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## α CALCITONIN GENE-RELATED PEPTIDE (αCGRP) PLAYS A PROTECTIVE ROLE IN THE ONSET OF ANGIOTENSIN-II INDUCED HYPERTENSION AND VASCULAR INFLAMMATION/REMODELLING

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Sensory nerve-derived neuropeptide calcitonin gene-related peptide (CGRP) acts as a potent vasodilator, and is suggested to be protective in models of hypertension. The aim of this study was to learn of the vascular mechanisms by which αCGRP is protective in an angiotensin-II (Ang II) model of hypertension. Matched C57BL/6 wildtype (WT) and αCGRP knockout (KO) mice were infused with Ang II (1.1 mg/kg/day for 14 days) or vehicle (saline) via the osmotic minipump. Blood pressure was recorded by tail-cuff plethysmography until day 14 when the experiment was terminated. Vascular hypertrophy was assessed by histology and RT-qPCR. Data were analysed using ANOVA plus Bonferroni's post test.

WT and αCGRP KO mice did not show any difference in systolic pressure under baseline recordings. However systolic pressure was elevated after 14 days Ang II infusion in WT (129±3.84) and αCGRP KOs (140±7.23, $p<0.001$), this being significantly enhanced in the CGRP KOs ($p<0.001$). αCGRP mRNA expression was upregulated in the aorta of hypertensive WTs ($p<0.01$), and localisation of CGRP was visible in endothelial and smooth muscle cell layers of the vessel wall. Vascular inflammation/remodelling and markers of oxidative stress was also apparent in hypertensive subjects, characterised by increased collagen III, glutathione peroxidase 1 (GPX1) and NOX 2 mRNA expression. Remodelling and expression of these markers was exacerbated in Ang II-treated αCGRP KOs ($p<0.001$). This study provides evidence that deletion of αCGRP is associated with enhanced Ang II-induced hypertension and vascular injury.