

Appendix for *Epigenomic landscape of single vascular cells reflects developmental origin and disease risk loci*

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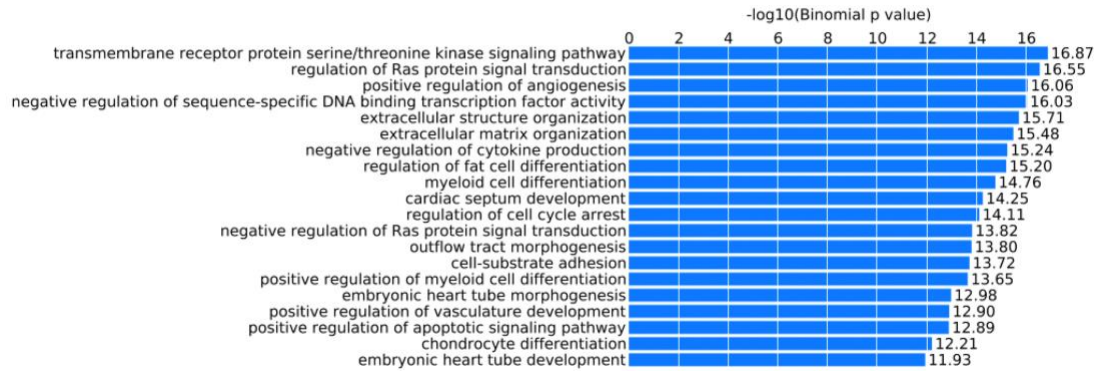
