ANTIBODY

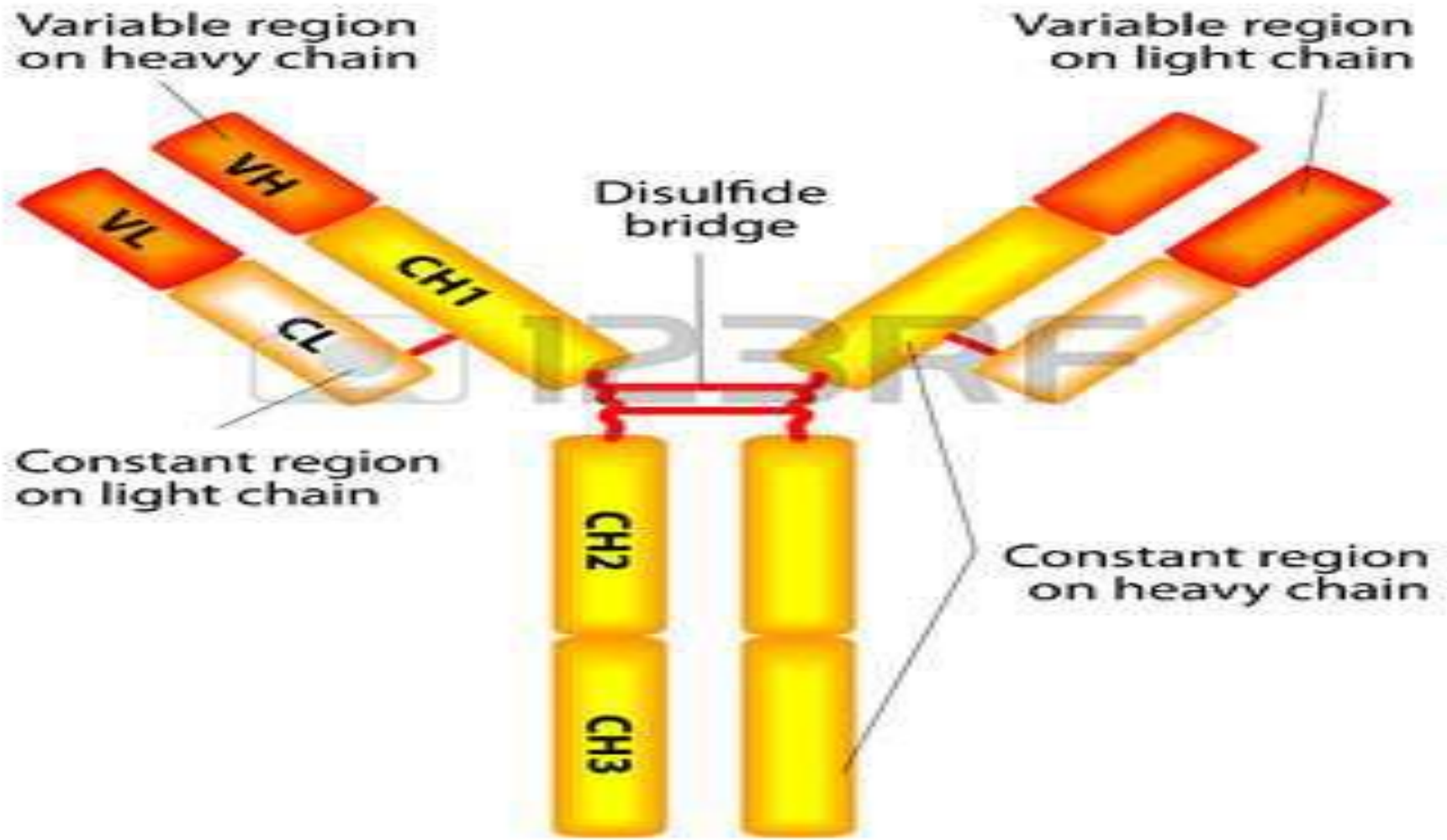
Antibodies: are synthesized by B lymphocytes (B cells) and are both synthesized and secreted by plasma cells. Plasma cells are B cells that have terminally differentiated. The term antibody is applied to an immunoglobulin molecule with specificity for an epitope of the molecules that make up antigens. Antibodies noncovalently bind to antigens to immobilize them, render them harmless, or “tag” the antigen for destruction and removal by other components of the immune system

- In doing so, antibodies facilitate the ability of other cells and molecules in the immune system to identify and interact with antigens. Because antibodies are often in soluble form, they are important components of humoral (soluble) immune responses.
- Basic structure: Human immunoglobulin contains four polypeptides: two identical light chains and two identical heavy chains linked by disulfide bonds to form a monomeric unit.

