Freshman Seminar 50q
Gut Reactions: Discovering Chemistry from the Human Microbiota
Spring 2017

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Course website: **https://canvas.harvard.edu/courses/22912**

Class: Tuesday, 2:30-5:30 pm (plus extra time in the lab as desired)
Room 152 Northwest Building (first floor)

The human gut is colonized by trillions of microorganisms that exert a profound influence on our health. Notably, the chemical capabilities of gut microbes extend beyond those found in our own cells, playing roles in nutrition, directing immune system development, and protecting against pathogens. However, we still do not understand how the vast majority of this microbial chemistry actually takes place, which stands in stark contrast to our knowledge of human physiology. The aim of this laboratory-based seminar is to expose students to a cutting-edge area of research at the interface of chemistry and microbiology. Over the course of a semester, students will work as in small teams to design and implement an experimental approach for discovering new enzymes from human gut microbes. We will using a strategy called 'functional metagenomics' as the basis for this work. Potential targets include enzymes involved in antibiotic resistance, metabolism of dietary components and pharmaceuticals, and modification of host metabolites. Students will pursue these goals in a fully equipped laboratory dedicated to undergraduate research. Course meetings will combine time in the lab with discussion of research literature and experimental techniques. Students will also have flexible access to the teaching laboratory to continue their experiments outside of the hours scheduled for the seminar. By having the opportunity to both explore a timely scientific problem and to drive the direction of their own research at a very early stage in their academic experience, students in this seminar will be extremely well prepared to seek out further undergraduate research opportunities and to pursue scientific career paths. *Students enrolled in this course will receive credit toward the Chemistry concentration.*

Texts on Reserve (Cabot Science Library):

Brock Biology of Microorganisms, 13th Edition. M. Madigan et al. 2012, Prentice-Hall, Inc. Englewood Cliffs, NJ.

I Contain Multitudes: The Microbes Within Us and a Grander View of Life. Ed Yong, 2016.

At the Bench: A Laboratory Navigator. Kathy Barker, 2004.

Readings:

1-2 journal articles or other readings per course session. Readings will cover the human gut microbiota and its functions, as well as enzymes and strategies for their discovery and characterization. Reading assignments will include a set of questions designed to guide thinking about the article and in-class discussion. These questions should be completed no later than an hour before class and submitted through the 'Discussion' section on the course website.

Research Proposal:

As a centerpiece of the course, students will formulate an idea for a functional metagenomics experiment aimed at uncovering new enzymes from the human gut microbiota. As preparation for attempting this experiment in the lab, students will write a two-page research proposal that provides an introduction to the activity being investigated, a rationale for the experimental design, a description of the experiments to be performed, and potential next steps and strategies for troubleshooting. A first draft of this proposal will be due on 3/3 and students will revise their proposal based on feedback (final version due on 3/24).

Final Poster Presentation:

Students will present the results they have generated in lab during the semester to other course participants and the broader Harvard community in a poster session. Students will work together in groups to generate and present their poster. Evaluation will be based both on the poster itself and the presentation. A draft version of the poster is due on 4/21 and the poster session will take place during the final class period on 4/25.

Collaboration Policy:

Discussion and the exchange of ideas are essential to academic work. In this course, you are encouraged to consult with your classmates on the choice of proposal topics and to share sources. You may find it useful to discuss your chosen topic with your peers, particularly if you are working on a similar topic as a classmate. However, you should ensure that any written work you submit for evaluation is the result of your own research and writing and that it reflects your own approach to the topic. You must also adhere to standard citation practices in

this discipline and properly cite any books, articles, websites, lectures, etc. that have helped you with your work. If you received any help with your writing (feedback on drafts, etc) from anyone outside of the FRSEMR 50Q teaching staff, you must also acknowledge this assistance.

Lab Safety:

Students must participate in lab safety training, adhere to all laboratory safety rules, and keep their lab space clean and organized. Several courses share the lab space we will be using, and each researcher must return their work area to a high standard of cleanliness and organization after each session of lab work.

Class Schedule

Session	Discussion	Reading	Lab
Session #1: 1/24	**What are 'microbiomes' and how can we study them?** **Introduction to enzymes and discovery methods**	Introduction to the human microbiota Part 1 Introduction to enzyme discovery	Lab safety, introduction to microbial cultivation
Session #2: 1/31	**Introduction to the human gut microbiota and its functions** **Introduction to functional metagenomics: discovery of antibiotic resistance genes in the human gut microbiome**	Introduction to the human microbiota Part 2 Functional metagenomics and the human gut microbiome **Tutorial: Searching and reading the scientific literature**	Day 1 of selection for antibiotic resistance Benchling tutorial
Session #3: 2/7	**Antibiotic production and resistance in the human microbiome**	Discovering antibiotic resistance genes in the human gut microbiota	Day 2 of selection for antibiotic resistance
Session #4: 2/14	**Functional metagenomics: selection/screen development for primary metabolism** **Tutorial: Research proposal writing**	Selection and screen development for functional metagenomics Discovery of primary metabolic enzymes using functional metagenomics	Day 3 of selection for antibiotic resistance
Session #5: 2/21	**Tutorial: Bioinformatics (BLAST + Geneious)** **Proposal brainstorming**	Introduction to DNA sequencing Introduction to BLAST	Day 4 of selection for antibiotic resistance
Session #6: 2/28 ***Draft proposal due on 3/3***	**Functional metagenomics: selection/screen development for secondary metabolism**	Discovery of microbial secondary metabolites using functional metagenomics	Preliminary experiments: screening for additional phenotypes

Session #7: 3/7	**Human gut microbiota in health and disease** **In-class feedback on proposals**	Studying the gut microbiota's role in disease Links to obesity	Day 1 of screening for additional phenotypes
Session #8: 3/21 ***Revised proposal due 3/24***	**Human gut microbiota and nutrition**	The gut microbiota and malnutrition	Day 2 of screening for additional phenotypes
Session #9: 3/28	**Human gut microbiota and xenobiotic metabolism**	The gut microbiota's role in drug metabolism	Day 3 of screening for additional phenotypes
Session #10: 4/4	**Gut-brain axis: Human gut microbiota and the nervous system** **Tutorial: Bioinformatics (multiple sequence alignments and homology modeling)**	Role of the gut microbiota in neurological disease, nervous system function	Day 4 of screening for additional phenotypes.
Session #11: 4/11	**The human microbiota: additional body sites**	The skin microbiota and its role in disease	Day 5 of screening for additional phenotypes
Session #12: 4/18 ***Draft poster due 4/21***	**Gnotobiotic models for studying the human microbiota** **Feedback on posters**	Germ-free model organisms and their use in microbiota research	Day 6 of screening for additional phenotypes
Session #13: 4/25	***Final poster session and reception***		