

CAMB705: Advanced Topics in Bacterial-Host Interactions

Wednesday 3:30-5pm from January 19, 2022 until March 23, 2022

Location: Johnson Pavilion room 209

Course Co-Directors:

Igor Brodsky

Associate Professor of Pathobiology

ibrodsky@vet.upenn.edu

215-746-8426 (office)

Sunny Shin

Associate Professor of Microbiology

sunshin@penntermedicine.upenn.edu

215-746-8410 (office)

Course Description: This course will delve into specific topics in general area of bacterial pathogenesis and bacteria-host interactions. We will explore key historical and current papers on topics related to bacterial invasion of and replication within host cells, bacterial interference with host cell signaling pathways, bacterial interactions with host mucosal tissues, and the role of bacterial colonization in shaping and instructing host immune responses. Each week, a student will lead the class in the discussion of a published paper on a specific topic. The format of each class will be a 10-15-minute introduction of the key background and underlying questions to be presented by a student, followed by a student-led analysis of the data presented in the research article involving participation by all members of the class. Students will be graded based on their presentation and active participation in the paper discussions. The papers listed below are recommendations. If students have alternative papers that they would like to present and discuss, please feel free to email your suggestions to Sunny and Igor.

Prerequisites: Strong background in cell biology, immunology and/or bacteriology fulfilled by 1st year CAMB courses. Course is limited to 2nd year and above doctoral students or advanced undergraduates with course director's permission.

The class will meet once per week for 1.5 hours, and will discuss 1 key papers for each topic, as well as relevant background.

Course Goals

Students who complete this course successfully will have gained:

- An in depth understanding of bacterial-host interactions
- Ability to discuss and analyze relevant primary articles in-depth

We respectfully ask that all members of our class work together to establish a supportive and inclusive environment that is welcoming for all, regardless of their race, ethnicity, gender identity, sexuality, religious beliefs, physical or mental health status, or socioeconomic status.

We would like our class to be a welcoming and safe space for everyone. We ask that everyone try their best to be respectful in their speech and actions, be considerate of others, and refrain from demeaning, discriminatory, or harassing behavior and speech.

It is also important to us that everyone who participates in this class has the resources to do so. Please let us know if you need any special accommodations in the curriculum, instruction or assessments of this course to enable you to participate fully. We will make a full effort to maintain the confidentiality of any information that you share with us.

Attendance Policy

Students are expected to attend the classes and paper discussions, as participation is an important aspect of the course. We understand that things can happen during the semester that may prevent

you from attending class. In that case, we ask that you contact us ahead of time to let us know if you are unable to attend.

Topics to be discussed:

Jan 19: General course background; introductory lecture on bacterial:host interactions

Background reading:

Falkow, S. (1988). Molecular Koch's postulates applied to microbial pathogenicity. *Reviews of Infectious Diseases*, 10 Suppl 2, S274–6.

Falkow, S. (2004). Molecular Koch's postulates applied to bacterial pathogenicity--a personal recollection 15 years later. *Nature Reviews Microbiology*, 2(1), 67–72.

Jan 26: Bacterial survival within the host cell: hijacking the host cytoskeleton

Discussion Paper:

L. monocytogenes-induced actin assembly requires the *actA* gene product, a surface protein. Kocks C, Gouin E, Tabouret M, Berche P, Ohayon H, Cossart P. *Cell*. 1992 Feb 7;68(3):521-31.

Background Paper:

Listeria monocytogenes: towards a complete picture of its physiology and pathogenesis. Radosheвич L, Cossart P. *Nat Rev Microbiol*. 2018 Jan;16(1):32-46.

Actin-based motility and cell-to-cell spread of bacterial pathogens. Lamason RL, Welch MD. *Curr Opin Microbiol*. 2017 Feb;35:48-57.

Feb 2: Bacterial secretion systems: intra-kingdom communication devices – Type III secretion

Discussion paper:

In Situ Molecular Architecture of the Salmonella Type III Secretion Machine. Hu B, Lara-Tejero M, Kong Q, Galán JE, Liu J. *Cell*. 2017 Mar 9;168(6):1065-1074.e10.

Background Paper:

Galán, J. E., & Wolf-Watz, H. (2006). Protein delivery into eukaryotic cells by type III secretion machines. *Nature*, 444(7119), 567–573.

Protein-Injection Machines in Bacteria. Galán JE, Waksman G. *Cell*. 2018 Mar 8;172(6):1306-1318. (read section pertinent to type III secretion).

Feb 9: Bacterial secretion systems: intra-kingdom communication devices – Type IV secretion

Discussion Paper:

Carey et al. (2011). The *Coxiella burnetii* Dot/Icm system delivers a unique repertoire of type IV effectors into host cells and is required for intracellular replication. *PLOS Pathogens*. May;7(5):e1002056.

