Isozymes and Zymogen

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Isozymes

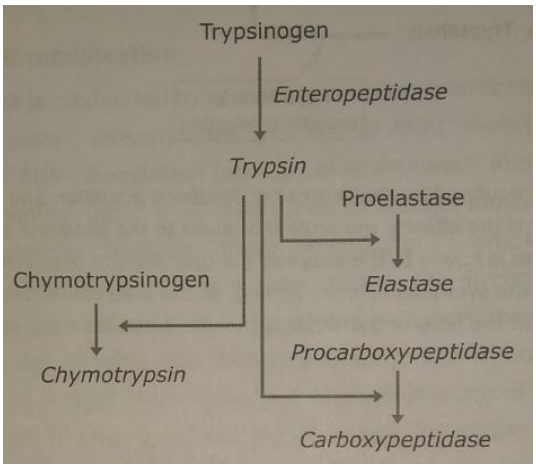
Isozymes (also known as isoenzymes) are enzymes that differ in amino acid sequence but catalyze the same chemical reaction. They are encoded by different genes located at different loci. These enzymes usually display different kinetic parameters or different regulatory properties. Isozymes differ from allozymes, which are enzymes that arise from alternative forms of the same gene i.e. alleles. A common example of an isozyme is lactate dehydrogenase (LDH) which catalyzes the reversible conversion of pyruvate to lactate. Human beings have two lysozyme polypeptide chains for this enzyme: **H polypeptide** and **M polypeptide**. The functional enzyme is tetrameric (homo- or heterotetramer). Two different subunits combine randomly with each other forming five isozymes. The kinetic properties of the various LDH isozymes differ in terms of their relative affinities for the various substrates and their sensitivity to inhibition by-products. Different tissues express different isozyme forms, as appropriate to their particular metabolic needs.

Isozyme	Nature of subunits	Location
LDH1	HHHH (H4)	In heart and RBCs
LDH2	HHHM (H3M)	In the reticuloendothelial system
LDH3	HHMM (H2M2)	In the lungs
LDH4	HMMM (HM3)	In the kidney and the placenta
LDH5	MMMM (M4)	In the liver and striated muscle

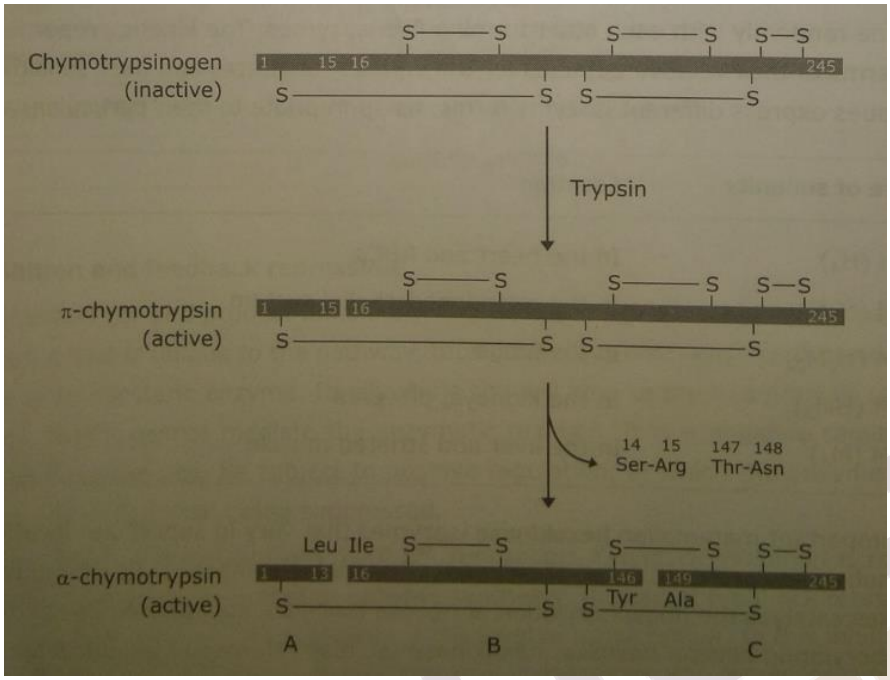
Similarly, there are four important mammalian hexokinase isozymes that vary in subcellular locations and kinetics with respect to different substrates and conditions. They are designated as hexokinase I, II, III and IV or hexokinase A, B, C and D. Hexokinase catalyzes the phosphorylation of hexose (such as glucose). While hexokinase I, II and III are capable of phosphorylating several hexoses, hexokinase IV (also referred to as glucokinase) acts only on glucose as hexose. Glucokinase is mainly expressed in liver and pancreatic β-cells and is characterized by a low affinity for its substrate glucose. Hexokinase I, II and III have high affinity for glucose even at low concentration and all three are strongly inhibited by their products glucose-6-phosphate. Glucokinase can only phosphorylate glucose if the concentration of this substrate is high enough.

Zymogen

An inactive precursor of an enzyme is called zymogen. Zymogen is cleaved to form the active enzyme. Many proteolytic enzymes like chymotrypsin, and trypsin are initially synthesized as inactive precursor chymotrypsinogen and trypsinogen. Specific cleavage causes conformational changes in the inactive precursor that expose the enzyme active site. In the duodenum, the pancreatic zymogens, trypsinogen, chymotrypsinogen, proelastase, and procarboxypeptidase are converted into active enzymes by enteropeptidase and trypsin.



Chymotrypsinogen, a single polypeptide chain of 245 amino acid residues, is converted to a-chymotrypsin, which has three polypeptide chains linked by two of the five disulfide bonds present in the primary structure of chymotrypsinogen.



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