Instructor: Michael Lynes, Ph.D. phone: 486-4350 Office: BSP 308 michael.lynes@uconn.edu
Class meetings T, Th BSP 131 (2-3:15 pm)
Teaching Assistant: Greg Marusov; Gregory.marusov@uconn.edu, 486-3648
Office hours: No scheduled hours. I am in my office by about 8AM, and usually stay until about 6.
Drop by my office, phone, or email to make an appointment.
course website: http://lynes.mcb.uconn.edu/classes.shtml

Guest Lecturers
Dr. William Fodor, MCB
Dr. Andrea Hubbard, Pharmacy
Dr. Lawrence Silbart, Animal Sciences

Recommended approach to studying this material:
1. skim assigned chapter before class, look at figures in chapter
2. take notes in class; copy notes over that night after class to ensure you understand what you wrote.
   If you have trouble taking good notes, consider bringing a tape recorder to supplement your notes.
3. following class, read assigned chapter for comprehension (don’t fall behind!)
4. be certain to read primary literature assignments before the assigned date! We discuss these papers in class.

Administrative notes:
1. please turn off your cell phone before class, do not bring cell phones, blackberry devices, or pagers to the examinations (you may leave your bookbags with these inactivated items in the front of the classroom if necessary).
2. exam seating will be designated at the beginning of each examination.

Grades
Examinations will focus on material presented in class, and from the supplemental assigned readings.
The final grade calculation will be made based on two hour exams (30% each), and the final examination grade (40%).

Statement on Academic Integrity
“A fundamental tenet of all educational institutions is academic honesty; academic work depends upon respect for and acknowledgement of the research and ideas of others. Misrepresenting someone else's work as ones own is a serious offense in any academic setting and it will not be condoned. Academic misconduct includes, but is not limited to, providing or receiving assistance in a manner not authorized by the instructor in the creation of work to be submitted for academic evaluation (e.g. papers, projects, and examinations); any attempt to influence improperly (e.g. bribery, threats) any member of the faculty, staff, or administration of the University in any matter pertaining to academics or research; presenting, as one's own, the ideas or words of another for academic evaluation; doing unauthorized academic work for which another person will receive credit or be evaluated; and presenting the same or substantially the same papers or projects in two or more courses without the explicit permission of the instructors involved. A student who knowingly assists another student in committing an act of academic misconduct shall be equally accountable for the violation, and shall be subject to the sanctions and other remedies described in The Student Code.”
(taken from the UCONN student handbook: http://www.dosa.uconn.edu)

Primary literature readings: see the MCB 211 website, or upload from the e-journal site at the UCONN library website

Semester Schedule

<table>
<thead>
<tr>
<th>Date</th>
<th>Topic</th>
<th>Readings</th>
<th>Lecturer</th>
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<tbody>
<tr>
<td>8/30</td>
<td>Introduction, overview of course</td>
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<td>Lynes</td>
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<td></td>
<td>A. Organization of the course</td>
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<tr>
<td></td>
<td>1. content: lecture with associated primary literature readings</td>
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<td>(references are noted in outline)</td>
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<td>2. additional resource materials: assigned text readings/note additional textbook features, websites</td>
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<td>3. course format: lectures and discussions during class: feel free to ask questions in class; you may tape the lectures if you wish.</td>
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<td></td>
<td>B. Historical roots of the study of Immunology</td>
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<td></td>
<td>1. Immunology is a relatively young science</td>
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<td></td>
<td>a. 1798 Jenner: cowpox immunization</td>
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<td>b. 1891 Koch: DTH vs tuberculin Ag</td>
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<td>c. 1895 Bordet: C' + Ab + bacteria = lysis</td>
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<td>d. 1901 Landsteiner: ABO blood groups</td>
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<td>e. 1914 Little: genetic theory of tumor transplantation</td>
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<td>f. 1936 Gorer: identification of MHC antigens</td>
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<td>g. 1939 Kabat and Tselius: Antibodies as gamma globulins</td>
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<td>C. Overview of immunological system activation</td>
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<td></td>
<td>1. Signal molecule • receptor molecule • information processing•</td>
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<td>tolerance or response</td>
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<td>2. signal molecule = antigen; smallest unit that is recognized as non-self</td>
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<td>3. Characteristics of the immune response</td>
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<td>a. specificity</td>
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<td>b. memory</td>
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<td>D. Current trends in immunological research</td>
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<td>1. manipulation of the response to disease</td>
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<td>a. AIDS</td>
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<td>b. cancer</td>
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<td>c. autoimmunity</td>
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<td>d. tissue transplantation</td>
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<td>2. antibodies as enzymes</td>
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<td>3. antibodies as probes of biochemical/cellular structure</td>
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<td>4. psychoneuroimmunology</td>
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<td>5. cytokine immunotherapies</td>
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<td>6. xenogeneic transplants of humanized tissues</td>
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<td>E. Lynes laboratory research interests</td>
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<td>1. mechanisms of immunotoxicity(role of metallothionein</td>
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<td>2. automated measurements of chemotaxis</td>
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<td>3. GCSPR protein microarray platform applications</td>
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</table>
a. use of the GCSPR platform for immune function characterization in 1G and microgravity
b. GCSPR pathogen biosensor
c. Cytometer on a chip

