

Vasomodulatory Dysregulation after Cardiopulmonary Bypass with Uncontrolled Hypertension



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Introduction

Cardiopulmonary bypass is known to cause dysregulation of vasogenic response in cardiac microvessels. Furthermore, it has been previously shown that this effect is preferentially upregulated in patients with uncontrolled hypertension compared to patients with either control over their hypertension or normotensive patients. Even in the presence of vasodilators, microvessels in the setting of cardiopulmonary bypass do vasodilate at expect levels, and more so in patients with hypertension. Although the vasomotor effects of vascular smooth muscle cannot be discounted, the chronic changes to vascular endothelium that are caused by hypertension may play a role in their response to the ischemic stress caused by cardiopulmonary bypass. Thus, there is a gap in understanding on whether there is a change in gene regulation of the vascular endothelium specifically in patients based on their hypertension status after cardiac surgery.

Objective

To determine which key genes, if any, are modulated in the vascular endothelium of hypertensive patients versus healthy patients after cardiopulmonary bypass and investigate their function

Methods

Atrial appendage tissue was collected via a double purse string technique both before cardiopulmonary bypass induction and after (post cross clamp removal) in twelve patients undergoing cardiac surgery at Rhode Island Hospital/Brown University Health. Patient tissues were flash frozen on liquid nitrogen and then processed for RNA sequencing via Singulomics Corporation. There were normotensive (N = 2) controlled hypertensive (N = 5) and uncontrolled hypertensive (N = 5) patients in this sample.

Reads were derived in fragments per kilobase per million mapped fragments (FPKM) in both pre and post tissue. Genes of interest were isolated from the TISSUES Text-Mining Database relevant to vascular endothelium. From there, fold changes were calculated for each group, and then compared using Welch's T-Test.

Results

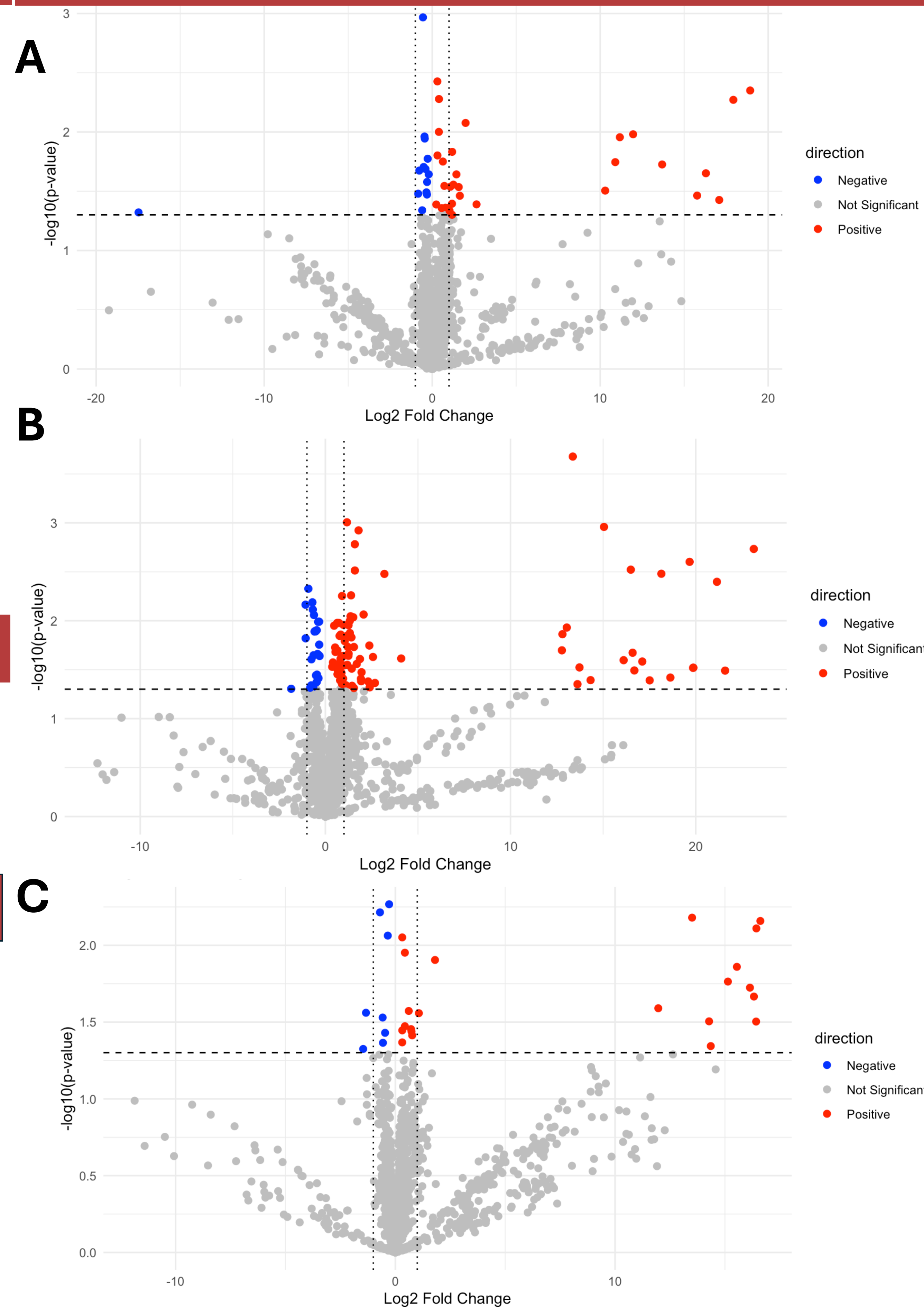


Figure 1 (A) Volcano plot of log2 fold change comparisons between uncontrolled hypertensive and normotensive patients after cardiopulmonary bypass (B) Volcano plot of log2 fold change comparisons between controlled hypertensive and normotensive patients after cardiopulmonary bypass (C) Volcano plot of log2 fold change comparisons between uncontrolled and controlled hypertensive patients after cardiopulmonary bypass