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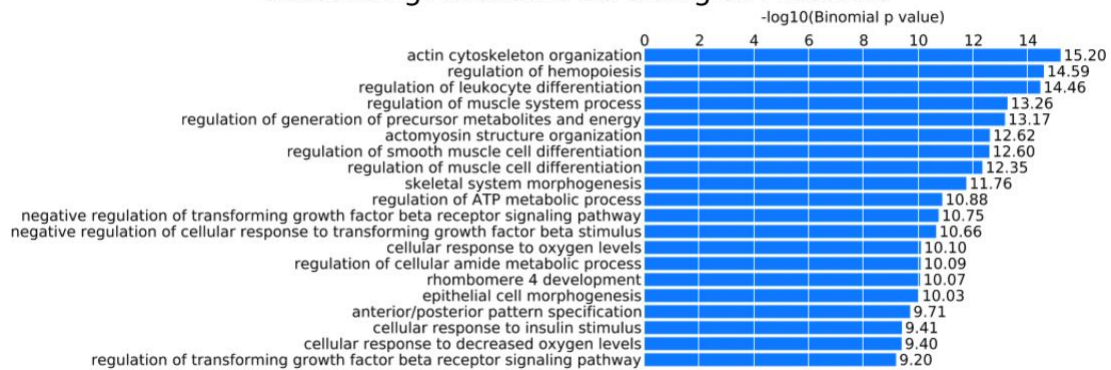
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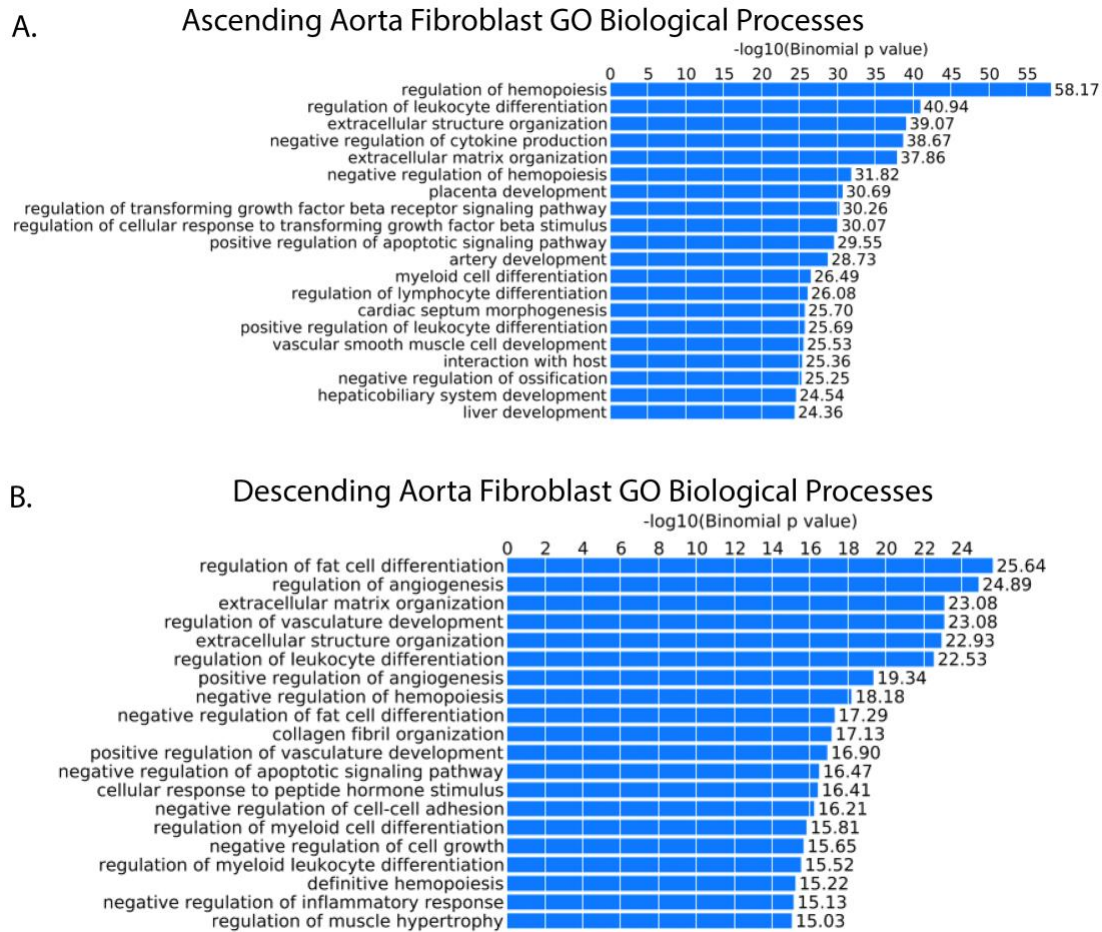
A. Ascending Aorta SMC GO Biological Processes



