MAST CELL PROTEASES AND THEIR INHIBITORS - BIOCHEMISTRY AND MEDICAL SIGNIFICANCE

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Tryptases and chymases comprise a group of serine proteinases that are highly and selectively expressed in mast cells and to some extent in basophils. They are stored fully catalytically active in secretory granules, are released in bacterial and parasitic infections as well as inflammation conditions, and have been implicated both in host defense mechanisms and in the pathogenesis of allergic and chronic disorders, e.g. asthma, psoriasis, and rheumatoid arthritis. The unique features of human β-tryptase that distinguish it from most other trypsin-like proteases, i.e. the activity as a heparin-bound tetramer, narrow substrate specificity and resistance to plasma antiproteinases, as well as the minute activity of the closely related α-tryptase have been well explained by their crystal structures. The structures have also clarified the interaction with the only known naturally occurring tryptase inhibitor that has been isolated from a blood-sucking parasite, *Hirudo medicinalis*, and guided the subsequent rational design of both synthetic and bioengineered tryptase inhibitors. Such compounds are now useful as tools to unravel the significance of tryptases in inflammatory disorders and as prototypes for clinically applicable drugs.

Key words: Mast cells, tryptases, chymases