2021-2022

Immunoglobulins

(1 of 2)

Immunoglobulins (Igs)

= antibodies

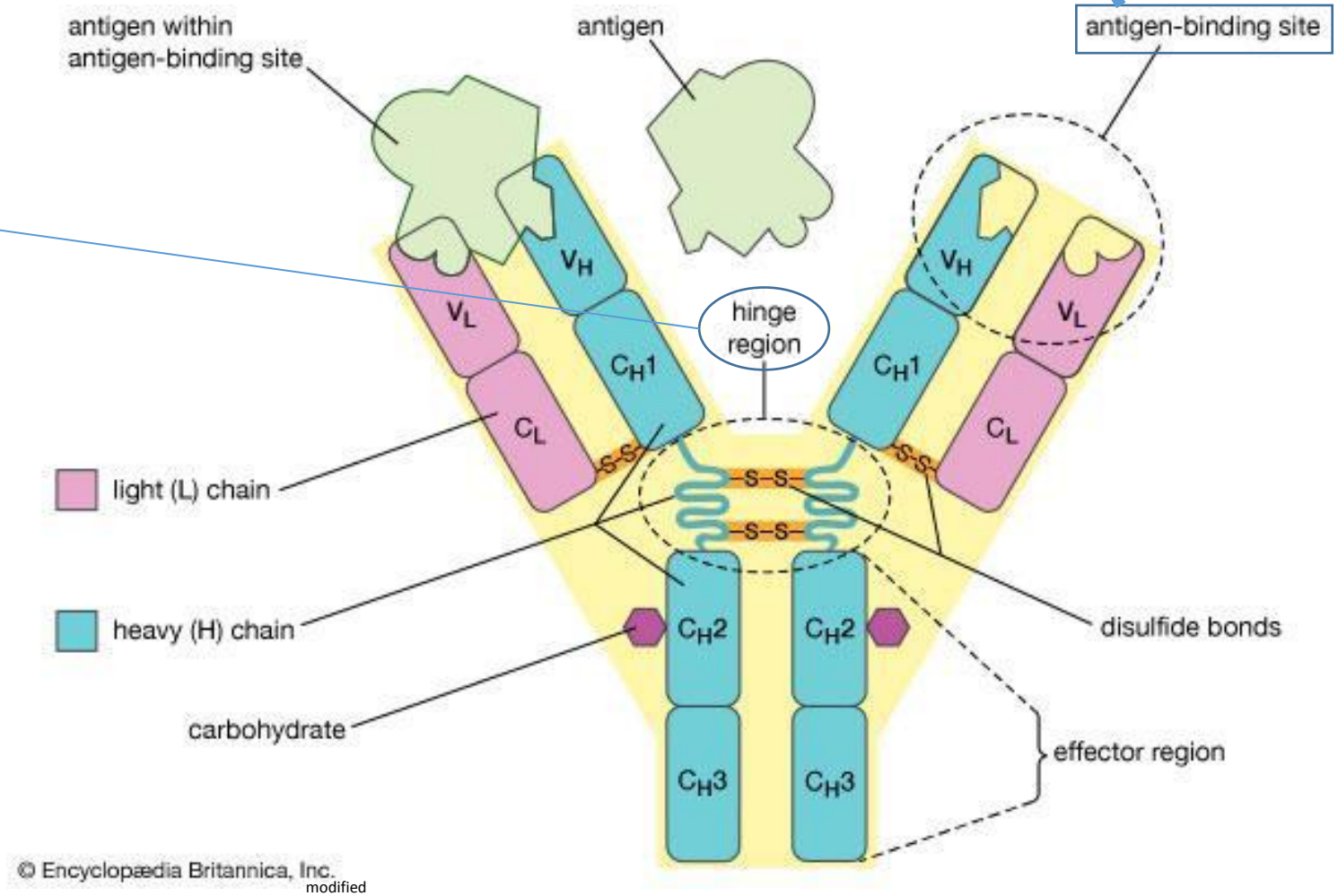
- Each B cell synthesizes Igs of single specificity for a specific epitope
- B cell receptors (BCRs) are the Igs on B cell surface
- Stimulated B cells → plasma cells → secrete soluble Igs → Humoral immunity

non-covalently bind to antigens → immobilize them (become harmless)

