Preliminary syllabus

PSYC G4498

Dr. Catherine J Peña

Fall 2016: Fridays, 2:10-4pm

I. Bulletin description

PSYC G4498. Behavioral Epigenetics (seminar).

4 pts. Fridays 2:10 – 4 PM in 405 Schermerhorn Hall

Prerequisites: Basic background in neurobiology (for instance PSYC 1010, 2450, 2460, 2480, and G4499) and the instructor's permission.

This course will provide an overview of the field of epigenetics, with an emphasis on epigenetic phenomena related to neurodevelopment, behavior and mental disorders. We will explore how the field of epigenetics provides a mechanistic bridge between early life experiences and enduring neurobiological and behavioral consequences. We will also discuss how epigenetics contribute to psychopathology throughout the life course, and the implications of behavioral epigenetic research for the development of novel pharmacotherapeutic approaches and preventive measures in psychiatry.

II. Full course description:

Epigenetics is the study of changes in gene expression and cellular phenotype through mechanisms that do not involve changes in DNA sequence. During development, epigenetic mechanisms are essential for the establishment of cell-specific gene expression patterns and cellular differentiation. In addition, epigenetic marks are responsive to environmental cues throughout the lifespan of an individual, and can be stably maintained leading to long-lasting effects of the environment on gene expression. In this course, we will explore the role of epigenetic mechanisms in regulating brain gene expression, brain development, and adult brain function. We will focus on the neuronal epigenome as a biological substrate through which environmental exposures can contribute to the development of altered behavior and psychiatric syndromes.

In the first part of the course, we will explore the major epigenetic mechanisms of gene regulation and the research tools that are used to study epigenetic modifications in different model systems, including humans. Following this introduction, we will discuss the most sensitive periods during which the epigenome can be disrupted by environmental factors, including prenatal and early-life development. We will further consider the role of epigenetic mechanisms in the dynamic regulation of the adult brain function, as well as epigenetic dysregulation that may underlie various psychiatric disorders. In addition, we will discuss the role of epigenetics in normal processes in post-mitotic neurons of the adult brain with a focus on learning and memory. Finally, we will discuss one of the most controversial topics in epigenetics: the hypothesis that environmentally-induced epigenetic modifications can be heritable, contributing to disease susceptibility of multiple generations.

The topics of the course will be introduced through overview lectures given by the instructor, followed by journal article presentations by students. The readings will consist of review articles and primary research articles, and will draw upon examples from both human and experimental/animal research. In addition to several classic papers to lay the foundation for Behavioral Epigenetics, the readings emphasize the most contemporary research and understanding of each topic area. The whole class is expected to have read the journal articles in advance and participate in discussion.

Finally, students will have the opportunity to explore and demonstrate a detailed understanding of a topic of their choice relevant to Behavioral Epigenetics through a final paper.

III. Rationale for giving the course:

This course is designed to familiarize the students with basic and more advanced concepts of an emerging and rapidly evolving field of behavioral epigenetics. Epigenetic research has recently been incorporated in the major neuroscience-related areas, such as studies of neurodevelopment, animal models of behavioral and psychiatric disorders, studies on learning and memory, neuroendocrinology, psychopharmacology, and psychiatric epidemiology. The first part of the course will cover basic epigenetic mechanisms of gene regulation and epigenetic techniques, and will prepare students for more specific topics as well as enable them to critically evaluate epigenetic literature. The second part of the course will provide a synthesis on the role of epigenetic mechanisms in regulating normal brain function and their contribution to the development of psychopathology. The readings will consist of both review articles and primary research articles. Throughout the course, we will explore the landmark studies that paved the way for the establishment of the field.

The primary goal of this course is to for students to gain in-depth understanding of Behavioral Epigenetics as it pertains to the fields of Psychology and Neuroscience, through introduction of twelve applied topics. In order to aid in *remembering*, *understanding*, and *applying* the knowledge gained from the readings and lectures, students will be encouraged to ask questions and participate in discussion throughout the lectures and journal article presentations. In-class small-group activities will give students further opportunity to discuss, *apply*, and *analyze* the topics. Through presentation of journal articles and leading class discussion, students will gain a detailed understanding of a topic, *draw connections* to other course topics, *evaluate* the research, and *create* their own framework for presenting it to the class. The final literature review paper on a topic of the student's choice will further enable students to *synthesize* information from multiple sources, critically *evaluate* it as a whole, and *author* their own review of the sub-field.

More broadly, students will learn how to read primary scientific research articles, think critically, synthesize information, and write organized, evaluative papers. These skills are necessary to be informed citizens in our increasingly technological society, and in all chosen post-graduate disciplines and careers.

