**MGY340H1-F          2024  Molecular Genetics**

**Total class time:** 36 hours (12 weeks; 3x 1hr lectures/wk)

**MWF 1:10 - 2 pm Med Sci Building MS... (TBD)**

Welcome to MGY340H: Molecular Genetics! This course gives students an in-depth understanding of how genetics, the study of mutations and their resulting phenotypes are used to probe and understand a variety of biological phenomena ranging from metabolism, to development, to cancer. The course focusses on examples from eukaryotic model organism genetics and covers the basic principles that underlie genetic analysis: mutation, complementation, suppression, enhancement, recombination, segregation and regulation. Using these tools, geneticists (and budding geneticists) ask fundamental questions about biology.

**Instructors:**

* Brigitte (Bri) Lavoie\* (weeks 1-4)     email: brigitte.lavoie@utoronto.ca
* Julie Brill            email: julie.brill@sickkids.ca
* Jeehye Park email: jeehye.park@sickkids.ca

\*course coordinator

**Getting help / communicating with your instructors**:

 We are happy to help. All of us are firmly committed to training the next generation of geneticists (ie you), and we enjoy doing that, but you need to do your part. If, after reviewing your notes and looking up concepts that seemed confusing to you (the "Genetic Theory ..." textbook in particular provides exceptionally clear explanations), you still remain confused about the material or an assignment--please ask questions! You can do this:

1. **During/after class** (before is trickier as our attention is focussed on setting up the equipment but once that's done, we are all ears)

2. **During office hours**: in person or by zoom

3. **By pre-arranged office visit** (or Zoom) at a mutually agreed upon time

4. **By email**: expect a 24H turnaround time during weekdays, longer on weekends

5. **Through the discussion boards**: It is not an academic violation to ask/answer a question in a class discussion board about how to do things, or to explain a concept to someone. Rather it provides independent evidence of engagement with the course & intellectual generosity--don't be fearful of making a mistake or of stating that you aren't sure. Others can chime in (respectfully of course--all voices are welcome in this class!). This is collaborative learning.

***NB*** *please do safeguard your work &* ***avoid sharing complete answers to*** *assignment questions that someone could simply copy/paste into theirs--it can be just too tempting to someone pressed for time and is considered an academic violation. When in doubt, don't hesitate to ask.*

**Text:**

 The required textbook for MGY340 is **Miller, DE, Miller, AL and R.S. Hawley (2023). Genetic Theory and Analysis: Finding Meaning in a Genome, 2d edn. ISBN: 978-1-394-15628-3 (Wiley Publishing)**

link here: [Genetic Theory ebook](https://www.wiley.com/en-ca/Genetic%2BTheory%2Band%2BAnalysis%3A%2BFinding%2BMeaning%2Bin%2Ba%2BGenome%2C%2B2nd%2BEdition-p-9781394156283)

This excellent book is geared to more advanced undergraduates and beginning graduate students. It has exceptionally clear explanations of how to perform genetic analysis--with lots of wisdom, strongly held opinions and science stories to keep it interesting. R. Scott Hawley is a geneticist's geneticist, and this is a fun book to read. It is available as both a hard copy textbook or a slightly cheaper ebook.

**Assessments:**

 Evaluations will be largely centered around data interpretation and problem solving. Short answer questions will assess understanding of precise genetic vocabulary (including nomenclature) in designing experiments, generating scientific models and conveying thoughts clearly and concisely, a fundamental aspect of scientific writing. A non-programmable calculator is allowed. **Midterms tests will be held during class time.** To encourage in class attendance, we will also have 8-10 short unannounced in class quizzes during the semester (~ 5' of class time) worth 5% of the final grade. We'll drop the two lowest marks in calculating the quiz grade.

