Structure and Function of Angiotensin Converting Enzyme and Its Inhibitors

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Abstract: Angiotensin converting enzyme (ACE, EC 3.4.15.1) is a membrane-bound, zinc dependent dipeptidase that catalyzes the conversion of the decapeptide angiotensin I to the potent vasopressor octapeptide angiotensin II, by removing two C-terminal amino acids. ACE is well known as a key part of the renin angiotensin system that regulates blood pressure, and its inhibitors have potential for the treatment of hypertension. This paper reviewed the characteristics of ACE in aspects of its structure-function relationship, gene polymorphism and inhibitor development. In particular, the catalytic mechanisms of the two active sites of somatic ACE in the cleavage of angiotensin I and bradykinin are different. Therefore, it would likely provide a new way for exploiting novel ACE inhibitors with fewer side-effects by specifically-targeting the individual active sites of somatic ACE.

Keywords: angiotensin converting enzyme, structure and function, gene polymorphism, inhibitor
1 ACE 的结构与功能

1.1 ACE 的分子结构

ACE(somatic ACE, sACE), (1306 aa) 2 3 ACE(testic ACE, tACE), 1 732 739

ACE(149.723 kD) sACE N N-catalytic domain C-catalytic domain (1257–1276 aa)

(1–30 aa), N 1232 C ACE . N , C ACE (soluble ACE) sACE tACE .

 ACE 2 80.073 kD, N (1–31 aa), 68 1.3  [1,2] 3 83.989 kD, N 2 657 657

ACE 1.2 ACE 的 mRNA 选择性剪切

ACE 17 q23 , 21 kb, 26 25 ACE sACE tACE [3], N sACE

ACE 1 12–14 14–26[tACE] 12 13–26 (tACE) 12 13–26

ACE 628 bp, tACE . sACE [4], sACE

1.3 ACE 的组织分布

Harmer et al(2002) RT-PCR ACE 72

sACE . tACE . sACE tACE . ACE

1.4 ACE 的生物学功能

Zn2+, ACE I(angiotensin I, Ang I) Phe6-His5 I (Ang I) II (Ang II)

His-Leu[1] II 1, ACE

Na+, K+

ACE 2 P

Alzheimer

Kondoh et al(2005) tACE . ACE

GPI ACE

GPI ACE

2 ACE 的基因多态性与疾病

ACE ID/DD AS 3 16 287 bp Alu

I (I/D), ACE

ACE
**Fig. 1** The role of ACE and its inhibitor in the renin-angiotensin system

ACE: angiotensin converting enzyme  ACEI: angiotensin converting enzyme inhibitor

**Fig. 2** Schematic drawing of human somatic ACE, testic ACE, ACE2, Drosophila AnCE, and Drosophila Acer

The sequence of tACE is identical to that of the C-domain of sACE, except for its first 36 residues. Human sACE and tACE-732 have the same carboxy-terminal transmembrane and cytosolic sequences, while tACE-732 and tACE-739 have the same amine-terminal and a distinct transmembrane and cytosolic sequences. None of the Drosophila AnCE and Acer has a membrane-anchoring sequence. The carboxyl end of ACE2 is homologous to collectin, a nonenzymatic protein associated with renal injury. N: amine-terminus; C: carboxy-terminus; SP: signal peptide; TM: transmembrane domain; HEMGH: the locations of the active-site zinc-binding motif; HEXXH: the locations of the active-site zinc-binding motif.
家族

ACE

ACE-like

M2家族

ACE

ACE-like

家族

ACE

ACE-like

ACE

ACE-like

ACE

ACE

ACE

ACE

家族

ACE

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ACE

ACE
ACEI, ACE, Ang II, Ang I, RXPA380, sACE, Ac-D-K-P

ACEI, ACE, Ang II, Ang I, RXPA380, sACE, Ac-D-K-P

5 结语与展望

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