heritable phenotypic variation at the somatic and/or germ levels. During the last decade, the study of epigenetic mechanisms has become a critical aspect in understanding how plants and animals develop and adapt to environmental changes and diseases, providing another layer of complexity to the flow of genetic information as classically defined by the central dogma of molecular biology.

This course opens with discussions of the basic concepts and overview of classical examples of epigenetic phenomena in eukaryotes. The initial part of the course will set the framework to examine the various molecular mechanisms that have recently been uncovered in a number of eukaryotic models including yeast, Arabidopsis, maize, *C. elegans*, Drosophila, and mouse. Molecular mechanisms involving histone modification and chromatin remodeling, DNA modification by cytosine methylation, genomic imprinting, paramutation, transposable element-induced gene silencing, position effect variegation, post-transcriptional gene silencing by small regulatory RNA molecules, and RNA-directed DNA methylation are highlighted in context of the current understanding of genome structure, function, regulation and evolution in plants and animals.

4. Purpose of the course

Fundamental principles governing the functions of genes and genomes as defined by the central dogma of molecular biology have greatly advanced our understanding of the cellular processes associated with growth, development, and responses to biotic and abiotic stimuli. During the last several decades, the study of

epigenetic mechanisms has expanded the realm of how genes and genomes function to define the phenotype, beyond the scope of the central dogma. This topic is not covered in-depth by traditional courses in genetics, molecular biology, physiology, and biochemistry. Epigenetics is now considered as the critical piece of the puzzle to fully understand the finer details of '*genotype x environment interaction*' that lead to phenotypic expression in plants and animals. Therefore, it is critically important for the continuous advancement of biotechnology and its various applications in agriculture (plant and animal breeding, health, nutrition, and production) and human medicine. Under these contexts, PSS 6325 aims to provide graduate students engaged in any aspect of plant and animal biological research enabled by the genomics paradigm, with a platform for understanding the recent paradigm shifts brought about by epigenetics, and not directly addressed by the central dogma. Successful completion of this course fulfills the requirements for graduate degrees (M.S., Ph.D.) in any basic or applied disciplines of plant and animal biosciences including genetics, biochemistry, molecular biology, plant/animal breeding, plant/animal/human nutrition, agronomy, horticulture and plant/animal conservation sciences. It can also be used to fulfill elective courses for graduate students in the areas of bioinformatics, biotechnology, and bioengineering.

5. Expected learning outcomes

This course is a platform for learning the fundamental differences of epigenetic regulatory mechanisms from genetic regulatory mechanisms, at a level sufficient to allow comprehension of both the conceptual and technical aspects of research papers that are rapidly accumulating in this vibrant area of research in modern biology. Upon successful completion of this course, students will be able to:

- a) **Recognize** the fundamental differences between genetic and epigenetic mechanisms and their significance to basic processes of growth, development, and responses to biotic and abiotic stimuli at the cellular and whole organismal levels.
- b) **Interpret** molecular biological and genomic data from research literature addressing questions about epigenetic mechanisms in plants and/or animals.
- c) **Formulate** original questions and/or hypotheses relevant to epigenetically regulated processes in plants and/or animals, and design experiments addressing those questions and/or hypotheses.
- d) **Demonstrate** the ability to articulate and explain their ideas of epigenetic mechanisms to other scientists.

6. Methods for assessing the expected learning outcomes

Expected learning outcomes will be assessed using a combination of approaches that includes the following:

- a) For each topic, individual students will be assigned to make an oral presentation on a research paper on epigenetic mechanisms that was **recently** published in any research journal. Papers must be chosen by the students themselves and must be approved by the instructor prior to class presentation at least one week

before the scheduled presentation. Students will also write a brief synthesis, analysis, and critique of the research paper which must include their own interpretation, conclusions, questions that were left hanging, and how those questions should be addressed with further research.

- b)** Students will take a one-on-one oral exam with the instructor after the completion of the theoretical aspects of modules 1, 2, 3, and 4 (midterm). Questions for this oral exam will include conceptual, problem-solving and/or integration types of questions.
- c)** Students will write a research proposal on an original idea addressing an important question/hypothesis on epigenetic mechanisms either on a plant or animal study system, in the style and format of either NSF, NIH or USDA-AFRI programs.
- d)** Students will orally present and defend the ideas behind their research proposal to a mock panel of experts consisting of invited guests from the faculty, postdocs and senior graduate students.

