ANTIGENS

Dr. Naci
Immunologist

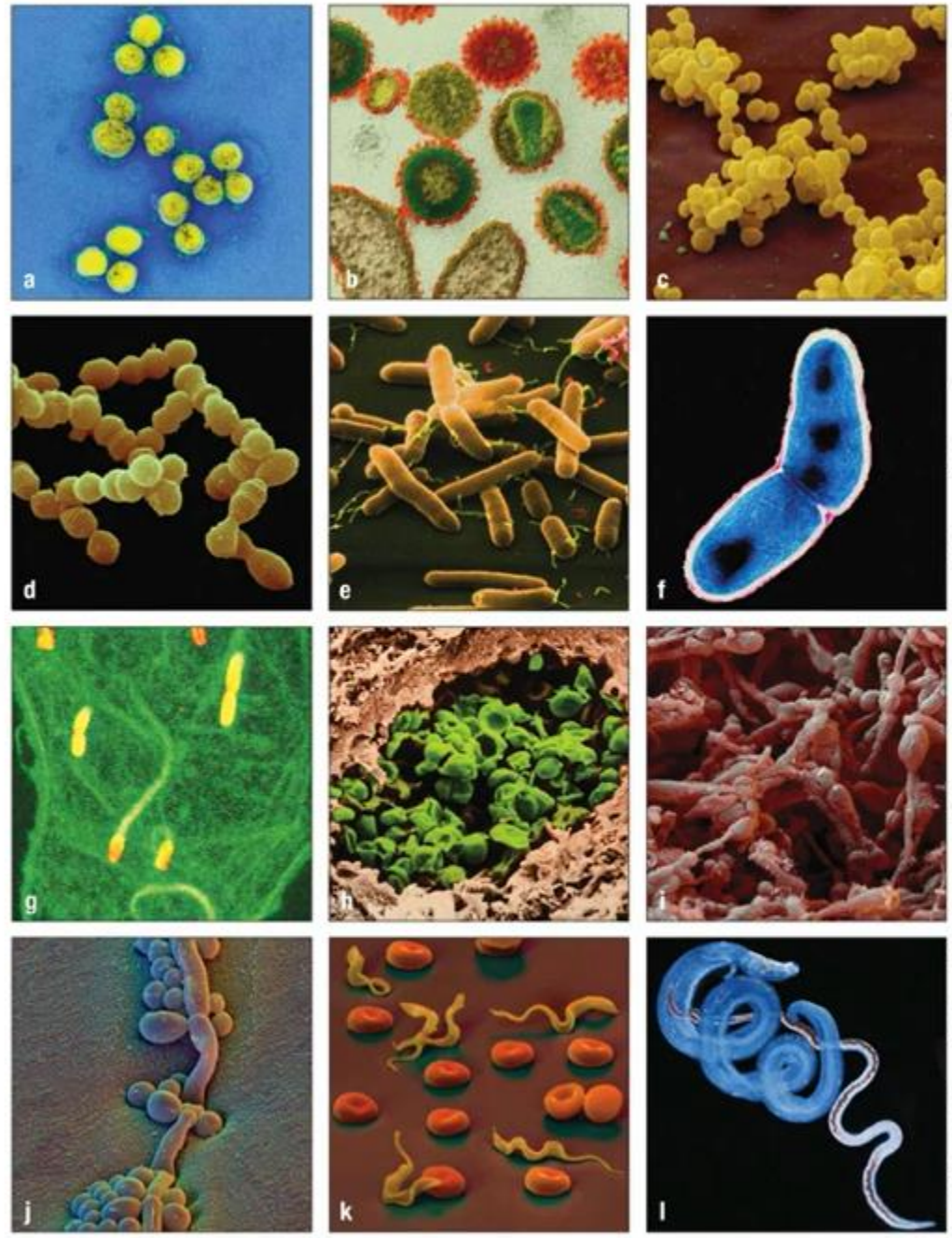
References
Abbass and Kuby Textbooks.

Antigen definition

“An antigen is a molecule that initiates the production of an antibody and causes an immune response.”

Antigens are **large molecules of proteins**, present on the surface of the pathogen- such as bacteria, fungi viruses, and other foreign particles.

When these harmful agents enter the body, it induces an immune response in the body for the production of antibodies.
For example: When a common cold virus enters the body, it causes the body to produce antibodies to prevent from getting sick.
Cellular Immunity: T-cell mediated immunity



Parham Figure 1.3

Types of Antigens
On the basis of Origin

- **Exogenous Antigens**

Exogenous antigens are the external antigens that enter the body from outside, e.g. inhalation, injection, etc. These include food allergen, pollen, aerosols, etc. and are the most common type of antigens.

- **Endogenous Antigens**

Endogenous antigens are generated inside the body due to viral or bacterial infections or cellular metabolism.

- **Autoantigens**

Autoantigens are the ‘self’ proteins or nucleic acids that due to some genetic or environmental alterations get attacked by their own immune system causing autoimmune diseases.

- **Tumour Antigens**

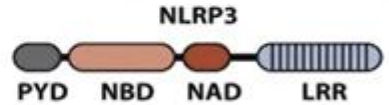
It is an antigenic substance present on the surface of tumour cells that induces an immune response in the host, e.g. MHC-I and MHC-II. Many tumours develop a mechanism to evade the immune system of the body.

- **Native Antigens**

An antigen that is not yet processed by an antigen-presenting cell is known as native antigens.

Groups of PRRs

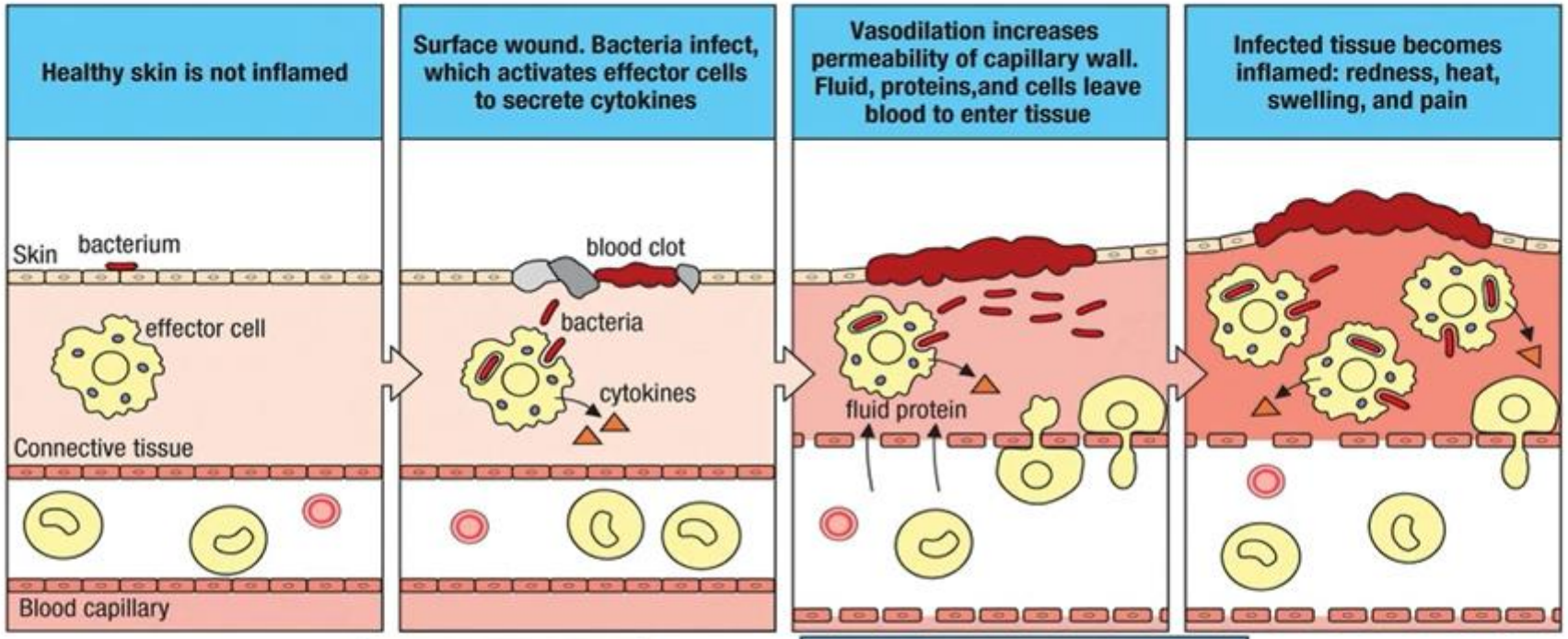
TABLE 3-2 Pattern recognition receptor families

	Full name	Cellular location(s)	Ligands	Cellular functions	Icon
TLR	Toll-like receptor	Plasma membrane, endosomes, lysosomes	Microbial carbohydrates, lipoproteins, fungal mannans, bacterial flagellin, viral RNA, self-components of damaged tissues, etc.	Production of antimicrobials, antivirals, and cytokines; inflammation	
CLR	C-type lectin receptor	Plasma membrane	Carbohydrate components of fungi, mycobacteria, viruses, parasites, and some allergens	Phagocytosis, production of antimicrobials and cytokines; inflammation	
RLR	Retinoic acid-inducible gene-I (RIG-I)-like receptor	Cytosol	Viral RNA	Production of interferons and cytokines	
NLR	Nucleotide oligomerization domain (NOD)-like receptor	Cytosol	Fragments of intracellular or extracellular bacteria cell wall peptidoglycans	Production of antimicrobials and cytokines; inflammation	
ALR	Absent-in-melanoma (AIM)-like receptor	Cytosol and nucleus	Viral and bacterial DNAs	Production of interferons and cytokines	

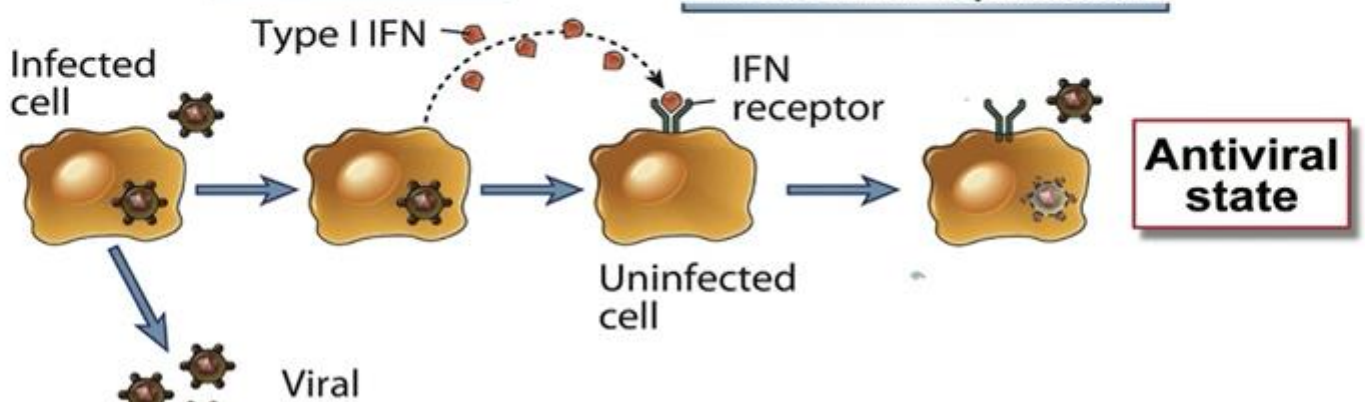
Kuby Table 3-2

Innate Immune Responses and Cytokine Production

Parham Figure 1.7



Abbas *Cellular and Molecular Immunology* Fig. 4-15



Properties of Antigens

IMMUNOGENECITY:

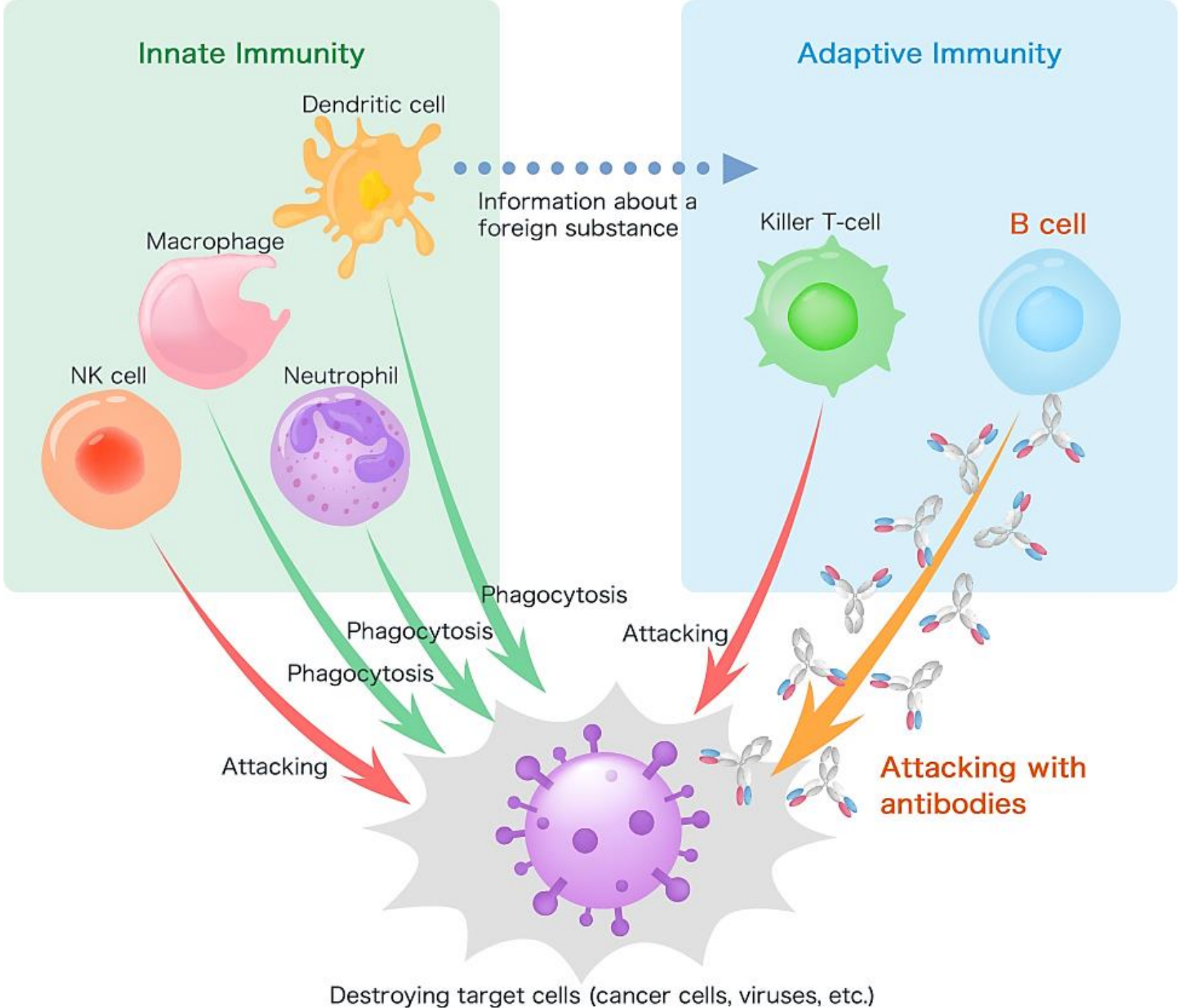
Ability of the substance to induce a specific immune response (Humorale or cellular)