* Term test 1 : Oct 4 **20%**
* Term test 2 : Nov 4 **20%**
* Assignments (equal value each part) **25%**
* Unannounced in-class quizzes **5%**
* Final Exam                                          **30%**

*The final exam will cover the entirety of the material, but will emphasize the last third of the course: marks on the final will be distributed approximately 1:1:8 between parts 1, 2, 3.*

**Late penalty policy:**10% per day. Assignments are not accepted if more than 3 days late.

**Missed term work policy:** During the academic term, if you are absent from your studies and unable to complete your course work, declare your absence on Acorn and email your instructor AND the course coordinator ASAP. If you have already used your absence declaration on Acorn for the term, use the [U of T Verification of Illness or Injury Form (VOI)](https://registrar.utoronto.ca/policies-and-guidelines/verification-of-illness-or-injury/) , and/or letter from your registrar or accomodation letter from accessibility services to support your request for consideration. Requests for accomodations/retakes will be considered on a case by case basis with appropriate documentation. Term work extensions/test retakes cannot be considered after feedback on the term work and/or the marks have been released.

Refer to the Arts and Sciences page on Student Absences for helpful links: [https://www.artsci.utoronto.ca/current/academics/student-absences](file:///Users/Bri2/Desktop/Dropbox/MGY340/MGY340%202024/%E2%80%A2%09refer%20to%20the%20Arts%20%26%20Sciences%20page%20on%20Student%20Absences%3A%20%20https%3A/www.artsci.utoronto.ca/current/academics/student-absences)

**MGY340H1 Course Outline**

MGY340 is taught in 3 parts, each with its own assignments and assessments. Each term test (there are two) will only encompass the section immediately preceding it. The final exam will comprise material from the entire course; however, the majority will be from section 3.

**Part 1   Learning outcomes:***Students will learn to perform genetic crosses in eukaryotic model organisms in weekly assignments & analyze the results to characterize mutants in a genetics simulator (StarGenetics).  Using data from crosses, students will determine inheritance patterns, assess whether phenotypes derive from single or multiple gene mutations, assess dominant vs recessive alleles, distinguish between autosomal vs sex-linked inheritance. Students will learn how to read/write genotypes in commonly used model organisms; how different methods of modifying DNA lead to different types of mutations and sort collections of mutants into complementation groups.*

***Week 1-2:*** Review of Mendelian Inheritance principles with a focus on the experiments (how do we know what we know?) and on **using** the principles of genetic inheritance (meiosis, segregation and recombination; genetic linkage; complementation) to characterize mutants.  *Textbook chapters 1, and 4. Assignments 1 & 2.*

***Week 3:*** Introduction to commonly used eukaryotic model organisms (yeast, worm, fly and mouse) including overview of nomenclature, genome structure and databases, experimental toolboxes, genome engineering technologies. *Textbook Appendix A (expanded). Assignment 3.*

***Week 4.***Introduction to mutant hunts & simple genetic screen design: review of mutagens and how they lead to different types of mutations. Examples of simple genetic screens in yeast, guided reading of paper(s). *Textbook chapters 1, 2 and 3.* *Assignment 4.*

**October 4, 2024:  Term Test 1 on part 1 material (20% of final grade)**

***Note: term tests will take place during regular class time. Please arrive a few minutes early so that we can start precisely on time.***

**Part 2  Learning outcomes:** *students will be able to design simple genetic screens; assign mutants to genes; design and interpret crosses to locate genes on chromosomes; make inferences about the role of a gene from mutant phenotypes; recognize epistatic interactions and interpret them to build models of genetic pathways*

***Week 5:*** Mutant screens in *C. elegans* and *Drosophila*; general design, examples; balancer chromosomes; assessing screen saturation; initial mutant characterization

***Week 6:*** Mapping and identifying the gene affected in a mutant; two-factor mapping; multifactor mapping with visible and molecular markers; deficiency mapping; mapping with whole genome sequencing; mutant rescue, RNAi phenocopy

