

Microbiology 202: Mechanisms of Bacterial Pathogenesis and Host Immune Response Harvard Medical School, Fall 2019

Tuesday and Thursday 10 AM-12 PM, NRB 1031

Course Description:

This course focuses on molecular mechanisms of bacterial pathogenesis and the host response to infection. The class consists of lectures and group discussions emphasizing themes of pathogenesis, methods, results, and interpretations of classic and contemporary literature. Subjects including bacterial secretion systems, mechanisms of entry into host cells, biofilm formation, and motility are viewed primarily from the pathogen's perspective, whereas topics including inflammasome activation, TLR signaling, and adaptive immune responses provide a host-centric view. Additional sessions are spent examining current methods of antibiotic discovery and vaccine development. The course also introduces students to the wide diversity of pathogenic bacteria. Organisms discussed include pathogenic *E. coli*, *Shigella* species, *Vibrio cholerae*, *Listeria monocytogenes*, *Chlamydia trachomatis*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*, as well as a discussion of the challenges presented by currently unculturable species.

The course is designed to complement Microbiology 201; however students who have not taken Microbiology 201 previously are welcome.

Course Objectives:

Our goal is for students to be able to

- Learn themes of microbial pathogenesis
- Recognize, describe, and interpret classic and modern experimental approaches for probing bacteria-host interactions
- Identify strengths and limitations of classic and modern experimental approaches for probing bacteria-host interactions
- Design and critically evaluate experimental studies
- Clearly communicate technical and conceptual aspects of experimental studies
- Describe mechanisms by which bacteria manipulate human hosts to cause disease
- Describe mechanisms by which hosts respond to bacterial infection
- Compare how mechanisms of pathogenesis are conserved or unique among different types of bacterial pathogens
- Describe how pathogen biology can be exploited to treat and control bacterial infections

Instructors:

Marcia Goldberg, MD (Course director, marcia.goldberg@mgh.harvard.edu); Darren Higgins, PhD; Jonathan Kagan, PhD; Michael Starnbach, PhD; Deepali Ravel, PhD (Curriculum Fellow, deepali_ravel@hms.harvard.edu), Brian Russo (Brusso1@mgh.harvard.edu)

Office Hours:

By appointment.

Assignments and Grading:

Students will receive a letter grade for this course. Final grades will be based on the following components:

Participation (60%)

Because this course is focused on class discussion of primary literature, attendance and active daily preparation/participation are required. Students will be provided a rubric with expectations for participation and will be given feedback on their participation mid-semester.

Students are allowed one excused absence. Additional absences will be considered by the course director and curriculum fellow on a case-by-case basis, and students will be asked to submit a one-page written summary and critique on the assigned readings for the session that is missed. We understand that illnesses and other conflicts can arise, and we encourage you to approach the instructors as early as possible so that we can make a plan that allows you to learn any content you miss.

Problem sets (30%)

Students will complete two problem sets – one at mid-semester and one at the end of the course. Each will be worth 15% of the final grade.

Framework activity (10%)

Over the course of the semester, students will generate a written “framework for pathogenesis” based on concepts from class readings, discussion, and lectures. Students will be provided with a template, rubric, and in-class time to work on this assignment in groups. At the end of the semester, this will be handed-in and graded.

Note about auditing: Auditors are welcome but must obtain prior approval of the course director. Because class discussion forms the core component of the course, auditors are expected to complete course readings and actively participate in class discussions.

Learning Community:

Community Standards

We acknowledge that the instructors, students, and authors of course materials all come to this course with their own diverse backgrounds and biases. Our goal is for this to be an open, collaborative, and inclusive learning community. Members of this class are expected to:

- share their own knowledge and perspectives
- value each other’s opinions and communicate in a respectful manner
- approach the instructors if elements of the course content, instruction, or course participants are barriers to this being an inclusive learning environment

Reasonable Accommodations

As an institution that values diversity and inclusion, our goal is to create learning environments that are usable, equitable, inclusive and welcoming. Harvard University complies with federal legislation for individuals with disabilities and offers reasonable accommodations to qualified students with documented disabilities and temporary impairments. To make a request for reasonable accommodations in a course, students must first connect with their local disability office. The primary point of contact for GSAS students is the Accessible Education Office (www.aeo.fas.harvard.edu). The HMS Director of Disability Services, Timothy Rogers (timothy_rogers@hms.harvard.edu) is another potential source of accommodation information for PhD students and is the primary contact for MD and master’s students.

