A lecture/seminar/discussion class on the emerging field of environmental epigenetics. Course will cover basic epigenetic mechanisms, methods in epigenetic research, epigenetic control of gene function, and the role of epigenetics in normal development and human disease.

Environmental epigenetics is a new field of study focusing on mitotically or meiotically heritable changes in gene regulation caused by environmental factors. There is evidence that epigenetic changes can occur through diet, toxicants (xenobiotics) and social factors (e.g. parental care). When such factors influence brain development, they can increase the risk for psychopathology throughout the lifespan. This course will focus on the environmental epigenetic mechanisms that impact human health and disease.

Office hours: Wednesdays: 1PM-3PM or by appointment. My office is in SW-548.

Course email address: epigeneticsD19@gmail.com

Lectures: BV-363 Mondays 3-5PM
A course calendar with the schedule for lectures and presentations will be available on Blackboard. This schedule is subject to change, so check back regularly.

• Weeks 1-2: Prof. McGowan’s lectures on (1) foundation topics in environmental epigenetics, (2) how to read/present a research article,
• Week 3: How to design and present a poster (Samantha Lauby)
• Weeks 4-10: Student seminars on research articles.
• Weeks 11-12: Poster presentations on research articles.

Textbook: There is NO textbook for this class. Prof. McGowan’s power point presentations and journal articles will be supplied on Blackboard as PDF files or linked.
Exams: There are NO exams in this class.

Grading scheme overview:

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<th>Assignments (4x2.5%)</th>
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<tr>
<td>Seminar presentations</td>
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<td>Seminar questions</td>
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<tr>
<td>Poster Presentation</td>
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<td>Attendance</td>
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Deadlines (3PM to course email):

Take-home assignments (3): Variable, but one week after assignment.
Seminar Presentation: Choice of articles (top 3): Monday September 12
Poster Presentation: Topic choice (top 3): Monday November 14
PDF of poster presentation: Thursday November 24

Take-home assignments: Four take-home assignments of short answer questions (brief: 3-5 sentences each question) addressing one of the articles presented in the class. You will be required to answer basic questions about the background, methods used, results and conclusions of the paper. The specific paper used for the questions is Prof. McGowan’s choice, and you will have one week after assignment to submit your answers. Each assignment will contribute to 2.5% of your final grade (total 10%).

Seminar Presentation: Seminars will be based on research articles chosen by Prof. McGowan, or you can suggest an article. Each person and a classmate will lead a 15 min discussion of a research article, followed by a 10 min question period. Only a maximum of 5 minutes should be spent on the introduction. When presenting, students are expected to provide handouts, which will be given to the class at the beginning of the seminar. Seminars will be graded based on clarity, style and delivery, use of visual aids, content, and ability to answer questions. Your slides and handout document must be submitted the night before your presentation via email (epigeneticsD19@gmail.com). The handout documents will be made available to the class by the instructor via Blackboard before the presentation. The seminar will contribute to 35% of your final grade.

Seminar Questions: An important part of your mark in this class is based on contribution to discussions. For each article presented, 4 students will be randomly assigned one week before the presentation to lead a 10-minute discussion (you won’t present and lead the discussion on the same article). Each student will lead 2 paper discussions during the course. You will be graded based on your capacity to engage other students into discussion, as well as on your critical analysis and understanding of the article. This mark contributes 15% to your final grade.

Poster: You and a classmate will design and present a poster based on an article from a list of articles provided on Blackboard. Alternatively, you can suggest an article. This will be a separate article from the one you present in class and cannot be repeated from any other
article presented orally or in poster format by your classmates. You and your partner will present the poster on-demand to your classmates and other interested people from the Biological Sciences department. Grading of your poster design, content and presentation will be performed by anonymous evaluators. You may be asked to evaluate some of your classmates posters on the day of the poster sessions. Your poster’s PDF file must be submitted 4 days before your presentation via email (epigeneticsD19@gmail.com). You are responsible for printing your own poster (dimensions 3ft x 4 ft). The poster presentation contributes 35% to your final grade.

**Attendance:** You are expected to be present on time in this seminar/discussion class. Attendance contributes 5% to your final grade.

**Foundation Reviews (Optional reading for background information):**


**Articles:**

Articles to present will be assigned on a first-come first-served basis. Send an email with your top 3 choices to: [epigeneticsD19@gmail.com](mailto:epigeneticsD19@gmail.com)

YOU CAN ALSO SUGGEST AN ARTICLE.

Deadline: **Monday September 12, 2016**. After the deadline, an article will be assigned to you.

**Nutrition:**


Illustrates the impact of methyl donors in the maternal diet on offspring DNA methylation and histone acetylation patterns, providing an important link between nutrition and gene regulation.

3. Dunn GA, Bale TL. Maternal high-fat diet effects on third-generation female body size via the paternal lineage. Endocrinology. 2011 Jun;152(6):2228-36. Epub 2011 Mar 29. PubMed PMID: 21447631; PubMed Central PMCID: PMC3100614. **This study implicates environmental influences on developmental regulation of growth and body size as the result of broad programming events at imprinted loci.**


**Xenobiotics:**


8. Dolinoy DC, Huang D, Jirtle RL. 2007. Maternal nutrient supplementation counteracts bisphenol A-induced DNA hypomethylation in early development. Proc Natl Acad Sci USA 104:13056–13061. **Shows that early developmental exposure to an environmental toxin can change offspring phenotype by stably altering the epigenome, an effect that can be counter-acted by maternal dietary supplements.**

Stress:

Describes the role of maternal care in epigenetic programming of the stress response and behaviours in rats.