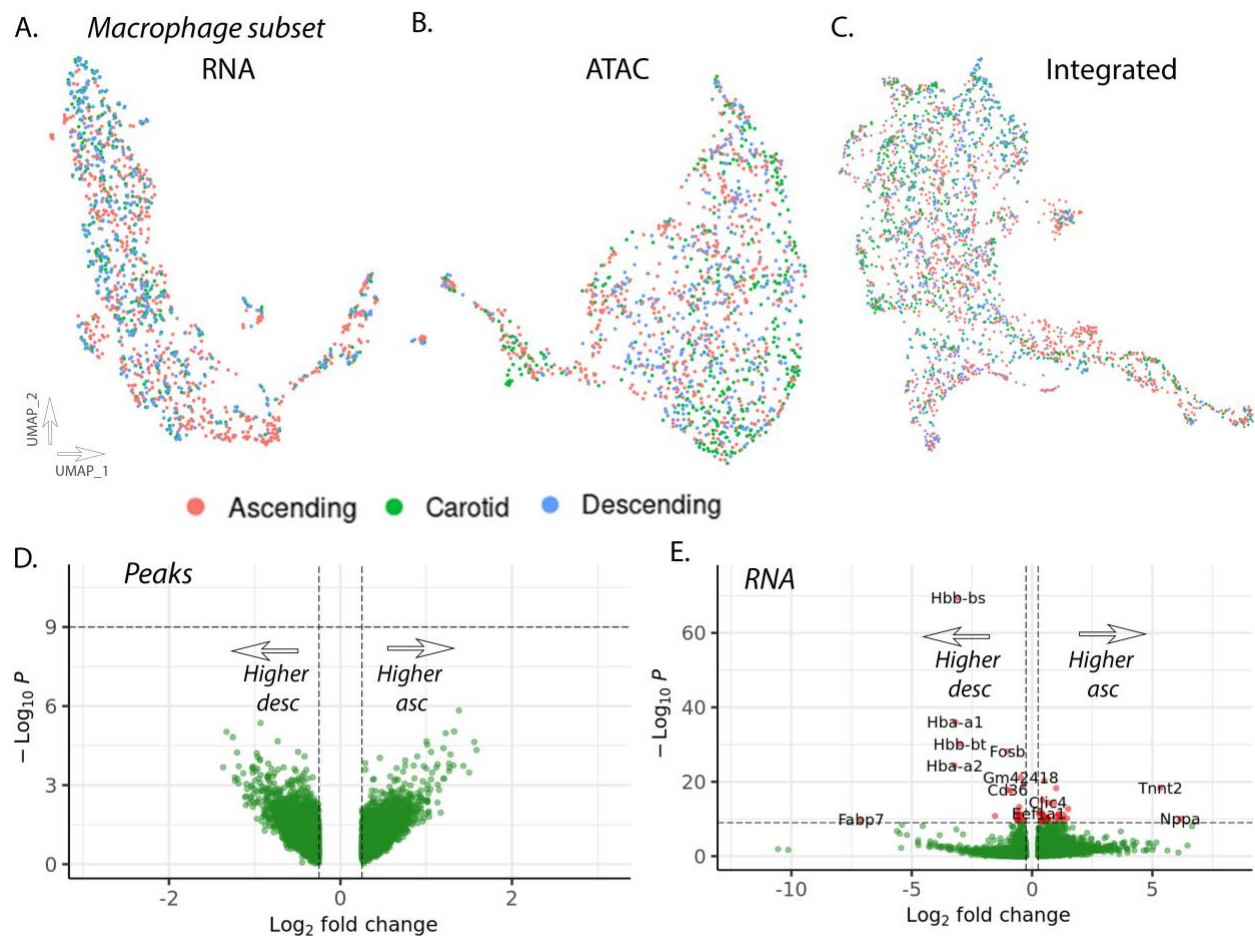
B. Descending Aorta SMC GO Biological Processes