9/1 Basic components of the Immune Response

A. Cells
   1. hematopoiesis
      a. lymphoid lineage
      b. other cells (erythroid and myeloid lineages)
   2. structure/function of cells
   3. organization of cells into tissues
   4. lymphocyte traffic
B. Soluble components of the immune system
   1. antibodies (structure/function)
   2. complement (structure/function)
   3. cytokines (structure/function)

9/6 The experimental system

A. The experimental animal
   1. phylogenetic studies
   2. commonly used mammalian systems
      a. mouse: mendelian inheritance and breeding manipulations
      b. other mammalian animal systems
   3. man
B. Artificial systems
   1. culture techniques: in vitro
   2. immunologically compromised animals (will discuss more fully on 11/27)
      a. immunological mutants
      b. radiation induced immunodeficiency
   3. transgenic animals

9/8 Antigenicity and Immunogenicity

A. Antigenicity vs. immunogenicity
B. Fundamental characteristics of antigens
C. Prototypical antigens
   1. mitogens as polyclonal activators
   2. T-dependent and T-independent antigens
   3. the MHC as an antigenic system

9/13 Antibodies: structure and function

A. Immunoglobulin structure
   1. subunit structure
   2. heavy and light chains
   3. Fc, Fab, and F(ab’)2
B. Antigenic determinants of immunoglobulins
   1. isotypes and subclasses
   2. idiotypes
   3. allotypes
C. Functions associated with antibody fragments
9/15 Antibody/antigen Interactions
A. Antibody-antigen binding
   1. parameters of binding
   2. structural contributions to binding
B. Assays of antibody binding
   1. Precipitation
   2. Agglutination
   3. Radioimmunoassay
   4. ELISA
   5. Fluorescent immunoassay/ Flow cytometry
   6. Western immunoblot analysis
   7. Immunohistochemistry/Immunoelectronmicroscopy
C. Monoclonal antibodies

9/20 Antibody/antigen Interactions (continued)

9/22 Sources of antibody diversity
A. Genetics of antibody synthesis (the B cell receptor)
B. Gene generation of antibody diversity
   1. germline vs. somatic mutation
      associational, junctional and combinatorial diversity

*****sample questions for the first examination will be handed out today in class*****

9/27 Major Histocompatibility Complex (MHC)
A. Discovery as a transplantation antigen, and genetics
B. Cellular expression/tissue distribution
C. Contribution to cellular recognition (genetic restriction)
D. Structure/function

9/29 •••••••• FIRST EXAM ••••••••••••••• will cover material through 9/23•••••••••••••••

10/4 Cell biology of the MHC/protein biology of the MHC; antigen processing and presentation
A. Mechanisms of antigen association with MHC molecules
   1. endocytic pathway (exogenous antigen)
   2. cytosolic pathway (endogenous antigen)
B. Interactions of antigen/MHC with the T cell antigen receptor

10/6 T cell/antigen interactions
A. structure of the TcR
B. genetics of TcR
C. Other molecular components of the TcR
D. Signal transduction following TcR engagement

10/11 Consequences of TcR engagement
A. T cell populations in the thymus and periphery
B. T cell maturation
C. Mechanisms of T cell activation
D. Products of T cell activation (see soluble mediators)
10/13 Cell mediated immunity (CMI)
   A. Cytotoxicity
   B. Delayed type hypersensitivity
   C. Immunological protection conferred by CMI

10/18 Soluble mediators of immunity
   A. Cytokines and lymphokines: structure and function
   B. Lymphokine receptors
   C. Complement

10/20 Humoral immunity
   A. Characteristics of humoral immune response
   B. Cells participating in humoral immune response
   C. Steps in B cell activation
   D. Affinity maturation and class switching

10/25 Immune responses to infections agents
   A. Viral
   B. Bacterial
   C. Protozoan
   D. Invertebrate parasites

10/27 Manipulation of the Immune Response
   A. Vaccines (live/attenuated/killed; protein;DNA)
   B. Drugs
   C. Irradiation
   Inappropriate immune responses
   A. hypersensitivities

11/1 Inappropriate immune reactions:
   A. Autoimmune disease
      1. Animal models
         2. Human diseases and treatment

11/3 Inappropriate immune reactions (autoimmunity, continued)

11/8 ··············· EXAM ··············· will focus on material from 9/27 through 11/3, and will depend on material from the first section of the course. Note that you are responsible for material in the required readings that are available from the reserve desk at the library, and as electronic documents.