7. Criteria for grading and grading scale

<u>Parameter</u>	<u>Total Points</u>	<u>% of Final Grade</u>
Oral presentation of research papers	50	10.0
Written critiques of research papers	50	10.0
Midterm oral exam	100	20.0
Written research proposal	200	40.0
Oral presentation/defense of proposal	100	20.0
Total	500	100.0

A = 91 to 100; **A-** = 86 to 90; **B+** = 81 to 85; **B** = 79 to 80; **B-** = 71 to 75; **C+** = 66 to 70; **C** = 61 to 65; **C-** = 56 to 60; **D** = 50 to 55; **F** < 50

Note: Grading scale may be adjusted according to the class median.

9. General information

Texas Tech University Statement of Academic Integrity

Academic integrity is taking responsibility for one's own work, being individually accountable, and demonstrating intellectual honesty and ethical behavior. Academic integrity is a personal choice to abide by the standards of intellectual honesty and responsibility. Because education is a shared effort to achieve learning through the exchange of ideas, students, faculty, and staff have the collective responsibility to build mutual trust and respect. Ethical behavior and independent thought are essential for the highest level of academic achievement, which then must be measured. Academic achievement includes scholarship, teaching and learning, all of which are shared endeavors. Grades are a device used to quantify the successful accumulation of knowledge through learning. Adhering to the standards of academic integrity ensures that grades are earned honestly and gives added value to the entire educational process. Academic integrity is the foundation upon which students, faculty, and staff

build their educational and professional careers. [Texas Tech University (“University”) Quality Enhancement Plan, Academic Integrity Task Force, 2010].

Texas Tech University Code of Conduct – Academic Integrity

“Academic dishonesty” includes, but is not limited to, cheating, plagiarism, collusion, falsifying academic records, misrepresenting facts and any act designed to give unfair academic advantage to the student. Students must understand the principles of academic integrity, and abide by them in all class and/or course work at the University. Academic integrity violations are outlined in the Code of Student Conduct, Part II, Section B1 and can be found here: www.ttu.edu/studenthandbook.

If there are questions of interpretation of academic integrity policies or about what might constitute an academic integrity violation, students are responsible for seeking guidance from the faculty member teaching the course in question.

University-wide Policies on Addressing Incidents of Academic Integrity

Texas Tech University policies and procedures regarding academic integrity can be found in the Student Handbook in Part II, section B and online here: www.ttu.edu/studenthandbook.

Any person becoming aware of alleged violations of academic integrity should report the allegation to the instructor of record in the course. The instructor in a course is responsible for initiating action in each case of dishonesty or plagiarism that occurs in that class. The instructor may contact the Office of Student Conduct to discuss the nature of the violation and the student’s record of academic integrity violations. The instructor should attempt to discuss the matter with the student and receive a response from the student about the allegations. Then, the instructor may assign academic sanctions including, but not limited to a assigning a paper or research project related to academic integrity, make-up assignment that is different than the original assignment, issue no credit for the original assignment, reduce the grade for the assignment and/or course, issue a failing grade on the assignment, and/or issue a failing grade for the course. All academic integrity violations will be referred to the Office of Student Conduct as a central clearinghouse of violations and for adjudication as a Code of Student Conduct violation where disciplinary sanctions, conditions, and/or restrictions will be assigned. These disciplinary sanctions could include suspension or expulsion from Texas Tech University.

Students with disabilities

Any student who, because of a disability, may require special arrangements in order to meet the course requirements should contact the instructor as soon as possible to make any necessary arrangements. Students should present appropriate verification from Student Disability Services during the instructor’s office hours. Please note that instructors are not allowed to provide classroom accommodations to a student until appropriate verification from Student Disability Services has been provided. For additional information, you may contact the *Student Disability Services Office* at 335 West Hall or 806-742-2405.

Discrimination policy

The University is committed to the principle that in no aspect of its programs shall there be differences in the treatment of persons because of race, creed, national origin, age, sex, or disability, and that equal opportunity and access to facilities shall be available to all. If you require special accommodations in order to participate, please contact the instructor. Students should present appropriate verification from “*AccessTECH*” located in the Counseling Center. No requirement exists that accommodations be made prior to completion of this approved University process. The URL for *AccessTECH* is: <http://www.accesstech.dsa.ttu.edu/default.asp>.

