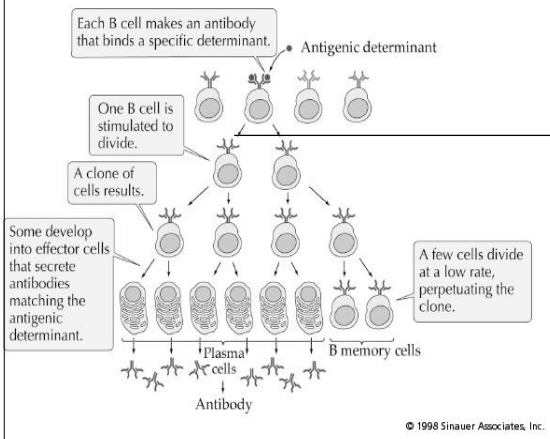
CLONAL SELECTION of B LYMPHOCYTES

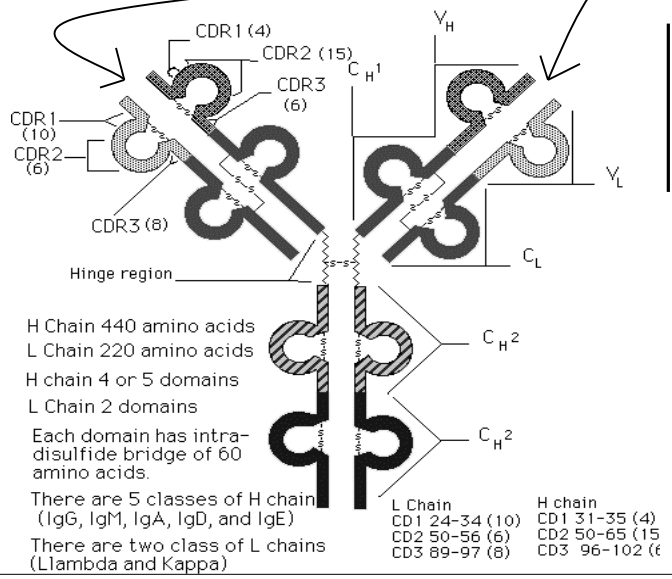
(Also true for T Lymphocytes)



1. **A vast repertoire of clones (~10^8) is generated in the absence of antigen.**
2. **Each clone has a unique recognition specificity conferred by its surface receptor (Ig for B cells; TCR for T cells).**
3. **Antigen binding SELECTS a clone whose receptor binds it.**
4. **Proliferation and differentiation of the clone follows antigen selection.**

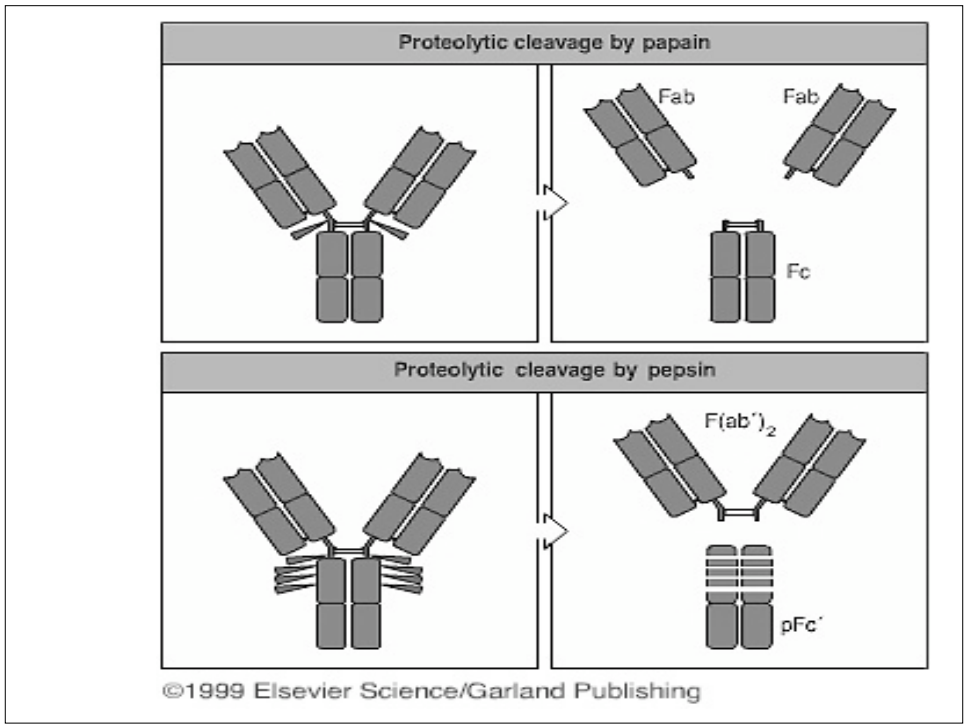
Immunoglobulin:

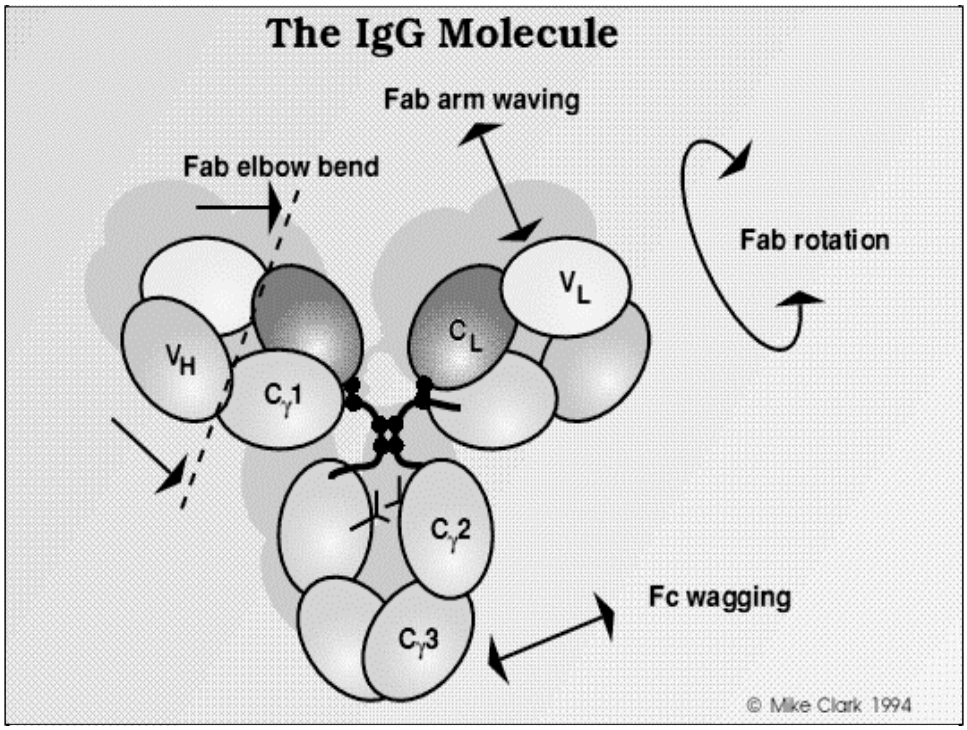
STRUCTURE AND FUNCTION



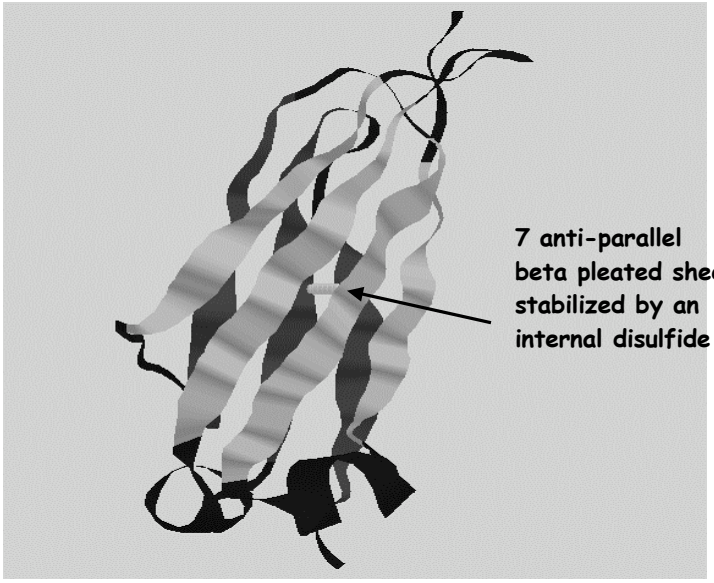
Antigen Recognition

Antigen Elimination

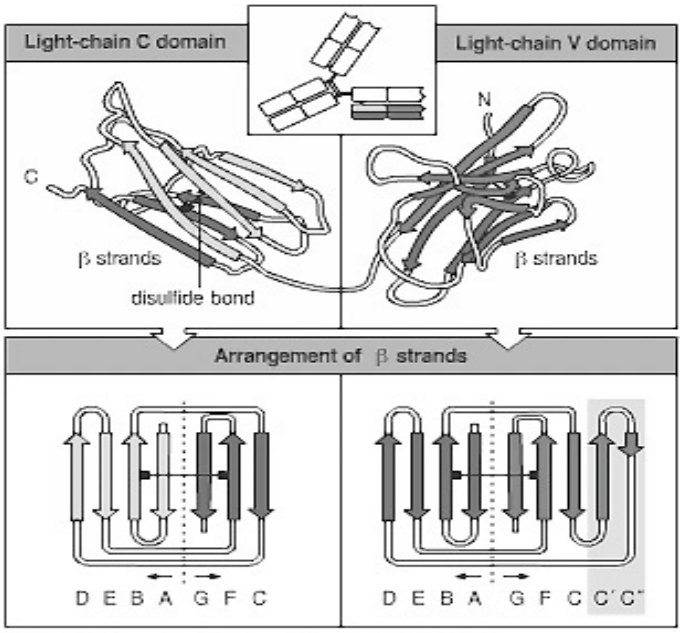

Proteolytic cleavage by papain
Fab
Fab
Fc
Proteolytic cleavage by pepsin
F(ab')2
pFc'
©1999 Elsevier Science/Garland Publishing