- 1. Light chains

An immunoglobulin monomer contains two identical κ or two identical λ light chains but never one of each. Light or L chains contain a variable (VL) domain and a constant (CL) domain. Each domain contains about 110 amino acids and an intrachain disulfide bond. Variable regions (in both heavy and light chains) are so named for their variation in amino acid sequences between immunoglobulins synthesized by different B cells..

IMMUNOGLOBULIN



2. Heavy chains

Heavy chains contain one variable (VH) and three or four constant (CH) domains. Heavy (H) chain variable domains (VH) are extremely diverse, and constant domains (CH) display a relatively limited variability for members of an isotype. The δ, γ,and α heavy chains contain three constant domains (CH1, CH2, CH3), and μ and ε heavy chains contain a fourth constant domain (CH4), making them both longer and heavier than δ, γ, and α heavy chains.

Antigen-binding sites:

A light chain variable domain and a heavy chain variable domain together form a pocket that constitutes the antigen (epitope)-binding region of the immunoglobulin molecule. Because an immunoglobulin monomer contains two identical light chains and two identical heavy chains, the two binding sites found in each monomeric immunoglobulin are also identical . The variability in the amino acid sequences of the VL and VH domains, together with the random pairing of light and heavy chain that occurs from one B cell to another, creates a pool of binding sites capable of recognizing a very large number of different epitopes.

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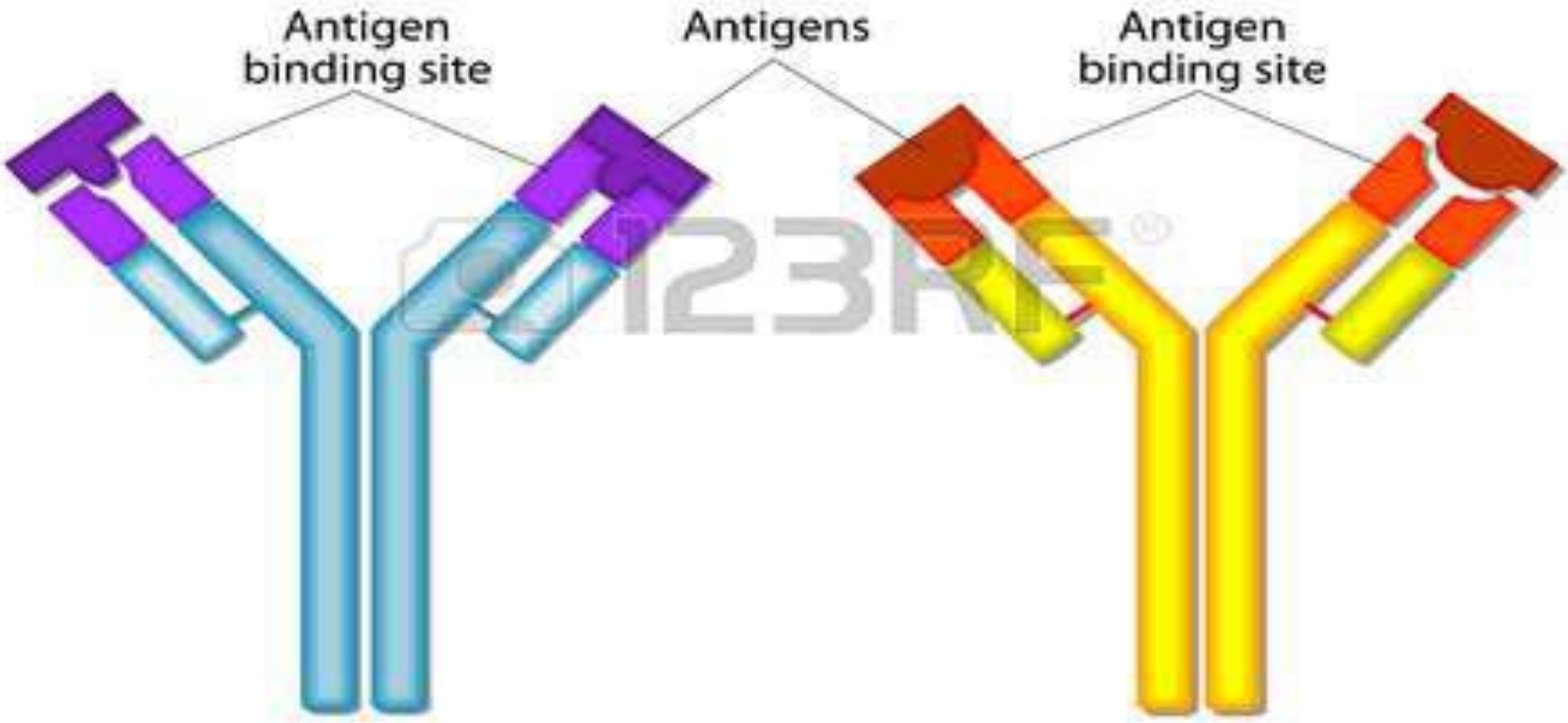


