STRUCTURE OF ANTIBODY

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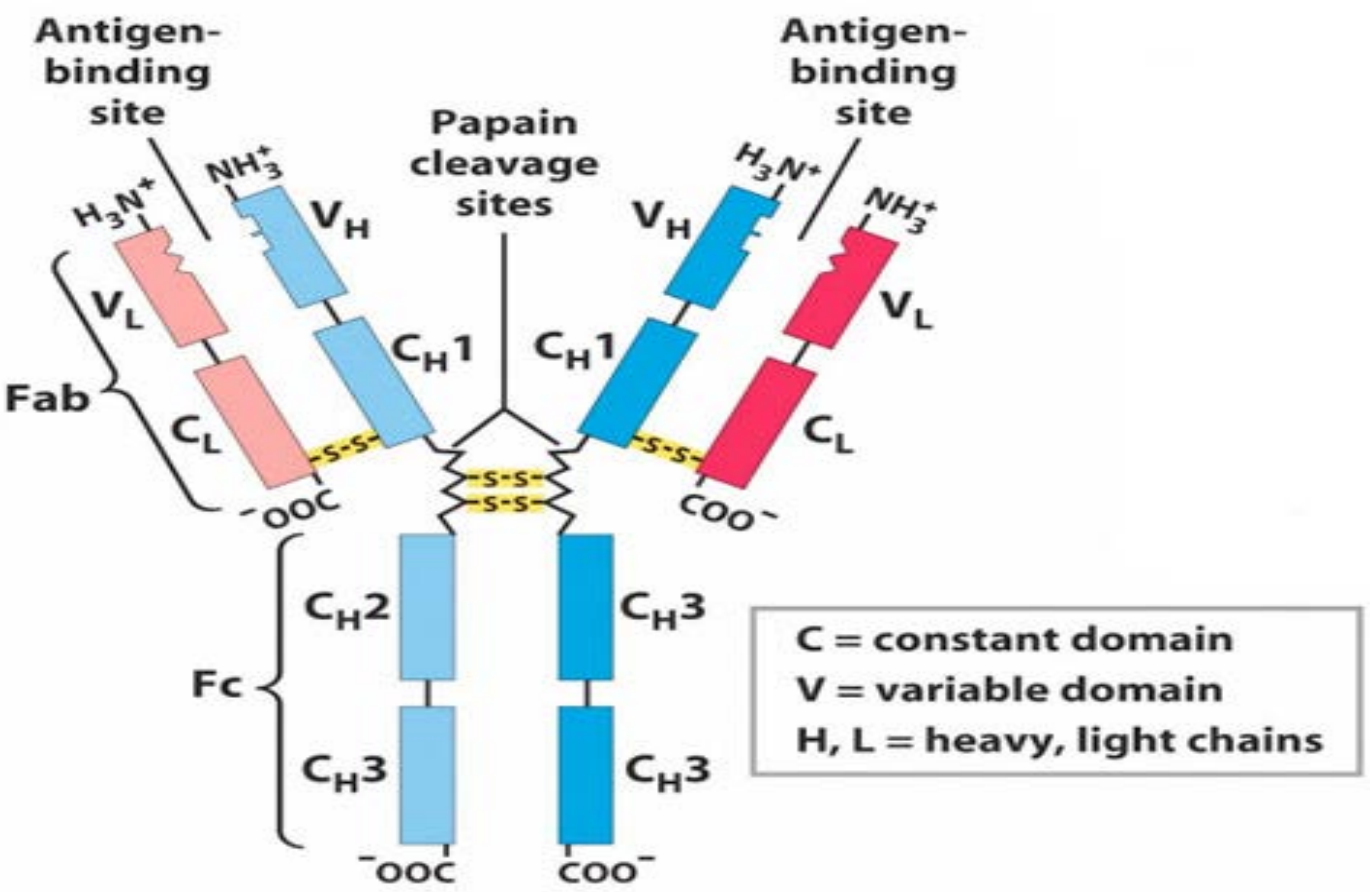
- Immunoglobulins are glycoproteins
- They are briefly represented as Ig
- Ig –may or not react with antigen
- When Ig react with an Ag it is called antibody
- When it does not react with an Ag , it is simply called Ig.
- Ab are found in the serum, body fluid and tissues
- They are produced by vertebrates only
- They are synthesized by B lymphocytes and secreted by plasma cells

Structure

- Rodney Porter (1962) proposed the basic structure of Ig
- Ig are Y- shaped. It has a stalk and 2 limbs
- The tip of the limbs is called the Ag binding site or paratope
- The tip of the stalk is called Fc. It binds to the phagocytes or complements.

