ANTIBODY: STRUCTURE AND FUNCTION

Antigen Recognition

H Chain 440 amino acids
L Chain 220 amino acids
H chain 4 or 5 domains
L Chain 2 domains
Each domain has intradisulfide bridge of 90 amino acids
There are 5 classes of H chain
(IgG, IgM, IgA, IgD, and IgE)
There are two class of L chains
(Lambda and Kappa)

Hinge region

\[ C_{H1} \]
\[ C_{H2} \]
\[ C_{L} \]

\[ C_{H1} \]
\[ C_{H2} \]

Antigen Elimination

Proteolytic cleavage by papain

Proteolytic cleavage by pepsin

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The IgG Molecule

Fab arm waving
Fab elbow bend
Fab rotation
Fc wagging

Ig CONSTANT DOMAIN
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)
<table>
<thead>
<tr>
<th>Non-covalent forces</th>
<th>Origin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electrostatic forces</td>
<td>Attraction between opposite charges</td>
</tr>
<tr>
<td></td>
<td>$\text{NH}_2$ $\text{COC}$</td>
</tr>
<tr>
<td>Hydrogen bonds</td>
<td>Hydrogen shared between electronegative atoms (N,O)</td>
</tr>
<tr>
<td></td>
<td>$\text{N} - \text{H} - \text{O} - \text{C}$</td>
</tr>
<tr>
<td>Van der Waals forces</td>
<td>Fluctuations in electron clouds around molecules oppose polarize neighboring atoms</td>
</tr>
<tr>
<td></td>
<td>$\delta^+ \leftrightarrow \delta^-$</td>
</tr>
<tr>
<td>Hydrophobic forces</td>
<td>Hydrophobic groups interact unfavorably with water and tend to pack together to exclude water molecules. The attraction also involves van der Waals forces</td>
</tr>
<tr>
<td></td>
<td>$\text{H}_2\text{O}$ $\delta^+$ $\delta^-$</td>
</tr>
</tbody>
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Antigen Recognition

Antibodies: Secreted or Transmembrane

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

Ig Polypeptides Are Encoded by
Multiple Gene Segments

<table>
<thead>
<tr>
<th>Variable</th>
<th>Constant</th>
<th>Light Chain POLYPEPTIDE</th>
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<tbody>
<tr>
<td>V</td>
<td>J</td>
<td>Light Chain GENE SEGMENTS</td>
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<td>D</td>
<td>C_H1</td>
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<td></td>
<td>C_H2</td>
</tr>
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**A Prototype Ig Gene: Murine Kappa**

About 10 V\(_{\kappa}\) gene segments

4 J Gene Segment s

1 C\(_{\kappa}\) Gene Segment

Multiple V gene segments, distant from J and C

A few J gene segments

One C gene segment

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**Murine Ig Heavy Chain Gene Organization**

~ 120 V Gene Segments

~20 Ds

4 Js

8 Constant Gene Segments

C\(_{\mu1}\) C\(_{\mu2}\) C\(_{\mu3}\) C\(_{\mu4/S}\) C\(_{\muM}\)
Human Ig Loci

**λ light-chain locus**
- L1
- L2
- L V<sub>1</sub>-30
- J<sub>λ</sub>1-5
- C<sub>λ</sub>

**κ light-chain locus**
- L1
- L2
- L3
- L V<sub>κ</sub>-40
- J<sub>κ</sub>1-5
- C<sub>κ</sub>

**Heavy-chain locus**
- L1
- L2
- L3
- L V<sub>γ</sub>-50
- D<sub>γ</sub>1-25
- J<sub>γ</sub>1-6
- C<sub>γ</sub>

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

**α chain**
- L V<sub>α</sub>70-80
- J<sub>α</sub>61
- C

**β chain**
- L V<sub>β</sub>32
- D<sub>β</sub>1
- J<sub>β</sub>6
- C<sub>β</sub>1
- D<sub>β</sub>2
- J<sub>β</sub>7
- C<sub>β</sub>2

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**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 and C gene segments.