- **Immunoglobulin landmarks:**
- Immunoglobulin molecules can be enzymatically cleaved into discrete fragments by either pepsin or papain. Disulfide bonds join the heavy chains at or near a proline-rich hinge region, which confers flexibility on the immunoglobulin molecule.

The fragments of immunoglobulin are as follows:

Fab or antigen (epitope)-binding fragment, produced by papain cleavage of the immunoglobulin molecule, contains VH, CH1, VL, and CL. Two Fab fragments are produced by papain cleavage of an immunoglobulin monomer; each fragment has an epitope-binding site. Fc or constant (crystallizable) fragment is produced by cleavage of the immunoglobulin molecule with papain. The Fc portion contains the CH2, CH3, and (sometimes) CH4 regions of the immunoglobulin molecule. It is responsible for many biologic activities that occur following engagement of an epitope.

Isotypes:

Heavy chain isotypes (μ, δ, γ, α, and ε) also determine immunoglobulin isotype or class (IgM, IgD, IgG, IgA, and IgE, respectively). Normally humans produce all five immunoglobulin isotypes. Of the two light chain isotypes, an individual B cell will produce only κ or λ chains, never both. B cells express surface-bound immunoglobulin monomers as epitope-specific receptors; B cells produce and display only one isotype, with the exception that unstimulated B cells express both IgM and IgD. When secreted into the body fluids, soluble IgG and IgE remain monomeric, soluble IgM forms a pentamer, and soluble IgA can be found in either a monomeric or dimeric form.

IgM: In general, IgM is the first immunoglobulin to be formed following antigenic stimulation. IgM is effective both at immobilizing antigen and in activating the classical pathway of complement.

IgD: has a monomeric structure and is almost exclusively displayed on B cell surfaces. Little is known of its function.

