ZYMOGEN

- A **zymogen** , also called a **proenzyme**, is an inactive precursor of an enzyme. A zymogen requires a biochemical change (such as a hydrolysis reaction revealing the active site, or changing the configuration to reveal the active site) for it to become an active enzyme.
- The biochemical change usually occurs in Golgi bodies, where a specific part of the precursor enzyme is cleaved in order to activate it.
- The inactivating piece which is cleaved off can be a peptide unit, or can be independently folding domains comprising more than 100 residues. .
- The pancreas secretes zymogens partly to prevent the enzymes from digesting proteins in the cells in which they are synthesised.
- Enzymes like pepsin are created in the form of pepsinogen, an inactive zymogen.
- Pepsinogen is activated when chief cells release it into the gastric acid, whose hydrochloric acid partially activates it.
- Accidental activation of zymogens can happen when the secretion duct in the pancreas is blocked by a gallstone, resulting in acute pancreatitis.
- In the duodenum, the pancreatic zymogens, trypsinogen, chymotrypsinogen, proelastase and procarboxypeptidase are converted into active enzymes by enteropeptidase and trypsin.
- Chymotrypsinogen, is single polypeptide chain of 245 amino acids residues, is converted to alpha-chymotrypsin, which has three polypeptide chains linked by two of the five disulfide bond present in the primary structure of chymotrypsinogen.

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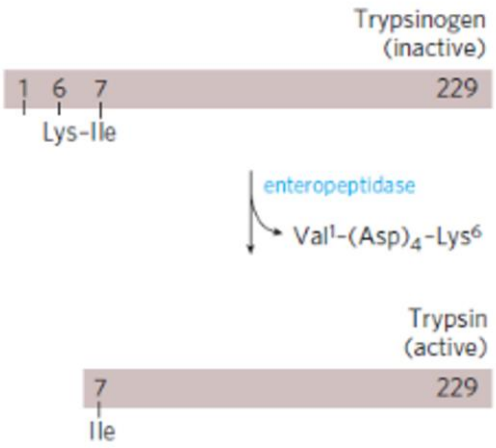
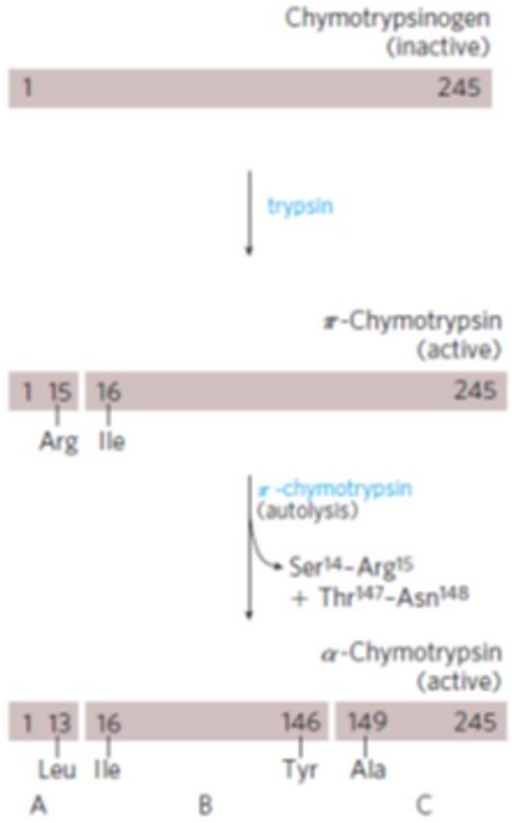
Trypsinogen is activated by enteropeptidase (also known as enterokinase). Enteropeptidase is produced by the mucosa of duodenum and it cleaves the peptide bond of trypsinogen after residue 15, which is a lysine. The N-terminal peptide is discarded, and a slight rearrangement of the folded protein occurs.