Appendix Figure S1. Top biological processes from GREAT for peaks marking SMCs isolated from the ascending aorta (A) and descending aorta (B).



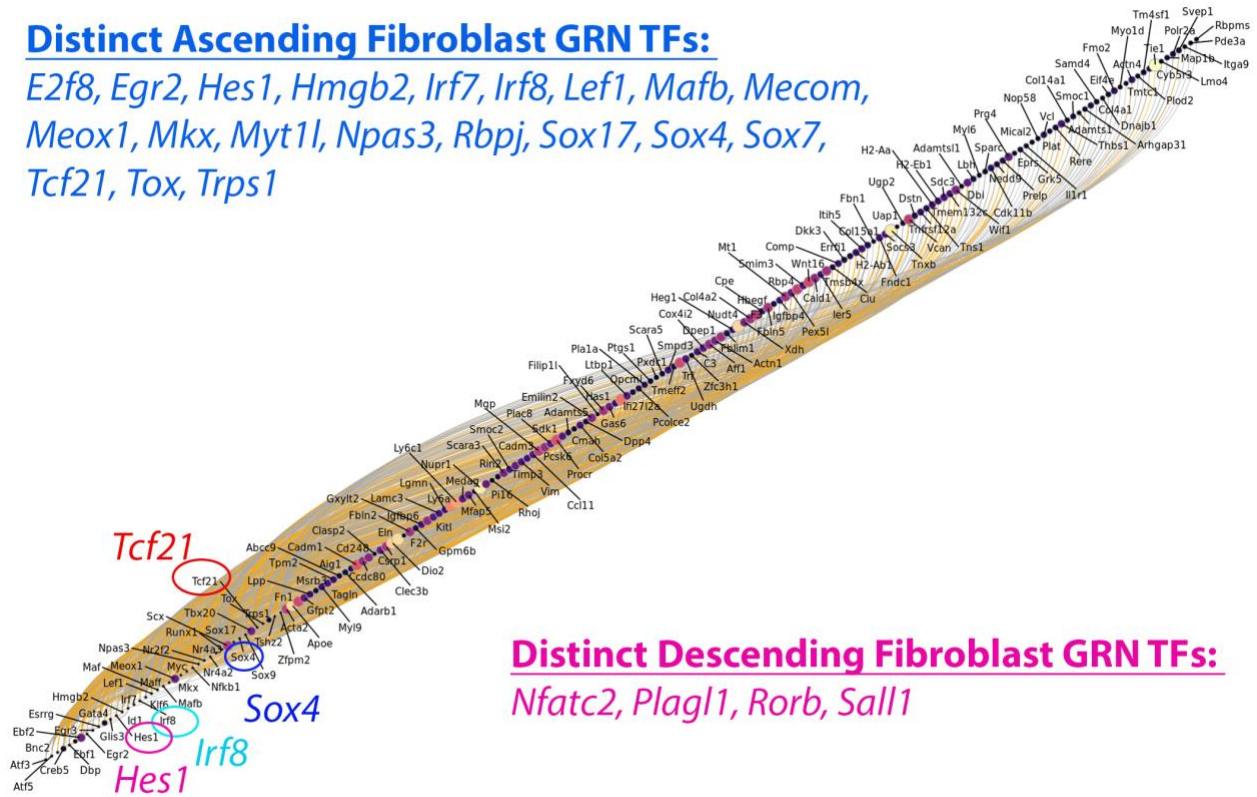
Appendix Figure S2. Top biological processes from GREAT for peaks marking fibroblasts isolated from the ascending aorta (A) and descending aorta (B).