Structure of antibody



FORMS

Ig exist in 2 forms

1. Soluble Ig
2. Membrane bound Ig

Soluble Ig are found in dissolved condition in the blood.

Ex serum and body fluids.

Membrane bound Ig are found on the surface of B cells.They are referred to as sIg or mIg.

Chemical in Nature

- Ig are glycoproteins
- It is made up of 2 pairs of polypeptide chains.
- Each polypeptide chains is made up of linear sequence of amino acids
  - 2 Light Chains (identical)
  - 2 Heavy Chains (identical)
- Each Light Chain Bound To Heavy Chain By Disulfide (H-L)
- Heavy Chain Bound to Heavy Chain (H-H)

L- chain

- L- chain of antibody is composed of about 214 aminoacids.
- Around 100-114 aminoacids are located at N-terminal (amino-terminal) and the aminoacids sequences varies among antibodies. This region of L-chain is known as variable (V) region.

- Light chains come in two major types κ or λ

  kappa and lambda
- In human 60% light chain are kappa and 40% are lambda whereas in mice 95% of light chain are kappa and 5% are lambda.

H-chain:

- Heavy chain is made up of 450 to 700 aminoacids.
- The H-chain has a central flexible region called hinge.
- Heavy chains come in 5 major types that have different tissue distributions and effector functions : α,γ, δ, ε, μ

