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The Isoforms of Human Neutrophil Elastase and Cathepsin G Differ in their Carbohydrate Side Chain Structures*

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Summary: The two proteinases found in human neutrophil granules, elastase and cathepsin G, each are normally isolated as a mixture of isoforms differing only in carbohydrate content. Elastase has two *N*-glycosylation sites occupied (Asn-45 and Asn-144), whereas cathepsin G has only one (Asn-64). Analysis of a minor form of elastase (E-1) and cathepsin G (C-1) indicates that the carbohydrate structures at each glycosylation site are complex-type bi-antennary chains usually associated with secretory glycoproteins. In contrast, the isoforms E-3 and C-3, the major forms of elastase and cathepsin G respectively, contain exclusively truncated, oligomannose-type chains at the same positions in the sequence of each protein. These data suggest the possibility that certain elastase and cathepsin G isoforms (E-1 and C-1) might be destined for secretory, others (E-3 and C-3) for lysosomal functions.

Key terms: Elastase, cathepsin G, carbohydrate, isozyme, neutrophil.

The two major proteolytic enzymes in human neutrophils, elastase (HNE) and cathepsin G (Cat G), are serine proteinases utilized in the degradation of foreign proteins during phagocytosis[1]. These enzymes can also digest elastin, collagen, and proteoglycan[2,3]. Therefore, their extracellular release from the neutrophil during phagocytosis or cell death could result in tissue damage. For this reason they have been strongly implicated in the development of connective tissue disorders, including emphysema and rheumatoid arthritis[4].

In order to develop specific inhibitors to HNE and Cat G for use in augmenting their control, detailed analyses of the structure and mechanism of action of each enzyme have been made[5–7]. The results clearly indicate that both are synthesized as a series of isoforms, each set having identical amino-acid sequences but different carbohydrate compositions. There are three potential *N*-glycosylation sites on HNE[5], only two of which are apparently utilized, whereas Cat G has only a single *N*-glycosylation site[7]. Since it seemed likely that the isoforms of each of the two enzymes differed because of alterations in the structure of attached carbohydrate side chains we undertook an analysis of each isoform. In this report we demonstrate that there are significant and potentially important differences in the carbohydrate structures attached to each of the major and minor forms of HNE and Cat G.

Abbreviations:
HNE, human neutrophil elastase; Cat G, cathepsin G; endo-F, endoglycosidase F; SDS-PAGE, sodium dodecyl sulfate polyacrylamide gel electrophoresis.

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