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Comparison of agonist-evoked, pericyte-mediated changes in vasa recta capillary diameter in mouse and rat live kidney slice models.

Introduction: Pericyte-mediated changes in vasa recta capillary diameter, following exposure of live kidney slices to a panel of known vasoactive agonists, have previously been well characterised in rat (1). However, it is well established that receptor expression patterns vary considerably between rat strains and rodent species. In the absence of a significant advancement in the generation of rat knockout models, we sought to characterise agonist-evoked pericyte-mediated changes in vasa recta capillary diameter in live kidney slices generated from C57BL/6J mice. The aim of this study was to compare agonist-evoked responses between mice and rats, and to provide a background profile of pericyte-mediated changes in vasa recta diameter for C57BL/6J mice for future studies in which data here will be compared to that yielded from studies utilising genetically modified mice.

Methods: All animals were killed humanely and in accordance with the Animals (Scientific Procedures) Act 1986. Post cervical dislocation, kidneys were removed from male C57BL/6J mice and 200 μm slices cut using a vibrotome. Slices were placed in a bath and anchored in place with a harp before being situated on the stage of an upright microscope continually superfused with physiological saline solution (PSS) bubbled with 95% O_2/5% CO_2. Slices were then exposed to the following compounds; ATP 2 mM, endothelin-1 (ET-1) 5 nM, prostaglandin E_2 (PGE_2) 10 μM, angiotensin-II (Ang-II) 300 nM and bradykinin 10 nM and DIC video images collected throughout the experiment. Videos were analysed off line and vessel diameter measured at pericyte and non-pericyte sites, with each vessel acting as its own control. Significance between data was calculated using a Student's t-test.

Results: A significantly greater constriction of mouse vasa recta was measured at pericyte sites compared to non pericyte sites in response to Ang-II 300 nM (15.89±3.29% vs 5.54± 2.88%, $p<0.05$, $n=21$), ET-1 5 nM (48.70± 11.04% vs 19.40± 9.41% $p<0.05$, $n=5$), ATP 2 mM (13.88± 2.40% vs 2.72 ± 1.14%, $p<0.005$, $n=6$), and a significantly greater dilation at pericyte sites compared to non-pericyte sites in response to PGE_2 10 μM (6.55± 0.47% vs 0.51± 0.32%, $p<0.0005$, $n=4$) and Bradykinin 10 nM (10.85± 0.58% vs 2.97± 1.02%, $p<0.05$).

Conclusion: Interestingly, the Ang-II- and ATP-mediated constriction of vasa recta measured at pericytes in the mouse is significantly less than that measured in rat ($p<0.05$), but the ET-1-mediated constriction of mouse vasa recta was greater than that measured in rat ($p<0.01$). Vasodilatory responses in mice were comparable to those measured in rat (1). Thus it is important to note for future studies that data yielded regarding pericyte-mediated constriction of capillaries in rat is not predictive of pericyte-mediated vasoconstriction in mice.

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(1) Crawford C *et al.* (2012). *Nephron Physiol* **120:** 17-31