-"tag" them for destruction and removal by other immune components

Structure (4 polypeptides)

= NH terminus of one heavy chain + NH terminus of one light chain



2 identical light chains and 2 identical heavy chains

Form one unit due to the disulfide bonds

Domains (the 3-dimensional subunits of the chains)

*Light chain contains 2 domains: VL (variable domain) & CL (constant domain)
*Heavy chain contains 1 variable (VH) & 3 or 4 constant (CH) domains
*Each domain = about 110 amino acids + intrachain disulfide bond

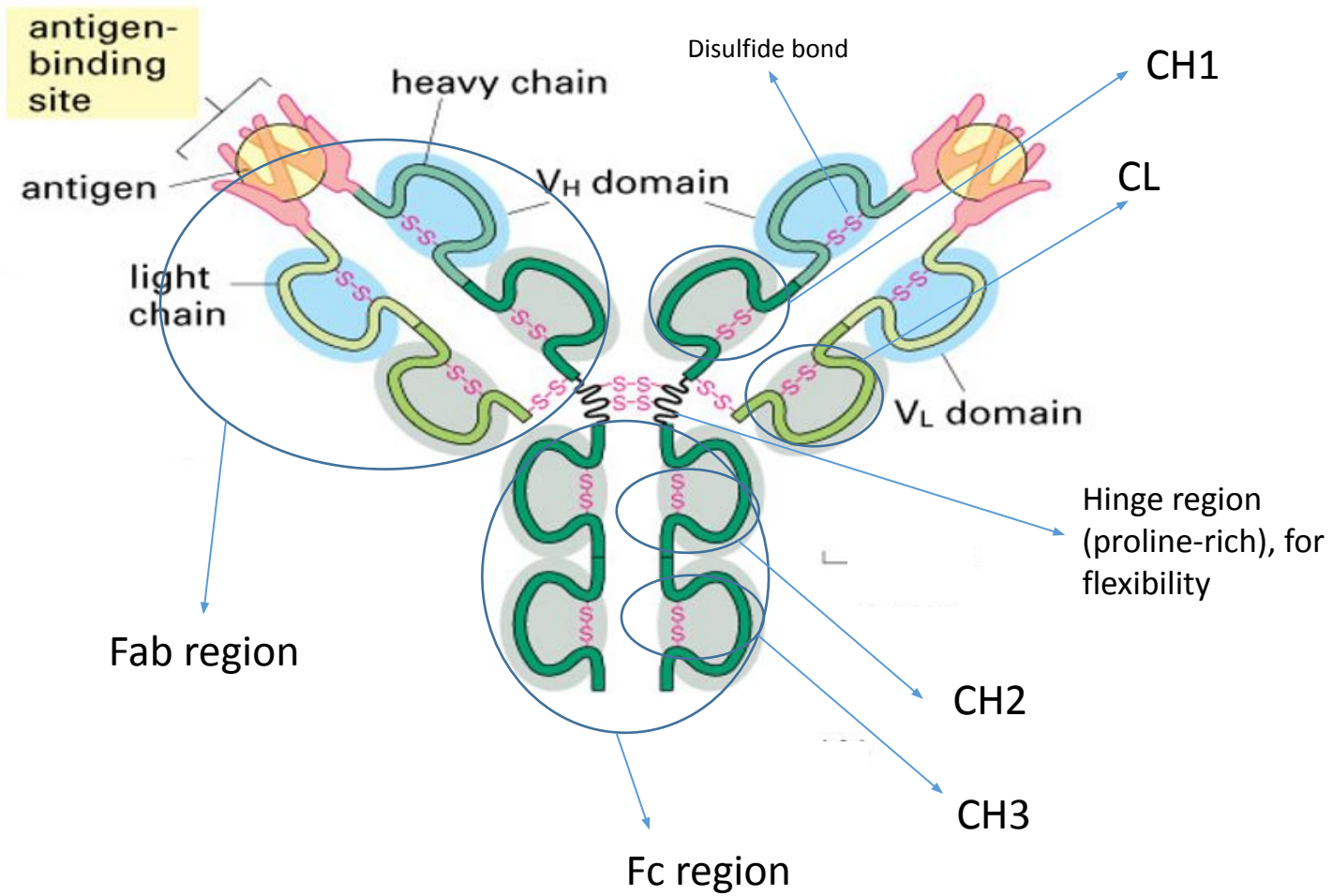


Figure 4-32 Essential Cell Biology, 2/e. (© 2004 Garland Science)

modified

Isotypes of light and heavy chains

- The light chain is one of 2 types (isotypes): Kappa or lambda

…kappa encoded on chromosome 2 and lambda on chromosome 22

…each Ig contains either two lambda or two kappa chains but not one lambda and one kappa