ANTIGENECITY:

Antigen is a complex of epitopes (or hapten carrier combination) that can be specifically recognized by the effector of the immune system (Antibodies, specific T-lymphocytes)

Properties of Antigens

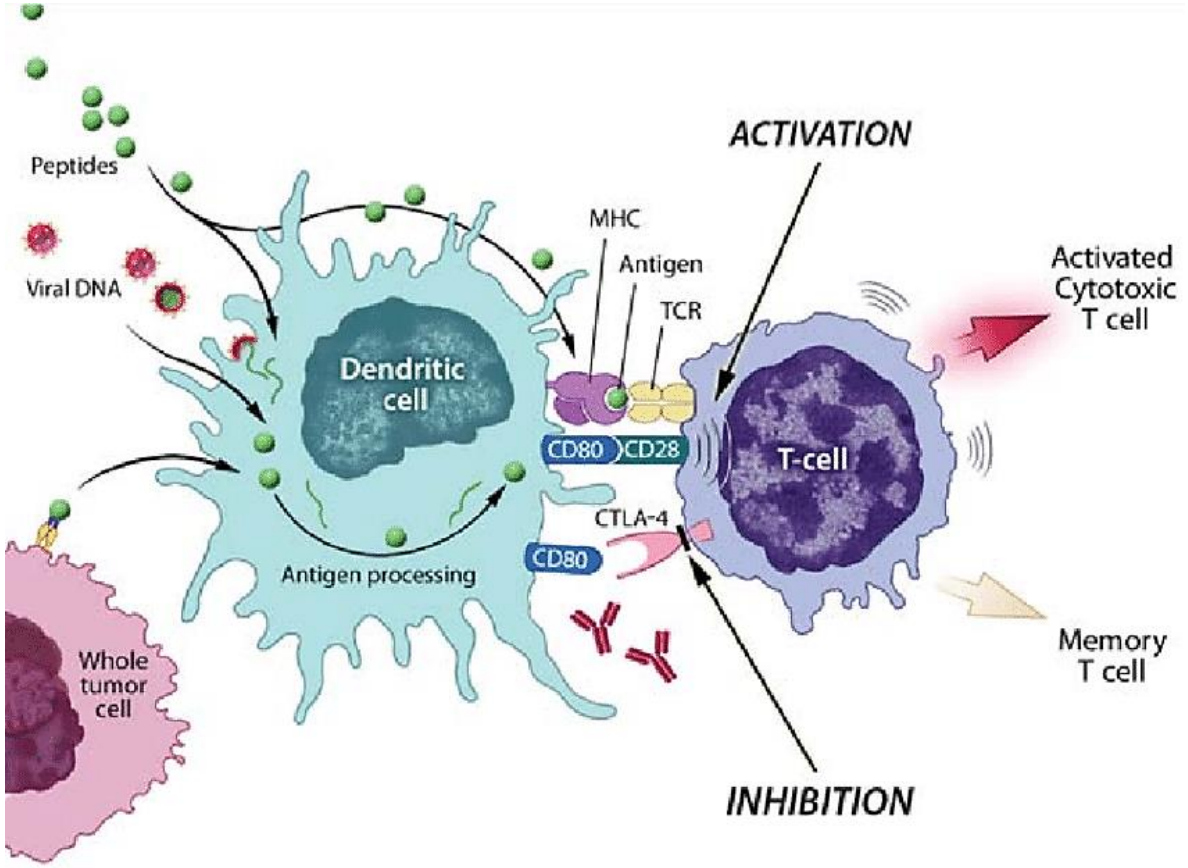
- The properties of antigens are as follows:
- The antigen should be a **foreign substance to induce an immune response**.
- The antigens have a **molecular mass of 14,000 to 6,00,000 Da**.
- They are mainly **proteins and polysaccharides**.
- The more **chemically complex** they are, the more immunogenic they will be.
- Antigens are **species-specific**.
- The **age influences the immunogenicity**. Very young and very old people exhibit very low immunogenicity.



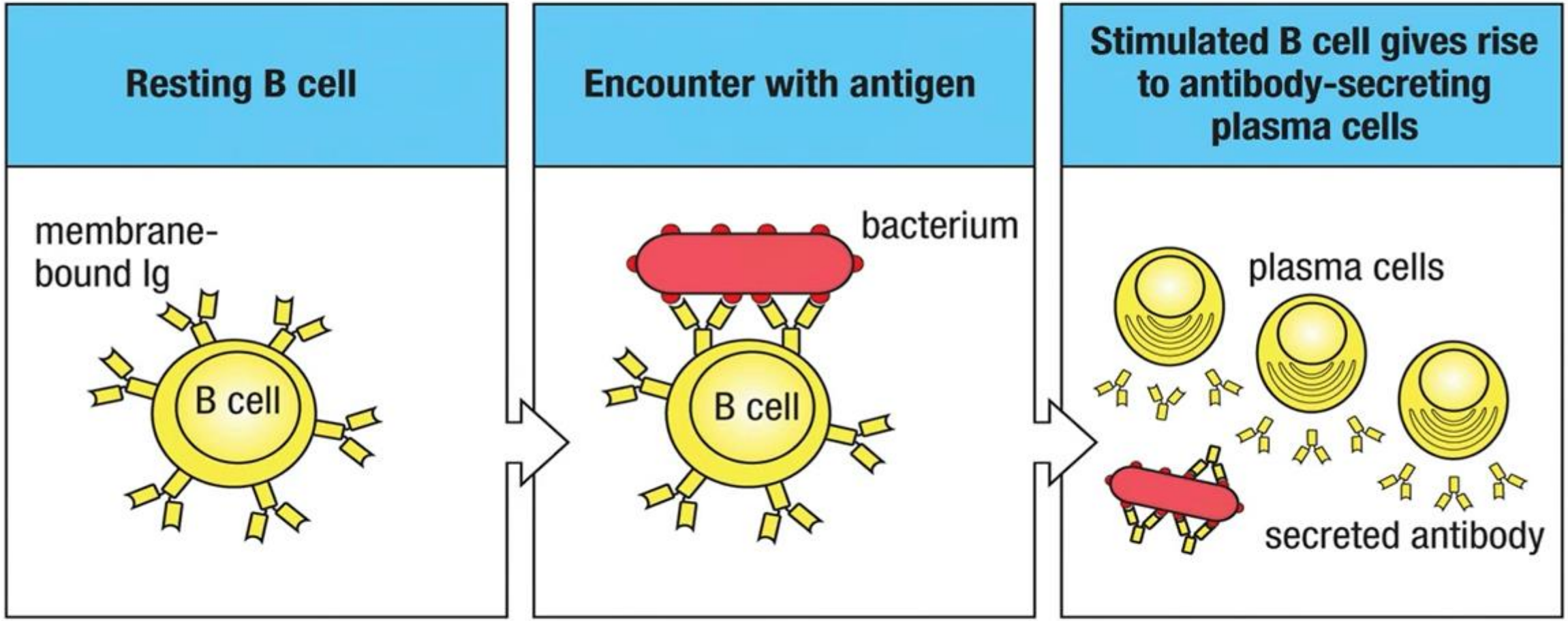
https://www.kyowakirin.com/antibody/basics/images/fig_basics01.jpg

Properties of Antigens

Cellular immune responses: mediated by CD4+ and CD8+ T-lymphocytes
Antigenic peptides recognized in the context of CMH restriction



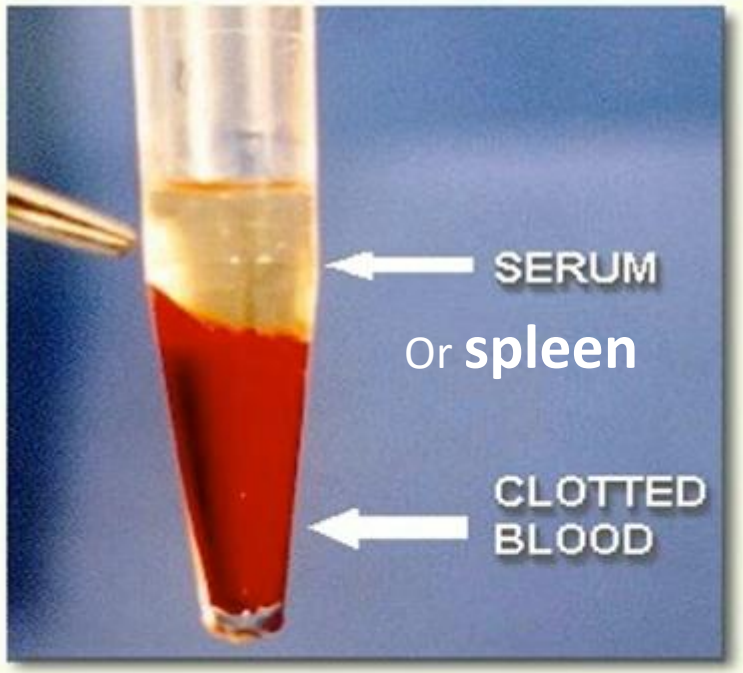
Activated B cells called plasma cells secrete antibodies

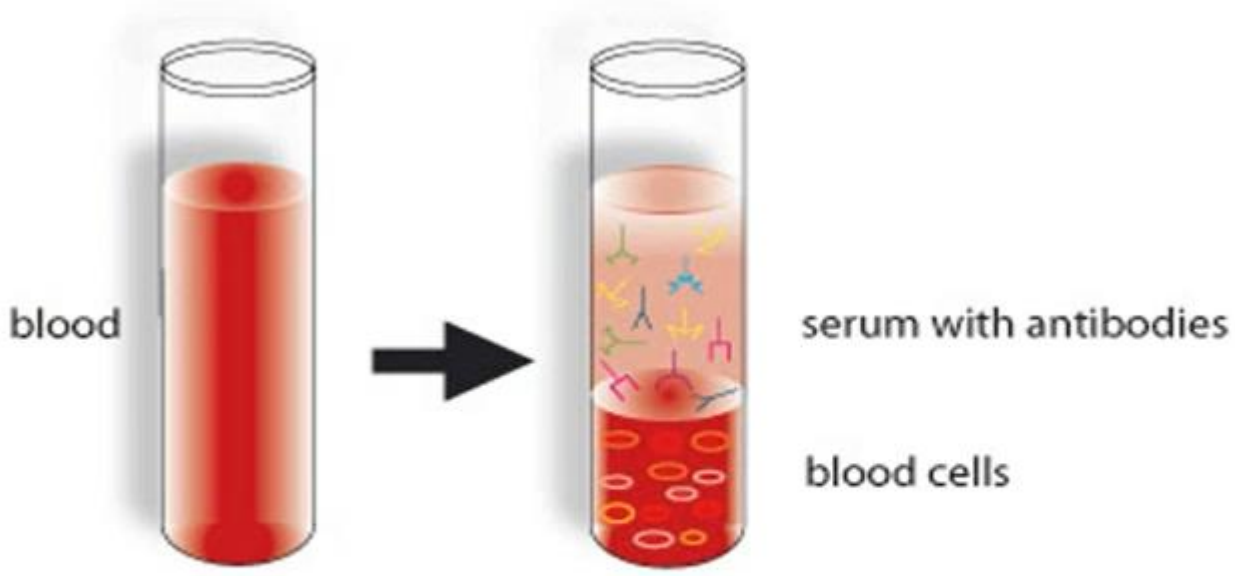


Parham Figure 4.1

1890s: von Behring and Kitasato

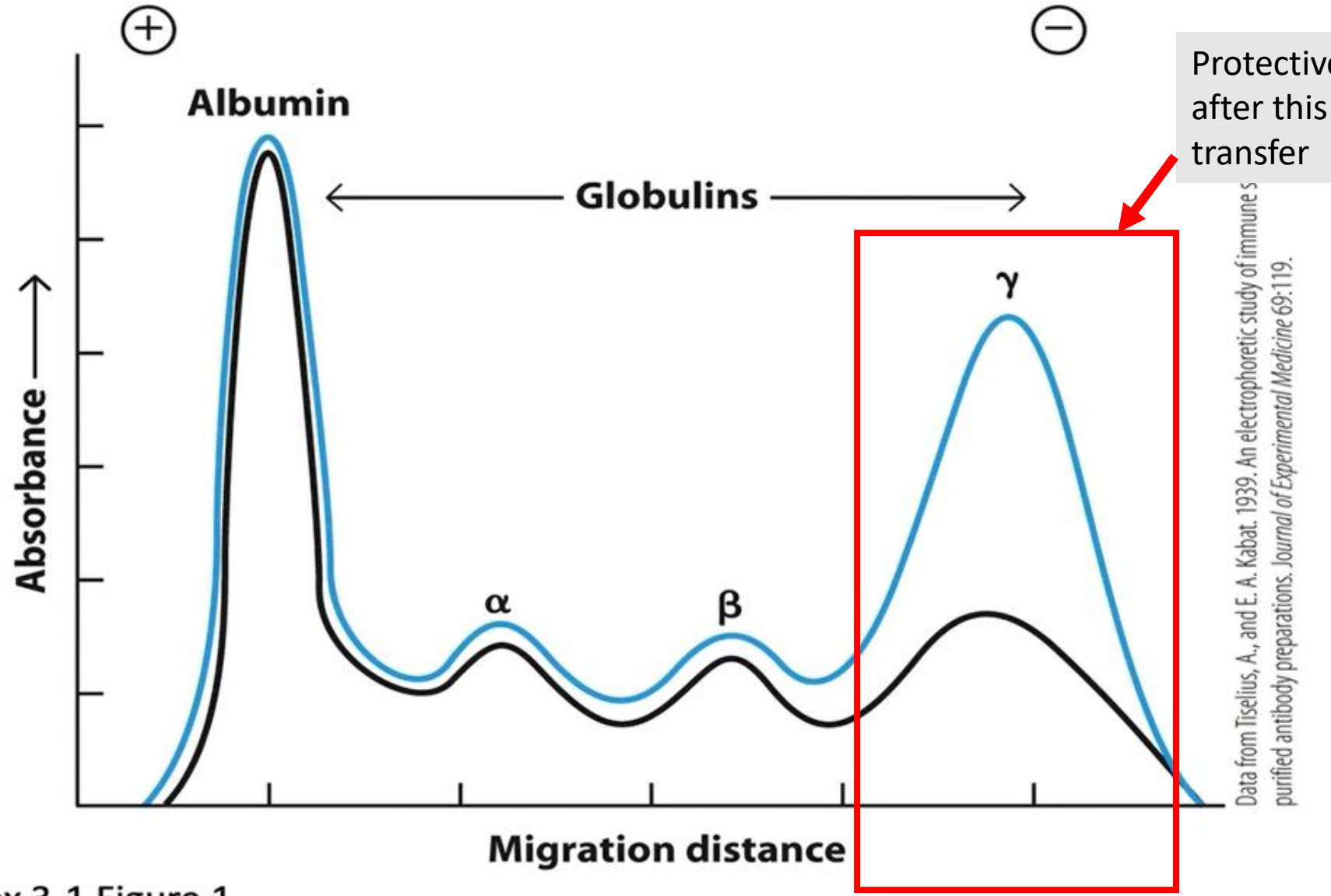
Clostridium botolimun
Clostridium betna
Low dose of antigen: rabbit lived and lived after injecting the highest dose but died after injecting the highest dose of Clostridium Betna: specificity of immune responses
High dose of antigen: Rabbit died





Serum is protective b
not the spl
not the cell

What is the molecule that can protect?