The Psychology Program Goals that will be advanced in this seminar (see http://www.columbia.edu/cu/psychology/dept/ugrad/goals.html) include 1. Knowledge preliminary syllabus base; 2. Research methods; 4. Critical thinking; 5. Values in psychology; 6. Application of psychology; 7. Communication skills—written; 8. Communication skills—oral; 9. Information and technological literacy.

PSYC G4498 is an advanced seminar, designed particularly for graduate students, for advanced undergraduates who are majoring in Psychology or in Neuroscience and Behavior, and for students participating in the Psychology Postbac Certificate Program. These students will have priority in registration, followed by junior majors followed by non-majors. The seminar will be well suited to students who have completed two or more lecture courses beyond W1001, such as W1010 (Mind, Brain, and Behavior), W2215 (Cognition and the Brain), W2450 (Behavioral Neuroscience), W2460 (Drugs and Behavior), or W2480 (Developing Brain). It will help ameliorate a serious shortage of advanced seminars giving students opportunities to develop their oral and written presentation skills.

<u>It fulfills the following degree requirements:</u>

• For Psychology Graduate Students, PSYC G4498 will apply toward the “two seriously graded seminars” requirement of the Master’s degree.

• For the Psychology major or concentration in the College and in G. S., for the Psychology minor in Engineering, and for the Psychology Postbac Certificate, G4498 meets the Group II (Psychobiology and Neuroscience) distribution requirement.

• For the Neuroscience and Behavior joint major, G4498 will fulfill the 5th Psychology requirement: “one advanced psychology seminar from a list approved by the Psychology Department advisor to the program.”

• For non-majors in the College and GS, G4498 – by virtue of its numbering in the 4400's--will count as one term of the natural science requirement, provided that students obtain the necessary permission and have taken the prerequisite psychology courses. Graduate students, and students who are majoring in Psychology or in Neuroscience and Behavior, and postbac certificate students will have priority over students who are taking the course for the science requirement. For this reason, as well as because of the course prerequisites, we anticipate the course will rarely be used for the science requirement.

• For the Psychology Postbac certificate, PSYC G4498 will fulfill the advanced seminar requirement.

• For the Barnard Psychology major, PSYC G4498 will fulfill the senior seminar requirement.

IV. Weekly outline of topics and readings [*subject to revision*]:

Schedule	Topic	Readings
Week 1 (9/9)	**Course orgaqnization, topic overview, expectations**	How To Read (Edwards)
	History of epigenetics, Epigenetic mechanisms of gene regulation	Waddington (1959); Jaenisch & Bird (2003); Jenuwein & Allis (2001); Esteller (2011)
Week 2 (9/16)	**Epigenetic techniques in neuroscience**	
	Tissue specificity of epigenetic marks	Chatterjee & Vinson (2012)
	Journal article assignments	
Week 3 (9/23)	**Epigenetic epidemiology**	Vaiserman (2015) Clin Epigenetics
	Lecture, article presentations, discussion	Heijmans et al. (2008) PNAS; Yehuda et al. (2014) Am J Psych
Week 4 (9/30)	**Epigenetic programming during perinatal development**	Reik, Dean, & Walter (2001), Science
	Lecture, article presentations, discussion	Whitelaw et al. (1999) Nat Genet; Nugent et al. (2015) Nat Neuro
Week 5 (10/7)	**Diet, obesity, and epigenetics**	Hajj et al. (2014) Reproduction
	Lecture, article presentations, discussion	Pankevich et al. (2010) Jneuro; Marco et al. (2013) PNE
Week 6 (10/14)	**The maternal environment and epigenetics**	Peña et al. (2013) Endo
	Lecture, article presentations, discussion	McGowan et al. (2009) Nat Neuro; Weaver et al. (2004) Nat Neuro
Week 7 (10/21)	**Epigenetic changes in depression and schizophrenia**	Peña et al. (2014) JMB
	Lecture, article presentations, discussion	Tsankova et al. (2006) Nat Neuro; Matrisciano et al. (2013) Neuropsychopharm;
Week 8 (10/28)	**Epigenetic changes in drug abuse**	Walker et al. (2015) Cur Opinions Neurobiology
	Lecture, article presentations, discussion	Chandrasekar & Dreyer (2011) NPP; Wang et al. (2010) NPP
Week 9 (11/4)	**Epigenetics in learning and memory**	Day & Sweatt (2010) Nat Neuro
	Lecture, article presentations, discussion	Day et al. (2013) Nat Neuro; Widagdo et al. (2016) JNeuro
	Due: Topics for papers, references	
No class 11/11	*Society for Neurosciene Meeting*	
Week 10 (11/18)	**Transgenerational epigenetic inheritance**	Bale (2015) Nat Rev Neuro
	Lecture, article presentations, discussion	Franklin et al., (2010) Biol Psych; Dias & Ressler (2014) Nat Neuro
No class 11/25	*Thanksgiving*	
Week 11 (12/2)	**Epigenetic therapy**	Kelly et al. (2010) Nat Biotechnol
	Lecture, article presentations, discussion	Weaver et al. (2006) PNAS; Li et al. (2006) Pharm Biochem Behav
Week 12 (12/9)	**Class wrap-up, discussion**	
	DUE: Review Paper	

