

Supplementary Materials for  
**Atlas of cardiac endothelial cell enhancer elements linking the  
mineralocorticoid receptor to pathological gene expression**

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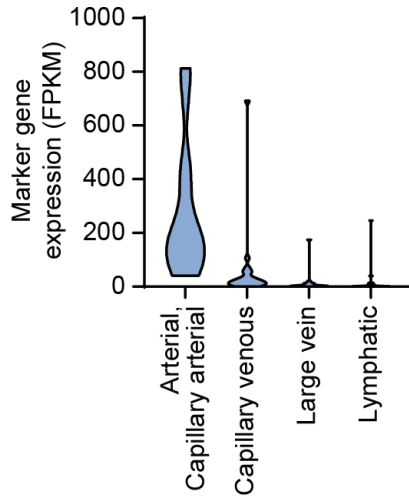
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**The PDF file includes:**

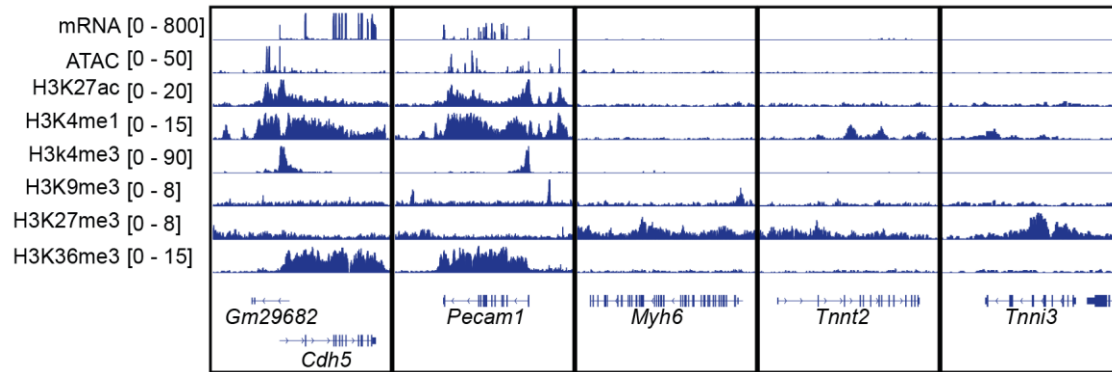
Figs. S1 to S7  
Legends for tables S1 to S3  
Tables S4 and S5  
Legend for data S1

