IJPT
1735-2657/02/12-30-39
IRANIAN JOURNAL OF PHARMACOLOGY & THERAPEUTICS
Copyright © 2003 by Razi Institute for Drug Research (RIDR)
IJPT 1:30-39, 2003

RIDR

Proceedings of Membrane Metalloproteases in Health and Disease Symposium

PART OF THE 4TH INTERNATIONAL CONGRESS OF PATHOPHYSIOLOGY, BUDAPEST, HUNGARY, JUNE 29-JULY 5, 2002

NEP, ACE and Homologues: The Pathophysiology of Membrane Metalloproteases

A.J. TURNER

Proteolysis Research Group, School of Biochemistry and Molecular Biology, University of Leeds, Leeds LS2 9JT, U.K.

ABSTRACT

The zinc metalloprotease, neprilysin (NEP), plays a role in the metabolism of cardiovascular, inflammatory and neuropeptides, including mitogenic peptides such as bombesin. In the cardiovascular system, NEP has a primary role in the inactivation of natriuretic peptides but also contributes to local metabolism of angiotensin, endothelins and bradykinin. Hence NEP is seen as a potential therapeutic target and drug development is facilitated by its recent structural solution. In prostate cancer, NEP is dramatically downregulated allowing mitogenic peptides to drive androgen-independent progression of the disease. NEP also contributes to the catabolism of the neurotoxic beta-amyloid peptide in Alzheimer's disease. Thus up- or downregulation of NEP activity critically affects peptide metabolism and can contribute to the pathophysiology of a number of diseases. The human genome contains seven NEP-like enzymes, including the endothelin converting enzymes (ECE) and aspects of their physiology and properties will be highlighted. We have also identified a novel human homologue of the zinc metalloprotease, angiotensin converting enzyme (ACE). This enzyme (ACEH) hydrolyses angiotensins I and II but not bradykinin and functions exclusively as a carboxypeptidase. Its localization and possible roles in regulation of the renin-angiotensin and other peptide systems will be described and compared with those of ACE itself.Abs text

Address correspondence to: Prof. A. J. Turner, Proteolysis Research Group, School of Biochemistry and Molecular Biology, University of Leeds, Leeds LS2 9JT, U.K. E-mail: a.j.turner@leeds.ac.uk

[Downloaded from ijpt.iums.ac.ir on 2026-11-13]