Hypertension and prolonged vasoconstrictor signaling in RGS2-deficient mice

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The authors wish to add the following information.

Table 1: The doses of antagonists used to treat wild-type and RGS2-knockout mice were hexamethonium at 5 mg/kg i.v., prazosin at 200 µg/kg i.v., and candesartan at 100 µg/kg i.v. Effective ganglionic blockade by hexamethonium was established as described previously, whereas blockade by prazosin or candesartan was demonstrated by the inability of a subsequent infusion of phenylephrine (10 µg/kg i.v.) or angiotensin II (1 µg/kg i.v.) to increase blood pressure of wild-type or RGS2-knockout mice.

Figure 3: Blood pressure responses were determined using anesthetized mice as described in Methods. In Figure 3a, the doses of vasoconstrictors used to treat wild-type and RGS2-knockout mice were 1 µg/kg i.v. for angiotensin II and 10 µg/kg i.v. for phenylephrine. These doses were determined empirically, as were those that elicited a near-maximal (>75%) increase in blood pressure (determined by dose-response experiments such as those shown in Figure 4a for phenylephrine). In Figure 3b, candesartan (100 µg/kg i.v.) was infused into wild-type and RGS2-knockout mice over a period of 10 seconds, after which blood pressure was recorded continuously over the time period indicated. In Figure 3c, the same dose of angiotensin II (1 µg/kg i.v.) was used to treat wild-type and RGS2-knockout mice in order to increase systolic blood pressure to similar absolute levels (160–170 mmHg) prior to antagonist infusion (candesartan, 100 µg/kg i.v.). This approach was established by the results shown in Figure 3a, in which MAP of wild-type mice increased from a resting value (prior to agonist infusion) of ~85 mmHg to a value of ~135 mmHg after angiotensin II infusion, and the MAP of RGS2-knockout mice increased from a resting value of ~135 mmHg to ~140 mmHg by the same treatment. After a maximal effect of angiotensin II on blood pressure was achieved (~1 minute), candesartan (100 µg/kg i.v.) was infused over 10 seconds, and decreases in blood pressure were recorded continuously over the time period indicated.