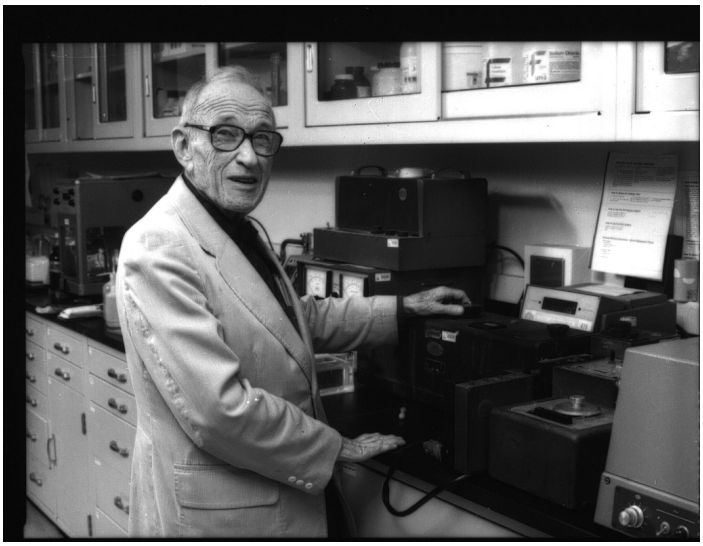

The IgG Molecule
Fab arm waving
Fab elbow bend
Fab rotation
VL
CL
VH
Cγ1
Cγ2
Cγ3
Fc wagging
© Mike Clark 1994

Ig CONSTANT DOMAIN



Ig VARIABLE DOMAIN

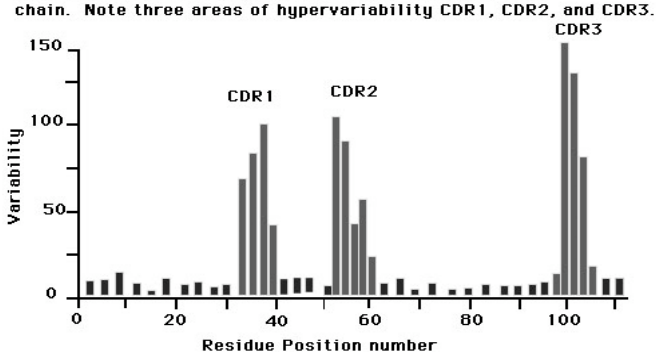




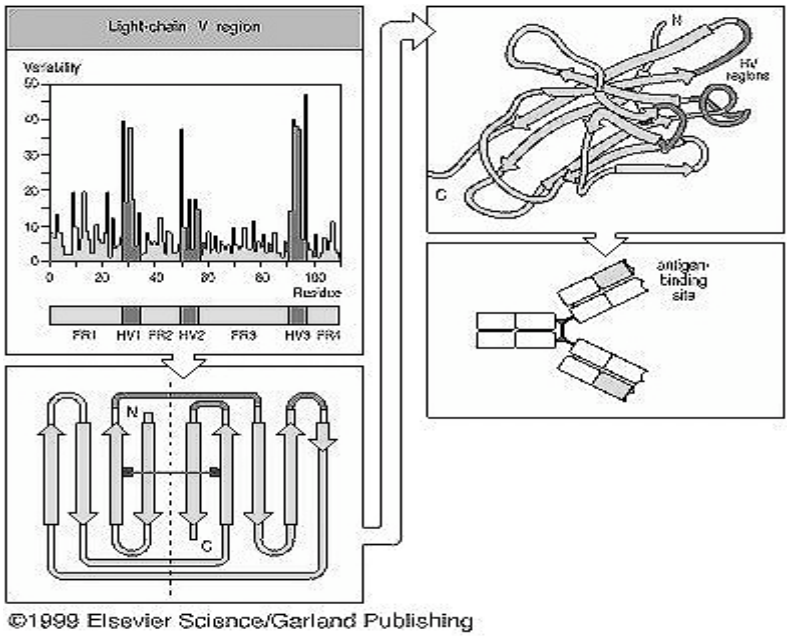
Dr. Elvin Kabat, Columbia University

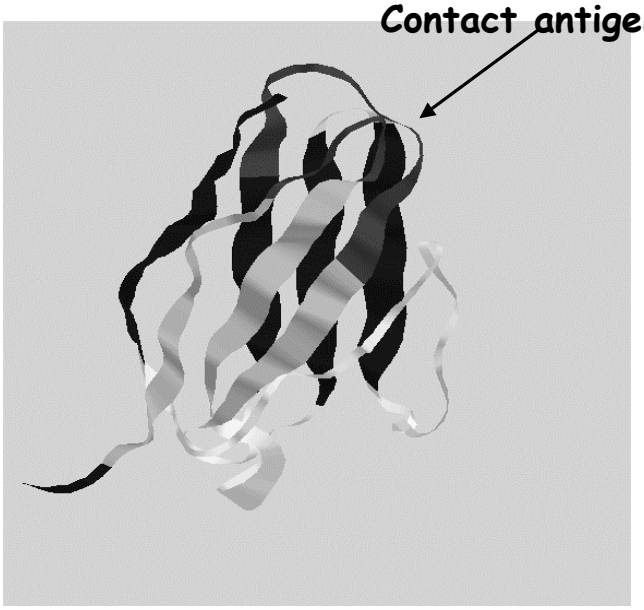
Hypervariable (HV) or Complementarity Determining Regions (CDRs)

