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EDITORIAL

A new face among our Associate Editors

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It is a great honor to introduce myself as an Associate Editor of Hypertension Research. I received my M.D. and Ph.D. degrees from Hiroshima University and started my research career there, studying abnormal intracellular calcium dynamics in patients with hypertension and animal models. I then developed my research specialization as a postdoctoral fellow under the supervision of Dr. Bradford C. Berk in the Cardiovascular Division at the University of Washington, focusing on the signaling mechanism for vascular remodeling in hypertension and atherosclerosis. I am currently conducting basic research focusing on DNA damage, inspired by research on atomic bomb survivors, with the goal of elucidating the pathophysiology of atherosclerosis.

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As part of my greeting, I would like to share a recent paper of interest in our journal. Hypertension is a multifactorial disease, impacted by environmental factors, genetics, and lifestyle, as well as a multisystem disease, involving the kidneys, central nervous system, and even the immune system [1–3], with the ultimate focal point being the blood vessels. This multifactorial nature makes it feasible to consider various strategies for the prevention and treatment of hypertension. In particular, the elucidation of the pathogenesis of hypertension related to the immune system and its therapeutic application has recently received much attention. For many years, it has been recognized that inflammation is involved in cardiovascular disease, and recently it has been reported that innate and adaptive immune responses are involved in the mechanisms of inflammation in hypertension [4]. Different subsets of lymphocytes and their cytokines, such as effector T cells including Th1 (interferon gamma-producing), Th2 (interleukin (IL) 4-producing) lymphocytes, Th17 (IL 17-producing), and regulatory T cells, are involved in the pathogenesis of hypertension [5]. Pro-inflammatory T lymphocytes are reported to be involved in the mechanisms of cardiovascular disease by mediating the effects of angiotensin II [6, 7] and mineralocorticoids [8]. Production of IL-17 is known to be dependent on IL-23, which is produced by activated dendritic cells [9]. The concept of an IL-23/IL-17 axis has been extensively investigated in chronic autoimmune diseases [10] and has recently received attention in the pathogenesis of hypertension [7].

Shokoples et al. hypothesized based on previous studies [11, 12] that angiotensin II-induced hypertension is associated with an increase in IL-17A-producing γδT17 cells in perivascular adipose tissue, and examined whether inhibition of the IL-23 receptor (IL-23R) blunts the angiotensin II-induced increase in blood pressure and reduces vascular damage [13]. They used *Il23r* knock-in (*Il23r*$^{gfp/gfp}$) mice lacking functional IL-23R by knocking in enhanced green fluorescent protein (gfp) in the intracellular domain of IL-

23R. Wild-type (WT) and *Il23r*$^{gfp/gfp}$ mice were infused with angiotensin II, their blood pressure was monitored, and vascular function and remodeling were assessed. Contrary to the hypothesis, *Il23r*$^{gfp/gfp}$ mice had smaller and stiffer mesenteric arteries, and angiotensin II-induced blood pressure elevation was not suppressed. While γδT17 cells were the most abundant subset of IL-17A-producing T cells in WT mice, functional loss of IL-23R resulted in fewer γδT17 cells and a lower frequency of Th17 cells with higher γ δT1, Th1, and cytotoxic Tc1 cells in perivascular adipose tissue than in WT mice, regardless of treatment with angiotensin II. Furthermore, angiotensin II infusion increased only IFN-γ-producing γδT1 cells in WT mice, but increased γδT1, Th1, and Tc1 cells in *Il23r*$^{gfp/gfp}$ mice. The angiotensin II-induced increase in blood pressure in *Il23r*$^{gfp/gfp}$ mice was partially suppressed by an anti-IFN-γ monoclonal antibody, indicating a contribution of IFN-γ to the more severe angiotensin II-induced hypertension seen in *Il23r*$^{gfp/gfp}$ mice.

This group conducted experiments by inhibiting upstream IL-23R signaling to clarify which subtype of T cells, γδT17 cells or γδT1 cells, contributes to the development of hypertension for future therapeutic applications in hypertension. The results suggested that inhibition of IL-23R provides no benefit in terms of protection against hypertension in a model of severe hypertension, which was consistent with previous studies [14, 15]. This study demonstrates that γδT1 cells, although a relatively small population of cells, may contribute significantly to angiotensin II-induced inflammation, elevated blood pressure, and vascular injury through the production of IFN-γ. As expected, the number of γδT17 cells was reduced in *Il23r*$^{gfp/gfp}$ mice, but γδT17 cells of IL-23R-independent embryonic thymic origin were detected. In contrast, since IL-23R is not required for the initial polarization of Th17 and Tc17 cells, loss of IL-23R function reduced the frequency of Th17 cells but did not alter the number of Th17 and Tc17 cells. The relatively high phenotypic plasticity of γδT17 and Th17 cells with respect to effector cytokine production and their ability to shift from IL-17A-producing cells to IFN-γ-producing cells may account for the increase in IFN-γ-producing T cells. These results suggest that an appropriate balance between T cell IL-17A and IFN-γ production is important for both blood pressure and vascular remodeling in angiotensin II-induced hypertension, and that this imbalance may be related to the pathogenesis of hypertension. Furthermore, other studies have shown that a high-salt diet can enhance the differentiation of immune cells toward Th17 cells, enhancing IL-17 production [16, 17], suggesting that sodium intake may be one of the most important lifestyle factors affecting hypertension.

As life expectancy extends due to improved medical standards, the incidence of cardiovascular diseases, leading eventually to heart failure, increases depending on lifestyle. Therefore, it has become increasingly important to ensure prevention through more rigorous guidance and treatment of cardiovascular risk factors such as hypertension. To achieve this, further extensive and detailed research on the causes and treatment of hypertension is essential. I encourage all researchers to submit your excellent papers to Hypertension Research for publication—it is a great honor for me to be involved in publishing such high-quality articles in Hypertension Research as an Associate Editor.

Compliance with ethical standards

Conflict of interest The author declare no competing interests.

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