Lecture 10 Introduction to Antibody Structure

- **Epitope**: Region on antigen that binds to the antibody.
- **Antigen**: Molecule/structure that is recognized by antibody.
- **Immunogen**: Antigen that evokes an immune response.

**B-cell Epitopes**: Membrane bound (and soluble) antibodies produced by B-cells are capable of recognizing a broad array of antigens. In general, B-cell epitopes must be exposed on the surface of the pathogen, such that they can interact with the antibody component of the B-cell receptor. The list of possible antigens, in the order of frequency of occurrence, is:
- Proteins
- Carbohydrates
- Haptens
- Lipids
- Nucleic acids

**Structure of Antibodies**: Antibodies, when found as membrane bound proteins as part of the B-cell receptor are referred to as **immunoglobulins**. Soluble antibodies are secreted by plasma cells. Immunoglobulin and antibody are often used interchangeably.

**Quaternary Structure**:
- 2 *Identical* Light Chains: $\lambda$ domain (~110 residues), Constant Domain, $\kappa$ (~110 residues).
  - Two forms of light chains, $\lambda$ (lambda) and $\kappa$ (kappa).
- 2 *Identical* Heavy Chains: IgG: $V_H$, constant domains $C_{H1}, C_{H2}, C_{H3}$.
- 5 different heavy chains classes (isotypes), each with a different biological function.
- All isotypes can be found as membrane or soluble. **Membrane bound** forms contain a transmembrane segment followed by a very short cytosolic segment.
- $V$ domains pair in heavy and light chains, as do $C_{\lambda}$ and $C_{H1}$.
- $C_{\lambda}$ and $C_{H1}$ linked by disulfide bond
- Variable region recognizes antigen, largely through hypervariable loops. (also called CDR, complementary determining regions). 3/chain.
- Constant region of heavy chain in Ab has effecter, or Biological Effect depends on type of heavy chain.
Quaternary structure:
- 2 Light + 2 heavy chains.
- Light chains are identical on any given Ab. There are two possible types of light chains, kappa and lambda.
- Heavy chains are identical on any given Ab. There are four major classes of heavy chain, IgM, IgG, IgE, IgA, each with a specific biological function, e.g., killing of pathogens.
- The first 110 residues in each chain are highly variable. The variable region of both heavy and light are responsible for binding antigen. The sequence of these differ from one antibody to the next, depending on the specificity.
- Two binding sites/molecule.
- Chains held together by disulfide bonds and non-covalent forces.

Primary structure.
- V-region, ~110 amino acids, different sequence between antibodies with different specificities.
  - Anti-flu: 1 QLYLQCPYVSSLGPRQNYTISGCGSHH+SN1GQRIAVVHPQCQPARKLLIHTDQFSGGV 59 (residue #)
  - Anti-ebola: 1 Q2ALQPSPSGGITVSCG76GIDN+SN1GQRIAVVHPQCQPARKLLIHTDQFSGGV 60 (residue #)
  - Anti-flu: 60 SDRFSGSGSAGLEALISIQLGSQEDAPYUCAHQQNSQITSGCG76GIDN+SN1GQRIAVVHPQCQPARKLLIHTDQFSGGV
  - Anti-ebola: 61 SDRFSGSGSAGLTDQSIQLEADAHYPCBYYTSGCG76GIDN+SN1GQRIAVVHPQCQPARKLLIHTDQFSGGV
- Hypervariable regions. 3 per V region, highly different sequences between antibodies with different specificities. The hypervariable loops are also called complementary determining regions (CDRs).
- Constant region - conserved sequence on all antibodies. 110 residues on L-chain, 330 residues on H-chain.

Super-Secondary Structure: Antibodies consists of linked domains, called Ig folds or Ig motifs. These are two beta-sheets held together by disulfide bonds.

Antibody Fragments:
- **F_{ab}** Fragment = light chain + ½ of heavy chain. Binds one antigen.
- **F_{v}** Fragment Variable regions from the heavy and light chain. The F_{v} domain is the smallest unit that can bind antigen.
- **F_{c}** Fragment = 2^{nd} part of heavy chains.
Isotypes of Antibodies:
- Five different heavy chain genes: γ, α, μ, δ, ε.
- Class of an immunoglobulin is defined by its type of heavy chain: IgG(γ), IgA(α), IgM(μ), IgD(δ), IgE(ε). These are termed isotypes.
- IgM is the initial isotype produced by B-cells.
- IgA is secreted as a dimer, IgM is produced as a pentamer.
- These may be found as soluble or membrane bound (BCR)
- All forms found in the BCR will be monomeric.

Lambda Light Chain Sequences:

Antibody A  QSVLTQFPSSSPHSGPQVTISGSGNV 61
Antibody B  QSALTQPASVSPGQTSGTSGS 62

A 62 SDRFSGSKSGTASLIGQDEADYYCWTTLGQKAAFSV 119
B 63 SNRFSGSNSATSLLTSGQLAEDARYYYCYTTTS-DTWPTGQKELVGQKAAFSV 119

Heavy Chain Sequences:

Antibody A  LVALRCLVQCC2V-LQVGGGVQFGSSRLQSCVTSQFTSFGGIDVRQRPGKGEWVAY 59
Antibody B  LVALRCLVQCC2V-LQVGGGVQFGSSRLQSCVTSQFTSFGGIDVRQRPGKGEWVAY 59

60 LSDGZNIN--YADSVKGRFTTVSRDTSKNTLSLAMNSLRLLEDATAVYCARQPRYFGDSGY 117
60 IEKSKKGYATIFRAVKSFGIRSSDSKNTALFQMDSLRDPDSTALYCTPEV-----E 114

118 YIDYVGQCGP 128
+ WG+GTL 115
125 SLRGCRCGL 125