Degree of variability in V regions of the H chains.
The degree of variability, at each different position, is graphically represented for the entire V region of Ig H chain. Note three areas of hypervariability CDR1, CDR2, and CDR3.

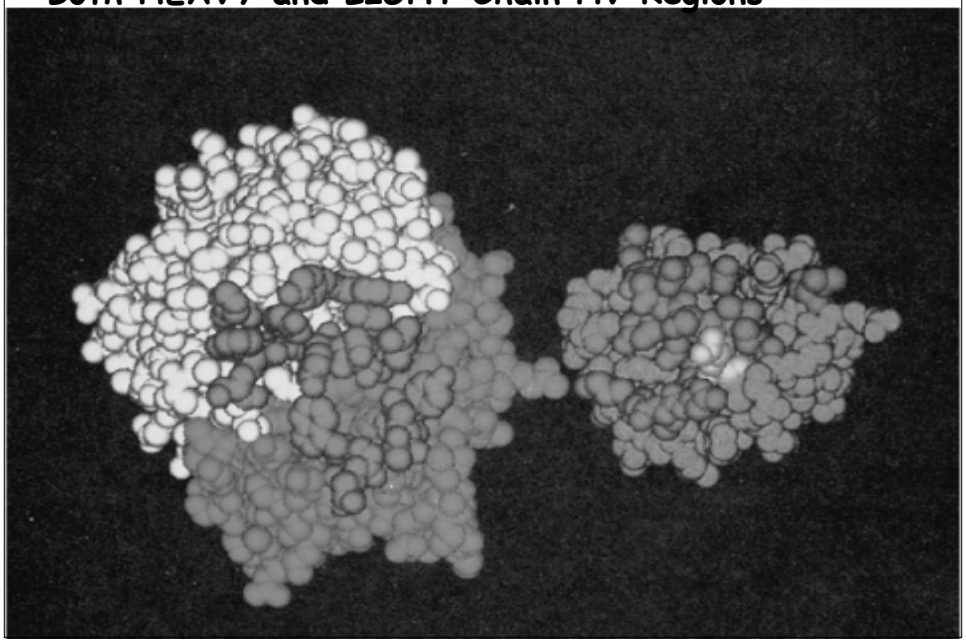


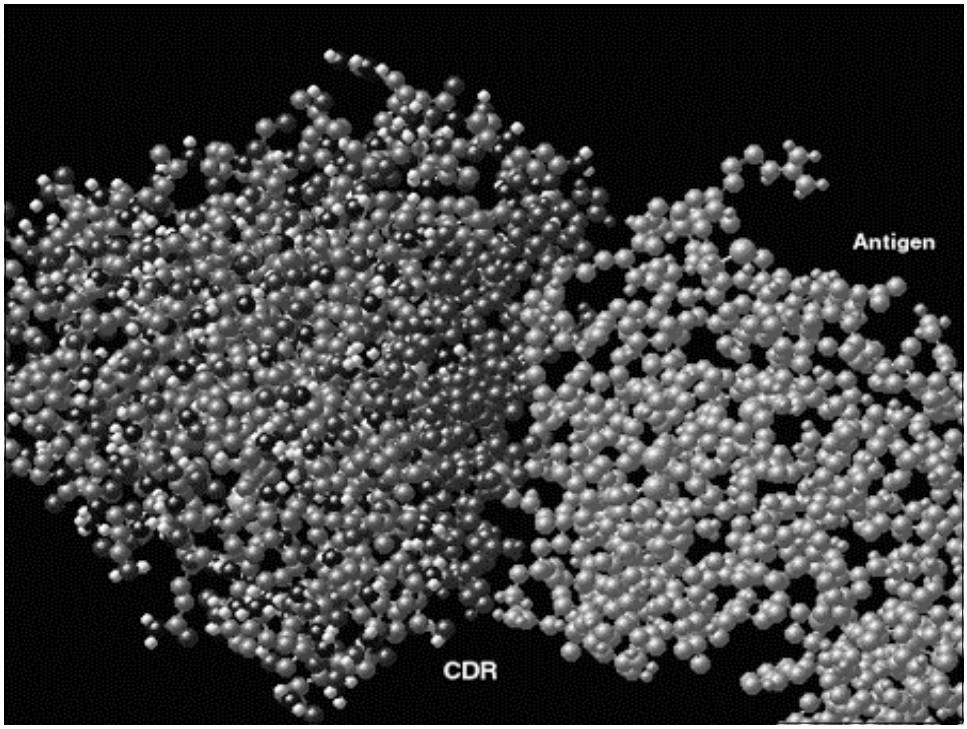
Complementarity-determining Regions (CDR)

