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). This course will focus on the environmental epigenetic mechanisms that impact human health and disease.

Office hours:
- Prof. McGowan (SW-548): Wednesdays: 1PM-3PM.
- Samantha Lauby (TA): TBD.

Course email address: epigeneticsD19@gmail.com
Please note that it may take up to 2 business days (48 hrs) for a response.

Lectures: BV260 Fridays 10AM-12PM
A course calendar with the schedule for lectures and presentations will be available on Quercus. 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) foundations part 2; how to read/present a research article,
- Week 3: Recap of core principles/methods. How to design and present a poster
- 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 Quercus.
Exams: There are NO exams in this class.

Grading scheme overview:

Assignments (4x2.5%) 10%
Seminar presentation 35%
Seminar discussion 15%
Poster Presentation 35%
Attendance 5%
100%

Deadlines (midnight to course email):
Take-home assignments (3): Variable, but one week after assignment.
Seminar Presentation: Choice of articles (top 3): Friday January 17
Poster Presentation: Topic choice (top 3): Friday January 24
PDF of poster presentation: Thursday before your Poster Session

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 presentation of a research article, followed by a 10 min discussion 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 Quercus before the presentation. The seminar will contribute to 35% of your final grade.

Seminar Discussion: 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 in discussion, as well as on your critical analysis and understanding of the article. This mark contributes 15% to your final grade.

Poster Presentation: You and a classmate will design and present a poster
based on an article from a list of articles provided on Quercus. 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):**


**AccessAbility statement:**

Students with diverse learning styles and needs are welcome in this course. In particular, if you have a disability/health consideration that may require accommodations, please feel free to approach me and/or the AccessAbility Services Office as soon as possible. AccessAbility Services staff (located in Rm SW302, Science Wing) are available by appointment to assess specific needs, provide referrals and arrange appropriate accommodations 416-287-7560 or email ability@utsc.utoronto.ca. The sooner you let us know your needs the quicker we can assist you in achieving your learning goals in this course.

**Academic Integrity:**

The University treats cases of cheating and plagiarism very seriously. The University of Toronto’s Code of Behaviour on Academic Matters (http://www.governingcouncil.utoronto.ca/policies/behaveac.htm) outlines the behaviours that constitute academic
dishonesty and the processes for addressing academic offences. Potential offences in papers and assignments include using someone else’s ideas or words without appropriate acknowledgement, submitting your own work in more than one course without the permission of the instructor, making up sources or facts, obtaining or providing unauthorized assistance on any assignment.

**Intellectual Property:**
Recording or photographing any aspect of this course without prior approval of all involved and written approval from the instructor is not permitted.

**Resources for Academic English:**
Academic English is nobody’s mother-tongue. Every student is expected to achieve a high level of Academic English to cope with the demands of their courses. The English Language Development Centre supports all students in developing better Academic English and critical thinking skills needed in academic and professional communication. Make use of the personalized support in academic writing skills development and Communication Café sessions to enhance your ability to do better in the various components of this course. Details and sign-up information available at [http://www.utsc.utoronto.ca/eld/](http://www.utsc.utoronto.ca/eld/)

**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
YOU CAN ALSO SUGGEST AN ARTICLE.
Deadline: **Friday January 17, 2019**. After the deadline, an article will be assigned to you.

**Nutrition:**


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.**

   Early life nutrition induces epigenetic changes that determine whether a honeybee will become a queen or worker bee.


   Examine the effects of vitamin C on the epigenetic machinery, including microRNA expression, in embryonic stem cells.


   Study of seasonal variations in methyl-donor nutrient intake of mothers in rural Gambia around the time of conception and their influence on 13 plasma biomarkers and DNA methylation.

Xenobiotics and infection:


   Demonstrates the ability of an endocrine disruptor to induce an epigenetic transgenerational disease phenotype for four generations.


   Shows that early developmental exposure to an environmental toxin can change offspring phenotype by stably altering the epigenome, an effect that can be counteracted by maternal dietary supplements.


   This study in primates finds that early exposure to lead (Pb) results in decreased DNA methyltransferase activity in the brain 23 years later.


   DNA methylome and transcriptome changes in a single individual were profiled over 36 months. Methylome changes were associated with infrequent blood glucose level alterations that rose to diabetic levels, whereas the transcriptome underwent dynamic changes during events such as viral infections.

Stress:

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


13. Rodgers, A. B., Morgan, C. P., Leu, N. A., & Bale, T. L. (2015). Transgenerational epigenetic programming via sperm microRNA recapitulates effects of paternal stress. *Proceedings of the National Academy of Sciences*, 112(44), 13699-13704. In this study, through zygote microinjection of nine specific sperm miRs previously identified in a paternal stress mouse model, the authors demonstrate that sperm miRs function to reduce maternal mRNA stores in early zygotes, ultimately reprogramming gene expression in the offspring hypothalamus and recapitulating the offspring stress dysregulation phenotype.


**Learning and Memory/Addiction:**


18. Lubin FD, Roth TL, Sweatt JD. Epigenetic regulation of BDNF gene transcription in the consolidation of fear memory. J Neurosci 2008;28:10576–10586. [PubMed: 18923034] 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:**

   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.

   This study examined the global and locus-specific differences in DNA methylation and histone acetylation of a large cohort of monozygotic twins. They find that, compared to differences in the early years of life, older monozygous twins exhibit greater differences in their overall content and genomic distribution of 5-methylcytosine DNA and histone acetylation, affecting their gene-expression portrait.
This study examined DNA methylation at more than 700 genes in placenta and cord blood and measured gene expression levels of a subset of genes that differed in methylation levels between children conceived in vitro versus in vivo.

Genome-wide epigenetic study of the contributions of stress and other factors in early life to epigenetic variability in humans stratified by socio-economic position.

Study reporting that adult blood DNA methylation profiles show more associations with childhood socio-economic position than adult socio-economic position.

Study of human pre-implantation embryo development at single cell resolution, revealing that the lineage path in the human embryo is distinct from that in the mouse.

Mental health (humans):

This study examined relationships between prenatal exposure to maternal mood and the methylation status of the human glucocorticoid receptor gene in newborns and HPA stress reactivity at age three months.

Reports that altered methylation profiles affecting the hippocampus are associated with major depressive disorder and shows the potential of the epigenetic twin model in neuro-psychiatric disease.

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:


Uses computational methods and DNA methylation microarray data to examine DNA methylation status as a predictor of chronological age in a variety of tissues.


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.


This study investigated the contribution of heritable influences and the combined effect of environmental and stochastic factors to variation in DNA methylation of the IGF2/H19 locus.


Addresses the tissue-specific nature of epigenetic modifications by examining methylation profiles in subsets of peripheral blood cells, which are commonly used in human clinical investigations.


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.


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.