PCB 3233
Exam 3 Study Guide

Chapter 5

1. BCRs are created in bone marrow, undergo somatic recombination, and migrate to secondary lymphoid tissue. TCRs mature in the thymus and also undergo somatic recombination.
2. An immunoglobulin consists of a heavy chain (variable and 3 or 4 constant domains) and a light chain (either kappa or lambda). A TCR consists of an alpha and a beta chain, each with 1 variable domain and 1 constant domain.
3. A TCR will recognize antigen peptide together with a MHC molecule. A BCR will recognize a specific antigen without it being presented by another cell. A BCR will recognize lipids, carbohydrates, and proteins, whereas TCRs will only recognize protein.
4. A TCR will have 2 epsilon, 1 gamma and 1 delta chain (CD3 complex) along with 2 zeta chains. All of these are used for intracellular signaling to the nucleus. Lack of functional delta and epsilon chains results in immunodeficiency.
5. The function of a TCR is to recognize peptide being presented to it on a MHC molecule, and then secrete cytotoxins to induce apoptosis or cytokines to activate a macrophage or B cell.
6. The CD3 complex consists of 2 epsilon chains, 1 gamma chain, and 1 delta chain. These proteins are used for intracellular signaling.
7. The TCR FAB is composed of the variable regions of the alpha and beta chain each with 3 CDRs, so one TCR has 6 CDRs. TCR diversity is dependent on variable region gene rearrangement and junctional diversity. Most variability is clustered into the CDR regions, and more specifically the CDR 3 region. After activation, T cell does not undergo somatic hypermutation or isotype switching.
8. Severe combined immunodeficiency syndrome: one of the RAG genes is not functional, so no functional T or B cells, infant usually dies very early on. Omenn syndrome is due to a RAG protein with partial enzymatic activity, causes red rash on shoulders and face. Bare lymphocyte syndrome is due to a non-functional TAP protein, so no MHC I is present on surface of cells, which results in poor responses to viruses. Heterozygosity of the HLA class 1 and 2 loci results in HIV taking a longer time to progress to AIDS.
9. The delta gene segment is located in between V and J regions of the alpha chain. If the V and J regions are rearranged, the delta gene segment is cut out. The gamma gene segment is located on chromosome 7. The delta and gamma chains have fewer V segments, but the delta chain makes up for this by rearranging up to 2 D gene segments (which results in more junctional diversity as well). Typically delta-gamma TCRs have much less diversity, but have potential for more.
10. Delta-gamma TCRs (1-5% of all TCRs) do not need antigen presented to them by MHC molecules, the delta chain can rearrange two D segments, and they can be dominant in the epithelial tissue.

11. MHC class 1 molecules present intracellular peptide, whereas MHC class 2 presents extracellular peptide. Class 1 molecules present to CD8 cytotoxic cells, and class 2 molecules present to TH1 and TH2 cells. Nearly every nucleated cell expresses MHC 1 molecules, but MHC class 2 are mainly expressed by dendritic cells, macrophages, and B cells (sometimes thymic epithelial cells.) MHC class II molecules can be produced by other cell types on exposure to the cytokine interferon-γ.
12. MHC class 1 consists of 3 alpha domains and beta 2 microglobulin (not encoded by MHC genes). Alpha 1 and 2 form the binding site, and alpha 3 and beta 2 microglobulin form the supporting structure. MHC class 2 consists of an alpha chain and a beta chain. Alpha 1 and Beta 1 form the binding site, and Alpha 2 and Beta 2 form the supporting structure. Supporting structure proteins also form binding sites for the CD4 and CD8 co-receptors (alpha 3 on MHC 1 and beta 2 on MHC 2).
13. MHC class 1 molecules can bind peptides 8-10 amino acids long which are pinned down at the ends of the structure. MHC class 2 can bind peptides 13-25 amino acids long because peptides are pinned along the groove of the binding site and extend through the ends of the binding site.
14. MHC molecules bind peptide non-covalently. In MHC class 2, peptide may extend to outside of the groove. The binding groove is made up of 8 antiparallel beta sheets and 2 antiparallel alpha helices. The peptide lies between the 2 alpha helices and parallel to them.
15. The promiscuity of MHC molecules allows for 1 MHC molecule to bind to up to 10,000 different antigens.
16. Intracellular pathogens are broken down and presented on MHC class 1 molecules to CD8 T cells. Extracellular pathogens are endocytosed, degraded, and presented on MHC class 2 molecules to either TH1 T cells which activate macrophages or TH2 T cells which activate B cells.
17. See # 16
18. Cytotoxic T cells leave the secondary lymphoid tissue and migrate to site of infection.
19. MHC class 1: proteasome breaks down peptide, TAP 1 and 2 transports peptide into endoplasmic reticulum, Calnexin (Calcium dependent) stabilizes MHC class 1 until B2 microglobulin is made, calreticulin and tapasin position MHC and helps load the peptide. Once a peptide is loaded, the molecule is exported to the cell surface. MHC class 2: peptide vesicles travel inwards, acidification of vesicles by a proton pump to make the enzymes functional, fuses with lysosomes to form phagolysosomes which degrade peptide, peptides bind to MHC class 2 which are exported to the cell surface.
20. Proteasome: degrades peptide for MHC class 1; TAP 1 and 2: transport peptides into the ER via hydrolysis of ATP; Calnexin: calcium dependent chaperone that stabilizes MHC 1 until B2 microglobulin is made; Invariant chain: blocks peptides from binding to MHC 2 in ER, and delivers class II molecules to endocytic vesicles (called MHC class II compartments or MIIC); HLA-DM: catalyzes the release of CLIP; CLIP: small fragment of the invariant chain left to block peptide binding; Chaperone molecules: proteins that assist