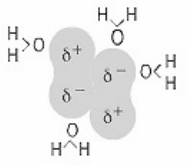


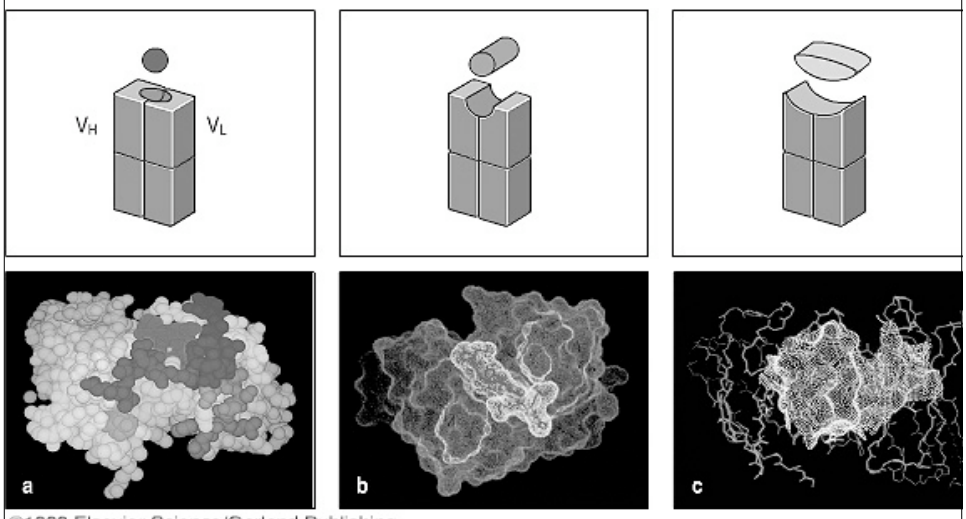


Antigen Binding Site Is Formed by a Combination of Both HEAVY and LIGHT Chain HV Regions

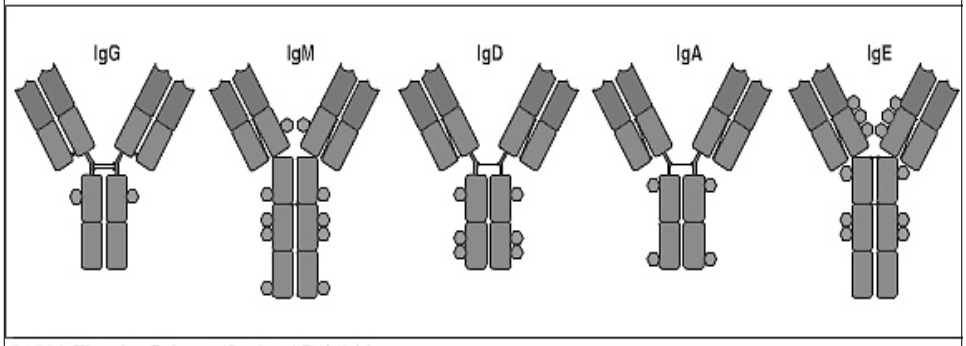




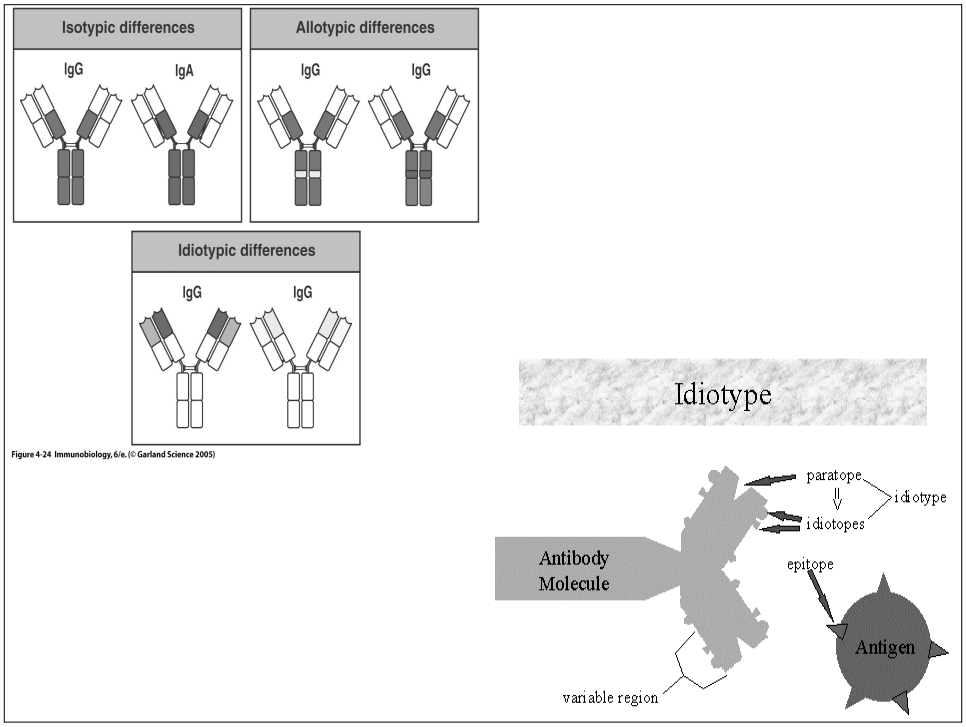
Non-covalent forces	Origin	
Electrostatic forces	Attraction between opposite charges	$-\overset{\oplus}{N}H_3 \quad \overset{\ominus}{O}OC-$
Hydrogen bonds	Hydrogen shared between electronegative atoms (N,O)	$>N-H\cdots O=C<$ (δ^- δ^+ δ^-)
Van der Waals forces	Fluctuations in electron clouds around molecules oppositely polarize neighboring atoms	δ^+ δ^- ⇄ δ^- δ^+
Hydrophobic forces	Hydrophobic groups interact unfavorably with water and tend to pack together to exclude water molecules. The attraction also involves van der Waals forces	