Five Basic Sequence Patterns

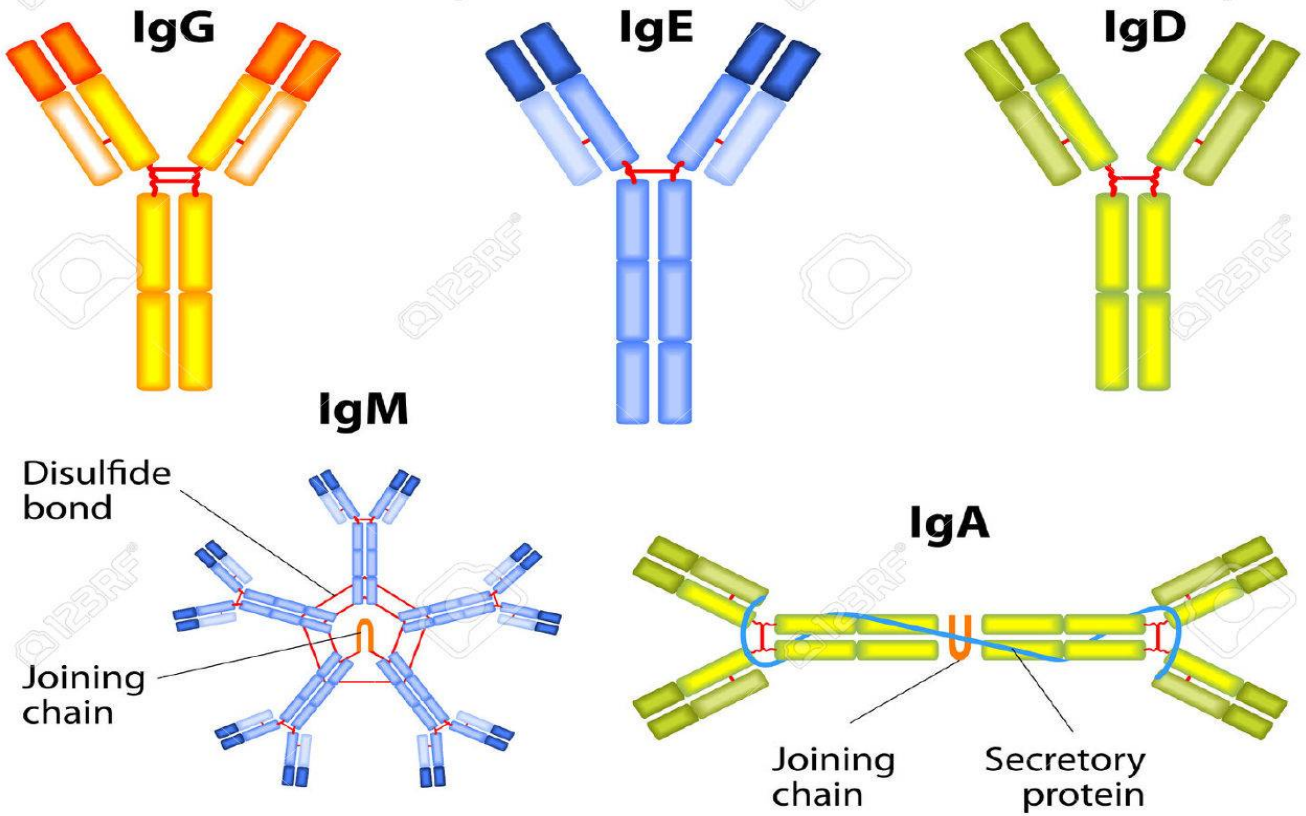
α,γ, δ, ε, μ

The above classes are called Isotype

Minor Differences Led To Sub-classes For IgA and IgG

IgA1, IgA2 and IgG1, IgG2, IgG3, IgG4

ANTIBODY CLASSIFICATION



Antibody Classes And Biological Activities

- IgG
  - Most abundant immunoglobin 80% of serum Ig
  - ~10mg/mL
  - IgG1,2,3,4 (decreasing serum concentration)
  - IgG1, IgG3 and IgG4 cross placenta
  - IgG3 Most effective complement activator
  - IgG1 and IgG3 High affinity for FcR on phagocytic cells, good for opsonization

- IgM
  - 5-10% of serum immunoglobulin
  - 1.5mg/mL
  - mIgM (also IgD) expressed on B-cells as BCR
  - Pentameric version is secreted
  - First Ig of primary immune response
  - High valence Ig (10 theoretical), 5 empirical
  - More efficient than IgG in complement activation

- IgA
  - 10-15% of serum IgG
  - Predominant Ig in secretions

    Milk, saliva, tears, mucus
  - 5-15 g of IgA released in secretions
  - Serum mainly monomeric, polymers possible not common though
  - Secretions, as dimer or tetramer+J-chain polyptetide+secretory component

- IgE
  - Very low serum concentration, 0.3μg/mL
  - Participate in immediate hypersensitivities reations.

    Ex. Asthma, anaphylaxis, hives
- Binds Mast Cells and Blood Basophils
- Binding causes degranulation (Histamine Release)

- IgD

  Expressed on B-cell Surface
- IgM and IgD, Expressed on B-cell Surface
- We Do Not Know Any Other Biological Effector Activity
- Low serum concentrations, ~30μg/mL

- Antigenic Determinants on Abs Fall in 3 Categories
  - Isotypic
  - Allotypic
  - Idiotypic
- Isotypic
  - Constant Region Of Ab
  - If you inject Ab in a different species Anti-Isotype is generated
  - If within same species, No Anti-isotype

