Chapter 6: Antibody Interactions

- **Antibody-antigen interactions depends on 4 non covalent forces**
  - hydrogen bonding
  - ionic bonding
  - hydrophobic interactions
    - water forces hydrophobic groups together
  - van der Waals interactions
    - electron clouds of two or more atoms interact
- **Cross-Reactivity**: occurs if two different antigens share same/similar epitope
- observed among polysaccharide antigens that contains similar oligosaccharide residues
  - Blood types
    - ex: ABO blood-group antigens are glycolipids expressed on rbc
    - blood type (A, B, AB, O) is equivalent to the type of antigens on an individual's red blood cells
    - the antibodies they have will be for the antigen they DON'T have (ex: Type A person will have anti-B antibodies) which is why they cannot take blood that is a different type
      - antibodies will precipitate out of rbc if given wrong type
    - Type AB has antigens A and B, so they do not have any antibodies (universal acceptor)
    - Type 0 has neither antigen A nor B, so they have both anti-A/anti-B antibodies (universal donor)

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- **Surface plasmon resonance (SPR) - measure rate of antibody-antigen binding = antibody's affinity**
  - sensitive, convenient, rapid way to measure antibody affinity
  - detects changes in reflective properties of surface of an antigen-coated sensor when it binds to antibody
  - beam of polarized light is directed through prism onto thin gold oil coated with antigen on opposite side
  - light is reflected off the gold film toward light-collecting sensor
  - some light will be absorbed by the gold (light energy transformed to waves)
  - dip in light intensity measured at resonant angle: will depend on several factors which SPR takes advantage of

    - binds to MHC I or II on dendritic cell causes choosing
  - **Stochastic Model**
    - random
- evidence for both models…**.likely that there is a blend of the two**

- once a functional T-cell receptor has bound to antigen, T-cell starts to alter gene expression
  - **immediate genes**: transcription factors that are turned on right away, cell starts making many different proteins
  - **early genes:** half hour-hour, cyclin (cell cycle protein) IL-2/IL-2 receptor
  - **late genes:** up to a day, cytokines
- all happens through T-cell receptor

- MHC + T-cell receptor
  - transmembrane domain (usually 10 C in phospholipids-will cluster together), but **T-cell receptor has longer than average ones**
    - lipid raft (long chain/congregation of phospholipids) —> *Lipid rafts is a blanket term used to describe distinct areas in the plasma membrane rich in certain lipids and proteins and which are thought to perform diverse functions.*
    - adhesion molecules begin to bind to hold T-cell receptor and MHC in place
  - T cells begin to cluster toward lipid raft…get island of T-cell receptors: **immunological synapse** … all start signaling at same time (reason why immediate genes turn on immediately)
  - P56-lock tyrosine kinase, adds phosphates to tyrosine residues in ITAMS
    - allows ZAP-70 to come and bind by creating docking site
    - once ZAP-70 activated, activates SLP-76, **PLC all go to plasma membrane to look for PIP 2**
      - **PLC cuts PIP2 into IP3 and DAG**
    - **GEF** turns on Ras kinase—-**MAPK/ERK pathway*** *chain of proteins in the cell that communicates a signal from a receptor on the surface of the cell to the DNA in the nucleus of the cell*
- cell needs signal 2 (co-stimulatory signal), cell otherwise won't fully activate
  - provided by antigen-presenting cell
  - **B7 is expressed on outside of antigen-presenting cells**
    - **has to interact with CD28** POSITIVE SIGNAL TO FULLY ACTIVATE T-CELL RECEPTOR (checkpoint…cell becomes anergic if doesn't happen)
- CTLA-4 does OPPOSITE…tells T-cell to stop (the "brakes")*
  - immediate expressed once CD28 and B7 interacts
- certain cells express B7 all the time, others only when induced

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- things happen to test tolerance (look for rearrangements that cause antibodies to bind to non-self peptides)
- 5 million B-cells/day leaving bone marrow
- Antigen-Independent Phase (maturation) in bone marrow
  - memory B-cells*
  - Antigen-Dependent phase follows in lymphatic vesicles
- STEPS
  - pro B-cells, don't express antibodies
    - outside of cells are simple
    - while maturing, rely on intimate contact with bone marrow stromal cells (create environment for pro B-cells to survive, provide with signals that tell them to do things)
      - **cannot mature to Pre B-cell without bone marrow stromal cells**
      - VLA-4 on Pro B-cell binds to VCAM-1 on stromal cell
      - ^promotes binding of c-Kit on Pro B-cell to SCF on stromal cell
      - ^triggers tyrosine kinase activity of c-Kit = differentiation of Pro B-cell to Pre B-cell
      - stromal cells begin to express IL-7 (must receive signals from IL-7 to continue) which binds to IL-7 receptors on B-cell; tells B-cell to downgrade expression
        - **down regulation occurs, but IL-7 is necessary for Pre B-cells to survive**
  - Pro B-cell
    - produce/insert into plasma membrane an **Ig alpha/Ig beta**
  - Pre B-cell
    - begin to express pre B-cell receptor
    - RAG-1/-2 for recombination, necessary for heavy and light chain rearrangement (expressed during pro-B and pre-B stages)
    - TdT turned off (which stops addition of nucleotides) to stop diversity from occurring, create same Vpre-B cells …. made heavy chain that can properly recognize
    - hypothesized that there is a **ligand that binds to Vpre-B**
      - **make surrogate light chains** (membrane M chain is associated with surrogate light chain to form light-chain-like structure)
        - pre-B-cell receptor
      - then stop making light chain, choose kappa or lambda
  - Immature B-cells—> Naive B-cells ("naive" means they have not encountered antigen)
    - kappa/lambda
    - fully mature and function IgM antibody

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