- The heavy chain is one of 5 isotypes (all encoded on chromosome 14):

Heavy chain types:

- IgG: gamma
- IgM: mu
- IgA: alpha
- IgD: delta
- IgE: epsilon

The immunoglobulin class or subclass is determined by the heavy chain isotype

Variable and constant domains

- Variable regions differ in their amino acid sequence between the Igs synthesized by different B cells…so called “variable”

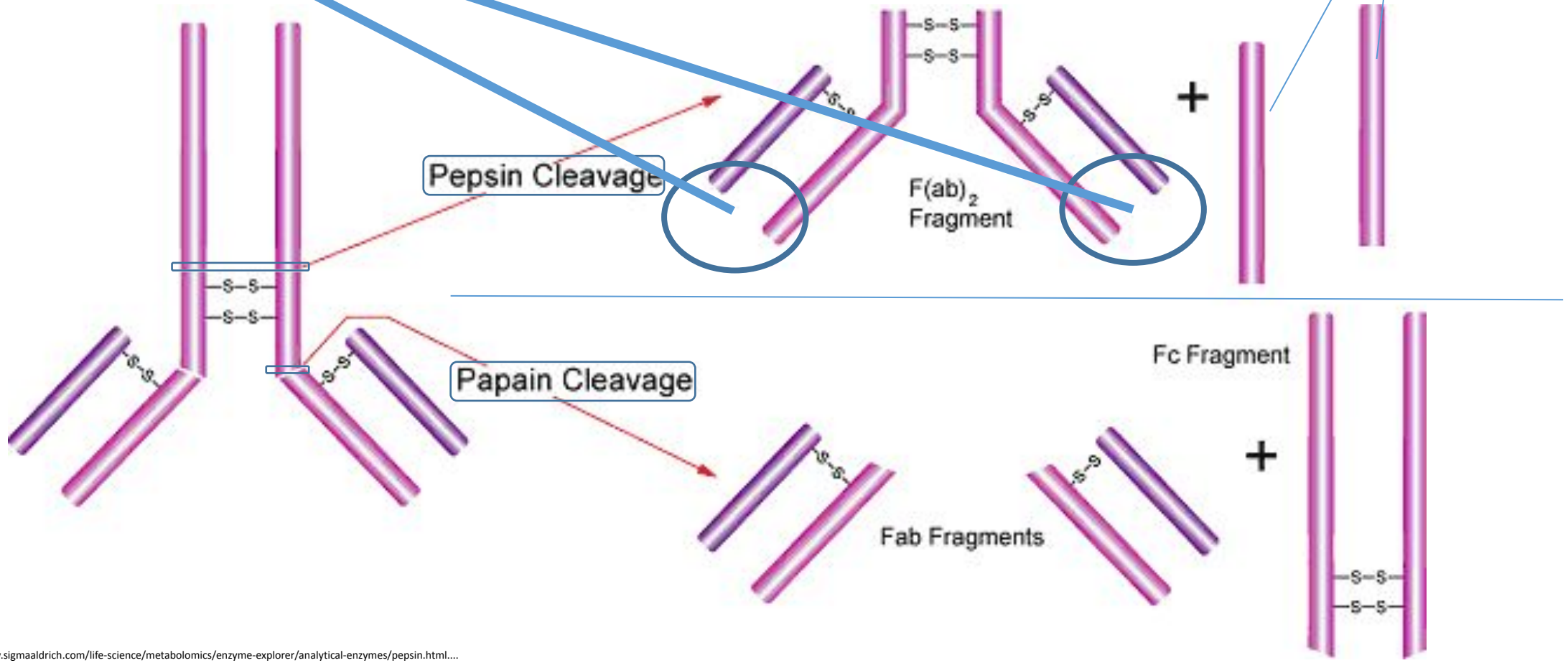
- Each of gamma, delta, and alpha heavy chains contains 3 constant domains (CH1-CH2-CH3)