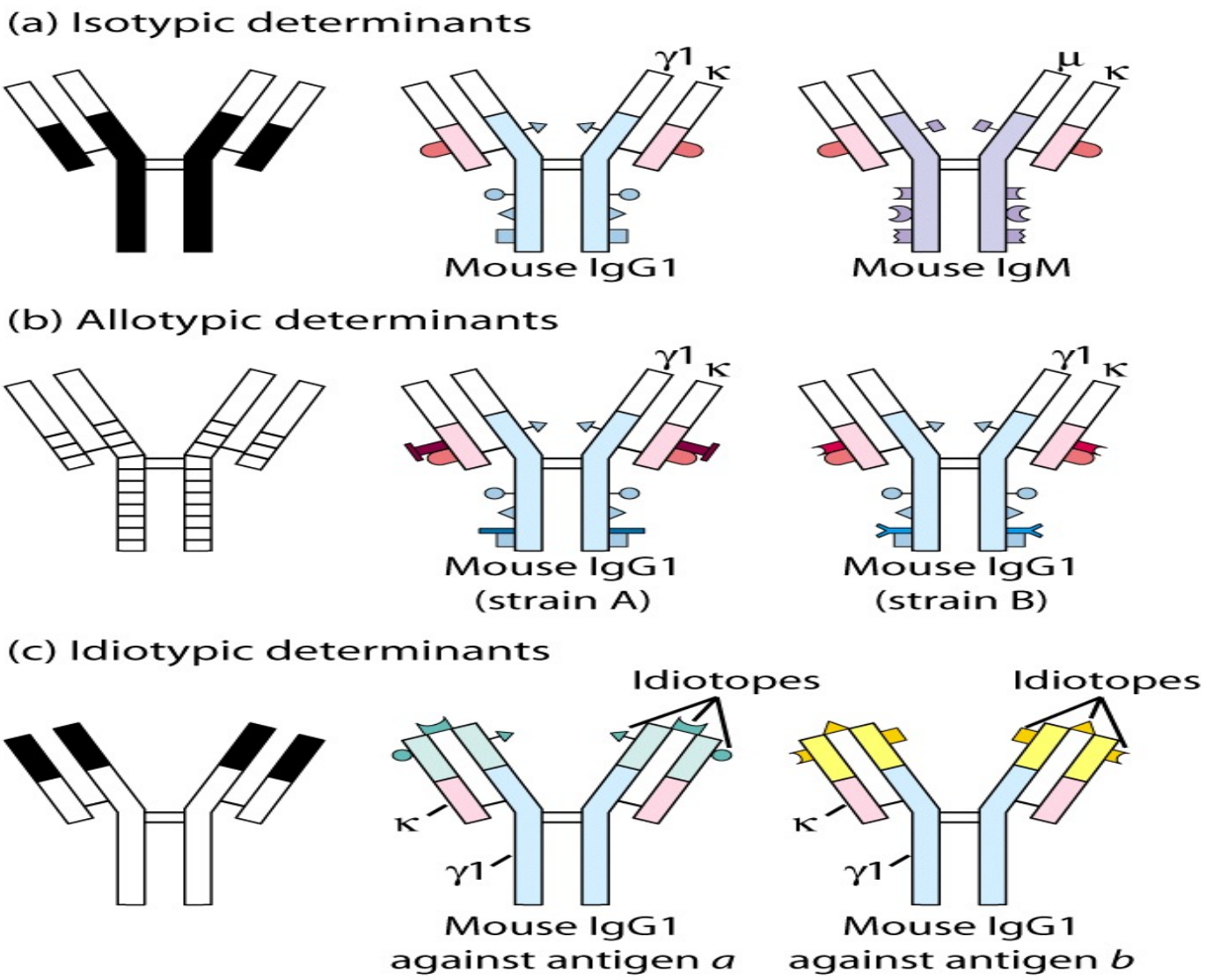
- Allotype
  - Even though same isotypes within one species small differences (1-4 a/a) arise in different individuals (form of polymorphism)
  - If injected with such Ab you generate anti-allotype Ab

    Ex.

    During pregnancy

    Blood transfusion

- Idiotype
  - Unique V_H and V_L binds antigen but can also behave as antigenic determinant
- If you inject a monoclonal antibody into a genetically identical recipient then anti-idiotypic antibodies are generated
- No anti-isotypic and no anti-allotypic Abs will be generated


(a) Isotypic determinants
γ1
κ
μ
κ
Mouse IgG1
Mouse IgM
(b) Allotypic determinants
γ1
κ
γ1
κ
Mouse IgG1
(strain A)
Mouse IgG1
(strain B)
(c) Idiotypic determinants
Idiotopes
Idiotopes
κ
γ1
κ
γ1
Mouse IgG1
against antigen a
Mouse IgG1
against antigen b