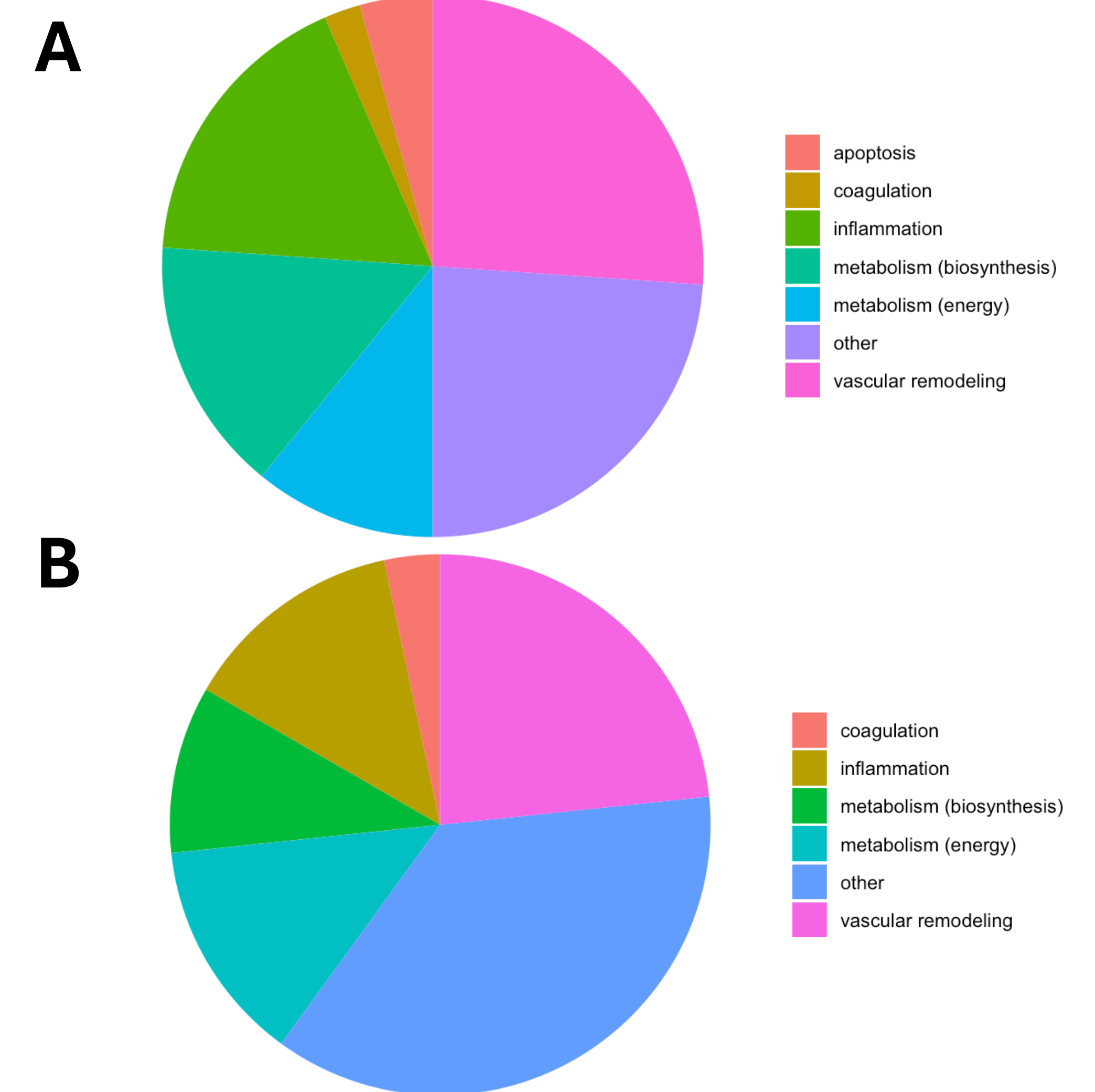


Figure 2: (A) Significantly differentially expressed gene functions in uncontrolled hypertension compared to baseline most commonly vascular remodeling genes (B) Significantly differentially expressed gene functions in controlled hypertension compared to uncontrolled hypertension most commonly with unspecific function

Conclusions

- Uncontrolled hypertensive patients show significant upregulations in inflammatory and vascular remodeling genes
- Controlled hypertensive patients also show upregulations in inflammatory process genes compared to baseline
- Surprisingly, controlled hypertensive patients do see upregulations in certain proinflammatory genes
- Further studies should increase sample size

References

