MICROBIOLOGY 308
Paradigms in Bacterial Pathogenesis
MICB 308 201 [3]

ACKNOWLEDGEMENT
UBC's Point Grey Campus is located on the traditional, ancestral, and unceded territory of the xwməθkwəy̓əm (Musqueam) people. The land it is situated on has always been a place of learning for the Musqueam people, who for millennia have passed on their culture, history, and traditions from one generation to the next on this site.

Homepage: http://canvas.ubc.ca (follow the links to MICB 308)

Location and time: M, W, F 12-12:50pm. Room: MCML 360. Lectures will not be recorded.

Instructors:
Dr. David Oliver
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Tutorials:
Dates and time TBA. Sample exam-type questions and opportunities to help you prepare your answers will be provided in tutorials.

Course content questions:
Please attend tutorials and office hours.

Textbook (Optional): Bacterial Pathogenesis: A Molecular Approach, 4th Edition (2019) by Wilson, Winkler and Ho. ISBN 9781555819408; e-ISBN: 9781555819415

https://www.vitalsource.com/en-ca/products/bacterial-pathogenesis-a-molecular-approach-brenda-a-wilson-malcolm-v9781683672883

$124.99 CAD (lifetime; does not expire; EPUB format, read aloud option)

Assessments:
Midterm Exam 1 [30%]: Monday February 12, 2024 (50 min during class, Vancouver time)
Midterm Exam 2 [30%]: Friday March 22th, 2024 (50 min during class, Vancouver time)
Final Exam [40%] 90 minutes. Final is cumulative

Exams will be essay-style, broken down where appropriate, into smaller short-answer sections.

Exam policies:
Midterm exams. If you are unable to write a midterm exam for any reason, to avoid getting a mark of zero, **please inform Dr. Oliver for midterm 1 and midterm 2 in writing – within one week of the midterm. A make-up midterm will be scheduled within 2 weeks.**

The expected answers to midterm exams will be provided. To request a re-grade of a midterm exam please compare your answers to the expected answers and, within one week of receiving your exam, indicate in writing why your exam should be re-graded.

Final exam. For missed final exams, and to view marked exams, please refer to UBC's policies for final exams.

University Policies:
UBC provides resources to support student learning and to maintain healthy lifestyles but recognizes that sometimes crises arise and so there are additional resources to access including those for survivors of sexual violence. UBC values respect for the person and ideas of all members of the academic community. Harassment and discrimination are not tolerated nor is suppression of academic freedom. UBC provides appropriate accommodation for students with disabilities and for religious observances. UBC values academic honesty and students are expected to acknowledge the ideas generated by others and to uphold the highest academic standards in all of their actions. Details of the policies and how to access support are available on **the UBC Senate website: https://senate.ubc.ca/policies-resources-support-student-success**

Proposed Course Outline

1. Introduction to course

- Importance of Infectious Diseases
- Definition of a pathogen
- Koch's postulates

2. Summary of key concepts of bacterial cells

- Importance of the cell membrane
- The central dogma
- Introduction to Genomics

3. Selected mechanisms of pathogenesis

- **Adherence**
  - Overview of ligands (afimbrial and fimbrial adhesins) and receptors
  - Direct binding vs binding to extracellular matrix proteins
  - Brief description of urinary tract infections, and the importance of adherence
  - Biogenesis of the pap-pilus (adhesin is at the tip; importance of chaperones)

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Microbial mechanisms for evasion of host defenses

- Summary of key concepts in innate immunity
- Bacterial virulence factors that alter NF-kB signaling
- Complement pathway
- Evasion of complement
- Phagocytosis (oxidative burst, oxygen-dependent and oxygen independent killing)
- Mechanisms to combat phagocytic killing
- Overview of bacterial mechanisms to avoid immune detection

- **Invasion**

- Overview of invasion mechanisms –zipper vs. trigger
- Brief description of Yersinia infections, and mechanism of zipper-mediated uptake by invasin.
- Importance of integrins, actin polymerization
- Brief description of Shigella infections and mechanism of trigger mediated uptake.
- Involvement of bacterial proteins in formation of filopodia, lamellipodia, actin cup, actin polymerization and depolymerization.

- **Intracellular Survival**
  - Brief overview of intracellular survival mechanisms (e.g. within professional phagocytes)
  - Focus on inhibition of phagosome-lysosome fusion (or remodeling of phagosome membrane) using *Legionella* and *Chlamydi*a (or *Salmonella*, or *Mycobacterium tuberculosis*) as specific examples, and escape from phagosome into the cytoplasm using *Listeria* and *Shigella* as examples.
  - Identification of both bacterial and host components where known.

- **Toxins**
  - Brief overview (concept of A-B toxins)
  - Cytolytic toxins.
    - Describe the mechanisms of enzymatic vs. non-enzymatic (iei.e. pore-formers) toxins
    - Cytotoxic toxins.
  - Describe the mechanisms of toxins that
    - inhibit protein synthesis (Diphtheria toxin and Pseudomonas exotoxin A, Shiga toxin)
    - interfere with signal transduction (cholera toxin, pertussis toxin)
    - interfere with actin polymerization (*C. difficile* toxins A and B)
    - proteases (neurotoxins tetanus toxin, botulinum toxin)
    - Anthrax toxin (unusual A-B toxin; how to inhibit its function)

4. Techniques for studying bacterial pathogens & their virulence factors

- Overview of bacterial genome structure and function
- Overview of models –advantages, drawbacks, limitations
- Koch's postulates –molecular version
- Gain of function/Loss of function experiments (advantages, limitations)
- Signature-tagged mutagenesis, TnSeq
- Promoter traps (in vivo expression technology (IVET) and differential fluorescence induction (DFI)
- Hybridization-based experiments and RNASeq
- Protein arrays?

5. Vaccines

- Summary of adaptive immunity
- Practical example of the *H. influenzae* B conjugate vaccine
- Designing vaccines (killed or attenuated, whole-cell or subunit, reverse vaccinology, adjuvants)
- DNA and RNA vaccines
- How to address bacteria that have multiple serotypes (molecular breeding/directed evolution).

6. Antibiotics

- Brief overview on antibiotics
- Focus on antibiotics that affect the cell wall
- Biogenesis of peptidoglycan and the cell envelope
- Beta-lactam antibiotic mechanism of action and resistance
- Glycopeptide antibiotics mechanism of action and resistance

7. Evolution of pathogens [Time-permitting]

- Pathogenicity Islands and phages
- General overview of how these are identified
- Impact of phages and pathogenicity islands on virulence *(V. cholerae*, *Staphylococci* as examples)

8. Tying it all together [Time-permitting]

- Seminars on the molecular mechanisms of pathogenesis for select bacteria

Learning Outcomes

By the end of the course, students will be able to:

- Describe the mechanism of action of antibiotics targeting the cell wall and primary mechanisms of resistance to these antibiotics

- Describe known human defenses and microbial strategies for evasion of these host defenses

- Describe the principles involved in generating vaccines and the advantages and limitations of different types of vaccines (e.g. killed vs. live, protein subunit vaccines, DNA/RNA vaccines, carbohydrate-protein conjugate vaccines, etc)

- Compare and contrast strategies for adherence, invasion and survival of select pathogens

- Describe the mechanisms of action of different classes of bacterial toxins

- Propose lines of research to design vaccines or new therapies against bacterial pathogens

- Describe techniques used for studying bacterial virulence factors and be able to appropriately propose their use in different scenarios

- Design experiments to test whether a putative virulence factor is indeed one