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DEPARTMENT OF BIOTECHNOLOGY
FACULTY OFENGINEERING & TECHNOLOGY

LT 9. Antigen Antibody interaction

Content Outline

1. Introduction & Definition
2. Chemical bonds involved in interactions
3. Factors Affecting interactions
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LT 9. Antigen Antibody interaction

➢The interactions between antigens and antibodies are known as ***antigen–antibody reactions***. The reactions are highly specific, and an antigen reacts only with antibodies produced by itself or with closely related antigens. Antibodies recognize molecular shapes (epitopes) on antigens. Generally, the better the fit of the epitope (in terms of geometry and chemical character) to the antibody combining site, the more favorable the interactions that will be formed between the antibody and antigen and the higher the affinity of the antibody for antigen. The affinity of the antibody for the antigen is one of the most important factors in determining antibody efficacy *in vivo.*

➢The antigen- antibody interaction is bimolecular irreversible association between antigen and antibody. The association between antigen and antibody includes various non-covalent interactions between epitope (antigenic determinant) and variable region (V_H/V_L) domain of antibody

Chemical Bonds Responsible for the Antigen–Antibody Reaction

The interaction between the Ab-binding site and the epitope involves exclusively non-covalent bonds, in a similar manner to that in which proteins bind to their cellular receptors, or enzymes bind to their substrates. The binding is reversible and can be prevented or dissociated by high ionic strength or extreme pH. The following intermolecular forces are involved in Ag–Ab binding:

Electrostatic bonds: This result from the attraction between oppositely charged ionic groups of two protein side chains; for example, an ionized amino group (NH_4^+) on a lysine in the Ab, and an ionized carboxyl group (COO^-) on an aspartate residue in the Ag.

Hydrogen bonding: When the Ag and Ab are in very close proximity, relatively weak hydrogen bonds can be formed between hydrophilic groups (e.g., OH and C=O, NH and C=O, and NH and OH groups).

Hydrophobic interactions: Hydrophobic groups, such as the side chains of valine, leucine, and phenylalanine, tend to associate due to Van der Waals bonding and coalesce in an aqueous environment, excluding water molecules from their surroundings. As a consequence, the distance between them decreases, enhancing the energies of attraction involved. This type of interaction is estimated to contribute up to 50% of the total strength of the Ag–Ab bond.

Van der Waals bonds: These forces depend upon interactions between the “electron clouds” that surround the Ag and Ab molecules. The interaction has been compared to that which might exist between alternating dipoles in two molecules, alternating in such a way that, at any given moment, oppositely oriented dipoles will be present in closely apposed areas of the Ag and Ab molecules.

Each of these non-covalent interactions operates over very short distance (generally about 1 Å) so, Ag-Ab interactions depends on very close fit between antigen and antibody.

Strength of Ag-Ab interactions

Affinity

Combined strength of totalnon-covalent interactions between single Ag- binding site of Ab and single epitope is affinity of Ab for that epitope.

Low affinity Ab: Bind Ag weakly and dissociates readily.

High affinity Ab: Bind Ag tightly and remain bound longer.

Avidity

Strength of multiple interactions between multivalent Ab and Ag is avidity. Avidity is better measure of binding capacity of antibody than affinity. High avidity can compensate low affinity.

Cross reactivity

Antibody elicited by one Ag can cross react with unrelated Ag if they share identical epitopeor have similar chemical properties.

Factors affecting interactions

The antigen-antibody reaction can be influenced by several factors. Some of the more common factors are:

Temperature

The optimum temperature for antigen-antibody reaction will depend on the chemical nature of the epitope, paratope, and the type of bonds involved in their interaction. For example, hydrogen bond formation tends to be exothermic. These bonds are more stable at lower temperature and may be more important when dealing with carbohydrate antigens.

pH

The effect of pH on the equilibrium constant of the antigen-antibody complex lies in the pH range of 6.5 and 8.4. Below pH 6.5 and above pH 8.4, the antigen-antibody reaction is strongly inhibited. At pH 5.0 or 9.5, the equilibrium constant is 100-fold lower than at pH 6.5 - 7.0. Under extreme pH conditions, antibodies may undergo conformational changes that can destroy the complementarity with the antigen.

Ionic strength

Effect of ionic strength on antigen-antibody reaction is particularly important in blood group serology. Here the reaction is significantly influenced by sodium and chloride ions. For example, in normal saline solution, Na^+ and Cl^- cluster around the complex and partially neutralize charges, potentially interfering with antibody binding to antigen. This could be problematic when low-affinity antibodies are used. It is well known that, when exposed to very low ionic strengths, γ-globulins aggregate and form reversible complexes with lipoproteins of red blood cells, leading to their sedimentation.

Types of Ag-Ab reactions

1. Agglutination
2. Precipitation
3. Complement Fixation
4. Enzyme inked Immunosorbent Assay
5. RadioImmuno Assay
6. Western Blotting

Cross reactivity

➢Antibody Cross reactivity: The ability of an antibody to react with similar antigenic sites on different proteins.

➢Cross-reactivity between antigens occurs when an antibody directed against one specific antigen is successful in binding with another, different antigen. The two antigens in question have similar three-dimensional structural regions, known as epitopes, which allow the antibody for one antigen to recognize a second antigen as being structurally the same antigen.

➢Cross reactivity can be beneficial if an individual develops immunity to several related pathogens despite having been exposed to or vaccinated against only one of them. For instance, antibody cross reactivity may occur against the similar surface structures of various Gram-negative bacteria. Conversely, antibodies raised against pathogenic molecular components that resemble self molecules may incorrectly mark host cells for destruction, causing autoimmune damage. Patients who develop systemic lupus erythematosus (SLE) commonly exhibit antibodies that react with their own DNA. These antibodies may have been initially raised against the nucleic acid of microorganisms, but later cross-reacted with self-antigens. This phenomenon is also called molecular mimicry.

References & Further reading

References

1. **https://microbenotes.com/introduction-to-antigen-antibody-reactions/**
2. **https://www.sigmaaldrich.com/technical-documents/articles/biology/antibody-antigen-interaction.html**
3. **https://bio.libretexts.org/Bookshelves/Introductory_and_General_Biology/Book%3A_General_Biology_(Boundless)/42%3A_The_Immune_System/42.3%3A_Antibodies/42.3B%3A_Antibody_Functions**

Further reading

1. Kuby, RA Goldsby, Thomas J. Kindt, Barbara, A. Osborne Immunology, 6th Edition, Freeman, 2002.
2. Brostoff J, Seaddin JK, Male D, Roitt IM., Clinical Immunology, 6th Edition, Gower Medical Publishing, 2002.
3. Janeway et al., Immunobiology, 4th Edition, Current Biology publications. 1999.
4. Paul, Fundamental of Immunology, 4th edition, Lippencott Raven, 1999.