- **Chymotrypsinogen** is an inactive precursor (zymogen) of chymotrypsin. Chymotrypsinogen is a single polypeptide chain consisting of 245 amino acid residues. It is synthesized in the acinar cells of the pancreas and stored inside membrane-bounded granules at the apex of the acinar cell.
- Release of the granules from the cell is stimulated by either a hormonal signal or a nerve impulse, and the granules spill into a duct leading into the duodenum.
- It is activated into its active form by another enzyme called trypsin.
- This active form is called π-chymotrypsin and is used to create α-chymotrypsin
- Trypsin cleaves the peptide bond in chymotrypsinogen between arginine-15 and isoleucine-16.
- This creates two peptides within the π-chymotrypsin molecule, held together by a disulfide bond.
- One of the π-chymotrypsins acts on another by breaking a leucine and serine peptide bond.
- The activated π-chymotrypsin reacts with other π-chymotrypsin molecules to cleave out two dipeptides, which are, serine-14–arginine-15 and threonine-147–asparagine-148.
- This reaction yields the α-chymotrypsin

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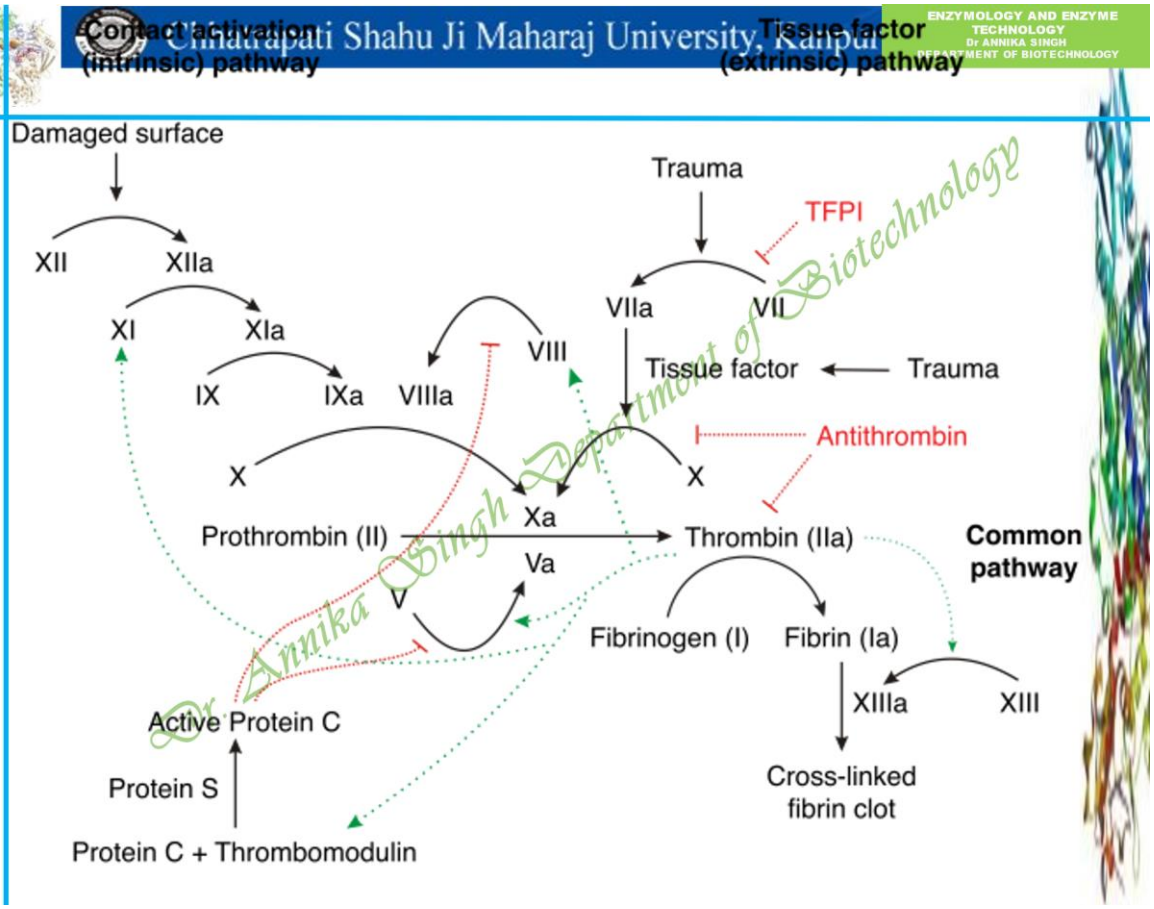
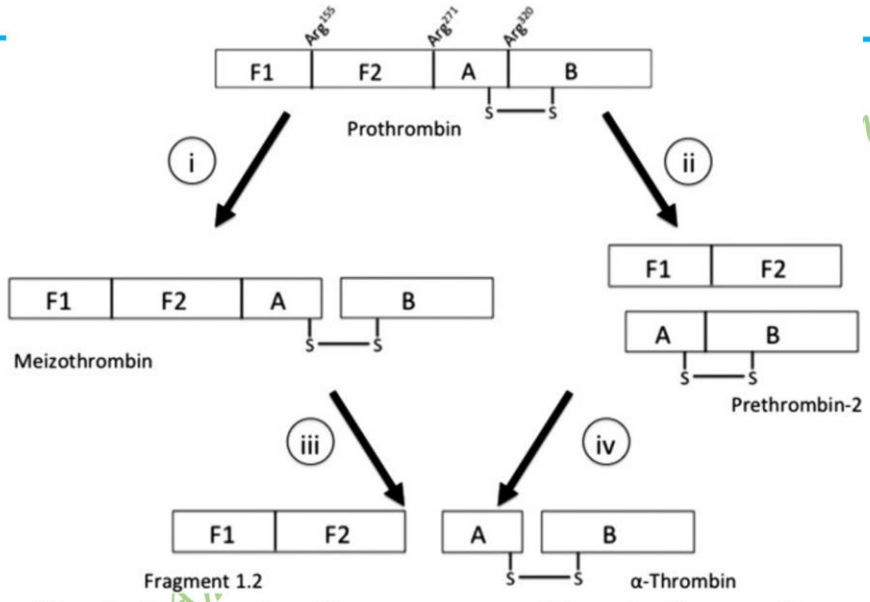
Prothrombin activation

