

**MICROBIOLOGY AND IMMUNOLOGY 640  
MOLECULAR AND CELLULAR IMMUNOLOGY**

**Course Objective**

To provide a didactic overview of key concepts underlying innate and adaptive immune responses, and in-depth discussions of related primary literature.

**Class Hours and Location**

5623 Med. Sci. II  
Monday and Wednesday 10-11:30 AM

**Contact Information for Instructors**

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**Office Hours**

Instructor Offices, Friday 1:30-2:30 PM

**Resources**

Class materials are posted at [ctools.umich.edu](https://ctools.umich.edu) (and follow the link to canvas in the top right panel) or use <https://umich.instructure.com/>  
Login in at with your unique name and password  
Find the MICROBIOLOGY 640 001 F16 site  
Click on left panels (Files) to Download relevant files

**Class Textbook**

Janeway's Immunobiology, 9<sup>th</sup> Edition

**Exams**

All exams will be in an open book format. Lecture notes and papers can be accessed on computers (internet access will not be allowed).  
Each section will constitute 33% of the final score, including assignments (for lectures and paper discussions) and exam.  
All students will be required to participate in paper discussions in class. Paper discussion-based assignments will each count towards 10% of the total score.  
Academic honesty will be handled strictly according to University and Rackham policies  
[http://www.rackham.umich.edu/policies/academic\\_and\\_professional\\_integrity/](http://www.rackham.umich.edu/policies/academic_and_professional_integrity/)

## **DR. RAGHAVAN, UNITS 1-10**

### **1. Basic concepts in immunology 9/7/16**

Overview of the immune system  
Janeway's Immunobiology, pages 1-24 and 32-35

## **ANTIGEN RECOGNITION**

### **2. Innate pattern recognition 9/12/16**

Molecular recognition by innate vs. adaptive responses  
Pattern Recognition Receptors  
Induced innate responses to infections  
Janeway's Immunobiology pages 77-81, 87-107 and 111-113

### **3. Paper discussion on innate pattern recognition 9/14/16**

Review article:  
The cell biology of inflammasomes: Mechanisms of inflammasome activation and regulation.  
Sharma D Kanneganti TD J Cell Biol. 2016 Jun 20;213(6):617-29. doi: 10.1083/jcb.201602089.

Paper for Discussion:

Hexokinase Is an Innate Immune Receptor for the Detection of Bacterial Peptidoglycan. Wolf  
AJ, Reyes CN, Liang W, Becker C, Shimada K, Wheeler ML, Cho HC, Popescu NI, Coggeshall  
KM, Arditi M, Underhill DM. Cell. 2016 Jul 28;166(3):624-36. doi: 10.1016/j.cell.2016.05.076.

### **4. Diversity in the immune response 9/19/16**

Antibody and T cell receptor structures  
Mechanism of V(D)J joining and generation of diversity  
Janeway's Immunobiology, pages 139-147, 152-154 and 173-190

### **5 and 6) Specificity in the immune response and Intracellular surveillance 9/21/16-9/26/16**

#### **Specificity in the immune response**

MHC restriction of antigen recognition by T cells  
MHC polymorphisms  
Transplant rejection  
Janeway's Immunobiology, pages 155-166, 231-240

#### **Intracellular surveillance**

Antigen Processing and Presentation I and II  
Non-classical antigen presentation  
Janeway's Immunobiology, pages 213-231, 243-251

**7: Paper discussion on mutated epitope presentation in cancers and their use in immunotherapy 9/28/16**

Review article: Mutanome directed cancer immunotherapy.  
Vormehr M, Diken M, Boegel S, Kreiter S, Türeci Ö, Sahin U.  
Curr Opin Immunol. 2016 Apr;39:14-22. doi: 10.1016/j.coi.2015.12.001.

Paper for Discussion:

Predicting immunogenic tumour mutations by combining mass spectrometry and exome sequencing. Yadav M, Jhunjhunwala S, Phung QT, Lupardus P, Tanguay J, Bumbaca S, Franci C, Cheung TK, Fritsche J, Weinschenk T, Modrusan Z, Mellman I, Lill JR, Delamarre L. Nature. 2014 Nov 27;515(7528):572-6. doi: 10.1038/nature14001.

