Regulation of Arterial Tone by Kv1 Potassium Channels

To the Editor:

We have read with interest the recent article published by Circulation Research entitled “Heteromultimeric Kv1 Channels Contribute to Myogenic Control of Arterial Diameter.” The study adds to an expanding body of evidence suggesting pivotal roles of the voltage-gated potassium channels (Kv channels) in vascular smooth muscle cells as regulators of arterial tone. Nevertheless, we feel it is necessary to point out some issues relating to representation of the literature by Plane et al.

A general sentiment conveyed by Plane et al is “This study indicates for the first time the importance of Kv1 [delayed rectifier potassium] channels composed of Kv1 subunits to normal function of arterial resistance vessels via controlling their role in myogenic reactivity.” However, although appropriate references are cited, it is not made apparent to the reader that this concept has been documented previously. For example, Cheong et al showed that murine pial arterioles express Kv1 proteins in the smooth muscle cells and that the recombinant toxins agitoxin-2 and margatoxin (highly-specific Kv1 blockers) cause vasoconstriction. Also, Kv1 proteins were shown in smooth muscle cells of rabbit pial arterioles, and correolide, a Kv1-specific blocker (also central to the work of Plane et al), caused vasoconstriction. This study included recording of the Kv1 potassium current, showing its block by correolide, and demonstrating specificity of correolide by heterologous expression studies. Finally, Albarwani et al found that rat small cerebral arteries express Kv1.6 proteins in the smooth muscle cells and that correolide inhibits the Kv1 currents. In this preparation, which exhibits a high level of myogenic tone, block of Kv1 channels by correolide depolarized and constricted the pressurized arteries.

Plane et al also do not discuss a potential discrepancy between their finding that mRNA encoding Kv1 channels decreases with progression along the rat mesenteric arterial tree and findings supporting the opposite pattern of increased expression of Kv1 channels from aorta to mesenteric arteries of the rat or mouse. Additionally, there are numerous errors in the description of the work of other laboratories. A partial list includes:

1. Page 1 to 2: “Expression of these transcripts . . . was reported . . . including Kv1.1 and Kv1.6. References 7, 21, and 22 do not provide any data on transcripts. Reference 7 includes only patch-clamp data.”

2. Page 3: “Kv1.1 and/or Kv1.6 expression was reported for cerebral and mesenteric arteries. References 19 that transcripts for Kv1.1 and Kv1.6 could not be detected in rat mesenteric artery.”

3. Page 4: “Similarly, a lack of Kv1.1 protein expression by rat cerebral arterial myocytes was also evident using this antibody, contrary to previous reports.”

4. Page 7: “Evidence for contribution of Kv1.1 . . . was not obtained . . . contrary to studies of small arteries and arterioles.”

5. Page 8: “Inhibition of Kv1 by correolide was previously shown to elicit depolarisation and constriction of cerebral arteries and/or arterioles.”

We would like to stress that this letter is not a comment on the data in Plane et al. In fact, the findings of this article support previous conclusions that heteromultimeric Kv1 channels are expressed in vascular smooth muscle cells and regulate arterial tone. Our intention is, instead, to set Plane et al in perspective and take steps toward clarifying current knowledge for those who might read Plane et al as a primary source of information on this emerging and important aspect of vascular biology.

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