  …while each of mu and epsilon heavy chains contains 4 constant domains (CH1-CH2-CH3-CH4)…longer and heavier

Identifying important parts

2 identical epitope-binding sites

These fragments will be degraded



http://www.sigmaaldrich.com/life-science/metabolomics/enzyme-explorer/analytical-enzymes/pepsin.html....
see references in this page

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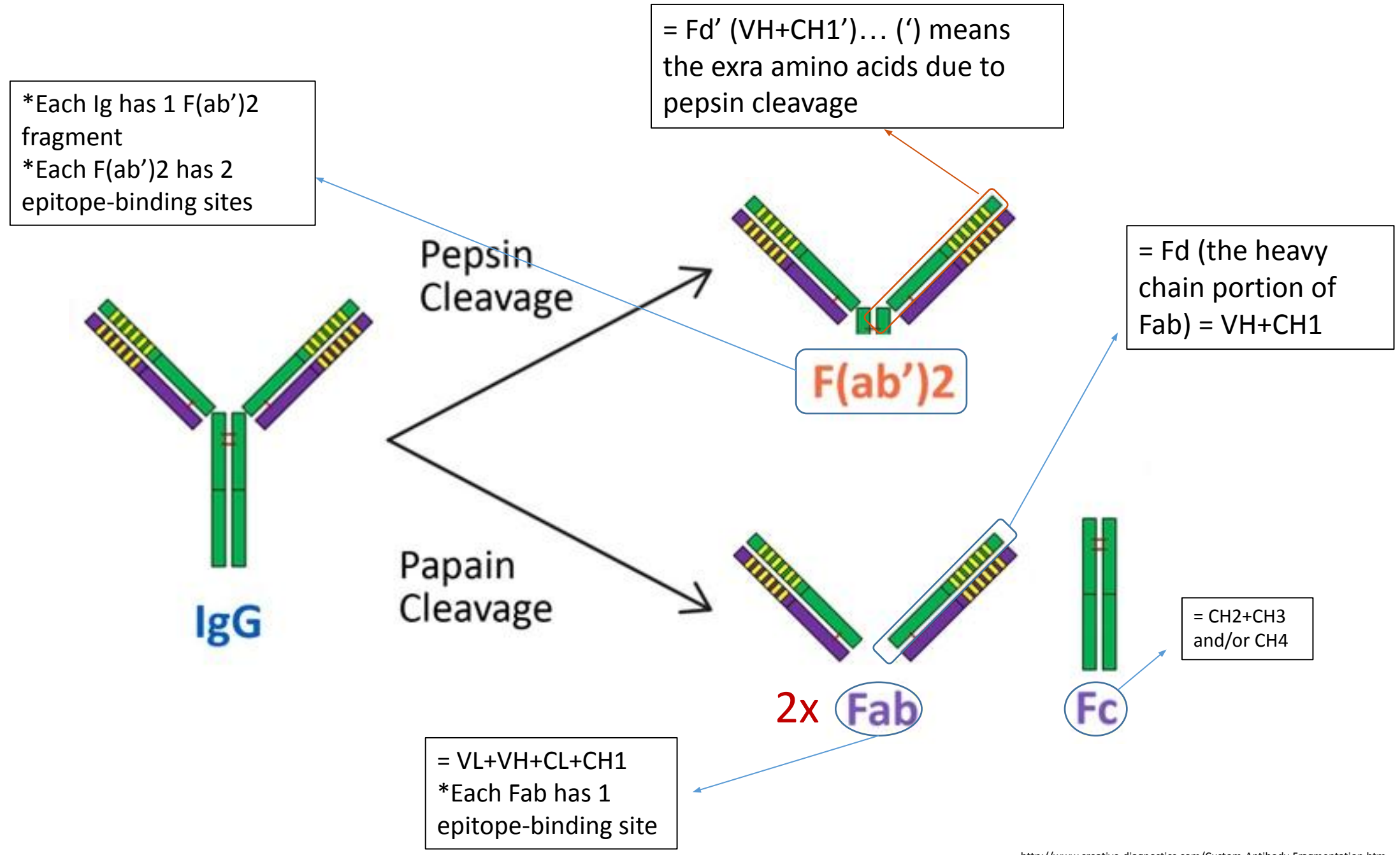


http://www.creative-diagnostics.com/Custom-Antibody-Fragmentation.htm
modified

Classes and isotypes

- Each B cell produces only 1 heavy chain isotype

  ...except: unstimulated B cells, express IgD and IgM

- When secreted (soluble Igs):