Appendix Figure S3. Single cell transcriptomic and epigenomic analysis of macrophage cells reveals notable homogeneity between vascular sites. UMAP visualization of macrophage cell subset for RNA (A), ATAC (B), and integrated (C) datasets. Volcano plots for differential peak accessibility (D) and RNA expression (E).

Distinct Ascending Fibroblast GRN TFs:

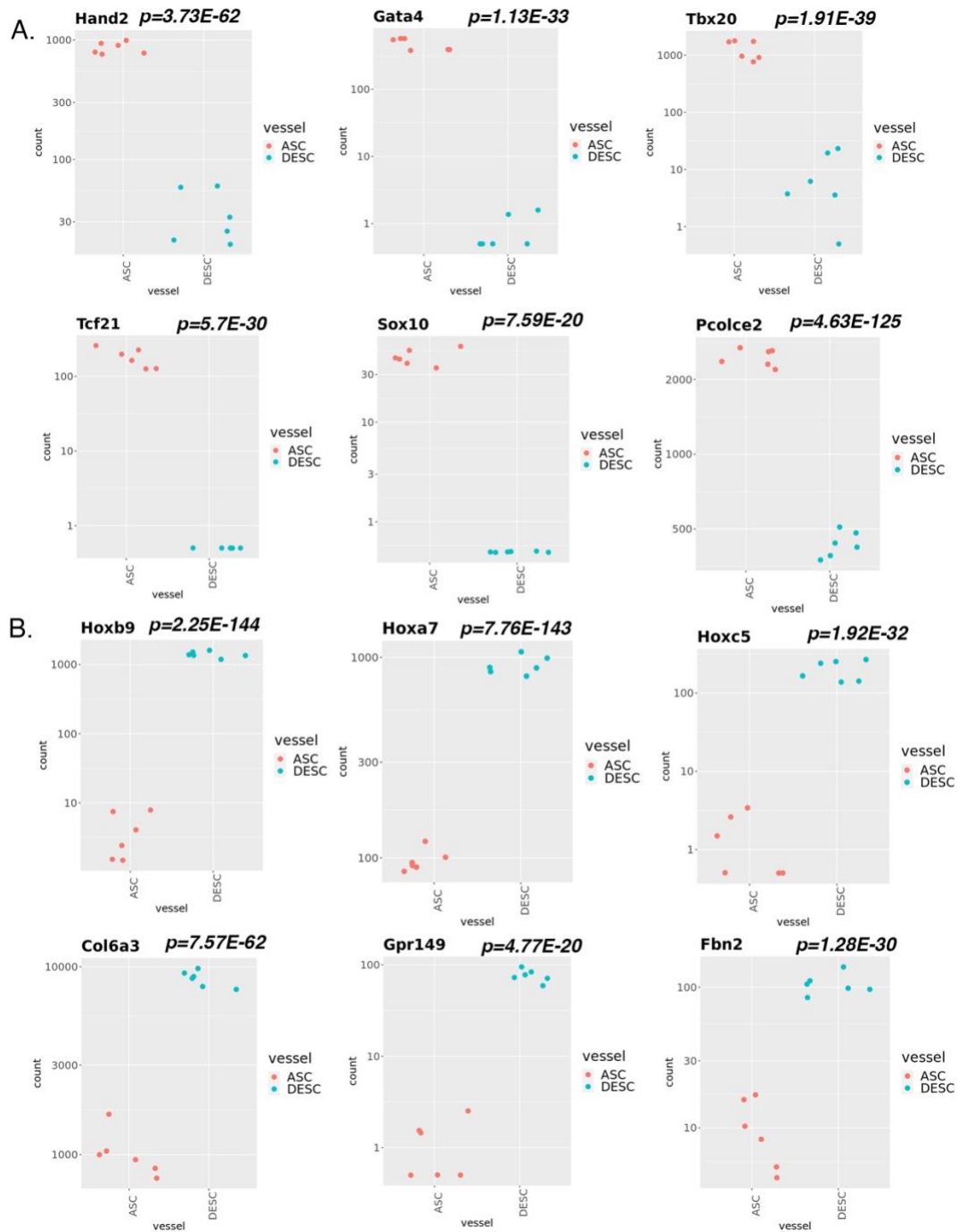
E2f8, Egr2, Hes1, Hmgb2, Irf7, Irf8, Lef1, Mafb, Mecom, Meox1, Mkx, Myt1l, Npas3, Rbpj, Sox17, Sox4, Sox7, Tcf21, Tox, Trps1



