**Distinct aortic endothelial cell subtype promotes vascular inflammation and remodelling during angiotensin II-induced aortic stiffening
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**Introduction.** Hypertension is the leading cause of death, affecting one third of adults worldwide. Aortic stiffening, inflammation and endothelial dysfunction are hallmarks of hypertension, however the interactions between these conditions remain largely unknown. **Aims**. We aimed to characterise endothelial cell (EC) heterogeneity and compare aortic EC phenotypes in healthy and hypertensive settings. **Methods**. Hypertension was induced by angiotensin (Ang) II (0.7 mg/kg/day) infusion into 12-week-old male C57BL/6 mice via osmotic minipump (*s.c.*). Normotensive control mice received saline. After 28 days, aortae were harvested and enzymatically dissociated into single-cell suspensions. Metabolically active live cells were collected using FACS and prepared for single cell RNA-sequencing using Chromium 10x and NovaSeq genomics platforms. **Results.** Single-cell analysis of 22,207 cells identified 17 cell types including 3 distinct Pecam1-expressing EC subclusters, one being a lymphatic EC. Interestingly, von Willebrand factor (vWF), a widely accepted EC marker, was solely expressed in one EC cluster (EC2). Immunofluorescence and flow cytometry confirmed the presence of three distinct EC populations. To determine regional heterogeneity, flow cytometry was performed on thoracic and abdominal aortas from male and female mice and showed male mice harboured a higher percentage of vWF+ ECs. Irrespective of sex, the abdominal aorta had a higher proportion of vWF+ ECs compared to thoracic aorta. Gene ontology analysis revealed hypertension enriched for biological processes associated with *ECM organisation*, *cell adhesion* and *migration* in EC2, suggesting a pro-fibrotic phenotype. Cell-cell communication analysis showed profibrotic signalling pathways enriched in EC2 from hypertensive mice including *Thbs1*, *Fn1*, *Bmp* and Icam1, which was uniquely associated with EC2-macrophage cross talk. **Discussion.** Characterising the distinct roles of aortic EC subtypes may provide crucial insights into EC- driven molecular mechanisms of aortic stiffening and inflammation in the context of hypertension.