11/10 Immunodeficiencies
   A. Animal models for congenital syndromes
      1. nude
      2. SCID
      3. beige
   B. Human congenital immunodeficiencies

11/15 Immunodeficiencies (continued)
   A. Acquired causes of immunodeficiencies
      1. Environmental
      2. Drug induced
      3. Viral
B. AIDS
   1. Etiology/viral replication cycle
   2. symptoms/immune effects
   3. epidemiology
   4. current and future therapies

Primary Literature Reference #4

11/17 AIDS (continued)

11/20-11/26 No class; Thanksgiving recess!

11/29 The immune response to cancer
   Immunobiology, C14 section 13-17
   Lynes
   A. Mechanisms of carcinogenesis
   B. Natural immune responses to neoplasia
   C. Immunological diagnosis of neoplastic disease
      1. tumor antigens
   D. Immunotherapies for neoplasia
      1. “magic bullets”: immune conjugates
         a. antibody/drug conjugates
         b. antibody/radionuclide conjugates
      2. anti-idiotypic antibodies
      3. irradiation and transplantation to reconstitute immunity
      4. TILs, LAKs
      5. Gene therapies

Primary Literature Reference #5

12/1 The immune response to cancer (continued)
   Lynes

12/6 Transplantation Biology
   Immunobiology, C13 sections 31-39
   Lynes
   A. Immunological mechanisms of histo-incompatibility
      Primary Literature Reference #6
   B. Manipulation of histoincompatibility
      1. General
      2. Specific
   C. Clinical value of transplantation

12/8 Overview and final comments
   Lynes

12/12-12/17 EXAM PERIOD; the date for the MCB 211 final exam to be announced

••••••••• the final exam will emphasize material from 11/10 through 12/8, and will cover
material from the entire course. Note that you are responsible for material in the required
reserve readings•••••••••

Required additional reading (primary references 1-6) from the scientific literature will be
posted on the MCB 211 website as pdfs

1. Kohler, G. and Milstein, C., Continuous cultures of fused cells secreting antibody of predefined
2. Davis, B.S., Chang, G.J., Cropp, B., Roehrig, J.T., Martin, D.A., Mitchell, C.J., Bowen, R., and
   Bunning, M.L., West Nile virus recombinant DNA vaccine protects mouse and horse from virus
   challenge and expresses in vitro a noninfectious recombinant antigen that can be used in enzyme-linked


BIBLIOGRAPHY

Required Textbook


Textbook website


Required additional reading from the scientific literature:

   http://jvi.asm.org/cgi/content/full/75/18/8752?view=full&pmid=11507220
   http://www.bloodjournal.org/cgi/content/abstract/98/8/2526
   http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6VJ0-42M793FDD&_user=669286&_handle=B-WA-A-A-EWY-MsSAYWA-UUW-AUECWBWWVVAUEWYABUVV-CDAZEBVZZ-EWYU&fmt=full&_coverDate=03%2F31%2F2001&_rdoc=348&_orig=browse&_srch=%23toc%236080%23232001%2323999669998%2323238189!&&cdi=6080&view=c&acct=C000036298&version=1&urlVersion=0&userid=669286&md5=70d12e41d850cda0a2e8e65145a42a90

Some website addresses of interest to immunologists:

Immunology techniques, biological materials, and instrumentation websites
1. http://flowcyt.cyto.purdue.edu/flowcyt/societes/index.htm {a list of worldwide flow cytometry associations}
3. http://www.bdfabs.com/home.htm {a home page for a flow cytometer manufacturer}
4. http://www.atcc.org/ {a homepage for the American Type Culture Collection; a source of cell lines and genetic resources}
5. http://www.jax.org {a resource of inbred mouse strains, transgenic and knockout mice}
7. http://flowcyt.cyto.purdue.edu/flowcyt/supplier/reagents.htm {a webpage listing of antibodies and other reagent suppliers}

**Immunology databases**
2. http://www.blacksci.co.uk/products/journals/jnltitle.htm {an HIV database hosted by Roche pharmaceutical}
2. http://cancernet.nci.nih.gov/ord/diseases.html {the office of rare diseases at NIH; for autoimmune diseases like Lupus, arthritis}

**Genome databases**
1. http://www.informatics.jax.org/userdocs/overview.shtml {mouse genome information}

**Scientific journal websites**
1. http://www.cell.com/ {the journal Cell}
3. http://www.jimmunol.org/ {The Journal of Immunology}
5. http://www.blacksci.co.uk/products/journals/jnltitle.htm {a host of journals from this publisher, including Immunology and Immunology and Cell Biology}

**Scientific funding websites**
1. gopher://gopher.nih.gov:70/77/gopherlib/indices/crisp/index? {a site from which to search for currently funded NIH grants}
2. http://www.nih.gov/grants/oer.htm {the National Institutes of Health website}

**Scientific document search engines**

**Scientific reagent and instrumentation companies:**
1. http://www.pharmingen.com/ {a supplier of monoclonal antibodies to human, mouse antigens; also a subsidiary of Becton Dickinson, a flow cytometry company}