V. Course requirements and grading:

Grades:

25% Participation in journal article discussions and in-class activities

25% Presentation of original research journal article

10% Topic and bibliographic citations for literature review

40% Literature review paper

Participation (25%): All students are expected to participate in weekly discussions. To effectively participate, it is expected that all students read the assigned articles in advance of the class. Each student should come prepared with at least one question for the original research article(s) being presented. If medical or other emergencies prevent students from attending a class, an email to Dr. Peña is required *in advance of class* to explain the absence.

Presentation (25%): Each student will present 1-2 original research articles and lead the class discussion. Journal articles are pre-selected by the instructor. Students are expected to walk the class through the background/rationale, methods, results, and discussion, including what is novel, and potential pitfalls/misinterpretation, and possible future directions. Students should try to engage class in discussion through questions. Each presentation should be ~30m.

Topic and references (10%): All students are required to select a topic relevant to Behavioral Epigenetics for a final literature review paper. The topic may expand on a topic presented in the course, may be a relevant topic not covered within the course, or may synthesize information across areas of the course. The student will submit the topic/title, a short rationale for its selection, and at least 10 FULL citations for their proposed literature review paper on or before the class meeting of **November 4th** with no exceptions. Topics will be approved by the instructor, and in some instances the instructor may suggest ways to broaden or focus the topic as appropriate. For the citations: review papers are acceptable but should be kept to a minimum.

Literature review paper (40%): All students will write a substantial, *original* 8-12 page paper (double spaced, not including references) on the chosen topic. At least 15 citations in APA format must be included. The paper will be submitted on the final day of class, with no exceptions.

Reading List (pdfs will be available via CourseWorks) (1-32)

0. Edwards PN. University of Michigan School of Information. (2013). *How to Read a Book, v5.0.* pne.people.si.umich.edu/PDF/howtoread.pdf.
1. C. H. Waddington, Canalization of Development and Genetic Assimilation of Acquired Characters. *Nature*. **183**, 1654–1655 (1959).
2. R. Jaenisch, A. Bird, Epigenetic regulation of gene expression: how the genome integrates intrinsic and environmental signals. *Nat Genet*. **33**, 245–254 (2003).
3. T. Jenuwein, C. D. Allis, Translating the histone code. *Science*. **293**, 1074–1080 (2001).
4. M. Esteller, Non-coding RNAs in human disease. *Nat Rev Genet*. **12**, 861–874 (2011).
5. R. Chatterjee, C. Vinson, CpG methylation recruits sequence specific transcription factors essential for tissue specific gene expression. *Biochim. Biophys. Acta*. **1819**, 763–770 (2012).
6. A. Vaiserman, Epidemiologic evidence for association between adverse environmental exposures in early life and epigenetic variation: a potential link to disease susceptibility? *Clin Epigenet*. **7**, 24 (2015).
7. B. T. Heijmans *et al.*, Persistent epigenetic differences associated with prenatal exposure to famine in humans. *Proceedings of the National Academy of Sciences*. **105**, 17046–17049 (2008).
8. R. Yehuda *et al.*, Influences of maternal and paternal PTSD on epigenetic regulation of the glucocorticoid receptor gene in Holocaust survivor offspring. *Am J Psychiatry*. **171**, 872–880 (2014).
9. W. Reik, W. Dean, J. Walter, Epigenetic reprogramming in mammalian development. *Science*. **293**, 1089–1093 (2001).
10. E. Whitelaw, H. D. Morgan, H. G. E. Sutherland, D. I. K. Martin, Epigenetic inheritance at the agouti locus in the mouse - Nature Genetics. *Nat Genet*. **23**, 314–318 (1999).
11. B. M. Nugent *et al.*, Brain feminization requires active repression of masculinization via DNA methylation. *Nat Neurosci*. **18**, 690–697 (2015).
12. N. El Hajj, E. Schneider, H. Lehnen, T. Haaf, Epigenetics and life-long consequences of an adverse nutritional and diabetic intrauterine environment. *Reproduction*. **148**, R111–20 (2014).
13. D. E. Pankevich, S. L. Teegarden, A. D. Hedin, C. L. Jensen, T. L. Bale, Caloric restriction experience reprograms stress and orexigenic pathways and promotes binge eating. *Journal of Neuroscience*. **30**, 16399–16407 (2010).
14. A. Marco, T. Kisliouk, A. Weller, N. Meiri, High fat diet induces hypermethylation of the hypothalamic Pomc promoter and obesity in post-weaning rats. *Psychoneuroendocrinology*. **38**, 2844–2853 (2013).
15. C. J. Peña, Y. D. Neugut, F. A. Champagne, Developmental Timing of the Effects of Maternal Care on Gene Expression and Epigenetic Regulation of Hormone Receptor Levels in Female Rats. *Endocrinology* (2013), doi:10.1210/en.2013-1595.