-IgG and IgE ⟶ remain monomeric

-IgM ⟶ pentamer

-IgA ⟶ monomer or dimer

*IgD: almost exclusively membrane-bound

IgM

- Cell surface-bound monomer or secreted pentamer
- Most unstimulated B cells display IgM on their surface
- The first Ig produced following antigen stimulation
- Functions:

-Immobilizing Ag (agglutination)

-Complement activation

…it is the most powerful class in these 2 functions (because of the 10 binding sites)

IgM pentamer

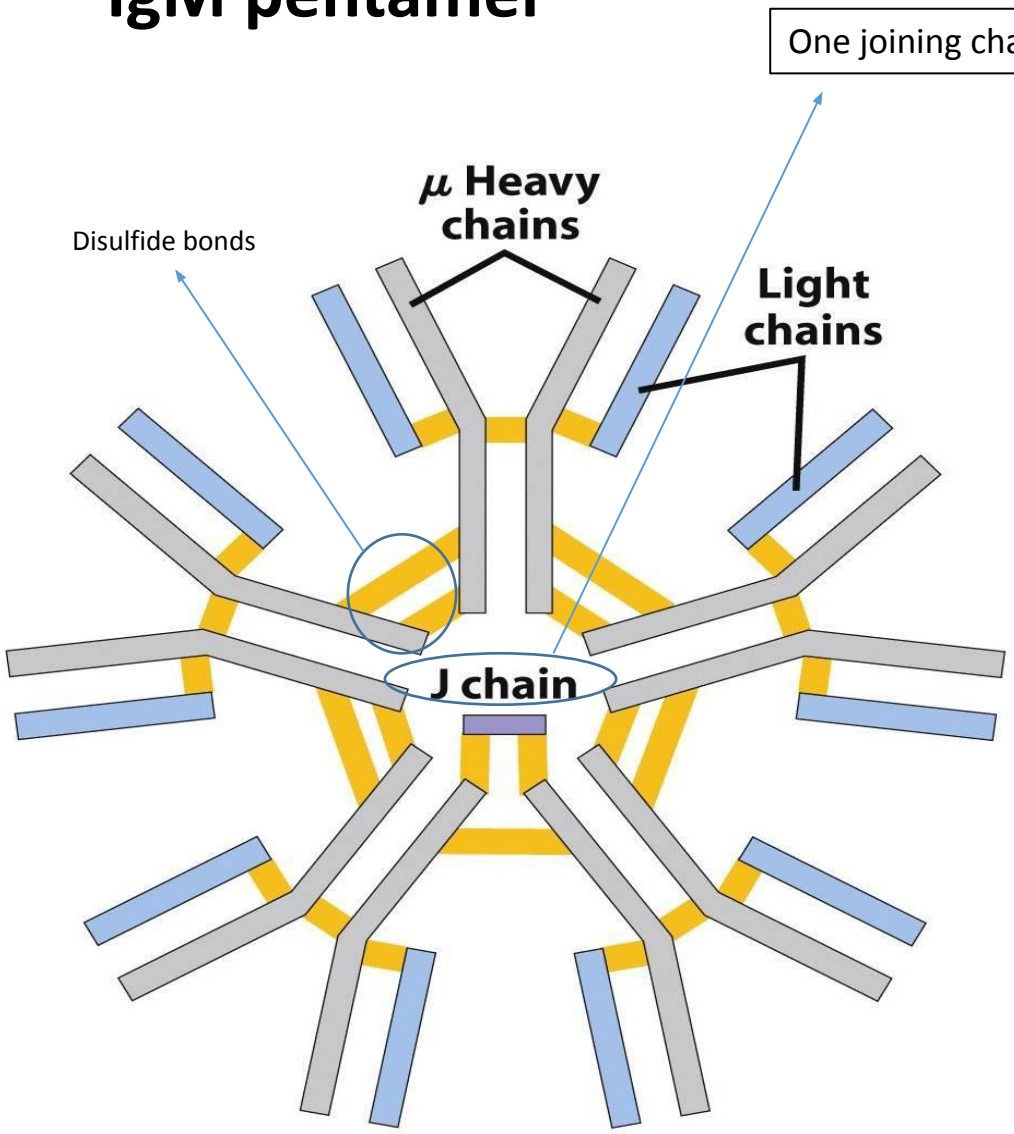


Figure 5-23
Lehninger Principles of Biochemistry, Fifth Edition

modified

IgG

- Cell surface-bound or secreted monomer
- 4 IgG subclasses (IgG1, IgG2, IgG3 and IgG4) due to 4 gamma heavy chain subclasses
- The greatest amount of Igs in serum, & the longest half-life
- Able to cross the placenta (maternal protection)
- Functions:

-Complement activation

-Opsonization

…binds to Fc receptors on phagocytes

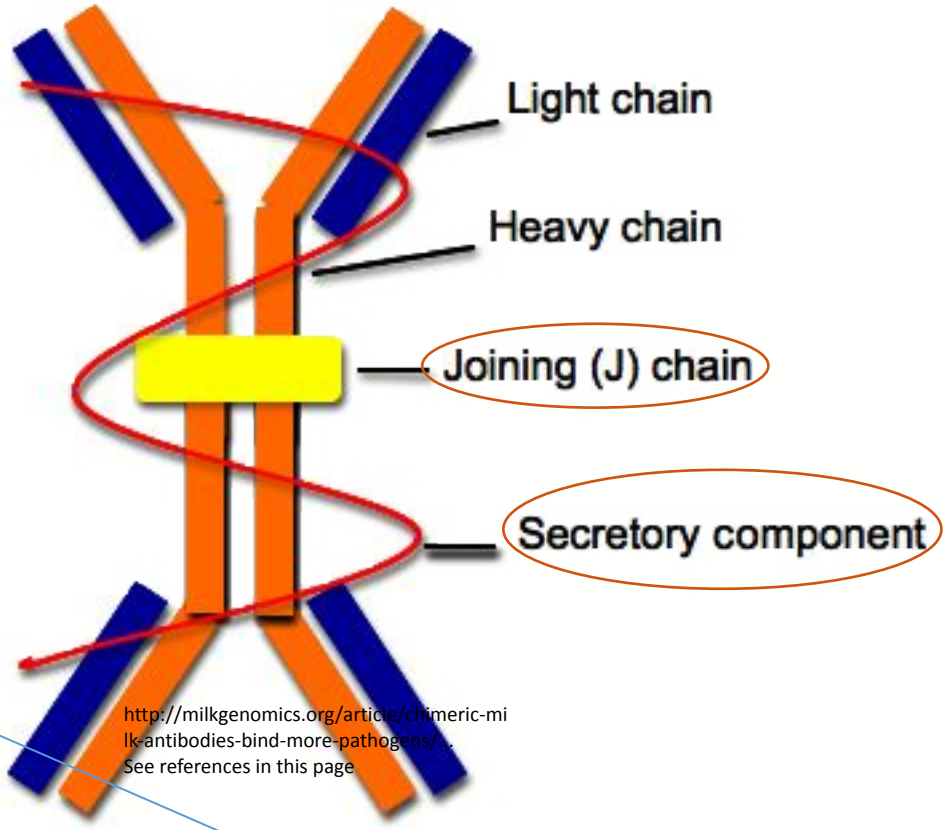
IgA

- Monomer in serum
- Dimer in secretions
- Special receptor in epithelial cell takes the dimer after it was formed using J chain then a portion of this receptor becomes a secretory component of the antibody which provides resistance against enzymes
- 2 isoforms (IgA1 & IgA2) due to alpha1 and alpha2
- Daily secretion quantity more than other classes altogether
- Functions:

-(Secretory): agglutination (immobilization) of antigens preventing them from binding To epithelial cell receptors

-(Serum): binding to Fc receptors on phagocytes

Blood & upper GI



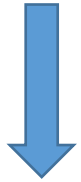
http://milkgenomics.org/article/chimeric-milk-antibodies-bind-more-pathogens/ ...
See references in this page

Lower GI

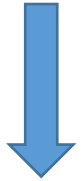
IgE

- Relatively low serum concentration
- Most of IgE produced is adsorbed onto mast cells and eosinophils
- Mast cells and basophils have **FcεRI** (**Fc epsilon RI)**
- Role against parasites (with eosinophils)

