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A new role for RGS-1 in vascular function and blood pressure regulation

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Background
The Regulator of G-Protein Signalling-1 (RGS1) controls G protein coupled receptor signalling by acting as a GTPase-activating protein for heterotrimeric G proteins. RGS1 has contrasting roles in haematopoietic and non-haematopoietic cells. We have previously shown that Rgs1 regulates macrophage accumulation in Angiotensin II (Ang II)-induced aortic aneurysms and Rgs1-/–ApoE-/- mice are protected from Ang II-induced aortic aneurysm rupture compared to ApoE-/– mice. Conversely, Ang II treatment increases systolic blood pressure to a greater extent in Rgs1-/–ApoE-/- mice than ApoE-/– mice and this is mediated by non-haematopoietic cells as indicated by bone marrow chimeras. However the precise role of RGS1 in hypertension and vascular-derived cells is unknown.

Methods and Results
We determined the effects of Rgs1 deletion on vascular function in ApoE-/- mice using wire myography. Rgs1 deletion led to enhanced vasoconstriction in aortas and mesenteric arteries from ApoE mice in response to PE and U46619 respectively. Rgs1 was shown to have roles in both endothelial and vascular smooth muscle cells (VSMCs), with endothelium-dependent vasodilation being impaired and endothelium-independent dilatation to SNP being enhanced in Rgs1-/–ApoE-/- mesenteric arteries. To address the downstream signalling pathways in VSMCs in response to Ang II-stimulated contraction, we assessed Erk phosphorylation in VSMCs isolated from thoracic aortas. Ang II induced rapid phosphorylation of Erk in Rgs1-/–ApoE-/- VSMCs in comparison to ApoE-/–VSMCs suggesting that Erk signalling is an major effector of Rgs1-mediated hypertension.

Conclusion
These findings indicate RGS1 is a novel regulator of blood pressure homeostasis and highlight RGS1-controlled signalling pathways in the vasculature that may be new drug development targets for hypertension.