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EDITED AND REVIEWED BY

Ayako Makino,
University of California, San Diego,
United States

*CORRESPONDENCE

DuoYao Cao,
✉ DuoYao.Cao@cshs.org

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Editorial: Role of angiotensin-converting enzyme in myeloid immune functions

DuoYao Cao* and Suguru Saito

Department of Biomedical Sciences, Cedars-Sinai Medical Center, Los Angeles, CA, United States

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Editorial on the Research Topic

Role of angiotensin-converting enzyme in myeloid immune functions

Angiotensin-converting enzyme (ACE) is best known for its effects on blood pressure regulation due to its ability to generate the potent vasoconstrictor angiotensin II. Besides cleaving angiotensin I, ACE degrades many substrates, including bradykinin, substance P, N-acetyl-seryl-aspartyl-lysyl-proline (AcSDKP), enkephalins, neurotensin, amyloid β peptide, and others (Bernstein et al., 2013). ACE is composed of two homologous catalytic domains termed the N- and C-domains, each domain has a specific catalytic preference (Bernstein et al., 2013). Recent research findings indicate that ACE impacts various physiological processes, including normal renal development, male reproductive function, hematopoiesis, aspects of the immune response, and metabolic functions in chronic diseases (Bernstein et al., 2018; Cao et al., 2020a; Cao et al., 2020b; Cao et al., 2021; Cao et al., 2022; Cao et al., 2023).

In this Research Topic, Danziger et al. discussed that myeloid ACE affects Alzheimer's disease (AD). ACE has demonstrated the ability to degrade A β 42, a neurotoxic peptide that caused AD, suggesting a potential neuroprotective function. Research in murine models has indicated that augmenting ACE expression within specific immune cells holds promise for reducing neuropathology and enhancing cognitive function in AD. This review may provide insights into the potential for therapeutic approaches in Alzheimer's disease based on ACE's natural capabilities.

The Renin-angiotensin-aldosterone system (RAAS) is a pivotal regulator of blood pressure, primarily influencing renal sodium reabsorption, vascular tone, and sympathetic output. Additionally, it is closely linked to the blood pressure response triggered by changes in salt intake. In the findings by Ertuglu et al., high sodium exposure *in vitro* resulted in the downregulation of renin, renin binding protein, and renin receptor expression. However, no significant alterations were detected when examining the genes of the renin-angiotensin system in response to dietary salt loading and depletion *in vivo*. Notably, salt-sensitive individuals tended to have lower plasma renin levels and a diminished response to the salt loading/depletion challenge. These results demonstrate that short-term dietary salt changes do not impact RAAS expression in myeloid immune cells.

A healthy body's immune system must address potential threats from both external and internal sources. When disturbances occur, such as blood pressure or electrolyte balance disruptions, the RAS system perceives danger signals, leading to increased blood

pressure. Blood vessel endothelial cells release abundant ACE into the bloodstream to regulate blood pressure and support immune cells circulating in the system, such as neutrophils and monocytes. These cells stand ready to combat infections and tumors. ACE as one of the most vital and extensively studied peptidases in the RAS, plays an important role in myeloid immune response. However, in recent years, evidence shows ACE has participated in many immune responses, especially in myeloid immune response, such as bacterial clearance, anti-tumor, and reduced atherosclerotic plaque (Khan et al., 2019; Cao et al., 2021; Cao et al., 2023).

Due to the effects of ACE in regulating blood pressure and other cardiovascular diseases, ACE inhibitors (ACEi) are extensively employed in the treatment of hypertension, heart failure, and various cardiovascular conditions. This raises concerns for patients who rely on ACEis for long-term blood pressure management and cardiovascular health. Intriguingly, recent investigations have suggested that ACE deficiency might compromise the immune functions of neutrophils and macrophages, particularly in the context of bacterial infections and tumor progression (Khan et al., 2019; Cao et al., 2020a; Cao et al., 2021; Cao et al., 2022). Conversely, myeloid cells with elevated ACE levels may enhance immune response and metabolic functions (Cao et al., 2020b; Cao et al., 2023). These studies suggest that ACE activity within myeloid cells is pivotal in modulating the immune response. However, our comprehension of the impact of ACE inhibition on myeloid cells during acute and chronic inflammation in patients receiving ACEi treatment (e.g., individuals with hypertension, heart failure, and diabetes) remains limited. Therefore, there is a compelling need for a more precise exploration of pharmacological treatments related to ACE inhibition, demanding further consideration.

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This Research Topic has the potential to draw increased interest in ACE functions and to encourage more individuals to dedicate their efforts to exploring ACE in immune cells.

Author contributions

DC: Writing–original draft, Writing–review and editing. SS: Writing–review and editing.

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Conflict of interest

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