Response to Angiotensin II Type 1a–Deficient Bone Marrow–Derived Dendritic Cells Produce Higher Levels of Monocyte Chemoattractant Protein 1

We thank Nahmod et al1 for their interest in our studies and for their intriguing experiments with dendritic cells that corroborate and complement our findings. One limitation of the bone marrow transfer strategy is that this approach does not elucidate which specific mononuclear cell populations are mediating blood pressure elevation and/or tissue damage. Therefore, experiments like those conducted by Nahmod et al1 will be crucial in defining the precise roles of angiotensin II type 1 (AT1) receptors on individual immune cell lineages in regulating inflammation. Reconciling the results of the diverse studies exploring the functions of AT1 receptors on immune cells is indeed challenging, but the divergent outcomes may accrue in part from the characteristics of the injury models used in these studies. For example, although AT1a deficiency was indeed detrimental in our model of autoimmune glomerulonephritis, we were not able to demonstrate a role for AT1 receptors on immune cells in that model, because AT1A receptor–deficient bone marrow chimeras had similar kidney injury to controls.2 Rather, we posited that glomerular AT1A receptors activated by high levels of angiotensin II in the AT1 receptor–deficient mice caused the exaggerated glomerular injury, because losartan therapy was protective in these animals. By contrast, in a model of antibody-mediated nephritis, Hisada et al3 found reduced kidney injury in AT1A receptor–deficient mice and in a follow-up study were able to demonstrate that AT1A receptors in a nonhematopoietic cell lineage were likely responsible for the AT1A-mediated kidney injury in their original study. This lack of a role for AT1A on immune cells in antibody-mediated disease is consistent with the finding of Guzik et al4 that B lymphocytes, which produce antibody, do not play a demonstrable role in the pathogenesis of angiotensin II–dependent hypertension. Therefore, we have focused on AT1 receptors in immune cell lineages that are involved in cell-mediated immunity, which include T lymphocytes, macrophages, and dendritic cells. Together, studies published to date suggest the paradox that AT1 receptors on immune cells play a more transparent role in nonimmune kidney disease (ie, associated with hypertension) than in immune-mediated kidney diseases. In addition to differences in injury models, discrepant reports regarding expression of angiotensin receptor isoforms on immune cell lineages greatly impact the interpretation of the studies in this field. For example, we have been unable to implicate the AT1A or the AT2 receptor in immune cell signaling because we cannot detect expression for these isoforms in T lymphocytes or macrophages using our RT-PCR primers (data not shown). By contrast, other groups using their own primers have found expression of both AT1A and AT2 receptors in mononuclear cell populations.5,6 Despite all of these discordant results, we are encouraged that the role of the renin-angiotensin system in regulating immune responses is now receiving considerable attention. Accordingly, careful and collective review of the growing number of studies including those conducted by Nahmod et al1 will undoubtedly lead to a clearer understanding of how AT1 receptors on immune cells impact the progression of kidney disease.

Sources of Funding
This work was supported by funding from the Veterans’ Administration Medical Research Service.

Disclosures
None.


Hypertension is available at http://hyper.ahajournals.org

DOI: 10.1161/HYPERTENSIONAHA.110.153544
Response to Angiotensin II Type 1a–Deficient Bone Marrow–Derived Dendritic Cells Produce Higher Levels of Monocyte Chemoattractant Protein 1

Steven D. Crowley, Young-Soo Song, Gregory Sprung, Robert Griffiths, Matthew Sparks, Ming Yan, James L. Burchette, David N. Howell, Eugene E. Lin, Benson Okeiyi, Johannes Stegbauer, Yanqiang Yang, Pierre-Louis Tharaux and Phillip Ruiz

Hypertension. 2010;56:e8; originally published online June 1, 2010; doi: 10.1161/HYPERTENSIONAHA.110.153544

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2010 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/56/1/e8

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/