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SEX OF THE ANIMAL IMPACTS RESPONSES TO ANGIOTENSIN II (ANG II), OXIDATIVE STRESS LEVELS AND NITRIC OXIDE (NO) BIOAVAILABILITY

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To the Editor

Oxidative stress has been implicated in the pathogenesis of renal and cardiovascular diseases, however there is still much to be learned. It is against this background that we read with great interest the article entitled “Superoxide dismutase 1 limits renal microvascular remodeling and attenuates arteriole and blood pressure responses to angiotensin II via modulation of nitric oxide bioavailability” by Carlstrom et al. (1). The goal of this paper was to determine the functional role of superoxide dismutase 1 (SOD1) in regulating renal microvascular function and blood pressure responses to Ang II. The authors found that SOD1 knockout mice had a greater initial increase in blood pressure to chronic Ang II compared to wild-type control mice. In addition, renal afferent arterioles from SOD1 knockout mice were significantly more sensitive to acute Ang II-induced vasoconstriction compared to wild-type, while arterioles from SOD1 transgenic mice were less sensitive to Ang II vs. controls. Altered vascular responsiveness was likely due to low levels of NO bioavailability in arterioles from SOD1-knockout mice and enhanced levels of superoxide.

While the authors are to be commended on their excellent work, we would like to call attention to the fact that experiments were conducted using both male and female SOD1-transgenic, SOD1 knockout, and wild-type littermate mice with an equal distribution of both sexes in all of the experiments. Based on known sex differences in blood pressure and vascular responses to Ang II (2) sex differences in NO bioavailability (3), and sex differences in oxidative stress and antioxidant potential (4) the inclusion of both sexes may be a confounding factor in the study. In fact, if only males had been included the differences between the SOD1-knockout and transgenic mice and the appropriate wild-type control groups may have been more dramatic. For example, female experimental animals have been shown to be less sensitive to Ang II-induced hypertension, therefore it would be interesting to know if the blood pressure data in figure 2 included 2 males and 3 females or 3 males and 2 females. The inclusion of both sexes may also contribute to the greater variability in the blood pressure data with Ang II infusion. In addition, we recently published that female SOD3 knockout mice maintain total SOD activity due to a compensatory upregulation of SOD1 activity (5).

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In closing, while we applaud the authors on the inclusion of females in their study, we encourage them to examine the data between the sexes separately. Based on existing data in the literature, they may find additional novel findings based on the sex of the animal.

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