Accommodations are determined through an interactive process and are not retroactive. Therefore, students should contact their local disability office as soon as possible, preferably at least two weeks before accommodations are needed in a course. Students are strongly encouraged to discuss their access needs with their instructors; however, instructors cannot independently institute individual

accommodations without prior approval from the disability office. Student privacy surrounding disability status is recognized under FERPA. Information about accommodations is shared on a need-to-know basis, and with only those individuals involved in instituting the accommodation.

Academic Integrity

All work in this course is governed by the academic integrity policies of GSAS (<https://gsas.harvard.edu/codes-conduct/academic-integrity>) and HMS (<https://mastersstudenthandbook.hms.harvard.edu/409-academic-dishonesty-and-plagiarism>). It is the students' responsibility to be aware of these policies and to ensure that their work adheres to them both in detail and in spirit. Unless otherwise specified by the instructor, the assumption is that all work submitted must reflect the student's own effort and understanding. Students are expected to clearly distinguish their own ideas and knowledge from information derived from other sources, including from collaboration with other people. If you have a question about how best to complete an assignment in light of these policies, ask the instructor for clarification.

Academic and other Support Services

We value your well-being and recognize that as a graduate student you are asked to balance a variety of responsibilities and potential stressors: in class, in lab, and in life. If you are struggling with experiences either in- or outside of class, there are resources available to help. Jackie Yun, the GSAS Director of Student Services (617-495-5005) is available to assist students navigating academic or personal difficulties and to connect students to university resources. HILS PhD students have access to free academic tutoring which can be arranged through the DMS office. A variety of academic support services are also available to GSAS students through the Bureau of Study Counsel (<https://bsc.harvard.edu/>) and the Center for Writing and Communicating Ideas (<https://gsas.harvard.edu/center-writing-and-communicating-ideas>).

All students have access to Counseling and Mental Health Services (CAMHS) available in Longwood, Cambridge or remotely via webcam or phone. The use of CAMHS is included in the student health fee, regardless of insurance, at no additional cost. More information is available at <https://camhs.huhs.harvard.edu> or by calling the main office at 617-495-2042. Urgent care can be reached 24/7 at 617-495-5711.

Course schedule (subject to change):

| Date | Instructor | Topic |
|-------------|-------------------|------------------------------------------------------------------|
| 9/3/2019 | Marcia Goldberg | Overview of bacterial infections and host pathogen interactions |
| 9/5/2019 | Jon Kagan | Disease tolerance |
| 9/10/2019 | Michael Starnbach | Overview of immune response to pathogens (innate and adaptive) |
| 9/12/2019 | Marcia Goldberg | Mechanisms of entry using type 3 secretion |
| 9/17/2019 | Marcia Goldberg | Type 3 secretion disruption of host signaling pathways |
| 9/19/2019 | Marcia Goldberg | Cellular trafficking and type 3 secretion |
| 9/24/2019 | Marcia Goldberg | Mechanisms of antibiotics and approaches to antibiotic discovery |
| 9/26/2019 | Jon Kagan | Mechanisms of living in a vacuole |
| 10/1/2019 | Jon Kagan | Toll-like receptors |
| 10/3/2019 | Jon Kagan | Inflammasome activation |
| 10/8/2019 | Jon Kagan | Manipulation of MAP kinase and NF κ B pathways |
| 10/10/2019 | Jon Kagan | Intracellular pathogens and cellular metabolism |
| 10/15/2019 | Michael Starnbach | Alteration of host ubiquitination |
| 10/17/2019 | Michael Starnbach | Autophagy |
| 10/22/2019 | Michael Starnbach | Regulation of chronic infection I |
| 10/24/2019 | Michael Starnbach | Regulation of chronic infection II |
| 10/29/2019 | Michael Starnbach | Bacterial manipulation of adaptive immunity |
| 10/31/2019 | Brian Russo | Bacterial toxins |
| 11/5/2019 | Deepali Ravel | Enteric pathogens/host-pathogen-commensal interactions |
| 11/7/2019 | Deepali Ravel | Bacterial killing via type 6 secretion systems |
| 11/12/2019 | Darren Higgins | Mechanisms of entry into cells (non-type 3 secretion mediated) |
| 11/14/2019 | Darren Higgins | Actin-based motility |
| 11/19/2019 | Darren Higgins | Bacteria and host cell death |
| 11/21/2019 | Darren Higgins | Biofilms |
| 11/26/2019 | Darren Higgins | Vaccine development and adjuvants |
| 11/28/2019 | | Thanksgiving |
| 12/3/2019 | Darren Higgins | Vaccine development and adjuvants |