Five Classes (or Isotypes) of Antibodies Are Determined by Different Heavy Chain Constant Regions

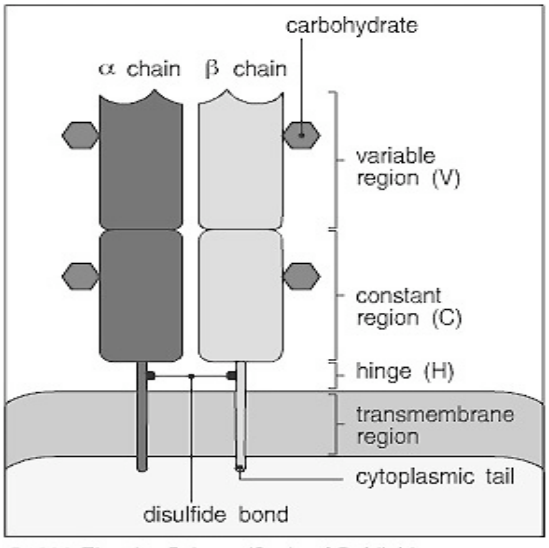


Ig isotypes have different antigen elimination properties.



T Cell Receptors Have ONLY ONE Function

Antigen Recognition



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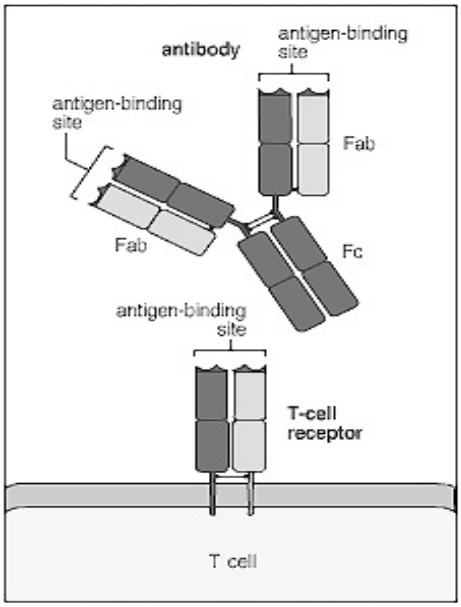
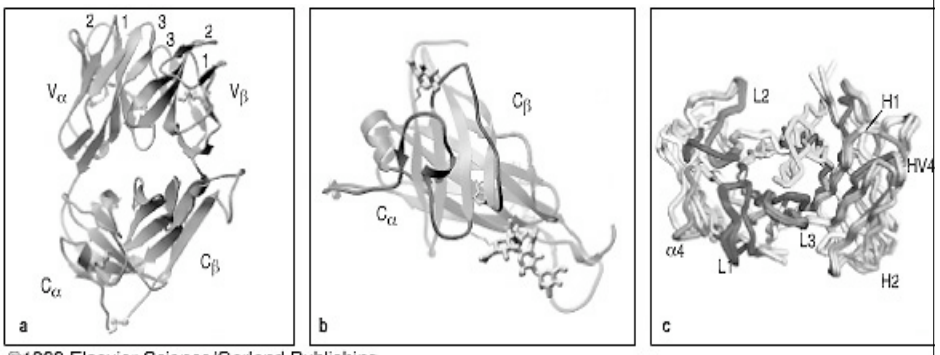
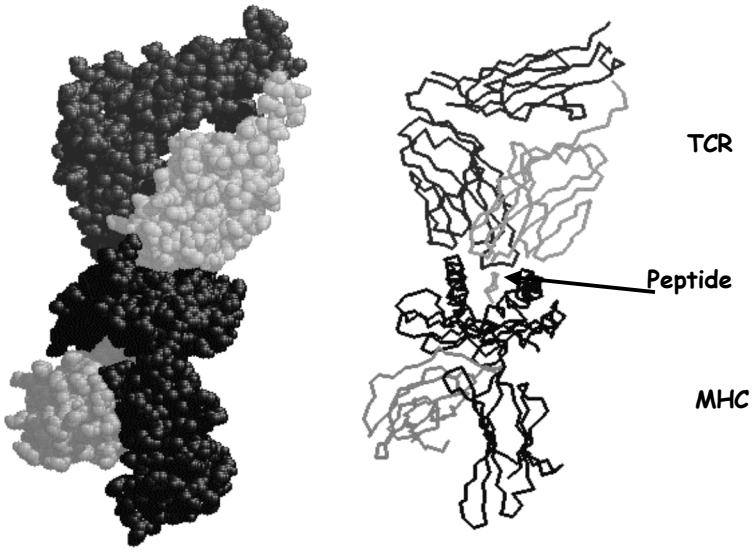
Antibodies:
Secreted or
Transmembrane