9. Topic outline

Module-1. Overview of epigenetic mechanisms

- a) History of epigenetics: From biological phenomena to scientific discipline
- b) Epigenetic phenotypes and models
- c) Genetics versus epigenetics
- d) Differentiating epigenetics from other non-Mendelian phenomena
- e) Drivers of epigenetic mechanisms: Chromatin environment, DNA methylation, regulatory RNA molecules
- f) Histone code hypothesis
- g) Gene expression and cellular reprogramming
- h) Big questions on epigenetics: Genotype by environment interaction
- i) Seminal observations of epigenetic phenomena
 - i) DNA is the same in all somatic cells
 - ii) X-chromosome inactivation
 - iii) Position effect variegation
 - iv) Genomic imprinting

Module-2. Molecular basis of epigenetic mechanisms – histones and chromatin

- a) DNA packaging and chromatin architecture
 - i) Basic questions
 - ii) Nucleosomes and histones
 - iii) Euchromatin versus heterochromatin
- b) Chromatin regulation by histone modification
 - i) Writers of histone modification: Histone acetyltransferases (HAT)
 - ii) Readers of histone acetylation: Bromodomains (BRD)
 - iii) Erasers of histone acetylation: Histone deacetylases (HDAC)
 - iv) Regulation of HDAC
 - v) HAT, BRD, and HDAC in plants
 - vi) Writers of histone modification: Histone lysine methyltransferases (HKMT)
 - vii) Erasers of histone methylation: Lysine demethylases (LSD)
 - viii) Readout of methyllysine epigenetic marks
 - ix) HKMT and LSD in plants
- c) Epigenetic phenomena by chromatin remodeling
 - i) Yeast as a model: Life cycle of yeast
 - ii) Histone acetylation and mating-type switch: Sir proteins
 - iii) Histone H4K16 acetylation and deacetylation by Sir proteins
 - iv) Inheritance of epigenetic states
- d) Seminal examples of plant processes regulated at the chromatin level
 - i) Control of photomorphogenesis
 - ii) Circadian oscillators
- e) Molecular and biochemical techniques for studying chromatin regulation

Module-3. Molecular basis of epigenetic mechanisms – DNA methylation

- a) Patterns of DNA methylation in eukaryotes
 - i) CpG islands across the genome and other CG contexts in plants

- ii) Modifications of cytosine in genomic DNA: DNA methyltransferases (DNMT)
 - iii) DNMTs in plants
 - iv) DNA demethylases (DMT, DEMETER)
 - v) Upstream regions, enhancer sequences, and DNA methylation
 - vi) Alleles versus epialleles
- b) Effects of DNA methylation on transcription
 - i) Proteins that interact with methylated DNA
 - ii) Transcriptional repression by methylated DNA-binding proteins
 - iii) Epigenome: Coordination of DNA and histone methylation marks

Module-4. Molecular basis of epigenetic mechanisms – Regulatory RNA

- a) Extended gene concept
- b) RNA silencing pathways
- c) Small non-coding RNAs (sncRNA) and post-transcriptional gene silencing (PTGS)
 - i) miRNA: Biogenesis and function
 - ii) siRNA/tasiRNA: Biogenesis and function
 - iii) siRNA-mediated defenses in plants
 - iv) sRNAs act as mobile signals in plants
 - v) Enhancer RNA molecules
- d) Small ncRNA and transcriptional gene silencing (TGS)
 - i) RNA-directed DNA methylation
 - ii) RNAi and heterochromatin assembly in *S. pombe* and Arabidopsis
- e) Long non-coding RNAs (lncRNA): Linking RNA with chromatin

Module-5. Epigenetically regulated processes – More detailed look at mechanisms

- a) Position effect variegation in *Drosophila*
- b) Dosage compensation in *Drosophila*
- c) Genomic imprinting in mammals
- d) Transcriptional regulation by Trithorax and Polycomb proteins in plants and animals
- e) Cellular memory and seasonal responses of flowering in plants
- f) Paramutation in maize and transposon taming in Arabidopsis