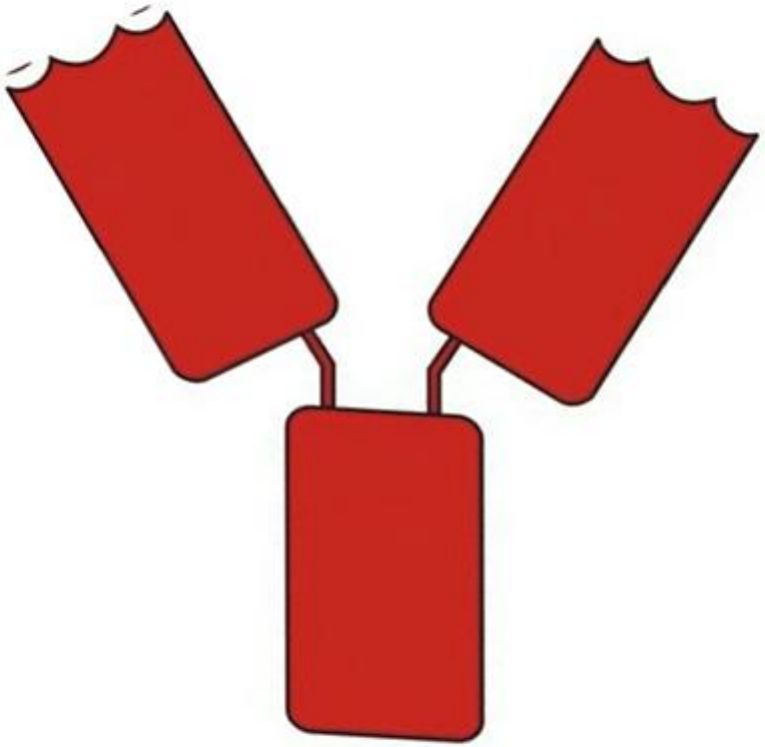


Protective ability after this fraction transfer

Kuby Box 3-1 Figure 1

Antibody

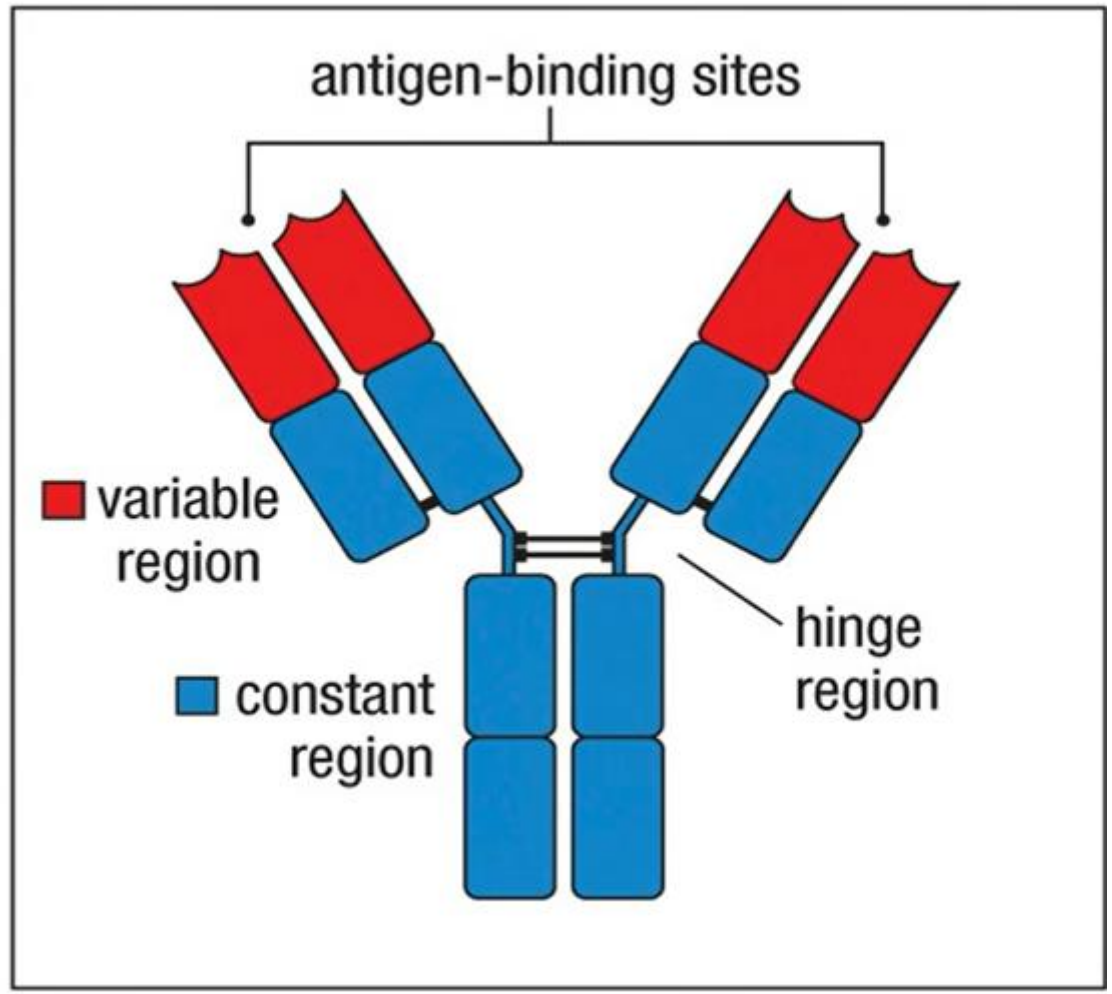
Roux *METHODS*: A Companion to *Methods in Enzymology* 10, 247–256 (1996)



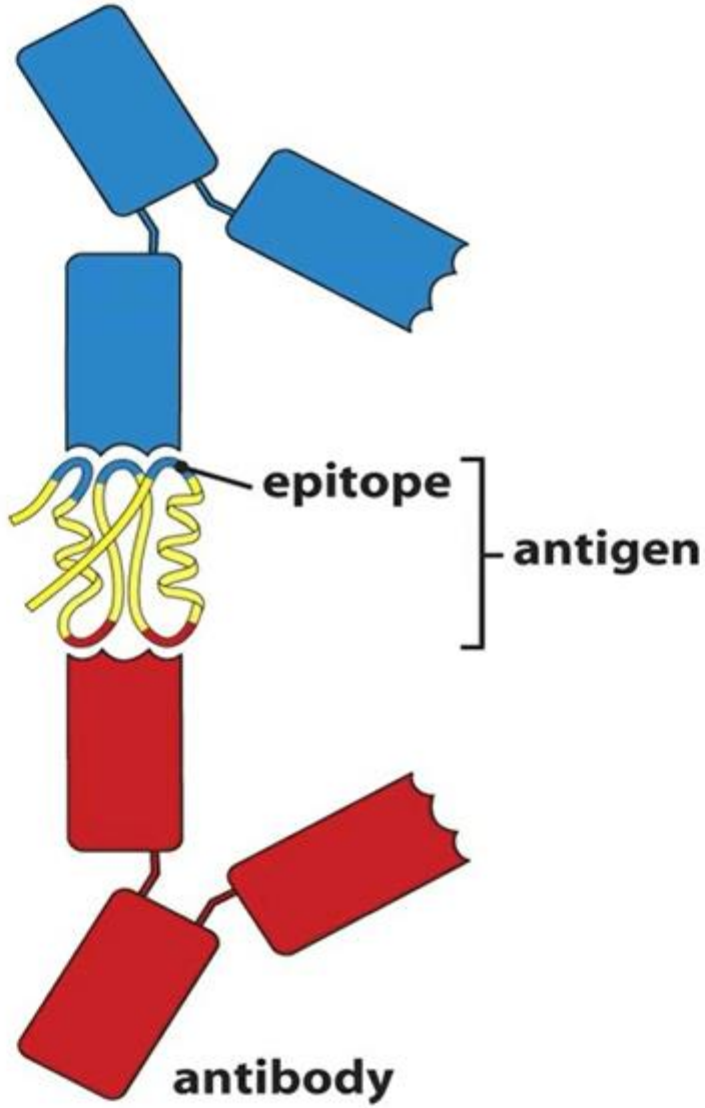
Adapted from Janeway Figure 1.15

Rudich et al. *J Exp Med*. 1988 Jul 1;168(1):247-66.