TCR: Transmembrane

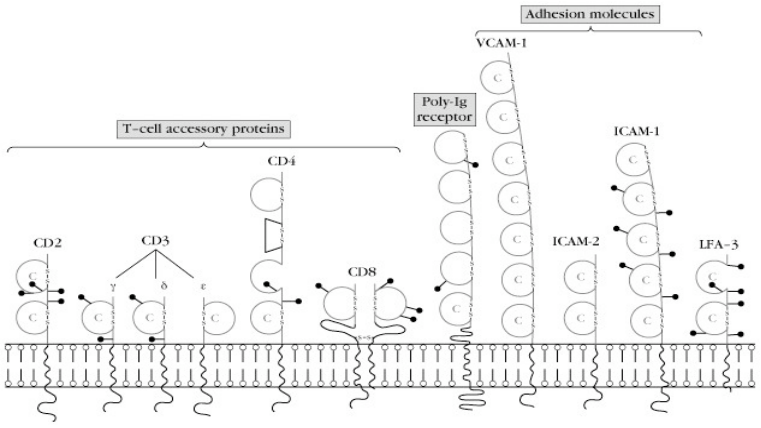




TCRs Recognize Peptides Associated with MHC Molecules on the Surface of Antigen Presenting Cells

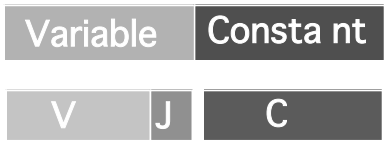


Evolutionary Conservation of Ig Domains: The Ig Supergene Family of Surface Proteins