IgE Abs bind to receptors on mast cells after initial exposure to an allergen



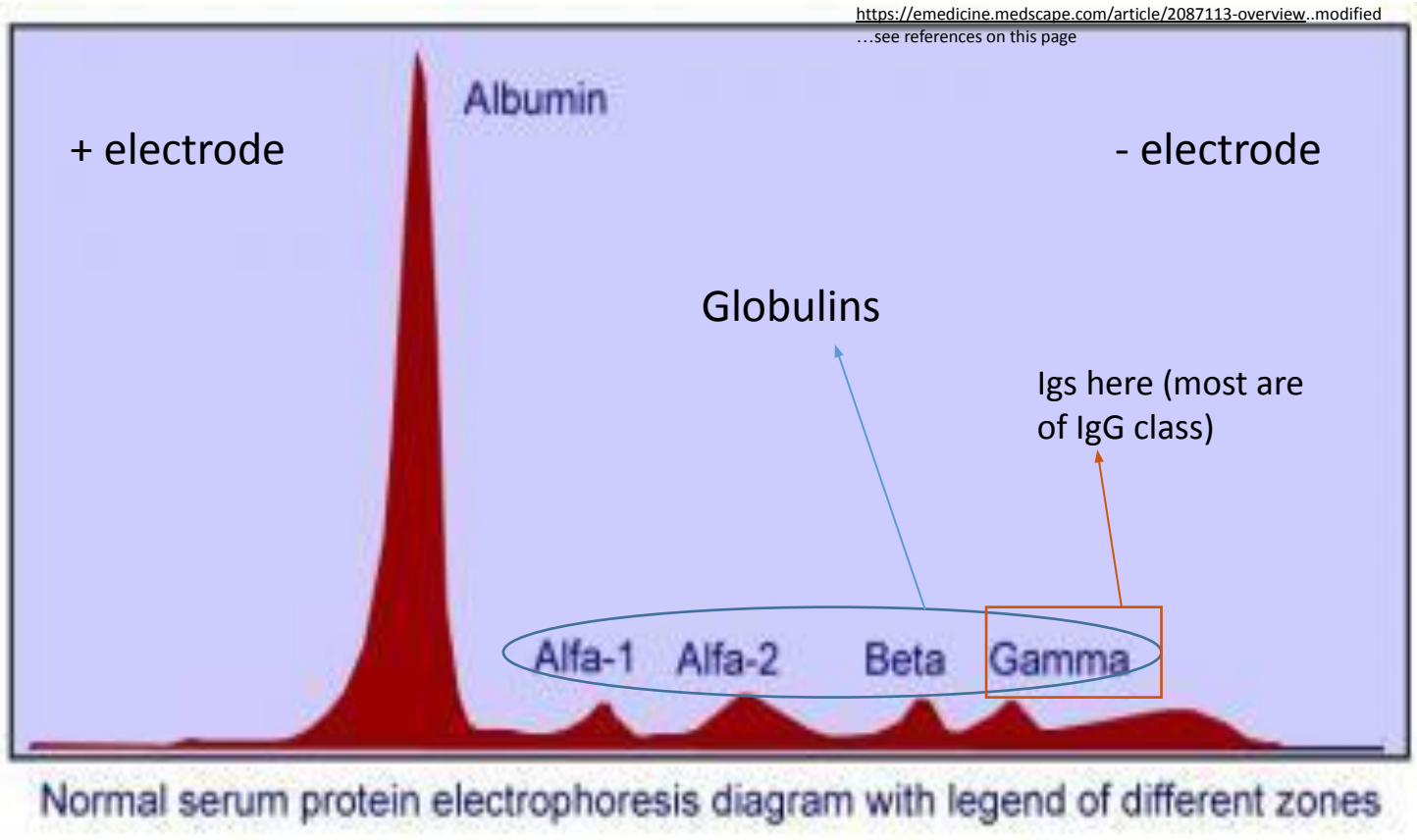
After subsequent exposure to the same allergen, IgE receptors attached to a mast cell bind the allergen



Cross-linking of adjacent IgE molecules induce mast cell degranulation…released histamine and other molecules lead to allergy symptoms

