Lecture 10: Immunoglobulin Structure and Function

Assigned reading in Campbell**: Chapter 14.5**

Key Terms:

- Hapten
- Epitope
- Antigen
- B cells/T cells
- Quaternary Structure: 2L+2H
- Immunoglobulin fold/disulfide bond
- Fab fragment/Fv fragment
- Hypervariable region/Complementary determining region (CDR)

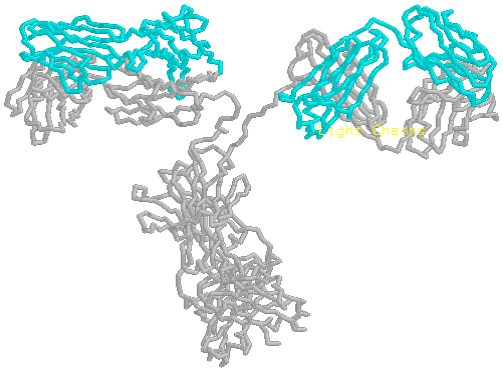
Overview of the Immune System

Three key terms

High diversity

High Specificity

Exclusion of Self



Some terms:

Antigen: Foreign material that is recognized by the immune system, it is usually a protein, but it can be a peptide, or carbohydrate.

Epitope: Region of a protein antigen to which the antibody binds.

Hapten: A small chemical that is an antigen.

2. Cellular immunity

We won't be concerned with cellular aspects of immunology in this course. However, you should be aware of the fact that B-cells produce immunoglobulins (antibodies) and that T-cells aid in the rejection of foreign material that is identified by antibodies (see 14.5). The HIV virus infects and kills T-cells, greatly reducing the ability to produce antibodies.

3. Antibody Structure:

3.1 Quaternary structure (2 Light + 2 Heavy chains). The two heavy and light chains are held together by non-covalent forces and covalent (disulfide) bonds. The light chain consists of two immunoglobulin folds and the heavy chain contains four of these domains: The overall shape is that of a 'Y'. Two antigen binding sites/antibody.

3.2 The Immunoglobulin fold is an example of a protein domain or a motif. It contains 7 □-strands that form a two sheet sandwich with 4 stands on one side and 3 on the other. A buried disulfide bond crosslinks the two faces.

3.3 Disulfide bonds covalently join the heavy and light chains, conferring stability on this secreted protein (Some antibodies are even secreted outside the body!)

3.4 CDR (hypervariable) regions The first immunoglobulin domain of the heavy and light chain contains three special

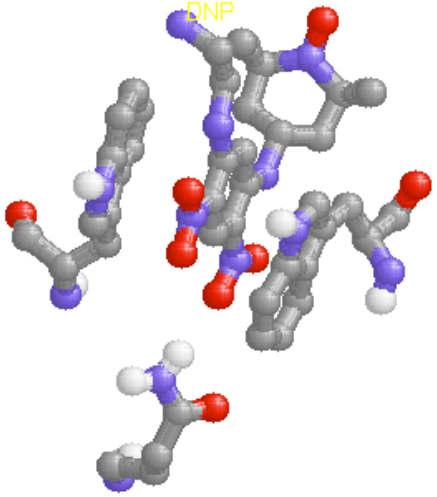
segments of primary sequence that vary in their primary sequence from one antibody to the next.

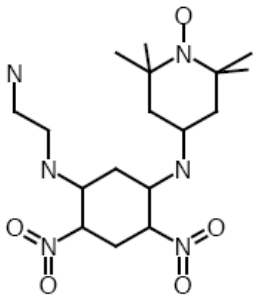
3.5 In the folded form of the antibody the three hypervariable regions of each chain come together in space to form the binding site for foreign material.

4. Antibody Fragments: Cleavage of the antibody at the junction between the antigen binding region produces two Fab fragments and one Fc fragment. The Fab fragments retain specific binding of antigen. Fab fragments can be further reduced to Fv fragments, consisting of the 1st immunoglobulin fold from the heavy and light chain. The Fv domain is the smallest unit that can bind antigen.

5 Antibody-hapten Interactions:

Specific interactions between Ab and DNP
This structure is an example of how an antibody binds a small chemical. Note the deep binding pocket.
In general, interactions between the antibody and haptens can include which of the following energetic terms?





- Hydrophobic effect
- van der Waals,
- hydrogen bonding
- electrostatic interactions.

6. Antibody-antigen Interactions:

Anti-lysozyme antibody
This structure is an example of how an antibody binds another protein. Note that the interaction surface is large and relatively flat. The **epitope** is the region on the surface of a protein that is recognized by the antibody. The interactions between an antibody and another protein can utilize *all* of the interactions we have seen in protein folding (as well as in antibody-hapten interactions)

7. Practical Uses of Immunoglobulins:

a. Fluorescence tagging (to label various components in the cell)
b. Purification of materials (More on this later)
c. Immunotherapy (see Campbell)
d. Novel chemical reactions (Some antibodies can actually perform chemical reactions)
e. Drug detoxification, see Chime page on Antibodies and Angel dust (PCP)