Antibody Structure

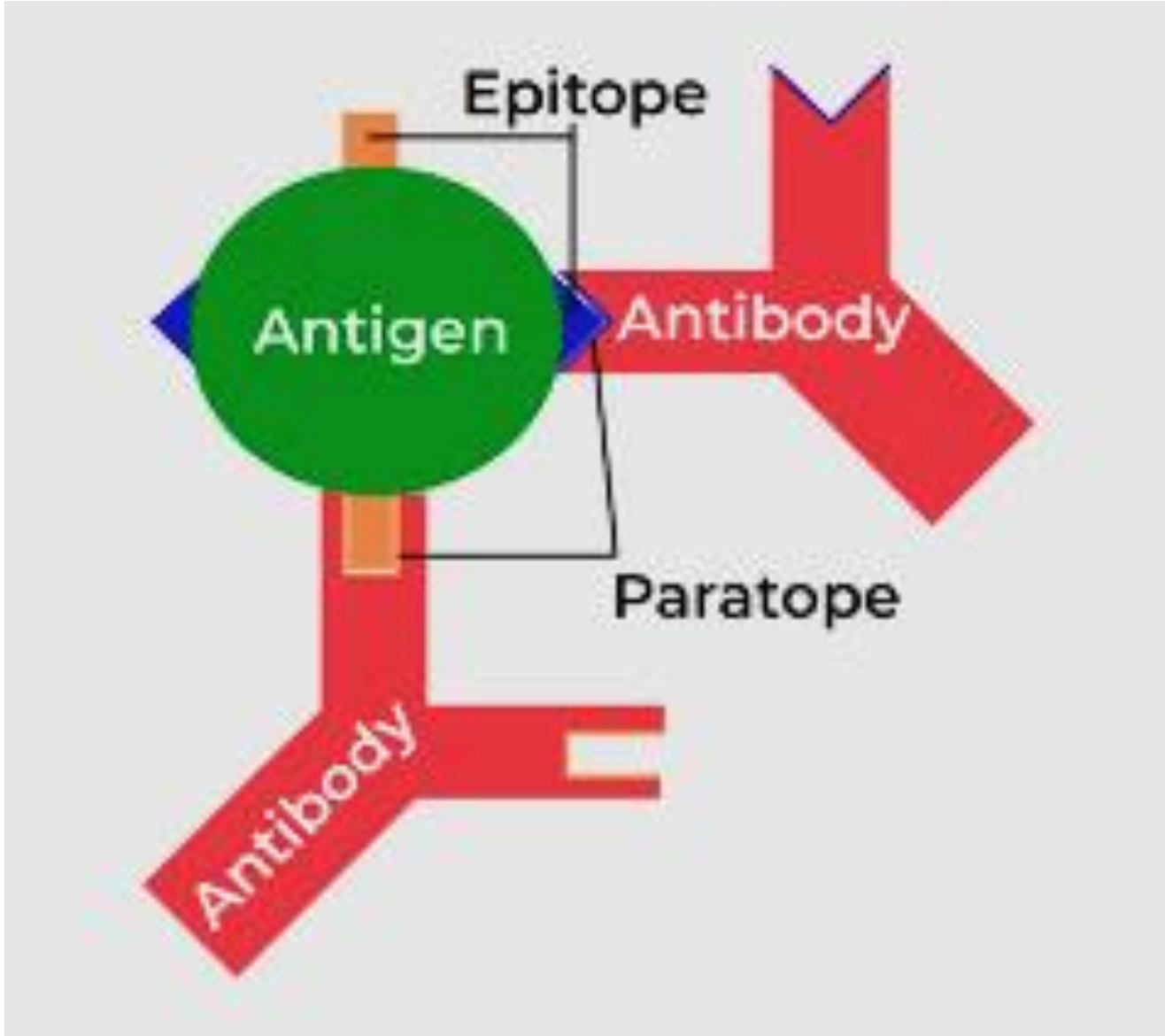


Epitope: The specific portion of the antigen that is contacted by antibody



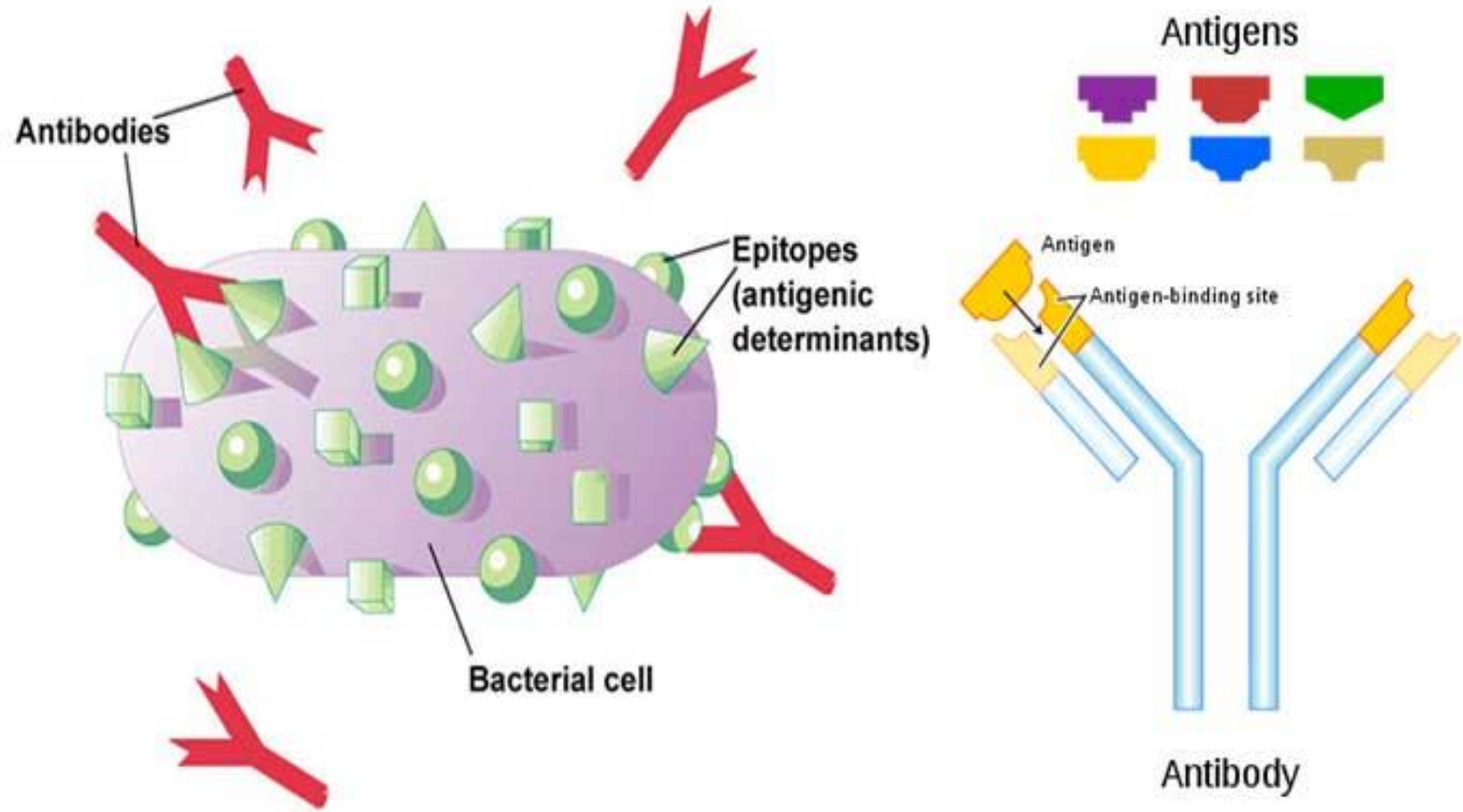
Janeway Figure 1.15

Figure 1.15 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

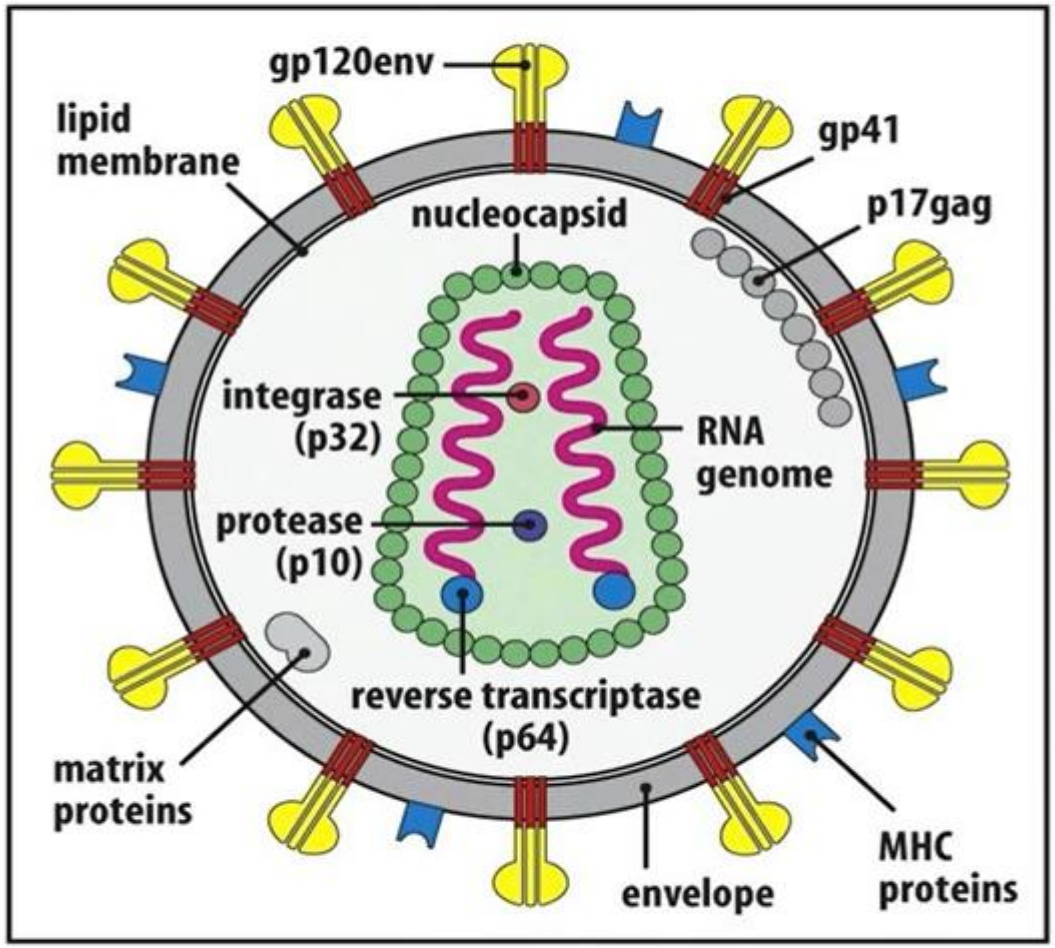

Epitope
Antigen
Antibody
Paratope
Antibody

Properties of Antigens

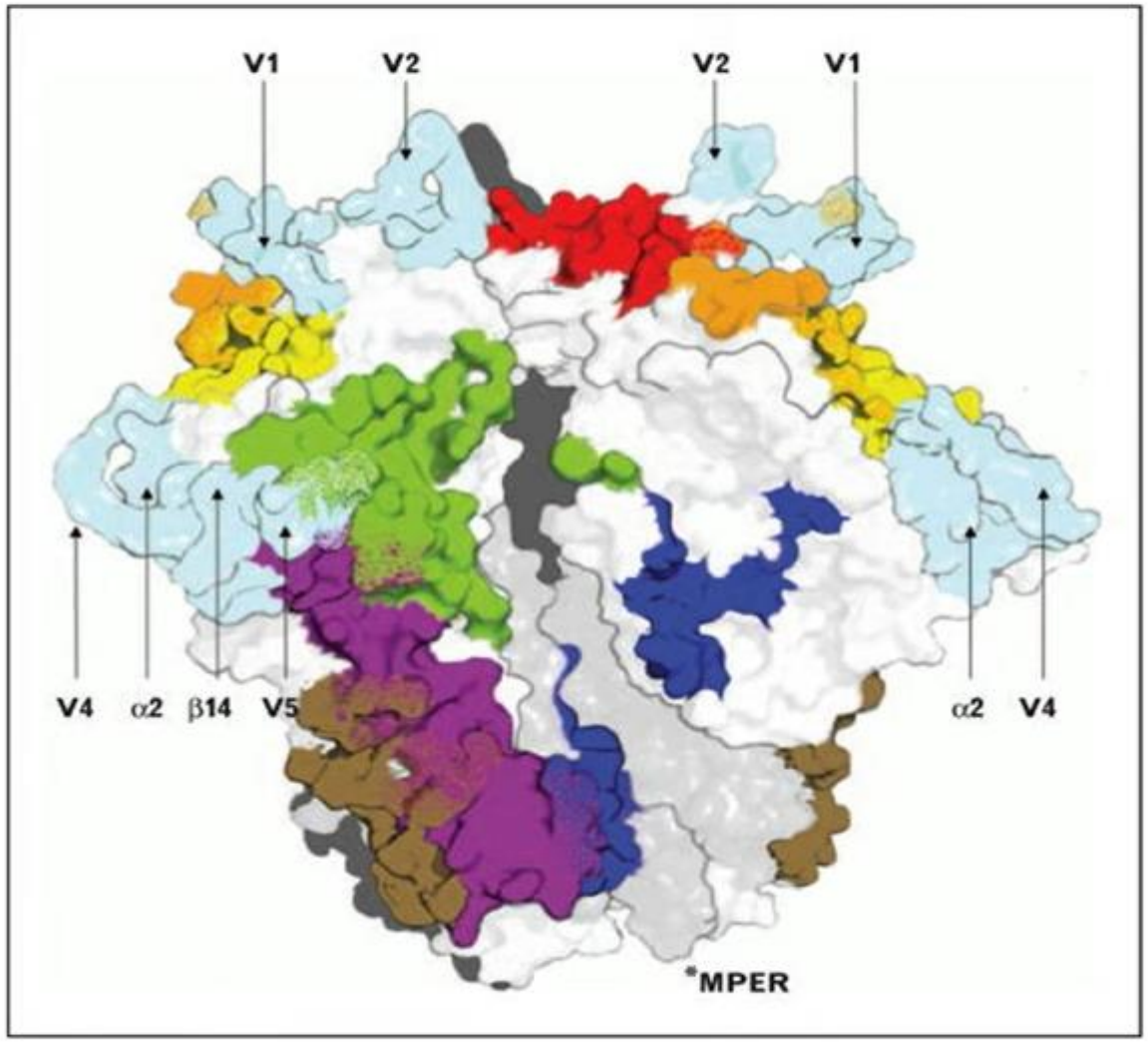
Humoral immune responses:



Antigens and epitopes



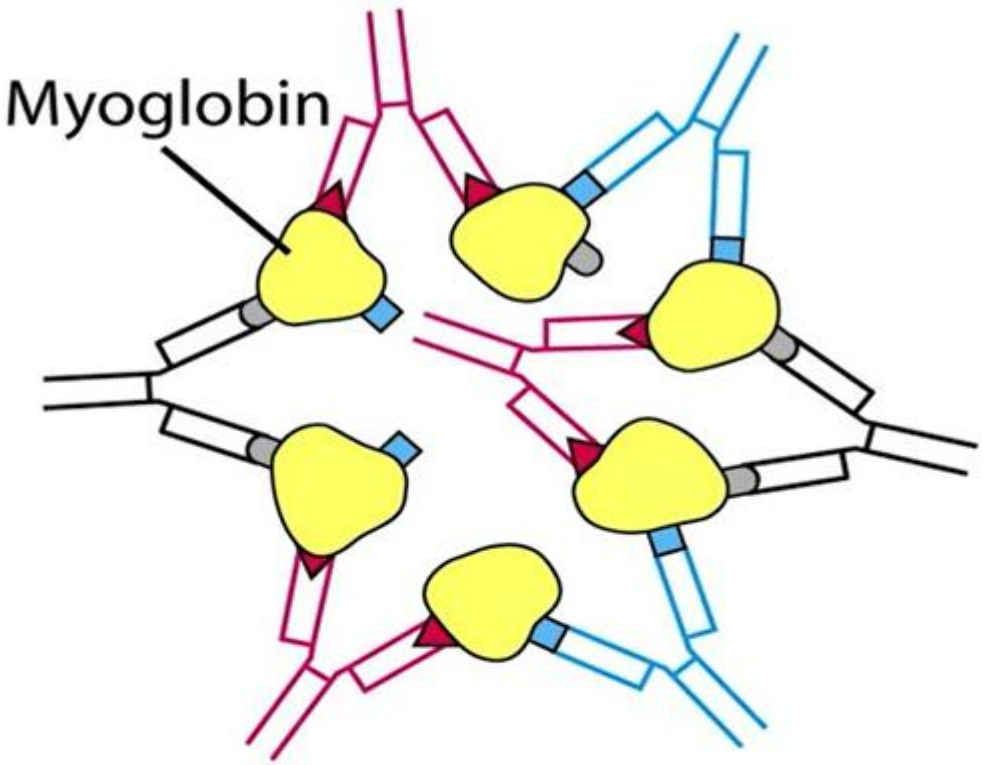
Janeway Figure 13.22



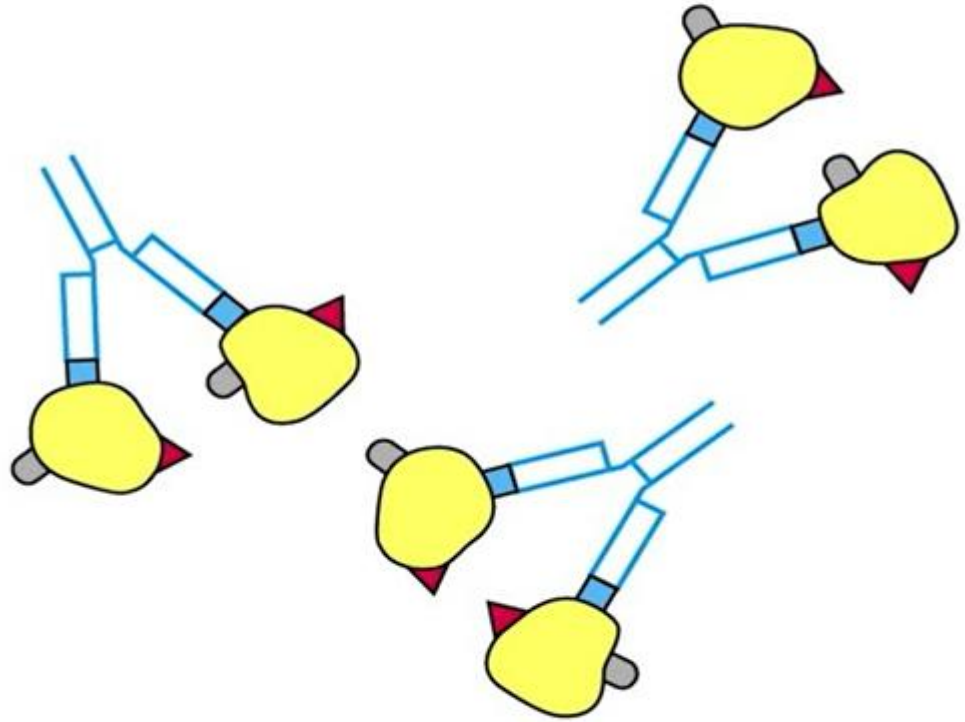
Wibmer et al. *Current Opinion in HIV/AIDS* Vol 10 (3) May 2015 p.135-143.