Ig Polypeptides Are Encoded by Multiple Gene Segments

LIGHT CHAIN



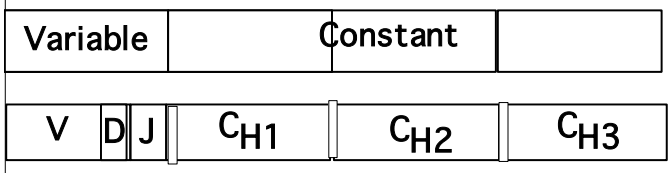
Light Chain POLYPEPTIDE

Polypeptide

Gene Segments

Light Chain GENE SEGMENTS

HEAVY CHAIN



H.C. POLYPEPTIDE

Polypeptide

Gene Segments

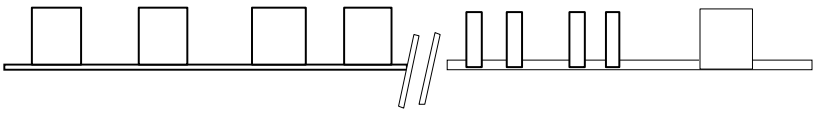
H.C. GENE SEGMENTS

A Prototype Ig Gene: Murine Kappa

About 10 0 V_κ gene segments

4 J Gene Segment s

1 C_κ Gene Segmen t

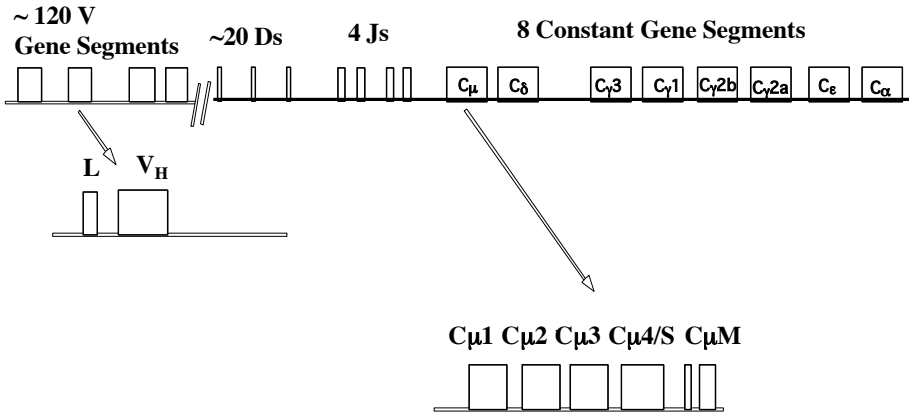


Multiple V gene segments, distant from J and C

A few J gene segments

One C gene segment

Murine Ig Heavy Chain Gene Organization



Human Ig Loci

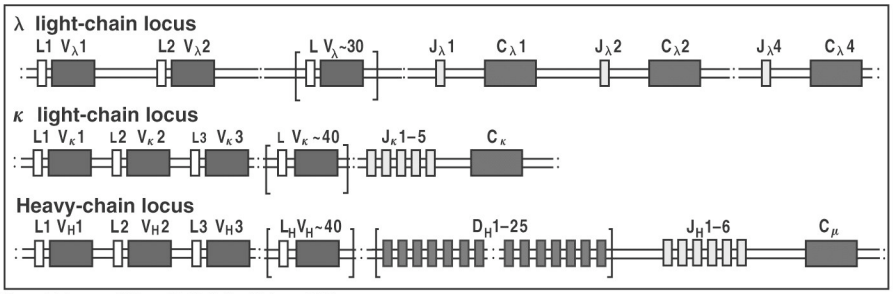
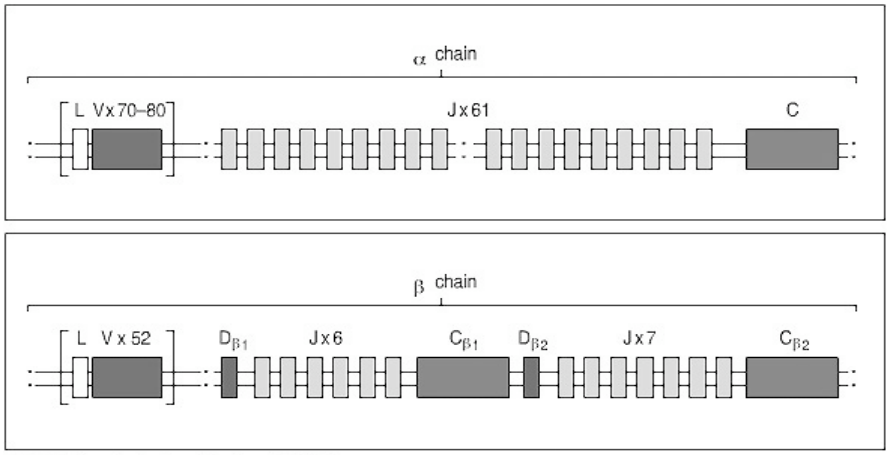
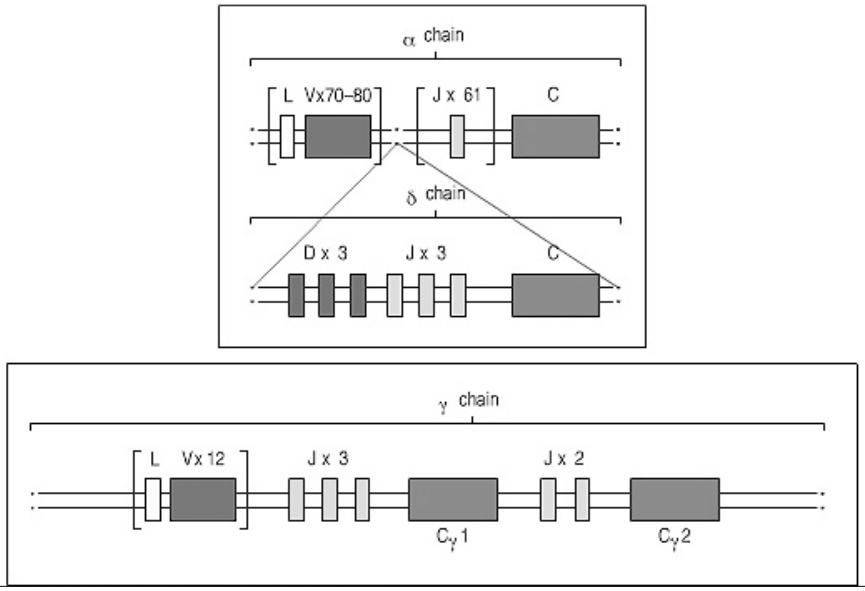


Figure 4-4 Immunobiology, 6/e. (© Garland Science 2005)

TCR Alpha and Beta Loci



TCR Delta and Gamma Loci



SUMMARY

1. Antibodies are comprised of 2 heavy and 2 light chain polypeptides.
2. N-terminal variable regions of antibodies recognize antigen and C-terminal heavy chain constant regions eliminate antigen.
3. Heavy and light chains are comprised of multiple Ig domains that have a characteristic beta pleated sheet structure.
4. Hypervariable amino acids in loops between beta sheets of variable regions contact antigen.
5. T cell receptors are comprised on one alpha and one beta chain and resemble Fab fragments of antibodies.
6. Genes encoding antibodies and TCRs are comprised of multiple V, D, J gene segments and one or a few C gene segments.