**Other Supplementary Material for this manuscript includes the following:**

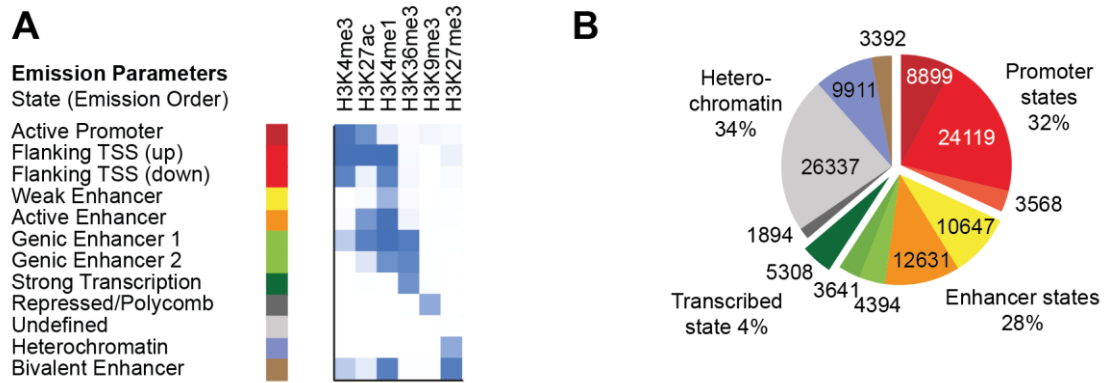
Tables S1 to S3  
Data S1



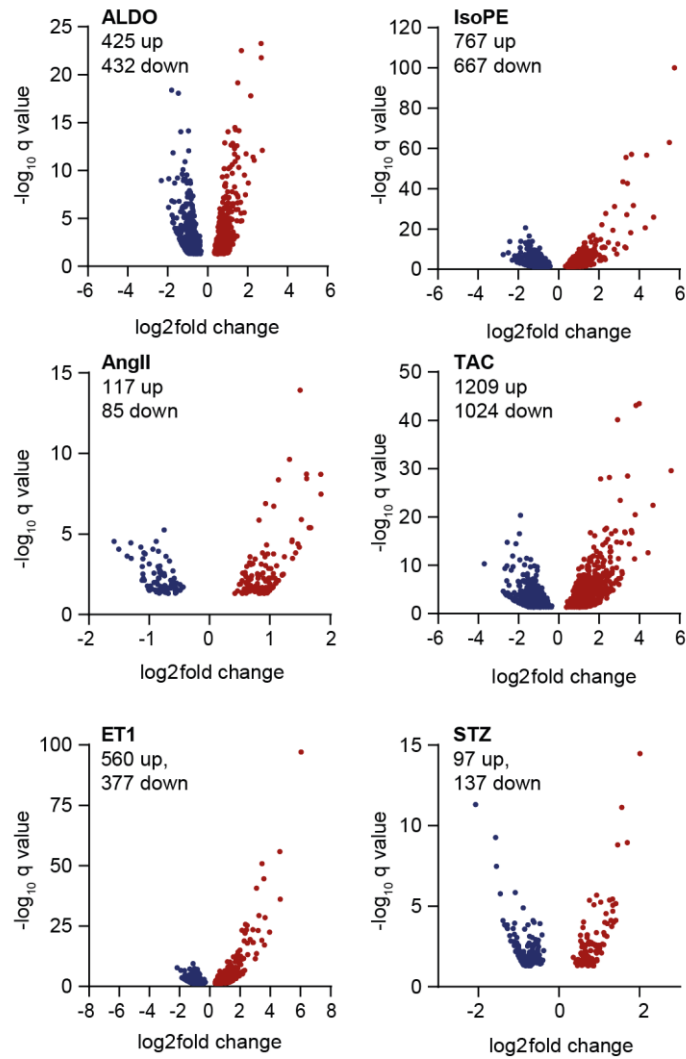
**Fig. S1. Endothelial cell subtypes marker gene expression.** mRNA expression of marker genes for arterial/capillary arterial, capillary venous, large vein, or lymphatic endothelial cells.



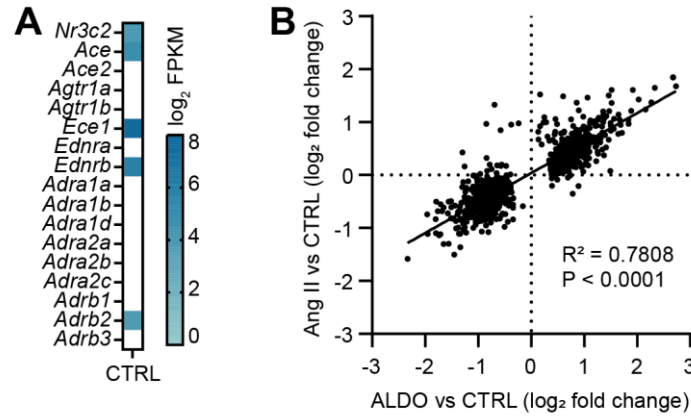
**Fig. S2. Gene expression and chromatin state at marker gene loci.** Representative traces showing mRNA expression levels, accessible chromatin (ATAC), and histone marks at the typical gene loci for cardiac endothelial cells, such as Cadherin 5 (*Cdh5*) and Platelet endothelial cell adhesion molecule 1 (*Pecam1*), as compared to typical cardiomyocyte gene loci, such as Myosin heavy chain (*Myh6*), Troponin T2 (*Tnnt2*), or Troponin I3 (*Tnni3*).



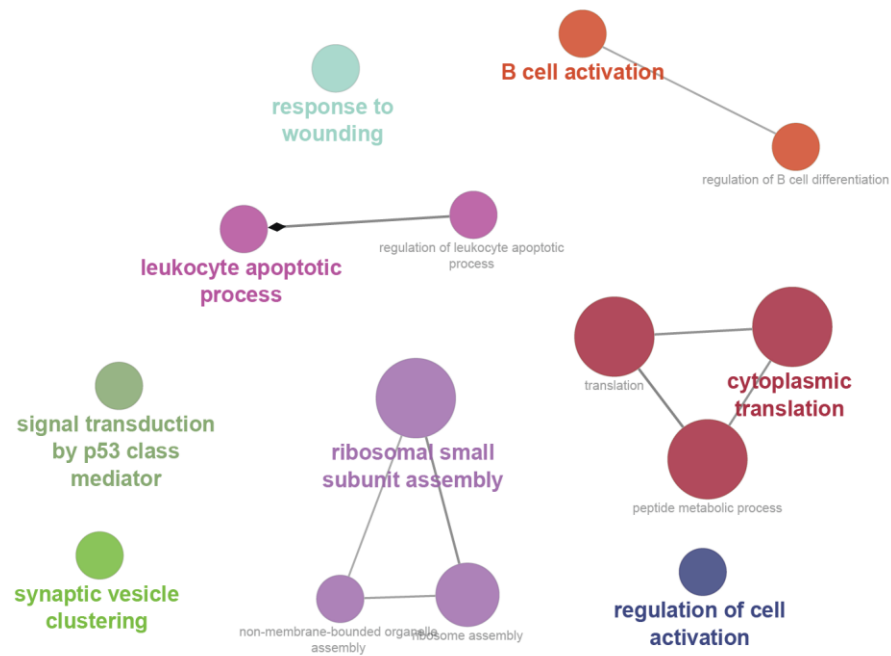
**Fig. S3. Chromatin state.** Analysis based on 6 histone marks characterize the epigenetic landscape with 12 different chromatin states in cardiac endothelial cells (A). Pie-chart illustrating the distribution of ATAC-peaks intersecting with distinct chromatin states (B).