Polyclonal vs. Monoclonal Antibodies

POLYCLONAL ANTISERUM

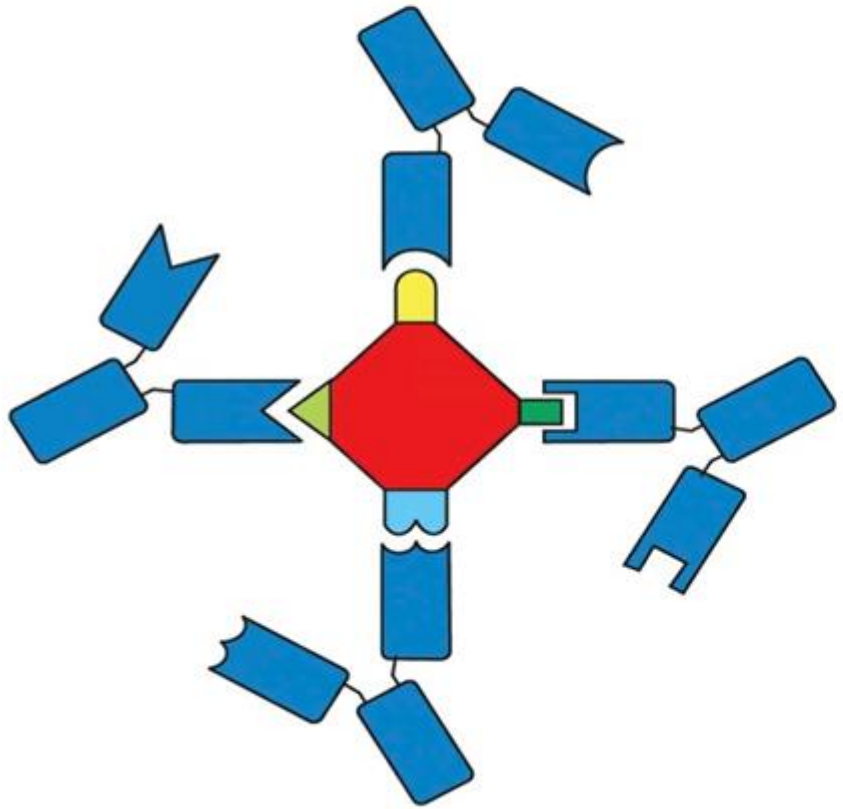


MONOCLONAL ANTIBODY

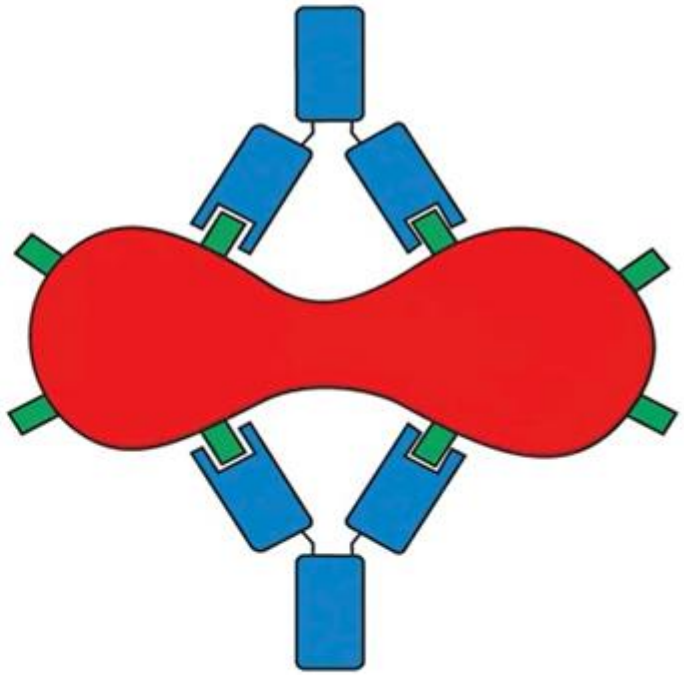


Antigens can contain multiple epitopes

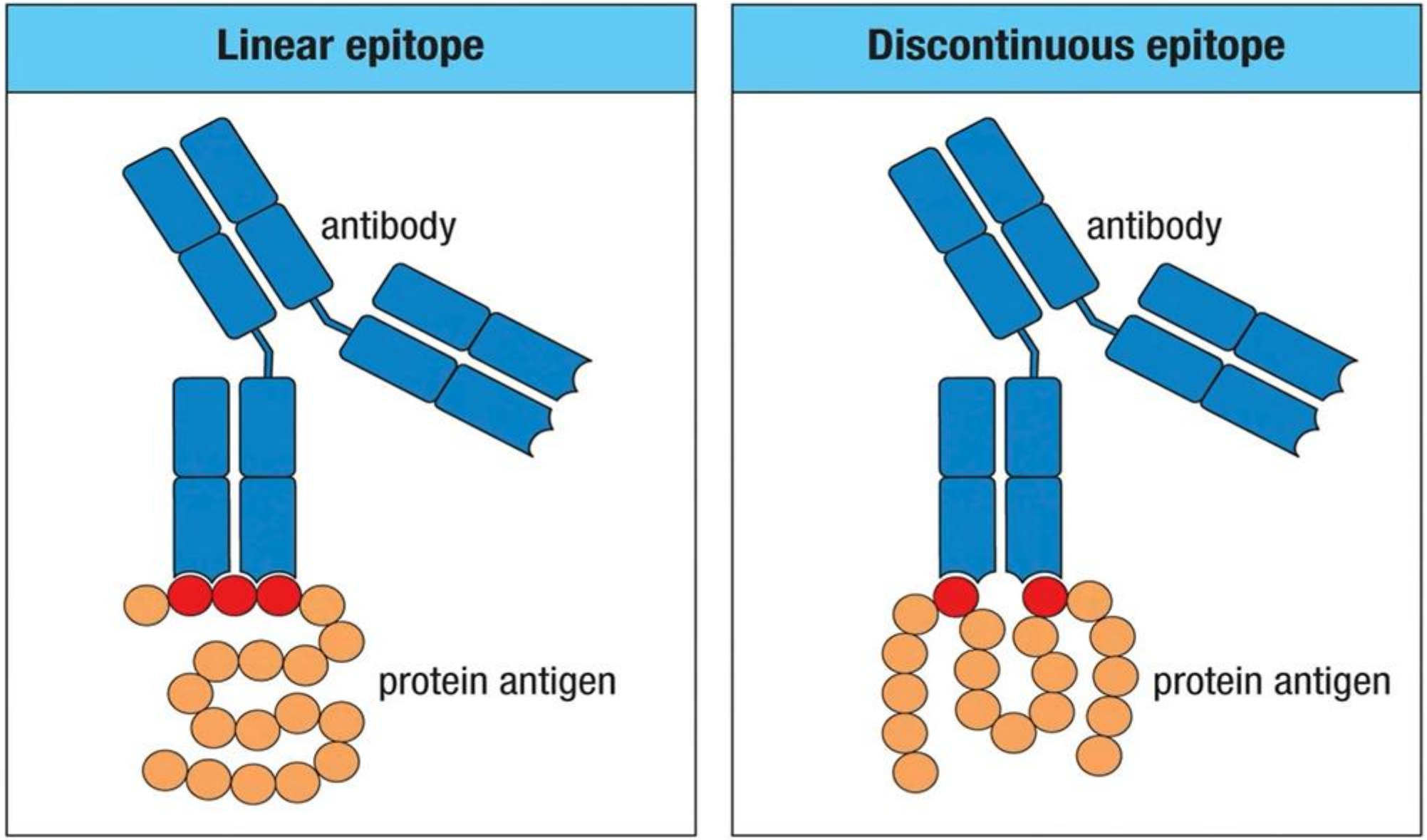
Multivalent antigen with different epitopes



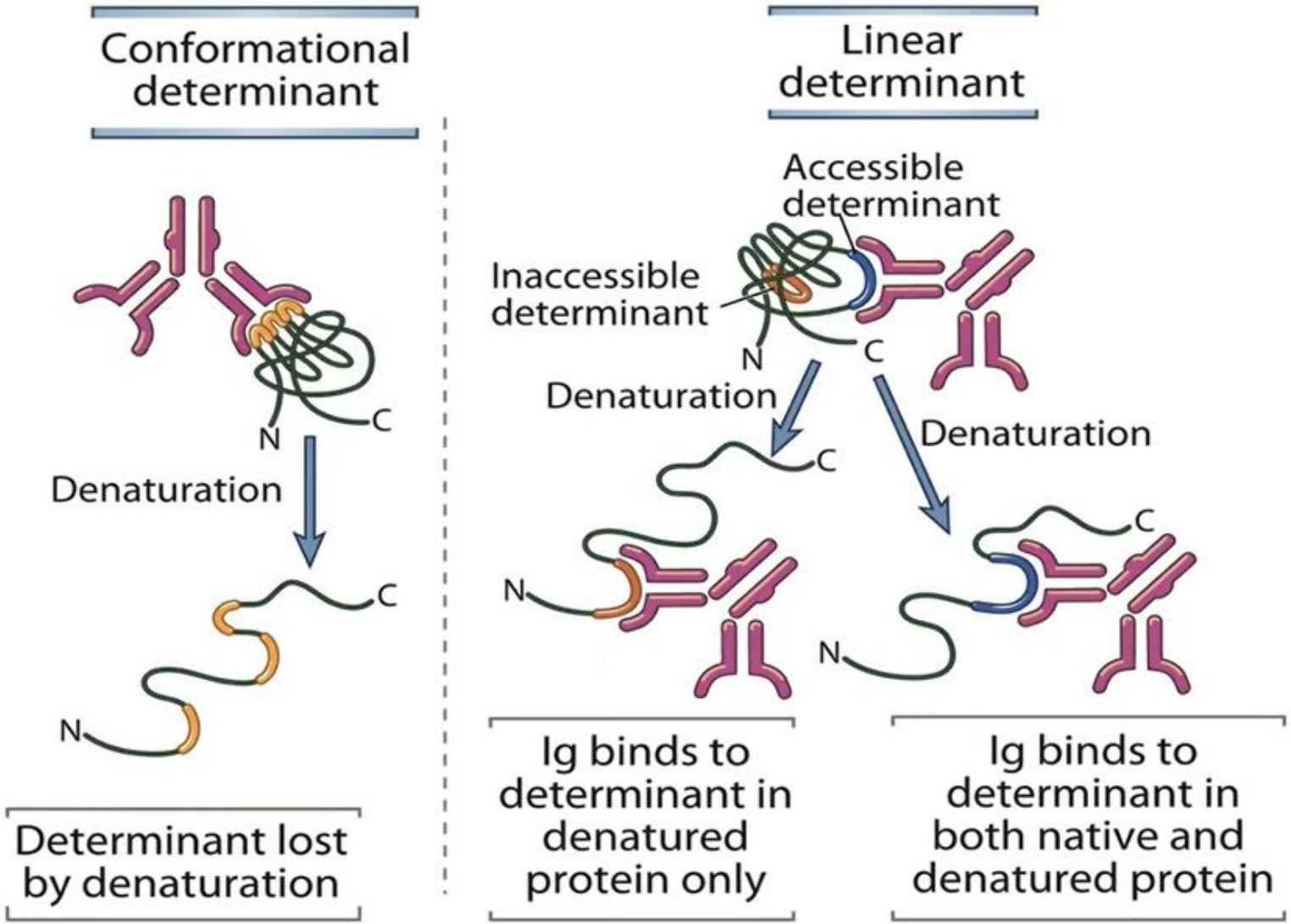
Multivalent antigen with a repeated epitope