Background:

Darbari and Waksman (2015). Structural Biology of Bacterial Type IV Secretion Systems. Annual Review of Biochemistry, 84:603-29.

Protein-Injection Machines in Bacteria. Galán JE, Waksman G. Cell. 2018 Mar 8;172(6):1306-1318 (read section pertinent to type IV secretion)

Feb 16: Life within the cell: Discovering the host targets of T3SS effectors

Discussion Paper:

Global Mapping of the Inc-Human Interactome Reveals that Retromer Restricts Chlamydia Infection. Mirrashidi KM, Elwell CA, Verschueren E, Johnson JR, Frando A, Von Dollen J, Rosenberg O, Gulbahce N, Jang G, Johnson T, Jäger S, Gopalakrishnan AM, Sherry J, Dunn JD, Olive A, Penn B, Shales M, Cox JS, Starnbach MN, Derre I, Valdivia R, Krogan NJ, Engel J. Cell Host Microbe. 2015 Jul 8;18(1):109-21.

Background Paper:

Chlamydia cell biology and pathogenesis. Elwell C, Mirrashidi K, Engel J. Nat Rev Microbiol. 2016 Jun;14(6):385-400.

Feb 23: Bacterial toxins and cell-surface receptors

Discussion Paper:

CCR5 is a receptor for Staphylococcus aureus leukotoxin ED. Alonzo F 3rd, Kozhaya L, Rawlings SA, Reyes-Robles T, DuMont AL, Myszka DG, Landau NR, Unutmaz D, Torres VJ. Nature. 2013 Jan 3;493(7430):51-5.

Background Papers:

The effects of Staphylococcus aureus leukotoxins on the host: cell lysis and beyond. Yoong P, Torres VJ. Curr Opin Microbiol. 2013 Feb;16(1):63-9.

Bacterial survival amidst an immune onslaught: the contribution of the Staphylococcus aureus leukotoxins. Alonzo F 3rd, Torres VJ. PLoS Pathog. 2013 Feb;9(2):e1003143

March 2: Setting up a persistent bacterial infection

Discussion Paper:

Salmonella-Driven Polarization of Granuloma Macrophages Antagonizes TNF-Mediated Pathogen Restriction during Persistent Infection. Pham THM, Brewer SM, Thurston T, Massis LM, Honeycutt J, Lugo K, Jacobson AR, Vilches-Moure JG, Hamblin M, Helaine S, Monack DM. Cell Host Microbe. 2020 Jan 8;27(1):54-67.e5.

Background Papers:

Helicobacter and salmonella persistent infection strategies. Monack DM. Cold Spring Harb Perspect Med. 2013 Dec 1;3(12):a010348. (Read the section on Salmonella)

March 9: Bacterial invasion and spread: crossing the blood-brain barrier.

Discussion Paper:

Blocking Neuronal Signaling to Immune Cells Treats Streptococcal Invasive Infection. Pinho-Ribeiro FA, Baddal B, Haarsma R, O'Seaghda M, Yang NJ, Blake KJ, Portley M, Verri WA, Dale JB, Wessels MR, Chiu IM. Cell. 2018 May 17;173(5):1083-1097.e22.

Background Papers:

Pain and immunity: implications for host defence. Baral P, Udit S, Chiu IM. Nat Rev Immunol. 2019 Jul;19(7):433-447.

March 16: Immune detection of bacterial virulence activity- Effector-triggered immunity

Discussion Paper:

Functional degradation: A mechanism of NLRP1 inflammasome activation by diverse pathogen enzymes. Sandstrom A, Mitchell PS, Goers L, Mu EW, Lesser CF, Vance RE. Science. 2019 Apr 5;364(6435).

Background Paper:

The NLRP1 inflammasome: new mechanistic insights and unresolved mysteries. Mitchell PS, Sandstrom A, Vance RE. Curr Opin Immunol. 2019 Oct;60:37-45

Effector-triggered immunity and pathogen sensing in metazoans. Lopes Fischer N, Naseer N, Shin S, Brodsky IE. Nat Microbiol. 2020 Jan;5(1):14-26

March 23: Interbacterial competition within the inflamed gut

Discussion Paper:

Microcins mediate competition among Enterobacteriaceae in the inflamed gut. Sassone-Corsi M, Nuccio SP, Liu H, Hernandez D, Vu CT, Takahashi AA, Edwards RA, Raffatellu M. Nature. 2016 Dec 8;540(7632):280-283.

Background Paper:

Control of pathogens and pathobionts by the gut microbiota. Kamada N, Chen GY, Inohara N, Núñez G. Nat Immunol. 2013 Jul;14(7):685-90.

G.I. pros: Antimicrobial defense in the gastrointestinal tract. Chung LK, Raffatellu M. Semin Cell Dev Biol. 2019 Apr;88:129-137.