**Fig. S4. Gene expression in different models of cardiovascular disease.** Volcano plots showing up- (red) or downregulated (blue) genes in endothelial cells isolated from mice subjected to aldosterone infusion (ALDO), angiotensin II infusion (Ang II), endothelin 1 infusion (ET1), isoprenaline and phenylephrine infusion (IsoPE), transverse aortic constriction (TAC), or streptozotocin treatment (STZ) compared to untreated CTRL ( $q < 0.05$ ,  $n = 3-4$  per group).



**Fig. S5. Correlation of aldosterone and angiotensin II-induced gene expression in cardiac endothelial cells.** Heatmap indicating the expression of the mineralocorticoid receptor (*Nr3c2*), angiotensin converting enzymes (*Ace*, *Ace2*), angiotensin receptors (*Agtr1a*, *Agtr1b*), endothelin converting enzyme (*Ece1*), endothelin receptors (*Ednra*, *Ednrb*), and adrenergic receptors (*Adra1a*, *Adra1b*, *Adra1d*, *Adra2a*, *Adra2b*, *Adra2c*, *Adrb1*, *Adrb2*, *Adrb3*) in untreated cardiac endothelial cells (n = 4) (A). Correlation of genes that are differentially expressed in endothelial cells treated with aldosterone (ALDO) or angiotensin II (Ang II) compared to CTRL (q < 0.05; n = 4 per group) (B).



**Fig. S6. Aldosterone-induced gene expression in MR-deficient endothelial cells.** Enrichment of biological processes ( $p < 0.05$ ) among genes that were differentially expressed in endothelial cells from untreated (CTRL) or aldosterone-treated (ALDO) MR<sup>Cdh5Cre</sup> mice ( $q < 0.05$ ,  $\pm 1.5$ -fold change,  $n = 5$  per group).





**Table S1. (separate file) Sequencing statistics for RNA-seq, ATAC-seq, ChIP-seq, and Hi-C data.**

**Table S2. (separate file) Endothelial cell gene expression in experimental models of cardiovascular disease as determined by RNA-seq.**

**Table S3. (separate file) Aldosterone-induced gene expression in endothelial cells from MR<sup>wildtype</sup> and MR<sup>Cdh5Cre</sup> mice.**

**Table S4. sgRNA sequences**

<b>FABP4 promoter</b>	sg_1	AATGCAGAGGCCGGTAATGA	forward
		TCATTACCGGCCTCTGCATT	reverse
	sg_2	GGAAGTTATCTGGACTCAAG	forward
		CTTGAGTCCAGATAACTTCC	reverse
<b>Enhancer 1</b>	sg_1	ACATGACTTCACATCAACTA	forward
		TAGTTGATGTGAAGTCATGT	reverse
	sg_2	GGTGGCTAAAATCAACAATA	forward
		TATTGTTGATTTTAGCCACC	reverse
	sg_3	CATTCATGTGCAGGTTGATA	forward
		TATCAACCTGCACATGAATG	reverse

**Table S5. qRT-PCR primer sequences**

<b>FABP4</b>	hFABP4ben_F	TGGGGGTGTCCTGGTACATGTG	forward
	hFABP4ben_R	ACTCTCGTGGAAGTGACGCCTT	reverse
<b>RPS29</b>	hRPS29_s	GGTTCTCGCTCTTGTCGTGTC	forward
	hRPS29_as	ATATCCTTCGCGTACTGACGG	reverse

**Data S1. (separate file) Homer Known Motif Enrichment Results.** Transcription factor binding motifs enriched within enhancer regions associated with genes that were differentially regulated in a given disease-model relative to the background of all endothelial enhancer regions.