Lecture 1
Immunoglobulin
Immuno globulins=Ig

They are a group of (glycoproteins) which present in serum, tissue and all body fluids of all vertebrates, that have Antibody (Ab) activities, specifically with the Antigen (Ag) that causes their production.

These Abs play a major role in defense mechanisms and protection against infections.

Ig are synthesized and secreted by plasma cell.
Which are the end stage of activated & differentiated B lymphocyte?
constitute about **20% of serum proteins** & consist of 82-96% polypeptide (back bone) 4-18% CHO which support them against proteolytic enzymes

Basic structure of Ig:

The backbone of Ig consist of **2 pairs of polypeptide chains** each pair are identical. One pair nearly double the molecular weight of the other pair so called **heavy & light chain** respectively.
Basic structure of Ig.
The 4 chains are hold together by inter chain disulphide bonds to give us this monomeric Structure.
Each chain has 2 terminals:
1- Amino ter. In which the a.a. are variable called (variable region)
2- Carboxy ter. In which the a.a. sequence rather consist & heterogeneous (constant region)
Hot spot (hyper variable region):
3 areas in the variable region of each chain
with a high variability in the a.a. sequence to form
the Ag binding site (paratope)

\textbf{Paratope=Ag binding site}

A cleft formed by 3 hot spots from the light chain &
a farther 3 from the adjacent heavy chain, it is
complementary to the specific chemistry & shape
of the epitope (Ag determinant)

\textbf{Idiotype }=\text{paratope +hot spots}
Constant region

Variable region

paratope

Variable R. light heavy

Constant region

Idiotypic

Paratope

Hot spot
Epitopes: Antigen Regions that Interact with Antibodies

Antigen-binding sites

Antigen

Antibody A
Antibody B
Antibody C

Epitopes (antigenic determinants)
constant region:

**Light chain** either:

- Kappa $\kappa$
- Lambda $\lambda$

**Heavy chain** either:

- $\gamma$
- $\alpha$
- $\mu$
- $\delta$
- $\varepsilon$

(5 classes)
The a.a. sequence in both light & heavy chains is not a linear sequence but there are domes or loops due to presence of **intra chain** disulphide bonds these globular areas called domains.
In the variable region of each chain there is only one domain VL or Vh
In the constant region of light chain there is one constant domain CL
In the constant region of heavy chain
There are 3 constant domains CH1, CH2, CH3 with exception IgM, IgE there is an extra domain CH4
antigen binding sites reside in the variable regions of the L & H chains

light chain (212 residues)

Complement fixation

Heavy chain (450 residues)

IgG1

C_H1

C_H2

C_H3

COOH

V_L

C_L

V_H

NPI_2

variable region

hinge region

Fc

Fab
Pepsin act to the right of hinge region leads to formation of FAB Dimmer (FAB)2 & FC fragment
Function of Ig

Ig is a bi-functional mol.

primary binding with Ag (recognition)

secondary biological activities to get rid of invasion Ag

Cytolysis:

Ag-Ab binding → activation of the complement sys. → Lysis of the cell
Opsonization

Ab coat the Ag → recognized by phagocytic cells (phagocytic cell like macrophage, monocyte, natural killer have receptor for FC fragment of Ig)

Neutrilization

Neutralize toxins & viruses

Blocking

block the reaction

Agglutination
Binding of antibodies to antigens inactivates antigens by:

- **Neutralization** (blocks viral binding sites; coats bacteria and/or opsonization)
- **Agglutination** of antigen-bearing particles, such as microbes
- **Precipitation** of soluble antigens
- **Complement fixation** (activation of complement)

Enhances:
- Phagocytosis

Leads to:
- Cell lysis
Ig classes they are classified:
On the bases of their heavy chain peptide str.

IgG:
- predominant Ig in serum 75%
- M.W. low 150000
- can extra-vassate easily to the extract vascular space so 1^{st} line of defense
- Only Ig can pass the placenta protect the fetus in the 1^{st} few month of life
- Long half time
  - Best opsonizing Ab, it binds the Ag with high affinity
Main Ig in the secondary immune response
The chain of IgG is subdivided into: 4 subclasses

<table>
<thead>
<tr>
<th>Subclass</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG₁</td>
<td>65%</td>
</tr>
<tr>
<td>IgG₂</td>
<td>32%</td>
</tr>
<tr>
<td>IgG₃</td>
<td>8%</td>
</tr>
<tr>
<td>IgG₄</td>
<td>4%</td>
</tr>
</tbody>
</table>
These subclasses differ in their secondary biological activity

- complement fixation (CH2) through classical pathway
  \[ \text{IgG} \quad \text{IgG} \quad \text{IgG} \]
  While IgG only fix complement through alternative path
  - crossing the plasenta (CH3, CH2)
    \[ \text{IgG} \quad \text{IgG} \quad \text{IgG} \]
  - binding to monocyte (CH3, CH2)
    \[ \text{IgG} \quad \text{IgG} \quad \text{IgG} \]
  - blocking IgE binding only IgG4
IgG is considered the most protective Ab: because

1- present in high amount in blood (75%)
2- Extra vassate easily to extra vascular space
3- can cross the placenta
4- Binds avidly with Ag (of high affinity)
5- Very efficient opsonizing Ab
6- Can activate the complement system through the classical path way
Opsonization:
Substances that bind to particles & make them more susceptible to phagocytosis:
1-complement compound C3b
2-Antibodies IgG, IgA
3-Fibronectin glycoprotein glue.
4-Leukotrienes B4
5-C. reactive protein
Ref.

Jawedez microbiology

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