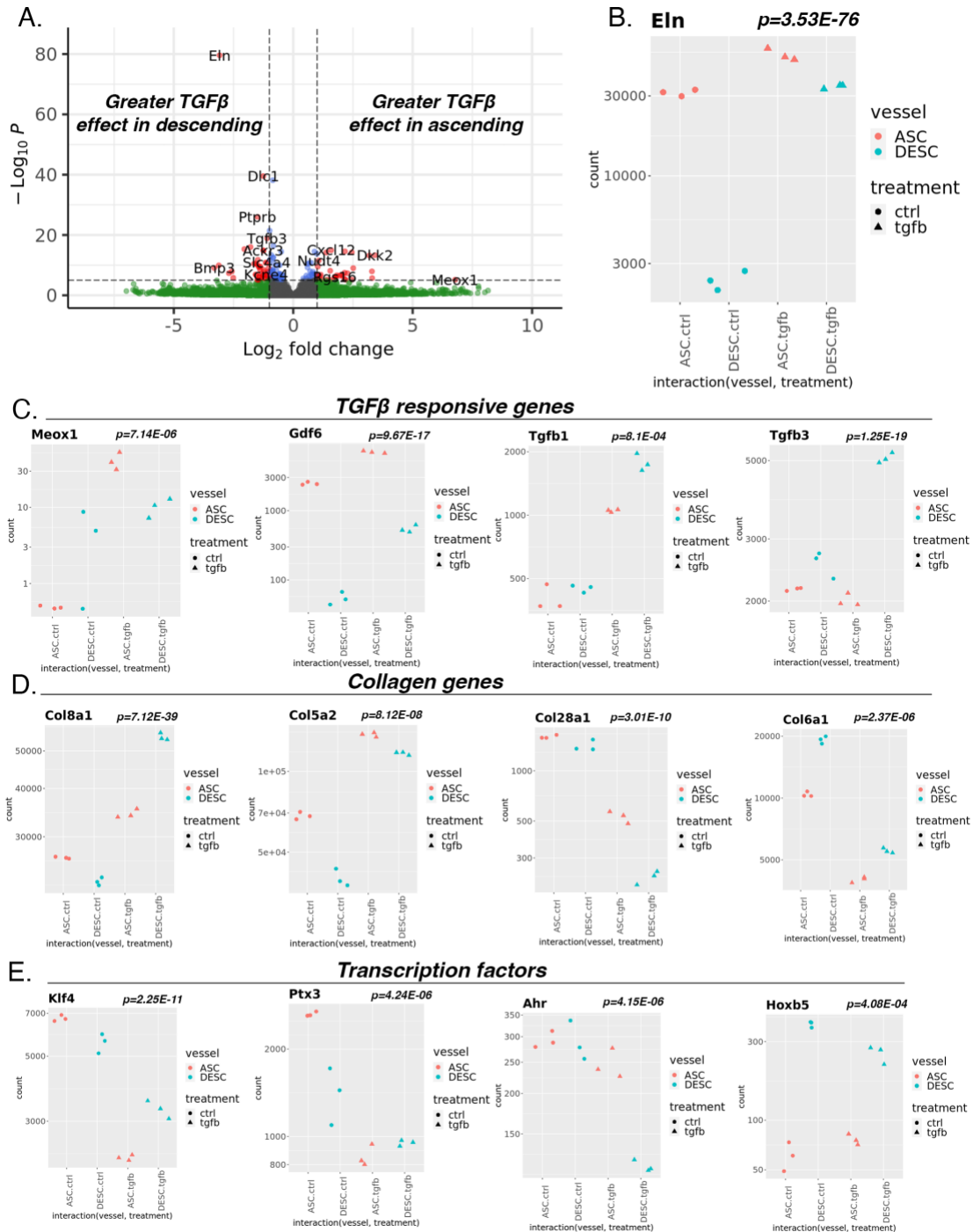
Distinct Descending Fibroblast GRN TFs:

Nfatc2, Plagl1, Rorb, Sall1

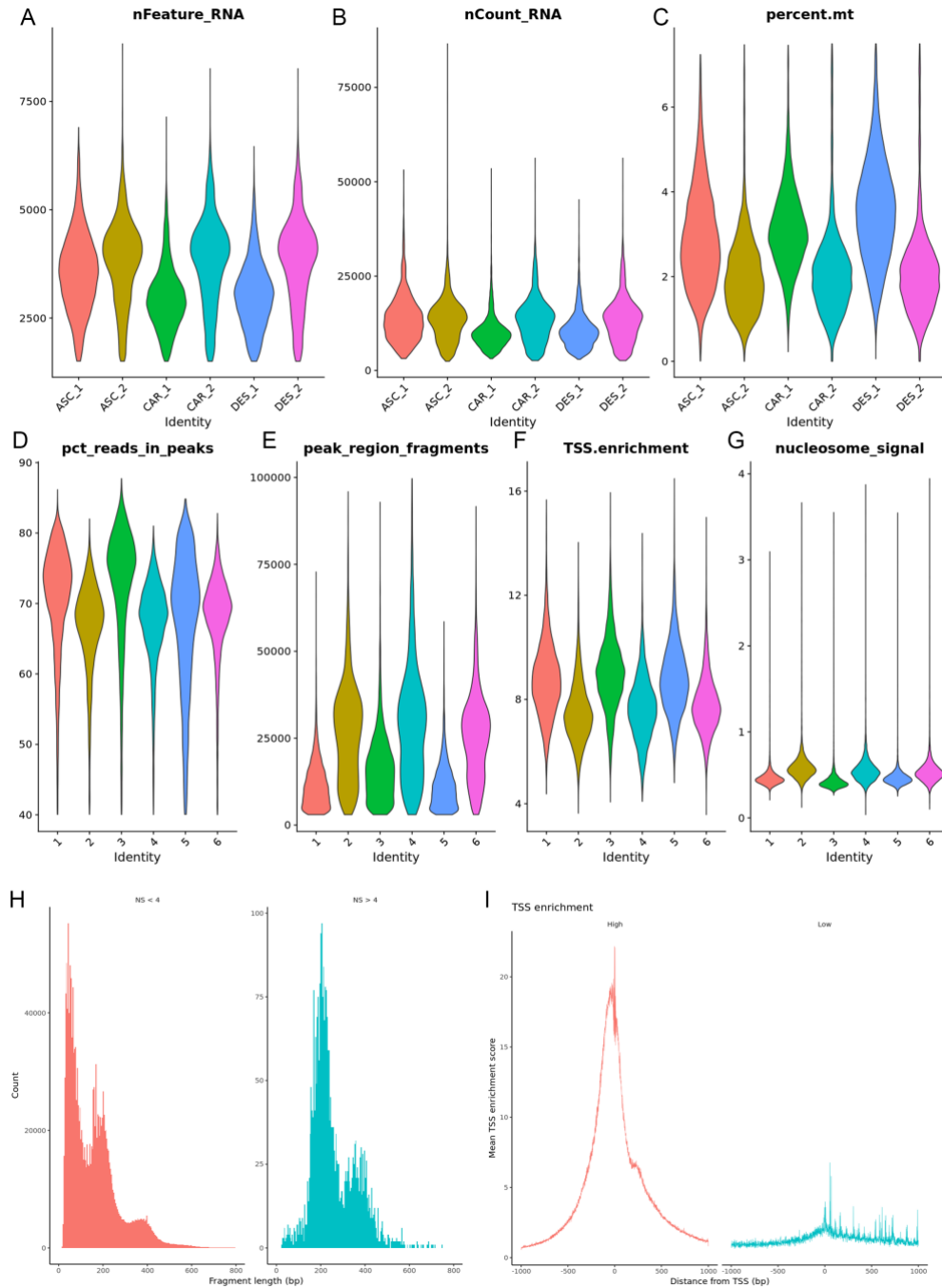
Appendix Figure S4. Distinct ascending fibroblast gene regulatory networks. GRN visualization for ascending fibroblasts network analysis, where each dot represents gene and/or TF, color represents regulatory strength (darker with higher strength), and size of dot reflects degree of centrality.



Appendix Figure S5. RNA expression from primary adventitial fibroblast in vitro culture highlighting genes with increased expression in ascending fibroblasts including *Hand2*, *Gata4*, *Tbx20*, *Tcf21*, *Sox10*, and *Pcolce2* (A), and increased expression in descending fibroblasts including *Hoxb9*, *Hoxa7*, *Hoxc5*, *Col6a3*, *Gpr149*, and *Fbn2* (B). Y-axis represents normalized read counts by DESeq2 shown on log10 scale. P-value for comparison shown for each gene.



Appendix Figure S6. Volcano plot of interaction analysis of RNAseq data revealing genes with differential response to TGF β by vascular site (log₂FC > 0 represents greater effect TGF β in ascending; log₂FC < 0 represents greater effect TGF β in descending) (A). RNAseq expression for top interaction gene *Eln* (B). RNAseq expression for TGF β responsive genes *Meox1*, *Gdf6*, *Tgfb1*, and *Tgfb3* (C) collagen genes *Col8a1*, *Col5a2*, *Col28a1*, *Col6a1* (D) and transcription factors *Klf4*, *Ptx3*, *Ahr*, and *Hoxb5* (E). Y-axis represents normalized read counts by DESeq2 shown on log₁₀ scale. P-value for interaction shown for each gene.



Appendix Figure S7. QC metrics for scRNAseq and scATACseq datasets. For scRNAseq datasets, violin plots for nFeature_RNA (A), nCount_RNA (B), and percent.mt (C) across 6 captures. For scATACseq datasets, violin plots for pct_reads_in_peaks (D), peak_region_fragments (E), TSS.enrichment (F), and nucleosome_signal (G). Fragment histogram of region chr1-1-10000000 in combined aggr dataset based on low and high nucleosome signal (NS <4, left, NS >4, right) (H). TSS plot for combined aggr dataset based on high and low TSS enrichment (TSS >2, left, TSS <2, right).