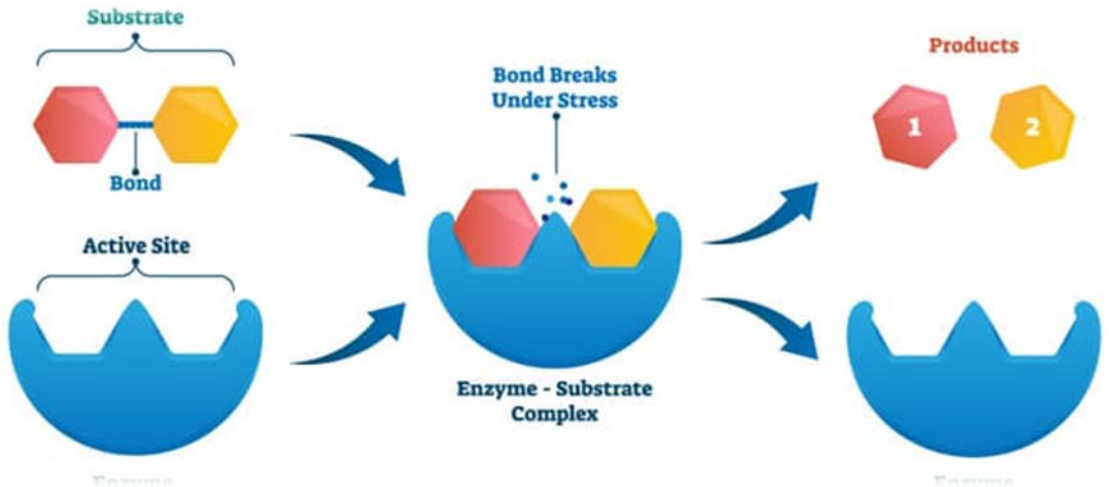
BIOCHEMISTRY - YEAR 2



Enzymes
Part 4
Lecture No: 17

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Regulation of Enzyme Activity

In any enzyme-catalyzed reaction, compounds are produced only in the amounts and at the times they are needed in the cell. This means that the rate of a catalyzed reaction must be controlled so it can speed up when more molecules of a compound are needed and slow down when an accumulation of that compound occurs. There are several factors in the cell that regulate enzyme activity.

Zymogens

Although most enzymes are active as soon as they are synthesized and acquire their tertiary structure, some are produced as inactive precursors called zymogens or proenzymes. Zymogens, which contain longer protein chains, are activated by the removal of peptide sections from the protein. Zymogens are often produced in an organ where they are stored and then transported to where they are needed, a which time they are activated.

Insulin

The protein hormone insulin is synthesized as inactive proinsulin. Recall that insulin contains two polypeptide chains linked by disulfide bonds. In proinsulin, the two chains are connected by a polypeptide of 33 amino acids. This peptide section is removed to form the active insulin hormone.

Digestive Enzymes

Several of the digestive enzymes including trypsinogen, chymotrypsinogen, and procarboxypeptidase are produced as inactive forms and stored in the pancreas. After food is ingested, it reaches the small intestine. Hormones trigger the release of the zymogens from the pancreas. In the small intestine, the zymogens are converted into active forms by proteases that remove peptide sections from their protein chains. The change in tertiary structure activates the enzyme. For example, an enzyme called enteropeptidase removes a hexapeptide from trypsinogen to give active trypsin. Trypsin in turn cleaves peptide sections from chymotrypsinogen to form active chymotrypsin and from procarboxypeptidase to yield active carbaxypeptidase.

Chymotrypsinogen $\xrightarrow{\text{Trypsin}}$ Chymotrypsin + 2 dipeptides

If the digestive zymogens were active in the pancreas, their catalytic action as proteases would digest the proteins of the pancreas. This can lead to conditions such as pancreatitis, which is an inflammation of the pancreas. Another zymogen, pepsinogen, is produced in the gastric mucosal cells that line the stomach. As food enters the stomach, HCI is secreted. Low pH levels cleave a peptide containing 42 amino acids from the pepsinogen protein to form pepsin, which digests proteins.

Pepsinogen $\xrightarrow{H^+}$ Pepsin + Peptides and amino acids

Most protein hormones such as insulin, enzymes involved in digestion, and enzymes that catalyze blood clotting are initially synthesized as zymogens.

Allosteric Enzymes

Certain enzymes known as **allosteric enzymes** are capable of binding a regulator molecule that is different from the substrate. The binding of the regulator causes a change in the shape of the enzyme and therefore in the active site. There are both positive and negative regulators. A **positive regulator** speeds up a reaction by causing a change in the shape of the active site that permits the substrate to bind more effectively. A **negative regulator** slows down the rate of catalysis by preventing the proper binding of the substrate. In **feedback control**, the end product acts as a negative regulator. When the end product is produced in sufficient amounts for the cell, some binds to the first enzyme (E_1), which is an allosteric enzyme. By inhibiting the reaction of the initial substrate, no intermediate compounds are produced for the other enzymes in the reaction pathway. The entire enzyme-catalyzed reaction sequence shuts down.

