Current Topics

Aminopeptidases in Health and Disease

Foreword

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Aminopeptidases hydrolyze N-terminal amino acids of proteins or peptide substrates. They are distributed widely in animal and plant tissues as well as in bacteria and fungi, suggesting that they play important roles in various biological processes. They are essential for protein maturation, the activation, modulation, and degradation of bioactive peptides, and the determination of protein stability. In addition, several aminopeptidases are known as differentiation antigens and control cell proliferation and differentiation.^{1,2)}

During the last decade, several mammalian aminopeptidases were cloned and molecular nature of respective enzymes was elucidated. Especially, enzymes belonging to the M1 zinc-metallopeptidase (gluzincin) family were characterized extensively. Gluzincin aminopeptidases share the consensus HEXXH(X)₁₈E zinc-binding motif essential for enzymatic activity. This growing family of mammalian zinc-containing aminopeptidase includes membrane-bound [insulin-regulated aminopeptidase (IRAP)/placental leucine aminopeptidase (P-LAP), aminopeptidase A (APA), aminopeptidase N (APN) and thyrotropin-releasing hormone degrading enzyme (TRHDE)], cytosolic [puromycin-sensitive aminopeptidase (PSA) and leukotriene A₄ hydrolase (LTA4H)], secretory [aminopeptidase B (APB)] and endoplasmic reticulum (ER)-resident [adipocyte-derived leucine aminopeptidase (A-LAP)/puromycin-insensitive leucyl-specific aminopeptidase (PILSAP), leukocyte-derived arginine aminopeptidase (L-RAP)] proteins (Fig. 1).

Molecular identification of the enzymes made it possible

Fig. 1. Phylogenetic Analysis of M1 Family of Aminopeptidases

to analyze their pathophysiological functions in detail. As a result, recent evidence facilitates new insights into the significance of the M1 family of aminopeptidases. In this mini-review series, we will summarize current topics on the functional studies of aminopeptidases, which include relevance to diabetes (Keller, S.), memory retention (Albiston, A. L. *et al.*), regulation of blood pressure (Mitsui, T. *et al.*), regulation of angiogenesis (Sato, Y.) and antigen-presentation (Hattori, A. *et al.*). It is expected that further elucidation of the molecular mechanisms of these functions and three-dimensional structure of the enzymes will allow the development of novel therapeutic approaches to several pathological conditions.

REFERENCES

- 1) Taylor A., *FASEB J.*, **7**, 290—298 (1993).
- 2) Shipp M. A., Look A. T., *Blood*, **82**, 1052—1070 (1993).