Antibodies recognize native epitopes

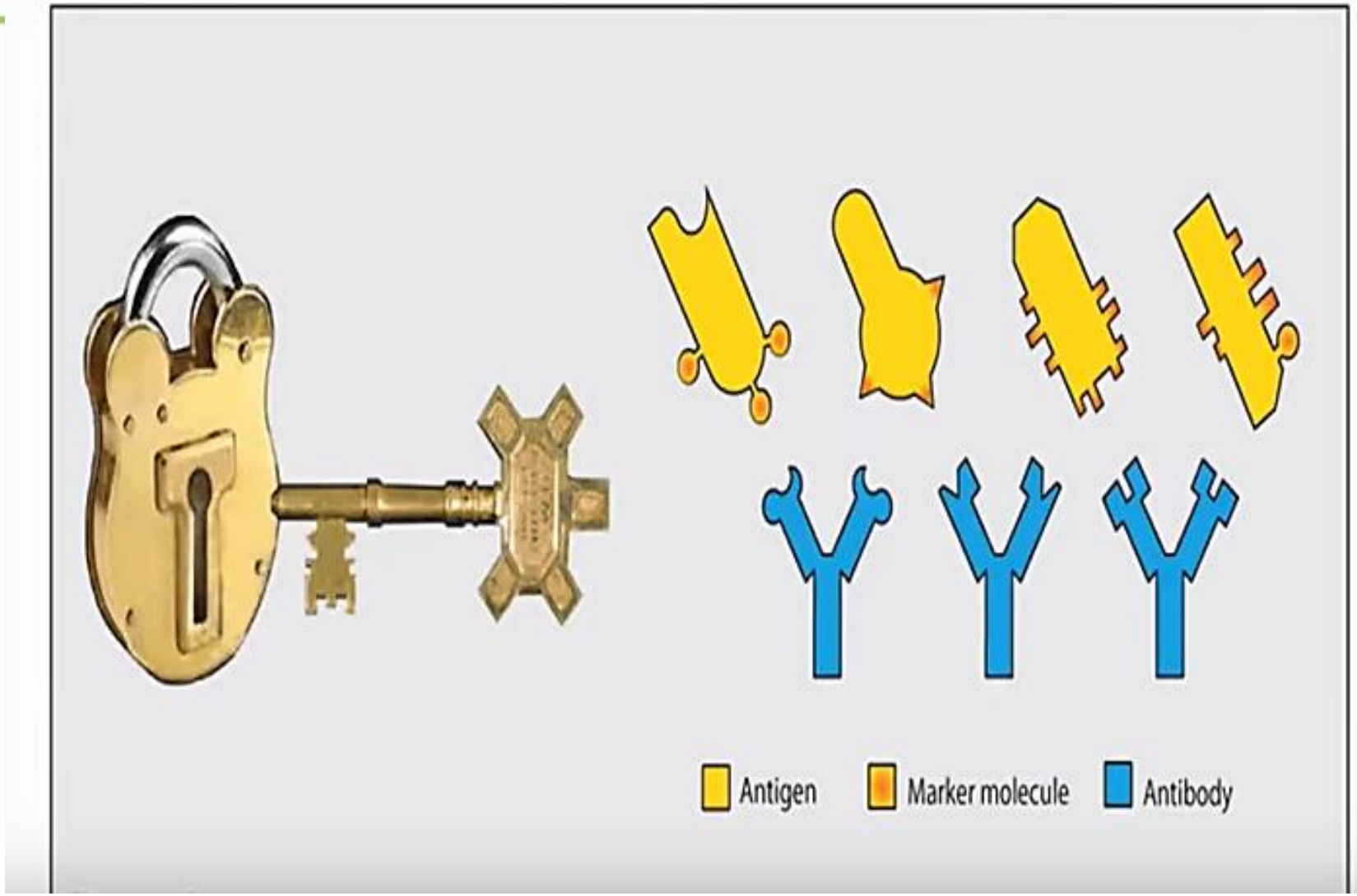


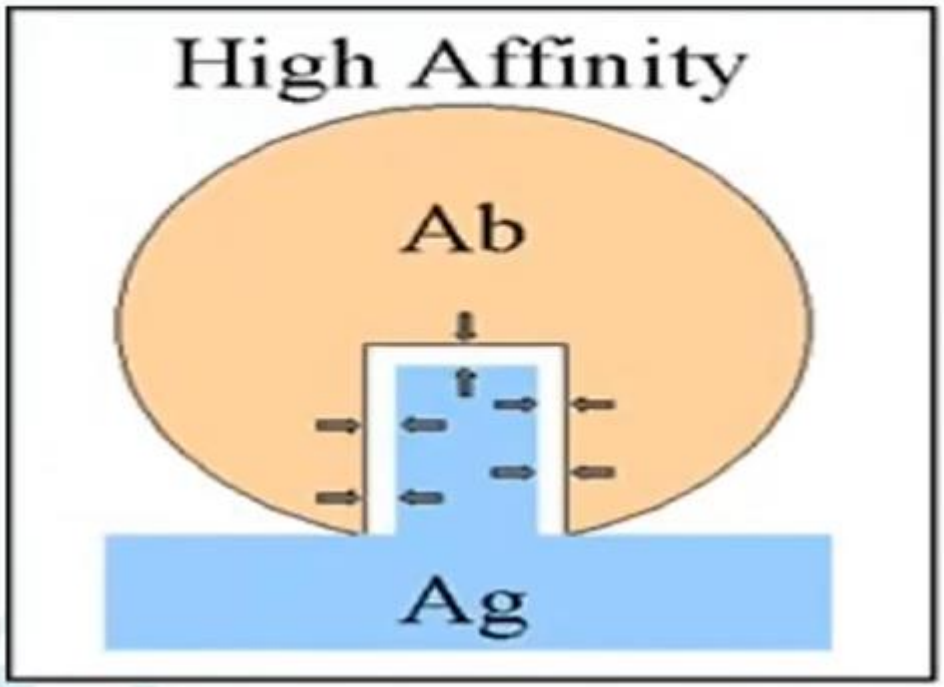
Linear and conformational epitopes

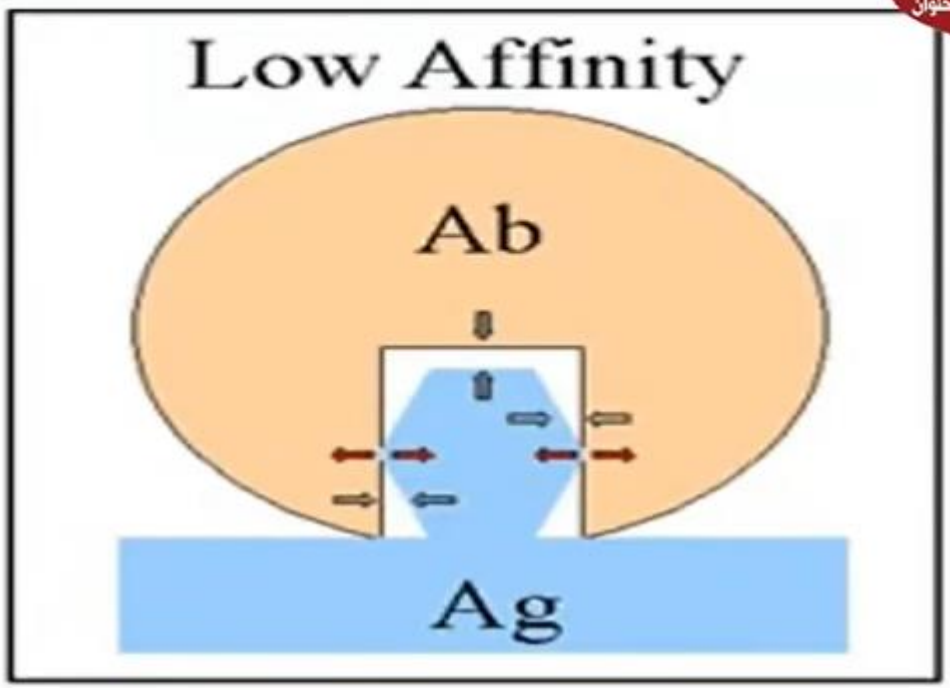


Abbas Fig. 5-12 A,B

Lock and key situation

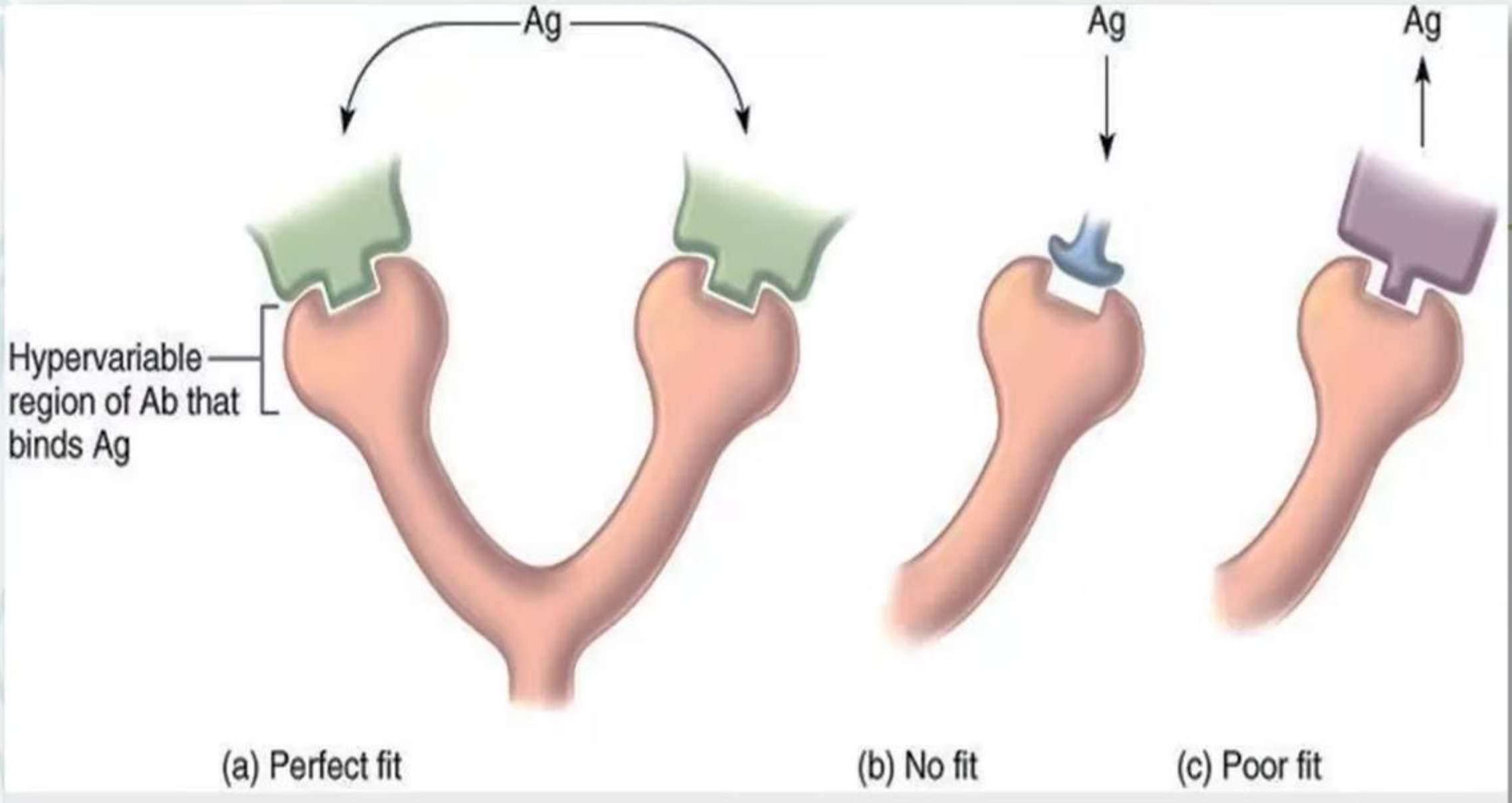




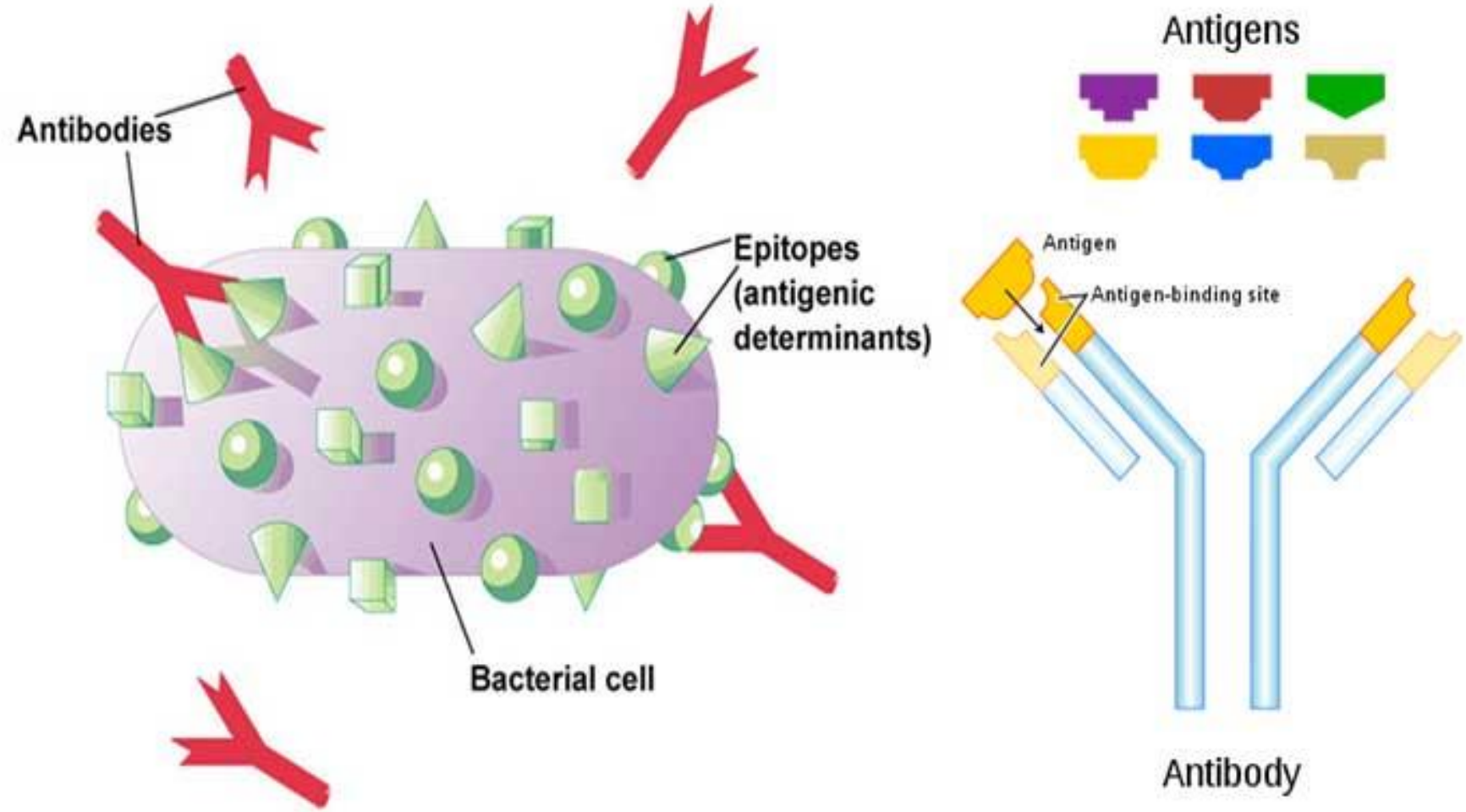


High affinity antibody

Low affinity antibody (poor fit)


Ag
Ag
Ag
Hypervariable region of Ab that binds Ag
(a) Perfect fit
(b) No fit
(c) Poor fit

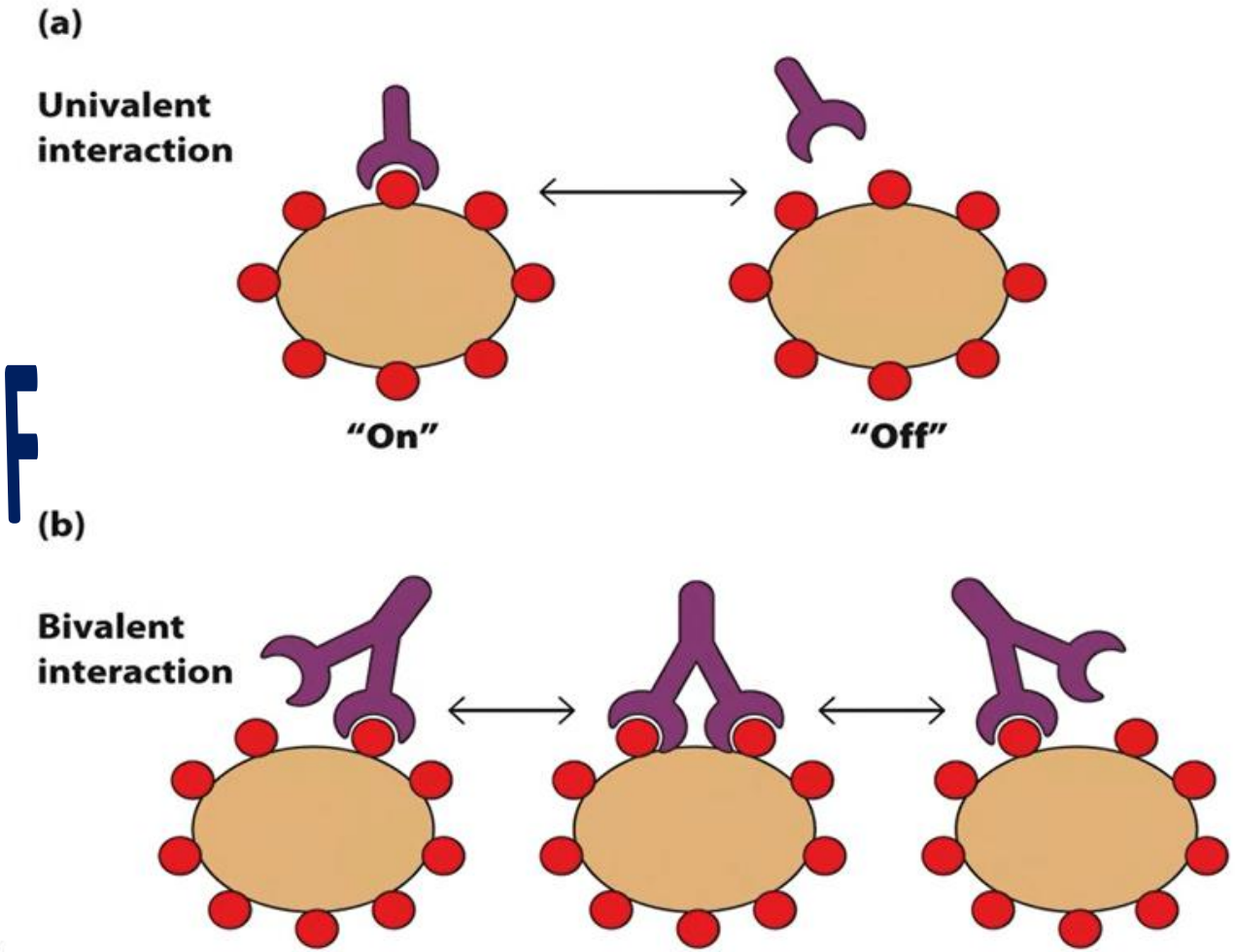
Affinity+ Affinity+…Affinity= Avidity



Why does it matter that an antibody has two arms?

