Module 13 / Regulation

75

Describe the major differences between a competitive and uncompetitive inhibitor.	Explain activation of enzymes by allosteric compounds as a method of regulation.	Distinguish regulation by non-covalent and covalent modification of enzymes.

It is essential that biochemical pathways are regulated, otherwise the cell would waste resources. Some general properties associated with the regulation of metabolic pathways are listed below

- At least one step is regulated, often in multiple ways.
- Essentially irreversible steps, i.e. those with large energy changes, are regulated. Consequently, once the pathway is turned on, metabolites that enter the pathway are committed to complete the pathway.
- In synthetic and degradative pathways a common step is performed by different enzymes, each of which are regulated in a coordinated fashion such that only one pathway is on at a time.

There are five general methods by which the flux through a step in the pathway can be regulated. These methods differ in how rapidly they can respond to changes in the environment. Each of these methods is discussed below, with the more rapid form of regulation at the top of the list.

- **Substrate availability.** For many enzymes, the intracellular level of substrate is below the level that half saturates the enzyme. Therefore, if the substrate concentration increases the rate of the reaction will increase due to the formation of additional enzyme-substrate complexes. If the substrate concentration is very low, the increase in the rate of the reaction is almost equal to the increase in substrate concentration.
- **Product inhibition.** In this case the product of the reaction inhibits the enzyme that generated it, preventing the accumulation of intermediates in a pathway. The product is a competitive inhibitor of the enzyme that just created it.

Question: How do product (competitive) inhibitors actually inhibit the reaction of the substrate with its enzyme? Complete the following Activity and then enter you answer on the My Response box below it.

Biochem version

learn by doing

Using the radio dials at the right, select increasing concentrations of substrate to investigate how the concentration of substrate affects the reaction velocity, v. The reaction velocity is just the rate of product formation/unit time, under steady-state conditions.

You can view the molecular events that occur in the upper animation and the velocity versus substrate is plotted on the lower graph.

Select [S]=2, and mentally note how frequently the four enzyme molecules have substrate.
Now make [S]=4

Now make [S]=4.

What happens to the average number of enzymes with substrate bound when [S] is increased from 2 to 4?

- Increases.
- Decreases.

NEXT »

Reset this Activity

new modern bio version version

learn by doing

How does enzyme activity change when the amount of substrate increases slightly?

- Increases
- Decreases
- Stays the same

NEXT »

Reset this Activity

old version

MY RESPONSE...

How do product inhibitors actually inhibit the reactions of the substrate with it's enzyme?

Submit and Compare

Reset this Activity

did I get this

Would you expect the product of an enzyme catalyzed reaction function as a competitive or non-competitive inhibitor?

Submit and Compare

Reset this Activity

- **Feedback inhibitors.**In this case, a compound that is further down the pathway, or even a compound in a separate pathway, will inhibit a reaction. Again, this prevents an accumulation of intermediates in a pathway. The binding of the feedback inhibitor usually causes a change in the shape of the enzyme; a feedback inhibitor is an example of a non-competitive inhibitor or an allosteric inhibitor.

Allosteric Binding

(definition) Allosteric binding causes conformational changes in an enzyme that can either inhibit or activate the enzyme.

Question: How do allosteric regulators differ from feedback inhibitors? Use the following activity to explore this difference.

Allosteric Binding

Allosteric Activation and Inhibition.

- **Enzyme phosphorylation**. The addition of phosphate groups to serine, threonine, and tyrosine residues on enzymes can cause a change in the shape of the active site of the enzyme. This change in shape is an allosteric effect. The change may lead to a more active enzyme (allosteric activator) or a less active enzyme (an allosteric inhibitor).
- **Enzyme levels**. Recall that the rate of product formation is proportional to the amount of enzyme. Enzyme levels can be increased by the conversion of inactive forms of the enzyme to active forms. This form of regulation occurs with digestive enzymes. These are made in an inactive form in the pancreas, but activated by cleavage in the small intestine. The levels of enzyme can also be varied by regulating the synthesis of the enzyme. This method of regulation is common during development, when certain enzymes are only present during defined developmental stages.

did I get this

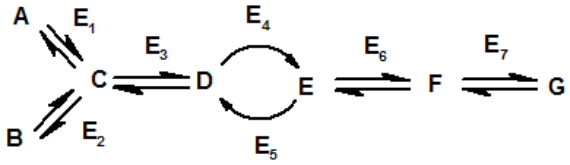
Which of the following is **not** a mechanism for altering the flux of metabolites through the rate-determining step of a pathway?

- Covalent modification of the enzyme.
- Genetic control of the enzyme concentration.
- Diffusional coupling between adjacent active sites.
- Allosteric control of the enzyme activity.
- Coordinate regulation of synthetic and degradative steps in the same pathway.

NEXT » Reset this Activity

did I get this

Which of the following enzymes are most likely to be regulated in the following pathway (select all that apply):



- E1
- E3
- E5
- E2
- E4
- E6

NEXT » Reset this Activity