- The intrinsic pathway consists of factors I, II, IX, X, XI, and XII. Respectively, each one is named, *fibrinogen*, *prothrombin*, *Christmas factor*, *Stuart-Prower factor*, *plasma thromboplastin*, and *Hageman factor*. The extrinsic pathway consists of factors I, II, VII, and X. Factor VII is called *stable factor*.
- The common pathway consists of factors I, II, V, VIII, X. The factors circulate through the bloodstream as zymogens and are activated into serine proteases.
- These serine proteases act as a catalyst to cleave the next zymogen into more serine proteases and ultimately activate fibrinogen.
- The factors II, VII, IX, X, XI and XII are serine proteases: factors V, VIII, XIII are not serine proteases.
- The intrinsic pathway is activated through exposed endothelial collagen, and the extrinsic pathway is activated through tissue factor released by endothelial cells after external damage.

Dr. Annika Singh Department of Biotechnology





Prothrombin activation by prothrombinase may proceed through either one of two pathways dependent upon the conditions of enzyme assembly. Prothrombin consists four fragments (fragment 1, fragment 2, A-chain, and B-chain). Initial cleavage at Arg-320 (pathway *i*) is characteristic of prothrombinase assembled on synthetic phospholipid vesicles and results in the formation of the catalytically active intermediate meIIaInitial cleavage at Arg-271 (pathway *ii*) is characteristic of fIIactivation by fXa in the absence offVa or prothrombinase assembled on activated platelets and results in the formation of the non-catalytically active intermediate Pre-2. The secondary cleavage at Arg-271 or Arg-320, respectively, results in the formation of fully activated fIIa