16. P. O. Mcgowan *et al.*, Epigenetic regulation of the glucocorticoid receptor in human brain associates with childhood abuse. *Nat Neurosci*. **12**, 342–348 (2009).
17. I. C. G. Weaver *et al.*, Epigenetic programming by maternal behavior. *Nat Neurosci*. **7**, 847–854 (2004).
18. C. J. Peña, R. C. Bagot, B. Labonté, E. J. Nestler, Epigenetic Signaling in Psychiatric Disorders. *J. Mol. Biol.* (2014), doi:10.1016/j.jmb.2014.03.016.
19. N. M. N. Tsankova *et al.*, Sustained hippocampal chromatin regulation in a mouse model of depression and antidepressant action. *Nat Neurosci*. **9**, 519–525 (2006).
20. F. Matrisciano *et al.*, Epigenetic modifications of GABAergic interneurons are associated with the schizophrenia-like phenotype induced by prenatal stress in mice. *Neuropharmacology*. **68**, 184–194 (2013).
21. D. M. Walker, H. M. Cates, E. A. Heller, E. J. Nestler, Regulation of chromatin states by drugs of abuse. *Current Opinion in Neurobiology*. **30**, 112–121 (2015).
22. V. Chandrasekar, J.-L. Dreyer, Regulation of MiR-124, Let-7d, and MiR-181a in the accumbens affects the expression, extinction, and reinstatement of cocaine-induced conditioned place preference. *Neuropsychopharmacology*. **36**, 1149–1164 (2011).
23. L. Wang *et al.*, Chronic cocaine-induced H3 acetylation and transcriptional activation of CaMKIIalpha in the nucleus accumbens is critical for motivation for drug reinforcement. *Neuropsychopharmacology*. **35**, 913–928 (2010).
24. J. J. Day, J. D. Sweatt, DNA methylation and memory formation. *Nat Neurosci*. **13**, 1319–1323 (2010).
25. J. J. Day *et al.*, DNA methylation regulates associative reward learning. *Nat Neurosci*. **16**, 1445–1452 (2013).
26. J. Widagdo *et al.*, Experience-Dependent Accumulation of N6-Methyladenosine in the Prefrontal Cortex Is Associated with Memory Processes in Mice. *Journal of Neuroscience*. **36**, 6771–6777 (2016).
27. T. L. Bale, Epigenetic and transgenerational reprogramming of brain development. *Nat Rev Neurosci*. **16**, 332–344 (2015).
28. T. B. Franklin *et al.*, Epigenetic transmission of the impact of early stress across generations. *Biological Psychiatry*. **68**, 408–415 (2010).
29. B. G. Dias, K. J. Ressler, Parental olfactory experience influences behavior and neural structure in subsequent generations. *Nat Neurosci*. **17**, 89–96 (2013).
30. T. K. Kelly, D. D. De Carvalho, P. A. Jones, Epigenetic modifications as therapeutic targets. *Nat Biotechnol*. **28**, 1069–1078 (2010).
31. I. C. G. Weaver, M. J. Meaney, M. Szyf, Maternal care effects on the hippocampal transcriptome and anxiety-mediated behaviors in the offspring that are reversible in adulthood. *Proc Natl Acad Sci USA*. **103**, 3480–3485 (2006).
32. S. Li, Y. Murakami, M. Wang, K. Maeda, K. Matsumoto, The effects of chronic valproate and diazepam in a mouse model of posttraumatic stress disorder. *Pharmacol Biochem Behav*. **85**, 324–331 (2006).