AFFINITY

AVIDITY= SUM OF AFFINITIES



Kuby Figure 3-2

Types of Antigens
On the Basis of Immune Response

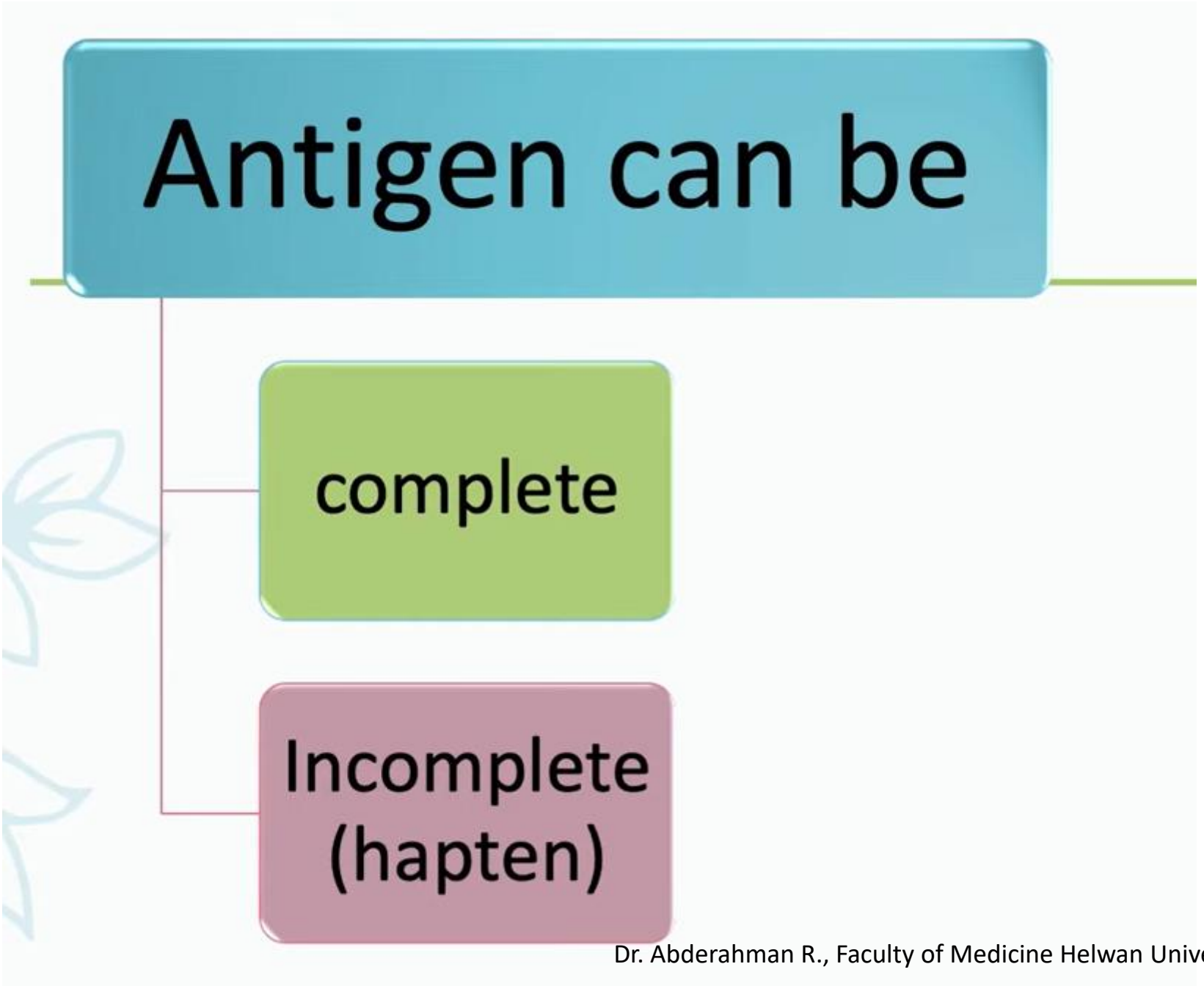
On the basis of the immune response, antigens can be classified as:

- **Immunogen**

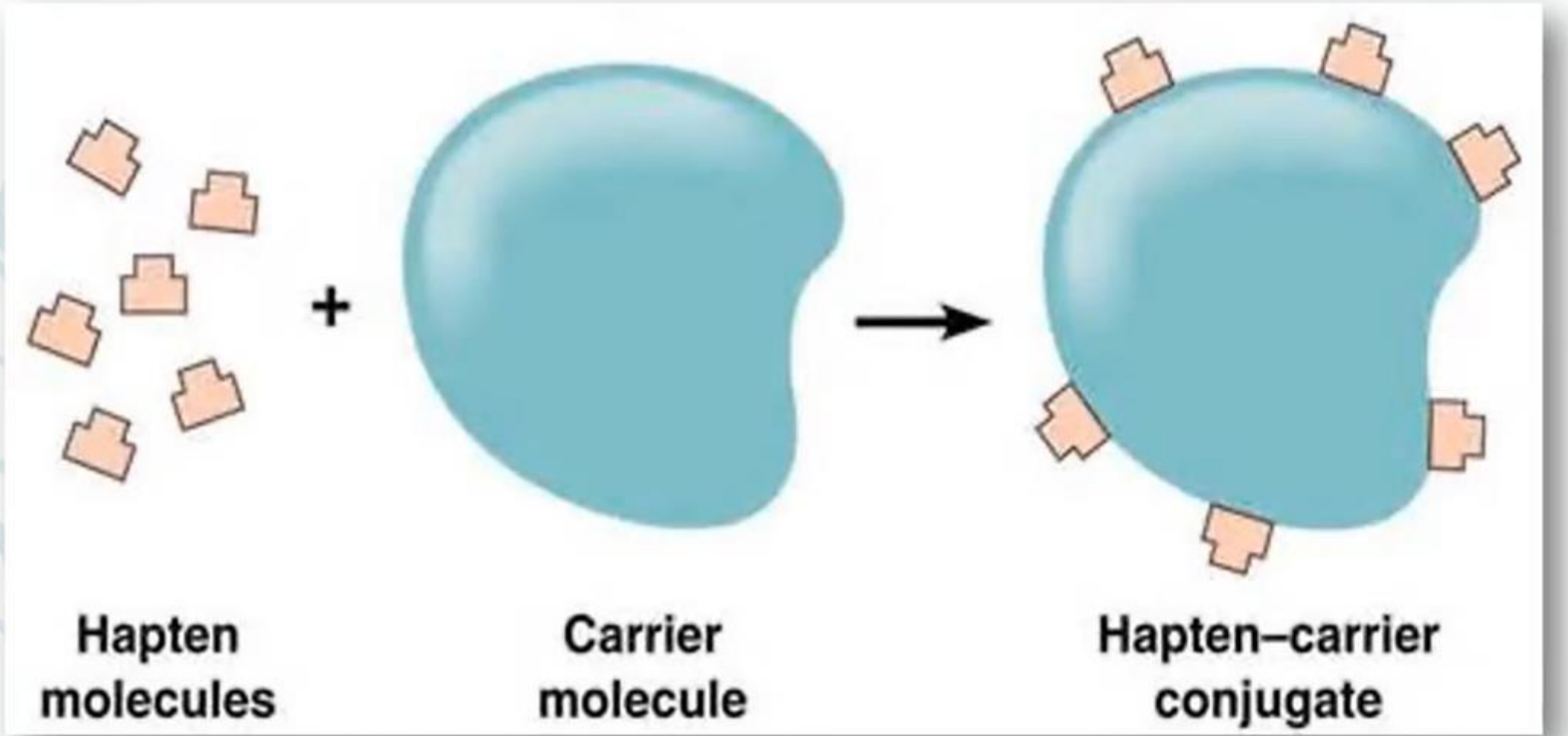
These may be proteins or polysaccharides and can generate an immune response on their own.

- **Hapten**

These are non-protein, foreign substances that require a carrier molecule to induce an immune response.

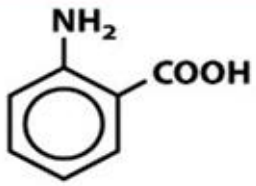
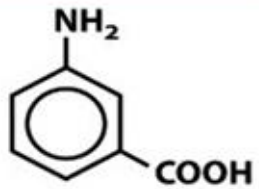
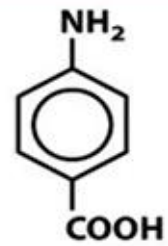

Antigen can be
complete
Incomplete (hapten)

Haptens:


+
Hapten molecules
Carrier molecule
Hapten–carrier conjugate

Specificity: Landsteinner (1900)

TABLE 4-1 Reactivity of antisera with various haptens

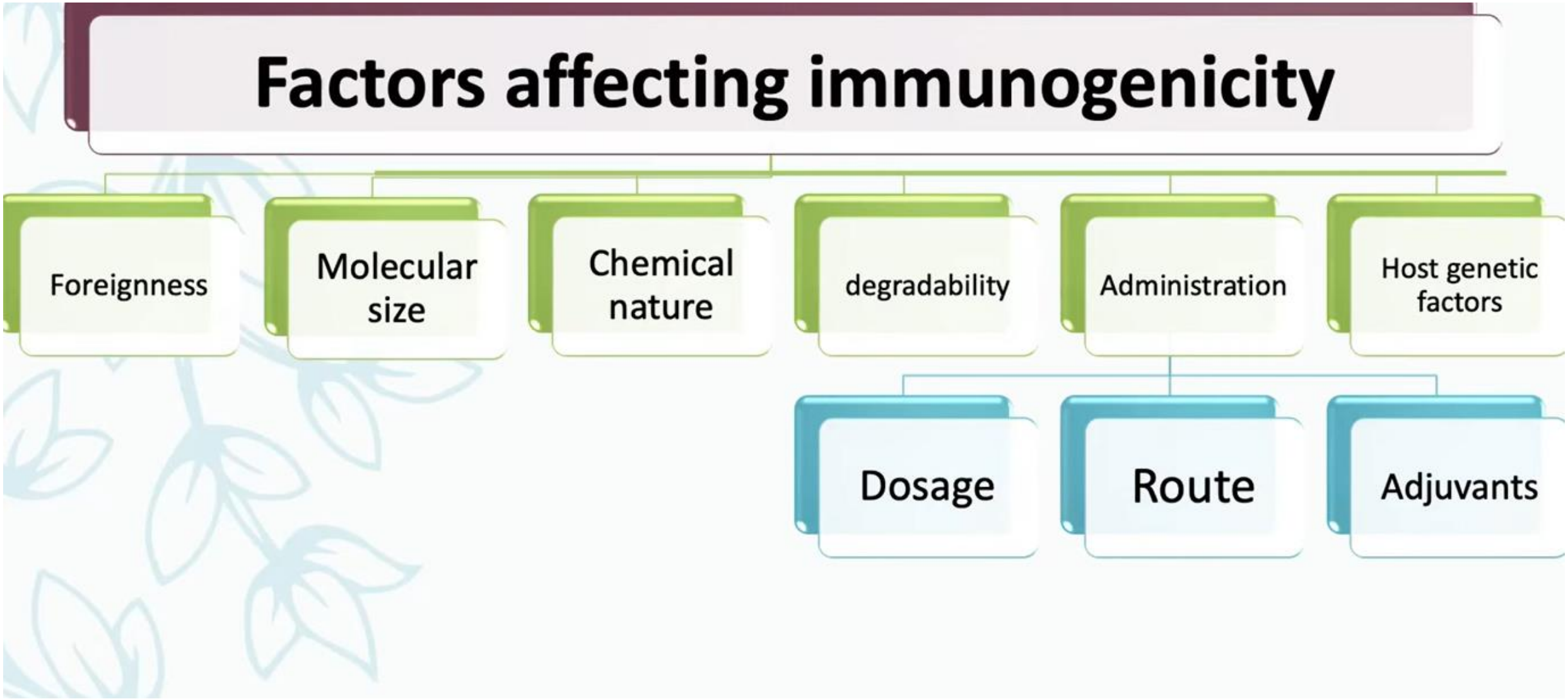
Antiserum against	REACTIVITY WITH: Aminobenzene (aniline) 	*o*-Aminobenzoic acid 	*m*-Aminobenzoic acid 	*p*-Aminobenzoic acid 
Aminobenzene	+	0	0	0
o-Aminobenzoic acid	0	+	0	0
m-Aminobenzoic acid	0	0	+	0
p-Aminobenzoic acid	0	0	0	+