***Week 7:*** Loss-of-function vs gain-of-function mutations; gene dosage tests; inferring the role of a gene from mutant phenotypes. Using existing mutations to obtain new alleles of a gene

***Week 8:*** Epistasis; building models of genetic pathways

**November 4, 2024: Term test 2 on part2 material only (20% of final grade)**

**Part 3  Learning outcomes:** *students will be able to recognize and interpret genetic interactions; design screens based on interactions; interpret mosaic phenotypes to infer focus of action and cell-autonomy or -non-autonomy; describe epigenetic effects of chromatin on gene activity; recognize and interpret paternal effect inheritance; explain mechanisms of dosage compensation*

***Week 9:*** Genetic interactions; suppression, enhancement; examples.Suppressor and enhancer screens; approaches to identifying new genes

***Week 10:*** Mosaic (clonal) analysis in *C. elegans* and *Drosophila*; identifying where the activity of a gene is required; mosaic screens for new mutations

***Week 11:*** Chromatin and gene regulation; histone code; heterochromatin, position effect variegation; polycomb genes; gene silencing

***Week 12:*** (Some of) Paternal effect inheritance; screens for paternal effect mutations; dosage compensation; epigenetic phenomena.

**FINAL EXAM: December Final Assessment Period, Date TBA**

***While all class material is included in the final exam, the majority focus will be on Part 3 material.  The exam will include a ~ 1:1:6 split between part 1, 2 and 3 questions.***

[**StarGenetics:**](http://star.mit.edu/genetics/screenshots/index.html)

 We will be using a Mendelian Genetics Simulator created by MIT for several assignments in part 1 of the course to give you practical experience in using crosses to determine the mode of inheritance of unknown mutants. You can download the software from [*http://star.mit.edu/genetics/screenshots/index.html*](http://star.mit.edu/genetics/screenshots/index.html) onto your own computer if you like. Because StarGenetics is JAVA based, an updated version of JAVA is required and you will also have to reset the permissions to allow it to run (you will get warnings that MIT is considered an "unknown developer").

*Note: Newer laptops running advanced security systems like Windows 11 or newer Mac's have had issues running the software because the StarGenetics security certificate has expired: if it doesn't work for you (or you are using an iOS machine), don't waste time troubleshooting--access the software in person or remotely through the Sid Smith Computer lab (see below). The machines in Discovery Commons (3rd floor MSB3281) also have the software loaded onto them.*

 In person or remote access to Star Genetics is via the Sid Smith Computer lab (SSH561) [*https://labs.artsci.utoronto.ca/*](https://labs.artsci.utoronto.ca/) . You will need: your UTOR ID to login. Your password will be: AS!your student number (as in AS!100100100). If joining remotely, you can access StarGenetics on any device (phones and ipads included). Detailed instructions can be found on our course Quercus page. Note that remote access is granted by A&S IT team and is generally set up the week before class starts: **if you joined the course late, email Bri (brigitte.lavoie@utoronto.ca) ASAP with your Name, UTORID, Student number and email** so that I can request your StarGenetics access. If you have access but can't connect, it's likely that SSH561 is booked for a class or the machine you chose is already in use--you can check the schedule here: <http://lab.chass.utoronto.ca/schedules.php>. Choose another machine name or try later.

 *ProTip. If after doing the Star Genetics assignments in Part 1 you can characterise mutants in exercises 3 or 4 without any prompts telling you what to do, you have successfully learned what StarGenetics was meant to teach you. Do this with your study group & compare answers!*

**Expectations--how to succeed in MGY340:**

 Third year marks an important transition in your learning journey. While knowledge assimilation and comprehension are the hallmarks of introductory courses, knowledge application, analysis, and synthesis are the objectives of the more advanced third and fourth year curricula (refer to Bloom's revised taxonomy below--roughly, Yrs1-2 of UG are focussed on remember/understand/apply while yrs 3-4 focus on apply/analyze/evaluate with some exposure to create--> grad school is all about creating new knowledge. ). As students starting MGY340, you should be able to recite Mendel's laws, and be familiar with the basic genetic vocabulary (genes, alleles, dominance, recessive, segregation, recombination, complementation, suppression and epistasis etc). Our focus will be on using these principles to generate and interpret data to characterize mutants (and to understand the experiments that underlie prior knowledge).