in correct folding of proteins and assembly of other proteins, protection until they enter their respective cellular pathways and to carry out their intended functions

21. MHC genetic complex: MHC class 1 and 2 are closely linked, highly polymorphic, alleles are co expressed, B2 microglobulin and invariant chain not encoded here, HLA-A, B, and C have many different allotypes and present to CD8 cells, HLA – P, Q, and R present to CD4 cells, HLA – E and G present to NK cells, 2 HLA – DR-B alleles can be inherited. MHC gene region 3 doesn't encode for MHC molecules but for other immune functions.
22. MHC class 1 and 2 get diversity through polymorphism. The greatest diversities among the MHC molecules is in the beta sheets and alpha helices of the binding groove. In a HLA class 2 DR molecule, alpha chain is monomorphic.
23. Polymorphism among MHC molecules is the reason for graft rejection.
24. HLA A, B, and C present to CD8 T cells and form ligands for NK cells.
25. HLA DP, DQ, and DR present to CD4 T cells.
26. Class 2 region: genes encoding alpha and beta regions of the 5 isotypes of HLA type 2 molecules, 2 polypeptides of TAP, genes for tapasin, genes encoding proteasome (LMP2 and LMP7). Invariant chain and B2 microglobulin not encoded here.
27. B2 microglobulin encoded on chromosome 15 and invariant chain encoded on chromosome 5.
28. MHC restriction refers to TCRs recognizing both the peptide and MHC molecule, if one of these is changed, a TCR will most likely not recognize it anymore. This refers to T cells.
29. MHC polymorphism is the reason for MHC diversity. No 2 people will have the same MHC molecules because there are so many different allotypes. This is the reason for alloreactions and implant rejections. The different MHC molecules are alloantigens and the antibodies created in response are alloantibodies.
30. MHC genes are expressed co-dominantly. You can express HLA-DRB1 and potentially another one (HLA-DRB 3 4 or 5)
31. TH1 activates macrophages and goes to the site of infection, TH2 activates B cells and stays in the secondary lymphoid tissue.

Chapter 6

32. Pre-B cell receptor includes the mu heavy chain and Ig-alpha and Ig-beta and the surrogate light chain and leads to intracellular signals that halt rearrangement at heavy chain locus = allelic exclusion and stops RAG and tags RAG 2 for destruction. Surrogate light chain consists of a V pre B region and lambda 5 region.
33. Stromal cells provide specialize environment for B cells at various stages at maturation. Stem cells and early pro-B use VLA-4 to bind to VCAM-1 and interactions of other CAMS promote binding of Kit on the B cell to stromal cell which activates B cell to proliferate. IL-7 stimulates the growth and