KEY: 0 = no reactivity; + = strong reactivity

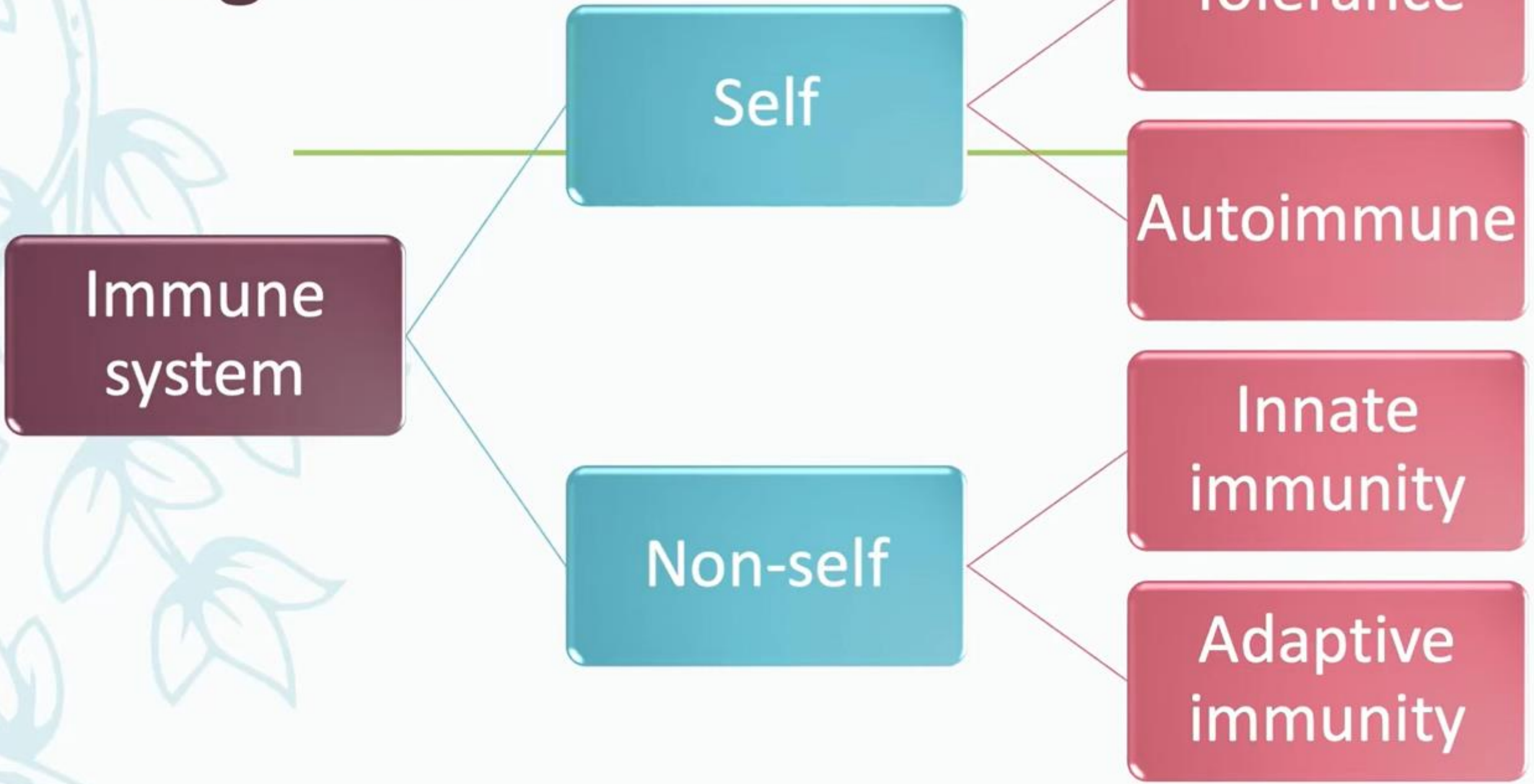
SOURCE: Based on K. Landsteiner, 1962, *The Specificity of Serologic Reactions,* Dover Press. Modified by J. Klein, 1982, *Immunology: The Science of Self-Nonself Discrimination,* Wiley.

Kuby 6th Edition Table 4-1

Factors affecting immunogenicity



1- Foreignness



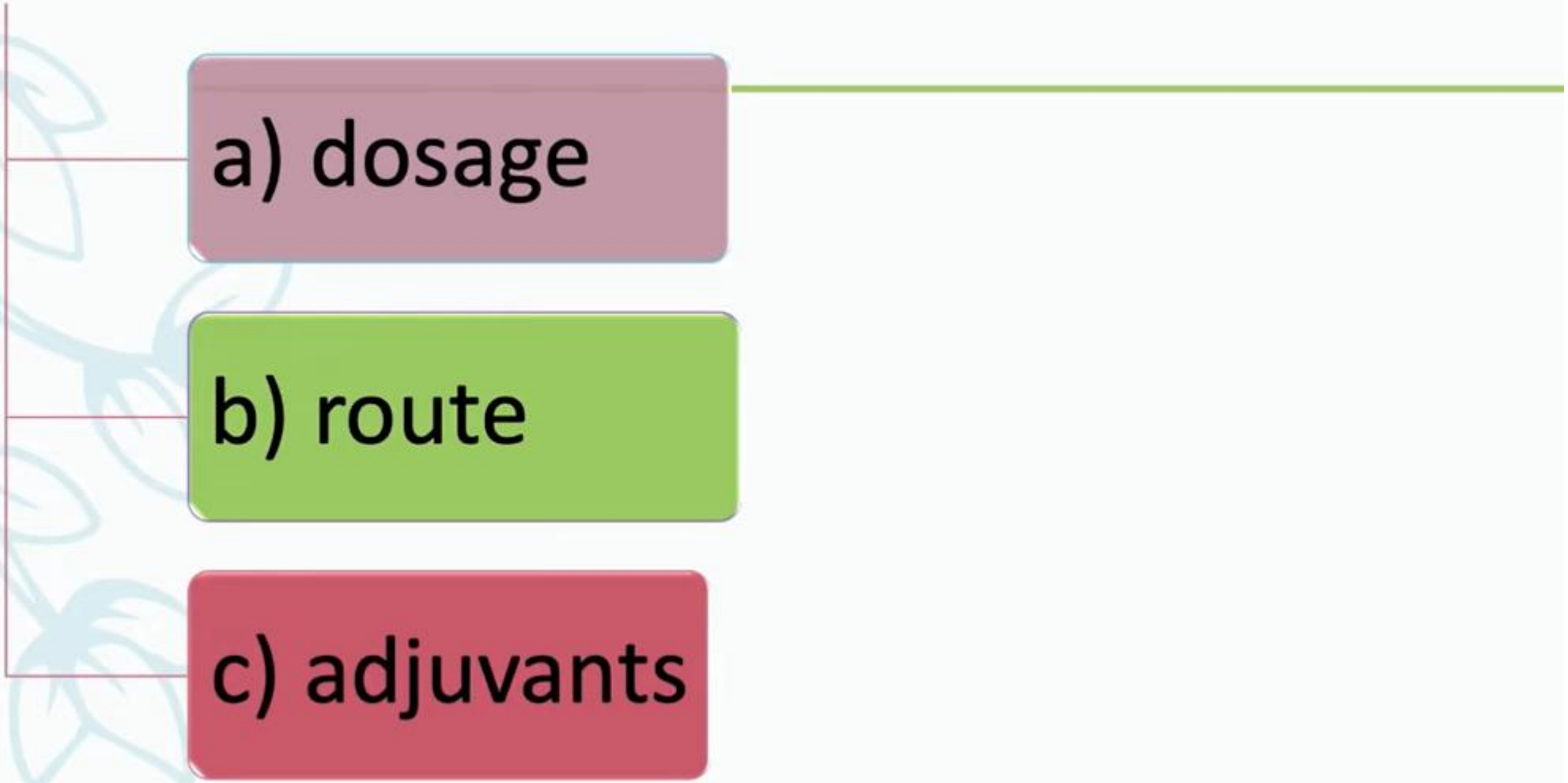
2- Molecular size

Small molecules such as amino acids or monosaccharides are usually not immunogenic. As a rule, molecules with a molecular weight of less than 5000-10,000, have no or only weak immunogenicity.

3- Chemical nature:

The most potent immunogens are proteins. Some polysaccharides of high molecular weight are immunogenic. More complex proteins are more immunogenic i.e. globular proteins are more immunogenic than fibrillar proteins.

5- Methods of antigen administration



a- Dosage: A state of antigen specific unresponsiveness (immunologic tolerance) can result if very high or very low doses of certain antigens are administered.

The number of doses administered also affects the outcome of the immune response.
Repeated administration of booster doses are required to stimulate a strong immune response.

b- Route of administration: Parenteral routes are preferred to oral routes for experimental immunogens as they induce stronger immune response.

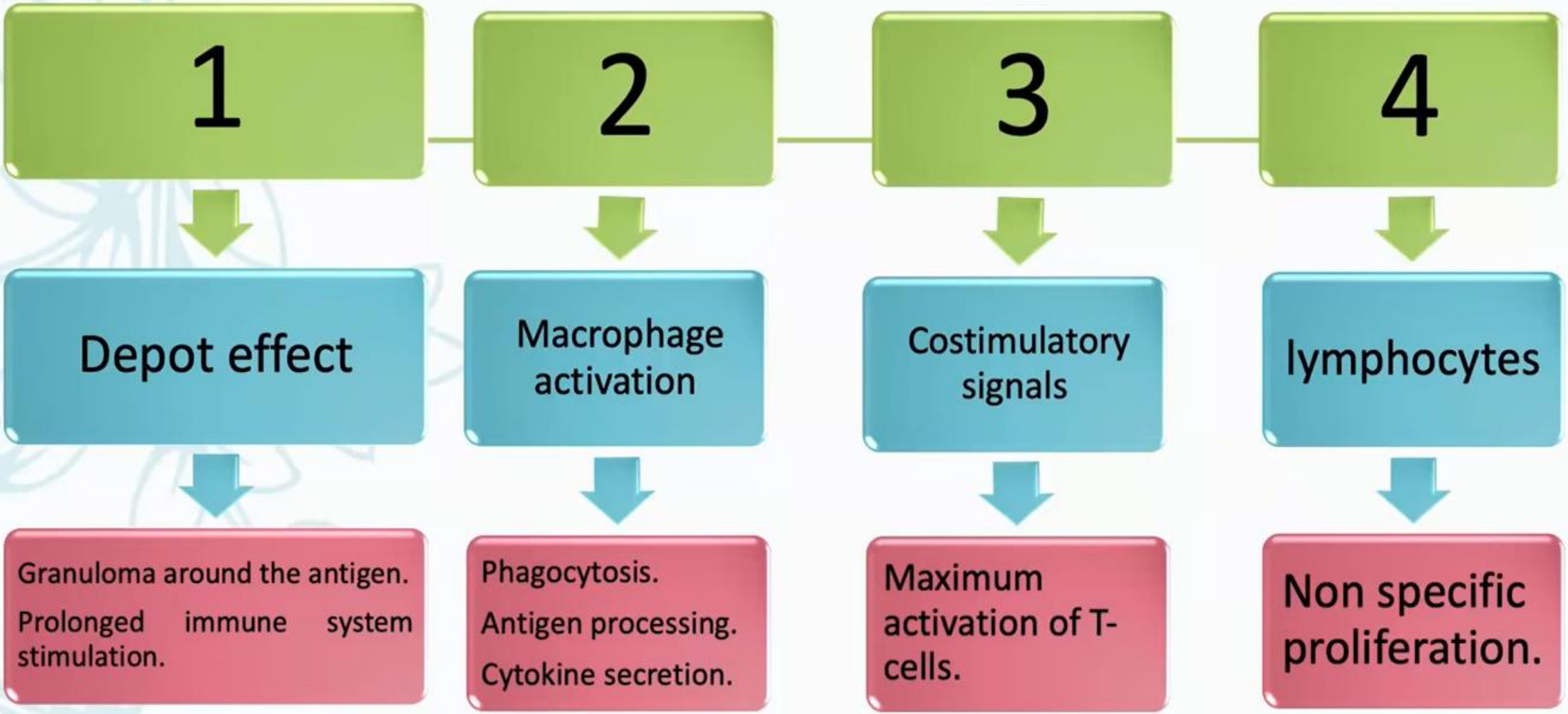
I.V. injected antigens are carried to the spleen while subcutaneously injected antigens are carried to the local lymph nodes.

Difference in the lymphoid cells that populate these organs may be reflected in the subsequent immune response.

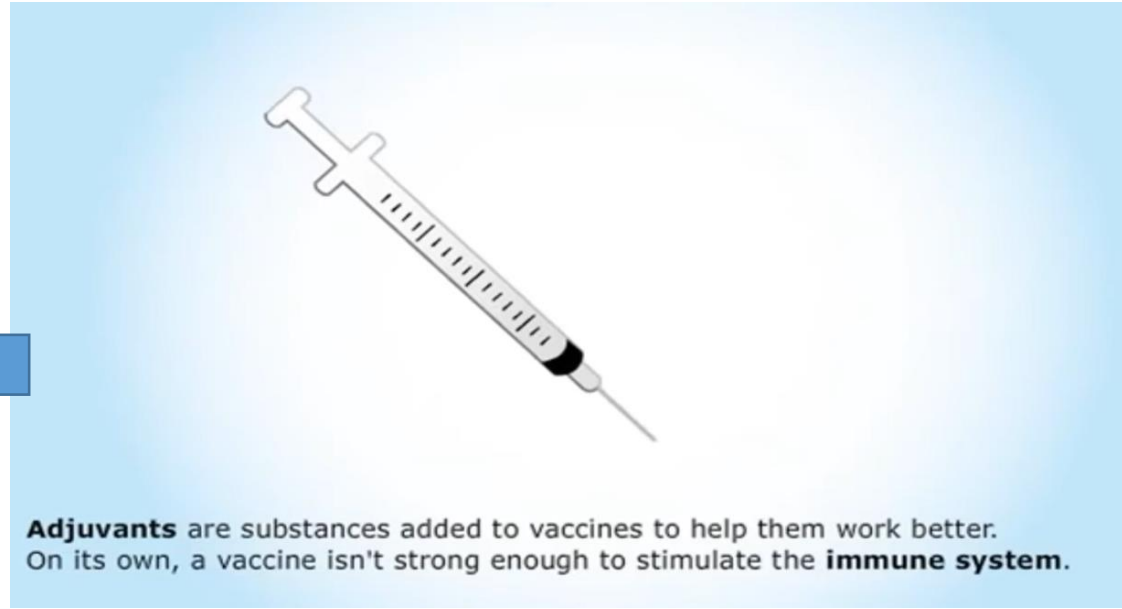
c- Adjuvants (to help): These are substances that, when mixed with an antigen before its administration will increase the immune response to that antigen.

Aluminum hydroxide is used to enhance the immune response as in the toxoid used for vaccination against diphtheria.

The mechanism of action of adjuvants



Notion of adjuvants in vaccines



Host genetic factors:

Different response between individuals:

- Strong responders.
- Weak responders.
- Non-responders.