[*https://uwaterloo.ca/centre-for-teaching-excellence/catalogs/tip-sheets/blooms-taxonomy*](https://uwaterloo.ca/centre-for-teaching-excellence/catalogs/tip-sheets/blooms-taxonomy)

You are here



 During your next two years of study, you will also progress from using textbooks to relying on the primary research literature for information. The data centric/ problem-based learning in MGY340 aims to support this transition. Reading the primary scientific literature *is* challenging for beginners (even senior scientists researching in a new area), so don't be discouraged by that. Anticipate that it will require sustained effort: it's not enough to know what the conclusions are, as scientists we need to critically assess how those conclusions were derived and importantly, how good the data that underlies them really is. We want to understand how we know what we know--what were the experiments, why were they done, and how convincing are they? Were all the necessary controls included? What are their limitations? Are there other possible interpretations? What should we (you) do next? This knowledge then serves as the foundation for designing your own experiments, testing your own scientific models and expanding our collective understanding of biology.

**To succeed in MGY340, you should:**

* **Attend class** (in person) as much as possible--carving out a dedicated time and giving your full attention to the material, your instructor and your classmates makes a huge difference. Expect to develop your notetaking skills, to ask and be asked questions and to huddle up into groups and participate in coming up with experimental strategies. *We will monitor participation through short (unannounced) quizzes (worth 5% of the total mark).*
* **Learn actively**: take notes that link concepts (not just a verbatim transcript), look things up, ask precise questions, **do the assignments (and reflect on what you learned from them!)** because the answer is less important than the process--please don't skimp on doing this thinking. The methods you learn (and tricks--should you start with a male or female mutant to show X-linkage?) are things you take forward. *Genetics is like math --the true value of the assignments isn't the answer you get, but in teaching you how to do things.*
* **Budget your time wisely:** per week, devote3H for in person lectures, ~2-3H review notes/reading textbook/study group, ~2H/assignment+study group. *Notice how no time is allocated to recorded lectures--that's because it's a lot more efficient to take notes in class and use the textbook to complete/expand them.*
* **Be proactive**: review your notes (READ the textbook) after each class, look things up & engage with your classmates (discussion boards, work through your assignments together & explain things to each other-- Study Groups are the best way to find your blind spots & promote the higher order learning we expect from 3rd year courses). Sustained effort beats last minute binge cramming every single time. *Remember that work* *piles up quickly and it's very hard to catch up--try not to fall behind (study groups are great for staying on track and for managing workload). The assignments illustrate fundamental genetic principles and provide you with sound experimental strategies:* ***reflect on the predictions and the approaches you can apply to other situations.******This is the learning you take forward****.*
* **Be curious and have fun:** read the primary literature (*Trends in Genetics* is a good place to start), and sign up for newsletters from *Science* or *Nature,* or try genetics podcasts (*Naked Genetics* is fun). Challenge yourself and attend some research seminars to broaden your interests and knowledge. *My favorite curated list of weekly seminars is maintained by the Biochem Dept:* [*http://cettesemaine.utoronto.ca/*](http://cettesemaine.utoronto.ca/)

**Learning & Assessment strategies:**

 **Recognized Study Groups:** Collaborative learning is a proven strategy that supports academic success. [Recognized Study Groups](https://sidneysmithcommons.artsci.utoronto.ca/recognized-study-groups/) are supported by Arts and Sciences and running /belonging to one demonstrates intellectual generosity & engagement. This not only looks good on your CV, but it's a good place to leverage skill sets among your classmates, discuss the material and the assignments, collaboratively define the key concepts to study and make up new problems for the group to solve, plus make like-minded friends (science is a team sport!). MGY340 is a problem solving course, and like math, the ability to generate and interpret data to find out new things benefits from practice. Learning how to solve different genetic problems is what this course is all about.

