**Microbial metabolite supplementation reduces blood pressure by improving vascular function**

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**Introduction**: Short-chain fatty acids (SCFAs), gut microbial metabolites derived from dietary fibre fermentation, reduce BP in mice and humans. In a clinical trial, total vascular resistance was reduced in the SCFA arm of participants untreated for hypertension. Whether this is a primary BP-lowering mechanism remains unclear.

**Aim**: To determine whether dietary SCFAs lower BP via vascular function in experimental hypertension.

**Methods**: Male C57BL/6 mice (n=16/group) received minipumps with angiotensin II (Ang II, 0.75mg/kg/day) or saline (sham) and drinking water with 0.9% sodium chloride for 4 weeks. Mice were fed on high-SCFA or control diet after surgery. Aortic elastin content was determined using Verhoeff van Giesen (VVG) staining, aorta contractile forces by wire myography and function by ultrasound. BP was measured by tail-cuff, immune system by flow cytometry, gut microbiome via 16S rRNA sequencing, and caecal SCFAs via NMR.

**Results**: SCFAs significantly increased elastin content in sham mice aortas (p=0.0041). Improved relaxation (*p*=0.0041) and resistive index (*p*=0.027) were observed with SCFAs, irrespective of hypertension status. SCFAs decreased BP (p=0.02) and increased caecal SCFAs (p=0.015) in Ang II-treated mice compared to control diet. The gut microbiome was significantly modulated by SCFAs, regardless of hypertension status (Shannon index, p<0.001; Weighted UniFrac distance, adjusted p-value<0.05). No significant changes to aortic immune cells were observed.

**Discussion**: SCFAs directly improves vascular function *in vivo*, via BP-reducing gut microbial metabolites.