**8: Recognition of pathogen-specific metabolites, and Induced-self and missing-self recognition 10/3/16**

NK activation, NK receptors  
Janeway's Immunobiology, pages 127-131 and lecture notes

**9: Review session for Antigen Recognition section 10/5/16**

**10/10/16 Exam 1**

**DR. CHANG, UNITS 10-17**

**CELLULAR IMMUNITY**

**10: T cell activation, differentiation and memory 10/12/16**

T cell /APC trafficking into lymphoid tissue  
Activation/differentiation of naïve cells by pathogen-activated dendritic cells  
Antigen receptor signaling following priming  
Janeway's Immunobiology: pages 265-287, 347-379

**Fall Study Break**

**11: Generation and function of effector T cells: cytokines and cytotoxicity 10/19/16**

Type and function of effector T cells  
Molecular mechanisms responsible for effector cell generation  
Janeway's Immunobiology: 380-392, 447-471,

**12: Paper discussion (Regulation of CD8 T cell fate by differential signaling) 10/24/16**

Asymmetric inheritance of mTORC1 kinase activity during division dictates CD8(+) T cell differentiation. Pollizzi KN et al. Nat Immunol. 2016 Jun;17(6):704-11.

**13. T cell selection: Self-Recognition and Tolerance 10/26/16**

T cell development in the thymus

Positive and negative selection of T cells  
Janeway's Immunobiology: 152-166, 187-191, 214-249, 315-336,

**14. Paper discussion (Treg development by commensal microbe) (10/31/16)**

Paper for Discussion:

Individual intestinal symbionts induce a distinct population of ROR $\gamma$ <sup>+</sup> regulatory T cells.  
Sefik E et al., Science. 2015 Aug 28;349(6251):993-7.

**15. Lecture on factors regulating T-cell mediated immunity 11/2/16**

**16. Paper discussion (Tumor immunity regulated by cell metabolism) (11/7/16)**

Paper for Discussion:

Metabolic Competition in the Tumor Microenvironment Is a Driver of Cancer Progression. Chang CH et al. Cell. 2015 Sep 10;162(6):1229-41.

**17. Review session for T-cell mediated immunity (11/9/16)**

**Exam 2 11/14/16**

**DR. GRIGOROVA, UNITS 18-24**

**HUMORAL IMMUNITY**

**GENERATION AND CONTROL OF HUMORAL IMMUNITY**

**18. B cell development and central tolerance 11/16/16**

Introduction to humoral responses (overview of B cell signaling, development, differentiation, T-dependent and T-independent responses, diversification of antibody responses: somatic hypermutation and class-switch recombination)

B cell development

Janeway's Immunobiology: 13-14, 173-186, 191-198, 279-282, 295-314, 364-365, 399-401, 419-422

**19. Cellular Cooperation: anatomy of B cell response 11/21/16**

Secondary Lymphoid Organs and their functions

Cognate interactions between B and T helper cells

Germinal centers and affinity maturation

Plasma cells and memory responses

Janeway's Immunobiology, pages 17-24, 347-351, 401-413, 418-419, 473-477, 493-501, 505-514

**Thanksgiving break**

**20. Paper discussion 11/28/16**

**B cell competition for T follicular helper (Tfh) cells in Germinal Centers**

1) Review paper to read:

Carola G. Vinuesa and Jason G. Cyster. How T cells earn the follicular rite of passage.  
*Immunity*. 2011. 35:671-680

- 2) Article to be discussed in the class:  
Victoria GD et al. Germinal center dynamics revealed by multiphoton microscopy with a photoactivatable fluorescent reporter. *Cell* 143:592-605

### **21. Paper discussion 11/30/16**

#### **Neutralizing antibodies and B cell memory**

- 1) Review paper to read:  
Lambert PH et. al. Can successful vaccines teach us how to induce efficient protective immune responses? *Nat Med.* 2005 Apr;11(4 Suppl):S54-62.
- 2) Article to be discussed in the class:  
Wrarmert et al. Rapid cloning of high-affinity human monoclonal antibodies against influenza virus *Nature* 453: 667-671 (2008)

### **22. Paper discussion 12/5/16**

#### **Peripheral B cell tolerance.** Review paper to read:

- 1) Yu D, Vinuesa CG. Multiple checkpoints keep follicular T cells under control to prevent autoimmunity. *Cell Mol Immunol.* 2010. 7(3):198-203
- 2) Article to be discussed in the class:  
Chan TD et al. Elimination of germinal-center-derived self-reactive B cells is governed by the location and concentration of self-antigen. *Immunity* 37(5): 893-904 (2012)

### **SPECIALIZATION OF THE ANTIBODY RESPONSES**

### **23. Antibody diversification and effector functions 12/7/16**

Secondary diversification of antibody response and class-switch recombination

Distribution and functions of immunoglobulin classes

Fc receptors and destruction of antibody-coated pathogens

Janeway's Immunobiology, pages 27-28, 413-417, 422-439

### **24. OVERALL CLASS REVIEW 12/12/16**

### **Exam 3: 12/14/16**