These findings highlight the negative impact of early stress on behavioral responses across generations and on the regulation of DNA methylation in the germline.

Illustrates alterations in DNA methylation of placental and brain tissue following exposure to gestational stress, providing a possible mechanism mediating the long-term neurobiological effects of prenatal exposure to elevated maternal stress response activity.

Study of the transgenerational impact of exposure to maternal abuse in infancy and the role of differential methylation of a growth factor gene in the prefrontal cortex in mediating these effects.

Shows that early life stress can dynamically control DNA methylation in neurons to generate stable changes in gene expression and phenotypic alterations that are frequent features in depression.

Study of effects of the 1998 Quebec Ice Storm on methylation in T-cells and saliva of children in utero at the time.

Learning and Memory/Addiction:

Rodent study showing that environmental enrichment increases histone acetylation in the hippocampus. Histone deacetylase inhibitors induce increased spatial memory in a neurodegenerative disorder mouse model.

Illustrates the dynamic changes to DNA methylation which occur during the process of learning and the critical role of these modifications in the consolidation of memory.

Study in mice examining the particular histone deacetylase target through which histone deacetylase inhibitors exert enhancements in synaptic plasticity and memory. The authors illustrate the importance of levels of this enzyme in mediating cognitive enhancement.

In a case of sex-linked epigenetic inheritance, paternal cocaine use results in a heritable increase in cortical Bdnf gene expression that confers a cocaine-resistant phenotype in male, but not female, progeny.

This study shows that when mice are taught to fear an odor, both their offspring and the next generation are born fearing it. The gene for an olfactory receptor activated by the odor is specifically demethylated in the germ line and the olfactory circuits for detecting the odor are enhanced.

Examines the epigenetics of pair bond formation in the monogamous prairie vole, and uses a pharmacological method to alter epigenetic status and partner preference.

Examines the role of histone variant exchange in memory in a mouse model.

Human Transgenerational/Health and Disease:

These two short reports (A-B) should be considered together. The first study demonstrates an inherited disease phenotype in humans that is potentially induced by an epigenetic phenomena. The second study follows on those data with evidence of a transgenerational response to ancestors’ nutrition as a main influence on longevity.

A genome-scale analysis of differential DNA methylation in whole blood after periconceptional exposure to famine during the Dutch Hunger Winter of World War II.

Human Development/Health and Disease:

A study of genome-wide epigenetic differences among twins.


Mental health (humans):


The first epigenome-wide association study of AD employing a sequential replication design across multiple tissues.


Study of the interaction between childhood maltreatment and PTSD, examining genome-wide gene expression and epigenetic signatures.


This study shows epigenetic alterations of a stress-sensitive gene in the brains of suicide victims in association with early life abuse or neglect.

Genetic, tissue-specific, and intergenerational sources of epigenetic variation:

36. Horvath S. DNA methylation age of human tissues and cell types. Genome Biol 2013; 14: R115. Uses computational methods and DNA methylation microarray data to examine DNA methylation status as a predictor of chronological age in a variety of tissues.

37. Orozco LD, Rubbi L, Martin LJ, Fang F, Hormozdiari F, Che N, Smith AD, Lusis AJ, Pellegrini M. Intergenerational genomic DNA methylation patterns in mouse hybrid strains. Genome Biol. 2014 Apr 30;15(5):R68. Concludes that the majority of DNA methylation differences among individuals are associated with genetic differences, and a much smaller proportion of these epigenetic differences are due to sex, imprinting or stochastic intergenerational effects.


40. Flanagan, J. M. et al. Intra- and interindividual epigenetic variation in human germ cells. Am. J. Hum. Genet. 79, 67–84 (2006). This study provides evidence for significant epigenetic variability in human germ cells, which warrants further research to determine whether such epigenetic patterns can be efficiently transmitted across generations and what impact inherited epigenetic individuality may have on phenotypic outcomes in health and disease.

41. Radford EJ, Ito M, Shi H, Corish JA, Yamazawa K, Isaganaitis E, Seisenberger S,
Hore TA, Reik W, Erkek S, Peters AH, Patti ME, Ferguson-Smith AC. In utero effects. In utero undernourishment perturbs the adult sperm methylome and intergenerational metabolism. Science. 2014 Aug 15;345(6198):1255903. **Reports that prenatal undernutrition can compromise male germline epigenetic reprogramming and thus permanently alter DNA methylation in the sperm of adult offspring at regions resistant to zygotic reprogramming. However, persistence of altered DNA methylation into late-gestation somatic tissues of the subsequent generation is not observed.**

**Accessibility:** Students with diverse learning styles and needs are welcome in this course. If you have a disability/health consideration that may require accommodations, please notify me and contact the AccessAbility Services Office (located in SW302) as soon as possible. I will work with you and AccessAbility services to ensure you can achieve your learning goals in this course. Enquiries are confidential, and the staff is available to assess your specific needs, provide referrals, and arrange appropriate accommodations (Tel/TTY: 416-287-7560 or ability@utsc.utoronto.ca).