 Study Groups (done well) promote the higher level learning expected in 3rd-4th year courses (apply, analyze, evaluate, create). Importantly, team study can help you find your blind spots (what you don't know you don't know!) and help you think about the course material from new and different angles, deepening your understanding. Working through assignments together allows you to explain to each other what you did and why, and then check your conclusions with your group. Making up new problems & working through them with your group is a great way to promote higher level learning. We've posted some links on Quercus that make the case for Study Groups and provide a framework for using them effectively.

Check it out here: <https://youtu.be/8vDrcQQyHGo?si=7YJZ-DE3rYpmcPu9>

 **Midterms/Assignments:** In high school, you may have heard that 1 mark = 1 line of text. **This no longer applies.** In MGY340, a question worth 10 marks reflects the amount thinking that goes into your answer (which could be just a couple of lines), not the amount of verbiage. A good Punnett square/ schematic is often more precise and compelling than a paragraph and takes less time to write out. **Aim to answer questions precisely and concisely.** **Take the time to read questions thoroughly and include everything you've been asked for in your answers** (show your data, draw a schematic, include a Punnett square etc). **And aim to keep it simple**--one can always hypothesize that a "hidden second or third mutation" underlies a phenotype through some convoluted genetic interaction, or that your WT isn't WT after all but harbors unknown random mutations that affect your analysis, but is this really likely? There's almost certainly a much simpler and far more likely answer (and at the bench, we always start with the most likely hypothesis, not the most far-fetched).

 Bottom line: No extra points will be awarded for extra correct information, but marks will be deducted for extraneous incorrect information. If a personal "cheat sheet" is allowed on a test, remember that you will likely not have time to refer to it. Rather, the value of a cheat sheet is in the prioritizing and organizing of information that goes into making it. This is why cheat sheets shouldn't be shared with others--the learning happens while you are making it. There's some evidence (though hardly rigorous) that notes and cheat sheets work better if handwritten (vs typed out)--certainly I remember things I've written better than things I've typed so maybe that's real.

 **StarGenetics** assignments are like lab reports. As scientists, your task is to generate straightforward hypotheses (Punnett square = hypothesis), and report on the crosses you performed to test them (always explicitly state the genotypes of the parents you crossed), the data you obtained (copy this from Star Genetics) and the conclusions you drew from the data. Write this out in a simple, clear, stepwise way so that your TA can easily understand what crosses you've performed and what you've concluded from the results, **just like you would in your lab notebook**. Bear in mind that it's our job as scientists to produce, evaluate and communicate data concisely and precisely. If your TA has to hunt through your assignments to know what experiments you performed, what data you produced and what you concluded from it, you've let yourself down.

***About reference letters: things I wish I'd known as a 3rd year undergrad***

 Many of you will be considering careers in research, medicine, biotech, education, etc. For most if not all post-grad programs, 2-3 reference letters will be required, and the better someone knows you in a scientific context, the more helpful the letter they can write.

 For those of you wishing to continue to graduate school, the most compelling letters of recommendation will come from your research advisors during summer or independent research projects. These advisors know you personally, can directly assess skills directly relevant to those needed for success in grad school and can discuss your research potential: your work ethic, organizational skills, attitude/resilience (experiments can be frustrating and working out the kinks takes effort), ability to learn new things, ability to ask for help when you need it, your experimental and data analysis skills as well as your communication skills.