Electrophoresis of human serum

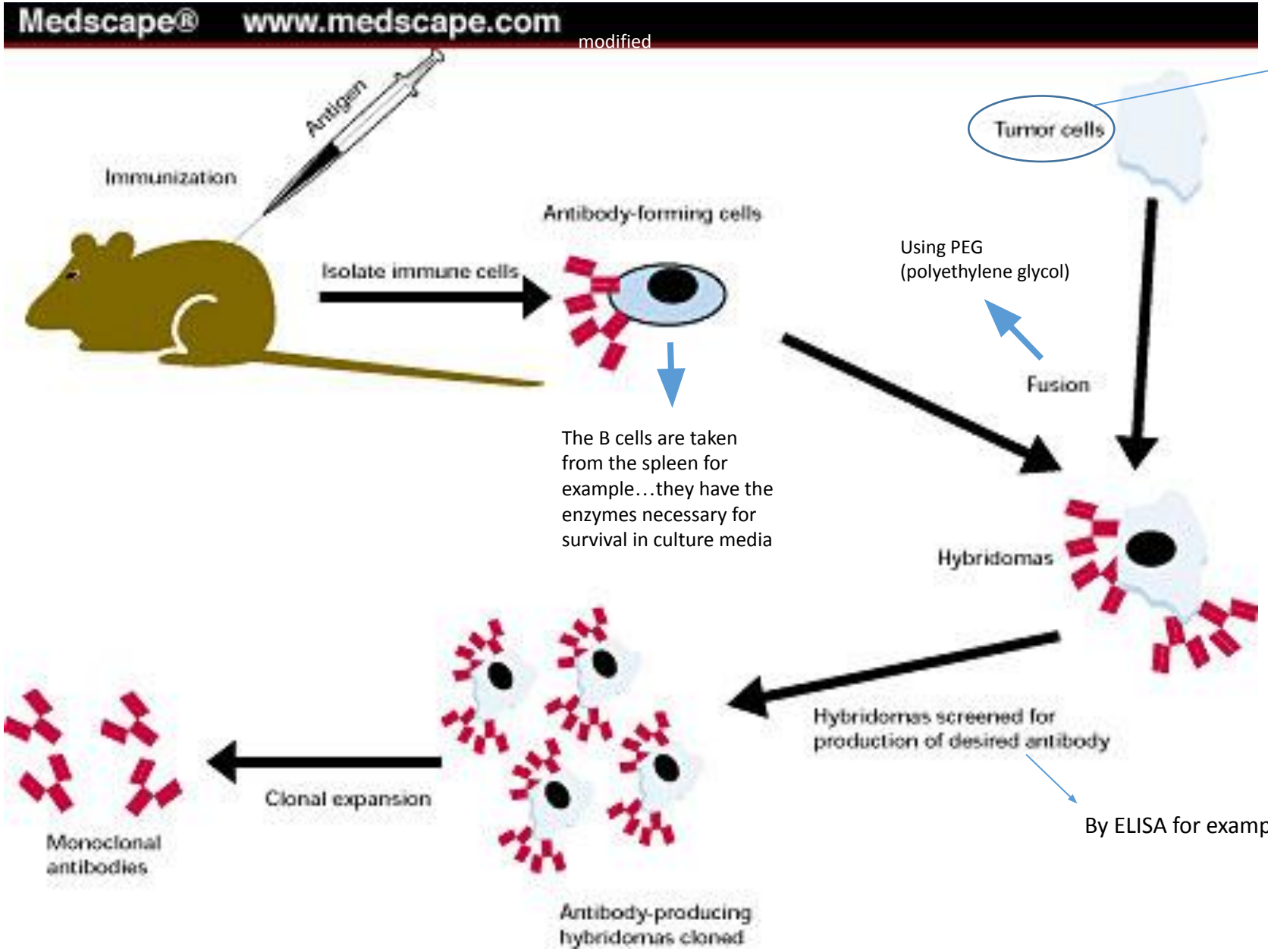
https://emedicine.medscape.com/article/2087113-overview..modified
…see references on this page



Normal serum protein electrophoresis diagram with legend of different zones

- What is the difference between serum and plasma?
- What is the difference between “monoclonal” and “polyclonal”?
- What is the difference between active immunity and passive immunity?

Hybridoma technology…for monoclonal antibody production



Thank You