Exam III Review Material:

Previous material that you should review:
1. Overview of the inflammatory response, e.g. activation and timeline.
2. Complement system.
3. Role of organ systems in the immune response (e.g. high conc T/B, cell migration to/from lymph nodes.
4. Antibody structure, e.g. comparison to TCR structure.
5. Activation of B and T-cells via MHC-TCR interactions – importance of diversity levels and specificity.
6. Important steps in B-cell development pre/post activation (checkpoints, affinity maturation, class switching)

Review Questions from Previous Exams:
- Exam III 2015: 6, 7, 8, 9, 10, 12, 13, 14, 15, 16, 18, 19, 21, 22, 23
- Exam III 2014: 3, 4, 5, 9, 10, 11, 17, 18, 19
- Exam II 2015: 3, 4, 5, 6, 7, 8, 12, 13, 19, 22, 24

New Topics for Exam III: Lectures 18 (antibody/antigen) - Lecture 27 (Infectious disease II)

A. Antibody-Antigen Interactions:
- Difference between how haptens and protein antigens interact with antibodies.

B. Antibody Technology:
- Polyclonal versus monoclonal antibodies
- What are hybridomas and how are they generated.
- What are some uses of antibodies (e.g. drug detoxification), catalytic antibodies
- How are antibodies/antigens detected (e.g. Precipitation, agglutination, ELISA, ELISPOT radioimmunoassay, Western)

FACS: How does a FACS machine work? Could you design an experiment to separate cell populations?
SPR: How does it work, and how could you use it to measure binding affinity.

Antibody Engineering: BiTE antibodies, generation of scFv.

C. TCR-MHC-Peptide Structure:
- β-chain on TCR = heavy chain on antibody.
- α-chain on TCR = light chain on antibody
  i) Overall structure similar to F_{aB} fragment, but membrane bound.
  ii) CDRs on TCR recognize both conserved and polymorphic residues on MHC and specific residues on peptide.
  iii) Direct binding experiments of altered peptides to MHC.
  iv) Use of transgenic mice to generate homogeneous receptors (B or T). Example was the determination of which chain of TCR contacted which region of peptide – MCC peptide.

D. T cell Development:
  i) Location of steps (thymus), experimental evidence (SCID/nude mouse), development affected by pathogens.
  ii) Order: β-chain, CD4/CD8, α-chain, positive selection (MHC), negative selection (self), CD4 or CD8 loss, (controlled by transcription factors).
  iv) Role of Fezf2 and Aire in expression of proteome on mTEC (Medullary thymic epithelial cells) for elimination of self-reactive T-cells: i) direct interaction, ii) transfer to thymic DC, iii) mosaic mTEC.
  v) General experimental approaches to show TCR is specific for self MHC and foreign peptides, e.g. the use of transgenic mice to produce cell populations with homogeneous T-cell receptors.
  Transplantation of bone marrow from a-b haplotype to inbred strains.
  v) You should be able to compare and contrast B-cell development and T-cell development, how are they the same (e.g. allelic exclusion of heavy/β-chain, negative selection for self), how are they different (CD4/CD8 expression, positive selection for MHC, VJ joining on β, N-base addition for α-chain).
T-Cell Subsets:
   i) Compare and contrast $T_{H1}$, $T_{H2}$, $T_{H17}$, $T_{Reg}$ in terms of overall function.
   ii) Cytokine selection of T-cell developmental pathway (IL-12, IL-4)
   iii) Cytokines produced by T-subsets and the role of cytokines in their function.

E. T-Cell Activation: Review B-cell activation – same steps. New features specific to T-cells:
   • Production of $\alpha$-chain (CD25) to make high affinity receptor ($\beta\gamma$ low affinity)
   • B7-CTLA-4 interaction to turn off activation process
   • Migration of activated T-cells to site of infection
   • Generation of T-memory cells.

F. Tolerance:
   Central Tolerance:
   o B- and T-cell development.
   o clonal deletion and anergy, role of AIRE transcription factor in T-cell tolerance.
   o Receptor editing (try new $V_L$ chains in Ig, new $\alpha$-chain in TCR).
   Peripheral Tolerance: (no activation of B and T-cells leads to tolerance.)
   o Anergy induced by non-activated B and T-cells.
   o Apoptosis of T-cells by Fas-FasL interactions.
   o $T_{reg}$ cells – e.g. B7-CTLA4 interaction, suppressive cytokines.

G. Vaccines
   Immunity; general concepts related to vaccination
   • Innate versus Acquired
   • Acquired: Passive versus Active
   The differences, pros and cons between passive and active vaccination approaches
   • maternally-transmitted immunity
   • antibodies generated in non-human hosts;
   • memory and recall immunity in active vaccination
   Active vaccines, how they are made; pros and cons of each type of vaccine approach below
   • live pathogens
   • live attenuated pathogens
   • killed pathogens (Polio as an example to compare pro/con between killed/attenuated pathogen in the type of immune response triggered (types of antibodies produced, risks to the person)
   • toxoids
   • subunit vaccines, polysaccharide vaccines
   • genetically-engineered subunit vaccines
   Why the whole pathogen stimulates a better and more comprehensive immune response and memory compared to subunits of a pathogen
   Lifetime protection versus transient protection; need for boosters/adjuvants
   Population effects; why vaccinate? - The Herd Effect

H. Transplantation:
   1. Blood group antigens: ABO.
   2. Reactions to transplant:
      i) GVHD – immune cells from the donor tissue attack the host tissue.
      ii) Hyperacute, occurs when blood types are not matched, rapid (2-4 d) type II hypersensitivity reaction. Blood group antigens develop due to cross reactivity to bacterial cell surface carbohydrates.
      iii) Acute – Type IV hypersensitivity.
         • Donor MHC II –peptide mimics self (recipient) MHC + foreign peptide.
         • Causes development of $T_{H0}$ to $T_{H1}$ cells that are sensitized to the donor MHC.
         • $T_{H1}$ cells migrate to transplant, secrete INF-gamma
         • Macrophages are attracted to transplant, and destroy it.
3. Detection of Rejection by MRI
   - Advantages: Rapid, non-destructive, and whole organ can be characterized.
   - Methods: Label macrophages (or T-cells) with contrast agent (USPIO) and look for accumulation of macrophages in transplant.

4. Immunosuppressive therapy.

5. Detection of histocompatibility.
   - HLA typing – Should know how it works and that it is limited to only detecting a subset of alleles.
   - Mixed lymphocyte assay – Should know how it works and why it is better than HLA typing.

I. Infectious Diseases:
   i) Immune response to extra-cellular and intra-cellular bacteria, viruses.
   ii) Antigenic shift, definitions and examples - e.g. bacteria pili, pandemic flu
   iii) Antigenic drift, definitions and examples – e.g. HIV, seasonal flu
   iv) Pathogen evasion/invasion mechanisms: pili for attachment, degradation of IgA, complement inactivation, intracellular growth, multiple serotypes, latent viruses, interference with presentation of viral antigens on class I and class II MHC.
   v) Immunology of Dengue fever, antibody-enhanced infection.