Allosteric Enzymes

Eventually the concentration of end product becomes too low, which causes the end product inhibitor to dissociate from the allosteric enzyme (E_1). As its shape returns to its active form, the catalysis of initial substrate begins once again. Through feedback control, the catalysis of the initial substrate undergoes reaction only when the end product is needed somewhere in the cell. There is no accumulation of the end product, which conserves the materials needed in other reactions. Let's look at the feedback control in a reaction pathway with five converts the amino acid threonine to isoleucine, another amino acid. enzymes that converts the amino acid threonine to isoleucine another amino acid.

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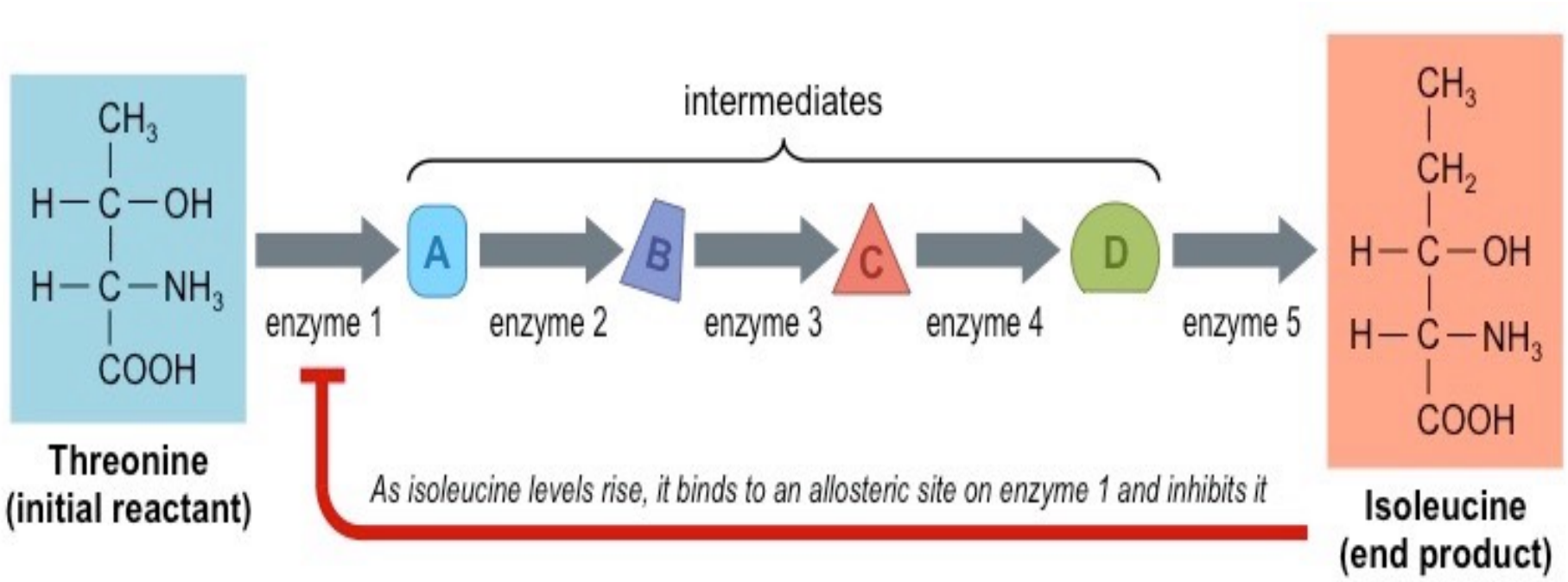

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When isoleucine begins to accumulate in the cell, it binds with the first enzyme (E_1) threonine deaminase in the pathway. The binding of isoleucine changes the shape of the deaminase, which prevents the substrate threonine from binding which the active site. The entire reaction pathway is turned off. None of the intermediate products from the other enzymes in the pathway can inhibit the first enzyme, As isoleucine is utilized in the cell, its concentration decreases, which causes the threonine deaminase to release the end product inhibitor. The tertiary shape of the deaminase returns to its active form and the reaction sequence once again converts threonine to isoleucine.

Enzyme Cofactors

Enzymes are known as **simple** enzymes when their functional forms consist only of proteins with tertiary structures. However, many enzymes require small molecules or metal ions called **cofactors** to catalyze reactions properly. When the cofactor is a small organic molecule, it is known as a **coenzyme**. If an enzyme requires a cofactor, neither the protein structure nor the cofactor alone has catalytic activity.

Metal Ions

Many enzymes must contain a metal ion to carry out their catalytic activity. The metal ions are bonded to one or more of the amino acid side chains. The metal ions from the minerals that we obtain from foods in our diet have various functions in catalysis. Ions such as Fe^{2+} and Cu^{2+} are used by oxidases where they lose or gain electrons in oxidation and reduction reactions. Other metals ions such as Zn^{2+} stabilize the amino acid side chains during hydrolysis reactions.

Let's look at an example of a metal ion in an enzyme-catalyzed reaction. The enzyme carboxypeptidase A cleaves the C terminal amino acid of a protein when that amino acid has a bulky hydrophobic or aromatic side chain. With the substrate in the active site, the Zn^{2+} helps to stabilize the negative charge on the oxygen atom of the carbonyl group and promotes the hydrolysis of the peptide bond.

The End

Thank You All

Reference: General, organic,& biological chemistry structures of life.
Timberlake. Pearson Education. 2002