 In contrast, lecturers can comment on very different aspects of your skillset: your engagement with the material, your overall scientific curiosity, your generosity towards your classmates (are you a volunteer notetaker? run a study group? participate in discussion boards?) and your academic excellence, but we can't say much about research potential or bench skills, nor is it possible to comment on someone's communication skills if they don't engage with you. **Be mindful of this. Participate in class, during group discussions and lab meetings, be present on discussion boards, engage with your professors, and attend some talks (even better if you know nothing about the topic)!** Immunize yourself against ignorance whenever possible.

**Academic Integrity : When in doubt, please ASK!**

 [*"Generally, academic misconduct is any behaviour, intentional or otherwise, that gives a student unearned or unfair advantage in academic work over other students."*](https://www.artsci.utoronto.ca/current/academic-advising-and-support/student-academic-integrity/academic-misconduct)

 While every student is responsible for knowing the [Code of Behavior on Academic Matters](https://governingcouncil.utoronto.ca/secretariat/policies/code-behaviour-academic-matters-july-1-2019), a helpful list of real academic integrity risks can be found at <https://www.academicintegrity.utoronto.ca/perils-and-pitfalls/> . This includes sharing your or others' finished work (including posting on-line to any forum), and the use of generative AI (large language models or LLM) for a marked assessment. Be very aware that LLMs often make up facts and references, which is an academic offense in itself, as is submitting any work that isn't your own.

**A special note about Group work:** *"If you want to go fast, go alone. If you want to go far, go together."*

 Science is a team sport--and working with others a crucial aspect of the skillset every modern scientist must master. Group work was and remains an essential part of my own learning journey--explaining things to others boosts your own learning and helps you articulate your thoughts precisely and simply (a very important skill for explaining your answers on a test). It also makes important connections with your classmates who may very well end up being colleagues later on (or who you may want to collaborate with later). Working through assignment problems together and making up new ones for your study buddies to solve are an integral part of mastering the skills you need as geneticists. This type of collaboration helps you find your learning blind spots, and work through more complex problems than you could on your own. But the use of social media and electronic communication (and the convenience of sharing documents and screens) can also risk. The UT Academic Integrity website notes that: *"Students studying in groups should be careful to safeguard their own work, to avoid sharing copies of finished work or previous assignments, and to be cautious about transmitting electronic copies of their work to other students."*

So how do you get the advantages of group work while minimizing risk? Whenver possible do it in person instead of in writing! It's not only more fun but it avoids giving easy access to electronic copies of your work (including sharing files, photographs or scans)--social media & shared google docs are risky for this reason. **It is never OK to copy/paste answers that are not your own work and even posting your completed work to an e-forum to facilitate copying is a violation**. From experience, electronic copies are especially tempting to students running short on time, and implicate both parties in misconduct--for MGY340, this would include any students that took the course previously and shared their assignments with you! *In contrast, in person group work has all the benefits of team study (plus social benefits) while minimizing the risk of electronic transmission of your work without your permission*. Should you suspect that someone has shared or is using your work without attribution, contact your instructor. If you've made it this far in reading the syllabus, well done! As a reward, email Bri with the words cobra chicken in the header to be included in a draw for a prize.

**FYI: Recording Lectures/Photographing slides without permission is an academic violation**

From[*https://www.academicintegrity.utoronto.ca/smart-strategies/recording-lectures/*](https://www.academicintegrity.utoronto.ca/smart-strategies/recording-lectures/)

*"If a student wishes to tape-record, photograph, video-record or otherwise reproduce lecture presentations, course notes or other similar materials provided by instructors, he or she must obtain the instructor’s* ***written consent*** *beforehand. Otherwise all such reproduction is an infringement of copyright and is prohibited.* ***In the case of private use by students with disabilities, the instructor’s consent will not be unreasonably withheld.*** *Students with disabilities who request accommodation should contact Accessibility Services on their campus."*

Take home message: you've just leveled up in your learning journey--congratulations! We're all excited to meet you and are committed to helping you master what Hawley calls "the proper doing of genetics". C U in class!

 Bri, Julie and Jeehye