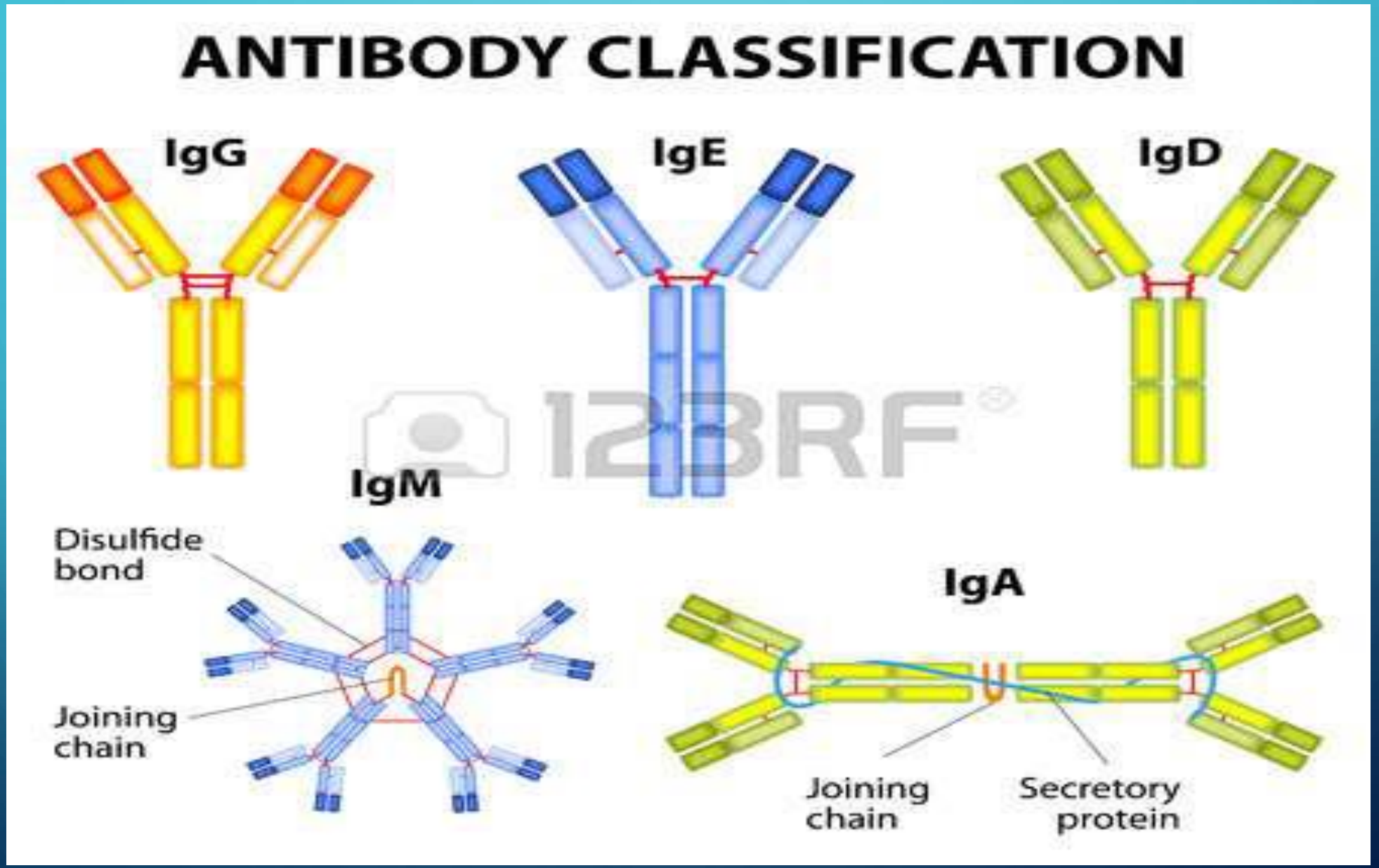
IgG: exists as both surface and secreted monomeric molecules. Four subclasses of γ heavy chains account for the four human IgG subclasses, IgG1, IgG2, IgG3, and IgG4. Collectively, IgG subclasses make up the greatest amount of immunoglobulin in the serum.

Many IgG antibodies are effective in activating complement , opsonizing and neutralizing microorganisms and viruses, and initiating antibody-dependent cell-mediated cytotoxicity, and they function in a wide variety of hypersensitivity functions.

IgA: is present in both monomeric and dimeric forms. Monomeric IgA is found in the serum. The addition of a J or joining chain to two IgA monomers forms a dimer. Epithelial cells use a specialized receptor to transport the IgA dimer to mucosal surfaces.

This specialized receptor becomes an accessory molecule that binds to the IgA dimers is known as secretory component (SC). Secretory IgA dimers are found in mucus, saliva, tears, breast milk, and gastrointestinal secretions. The SC provides increased resistance to enzymatic degradation. Two isoforms of IgA (α1 and α2) show slightly different functions. IgA1 predominates in the serum and in secretions above the diaphragm. Secretory IgA2 accounts for the majority of IgA found in the lumen of the lower portion of the gastrointestinal tract. Large amounts of IgA are synthesized and secreted daily at the mucosal surfaces of the GI tract, respiratory tracts, and other secretory epithelia. More IgA is produced daily than all the other isotypes combined.

IgE: is present in relatively low serum concentration; most is adsorbed onto the surfaces of mast cells, monocytes, and eosinophils. Mast cells and basophils have isotype-specific receptors (FcRε, CD23) for the Fc portion of free IgE molecules. Cross-linking of IgE on mast cell surfaces by antigen triggers the release of histamine and other inflammatory mediators, leading to immediate hypersensitivity (allergic) responses.


ANTIBODY CLASSIFICATION
IgG
IgE
IgD
IgM
Disulfide bond
Joining chain
IgA
Joining chain
Secretory protein

The most important functions of antibodies:-

1- neutralize toxins and viruses.

2- opsonize microbes so they are more easily phagocytosed.

3- activate complement.

4-prevent the attachment of microbes to mucosal surfaces.