

# Immunology and Virology (Bio 440) #6: Antibody Structure and Diversity

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## ***Terms you should know:***

antigen receptor (BCR)	isotypes	V(D)J recombinase
antibody	heavy chain ( $\alpha$ , $\delta$ , $\epsilon$ , $\gamma$ , $\mu$ )	combinatorial diversity
immunoglobulin (A, D, E, G, M)	light chain ( $\kappa$ , $\lambda$ )	junctional diversity
variable, constant regions	affinity, avidity	exonuclease
Fab, Fc domains	cross-reaction	TdT
hypervariable regions (CDRs)	somatic recombination	P-nucleotides

## ***Guide questions to help you prepare for lecture:***

1. What is the general function of an antigen receptor? For a B cell, what kind of molecule serves as the antigen receptor?
2. How many total polypeptides make up an antibody protein (of the IgG type)? How many *different* polypeptides make up an antibody protein?
3. Sketch the basic structure of an antibody molecule and identify: heavy chains, light chains, constant region, variable region, Fab domain, Fc domain, antigen binding sites.
4. How many “immunoglobulin fold” structures are there in an IgG antibody?
5. What is the hypervariable region of an antibody molecule?
6. What is the basic function of the variable region of an antibody? What is the basic function of the constant region?
7. How are the different immunoglobulin isotypes different from each other?
8. Why can the total strength of an antibody binding to an antigen be greater than the affinity of an antigen-binding site for its epitope?
9. How many different types (that is, specificities) of antibody can an individual B cell make?
10. An individual human needs to be able to make perhaps  $10^5$ – $10^6$  different types (specificities) of antibody protein. But there are only about 30,000 genes in the entire human genome. How is this diversity possible?
11. Show how somatic recombination occurs in a developing B cell and explain the ways in which diversity is introduced during the generation of its heavy- and light-chain genes.

## Problem Solving: Antibody Structure and Diversity

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1. By treating antibodies with mild reducing agents, disulfide bonds can be broken and the heavy chain can be separated from the light chain (leaving the disulfide bonds in the immunoglobulin folds intact). Or, by treating with a mild protease, the Fab portion can be separated from the Fc portion. Fill in the chart below, using a + or – in each cell to indicate what properties each of these parts of an antibody would have.

Property	Whole IgG	H chain only	L chain only	Fab only	Fc only
binds Fc receptor on macrophage	+				
binds complement	+				
has variable domain	+				
binds antigen	+				

2. In light-chain rearrangement, the V(D)J recombinase can join a V segment directly to a J segment. In heavy-chain rearrangement, the same V(D)J recombinase is used. However, in heavy-chain rearrangement, V is always joined to D, never directly to J. Suggest a simple mechanism for regulating this process so that the correct rearrangement occurs. Your mechanism should not require any additional proteins, just the V(D)J recombinase and DNA.