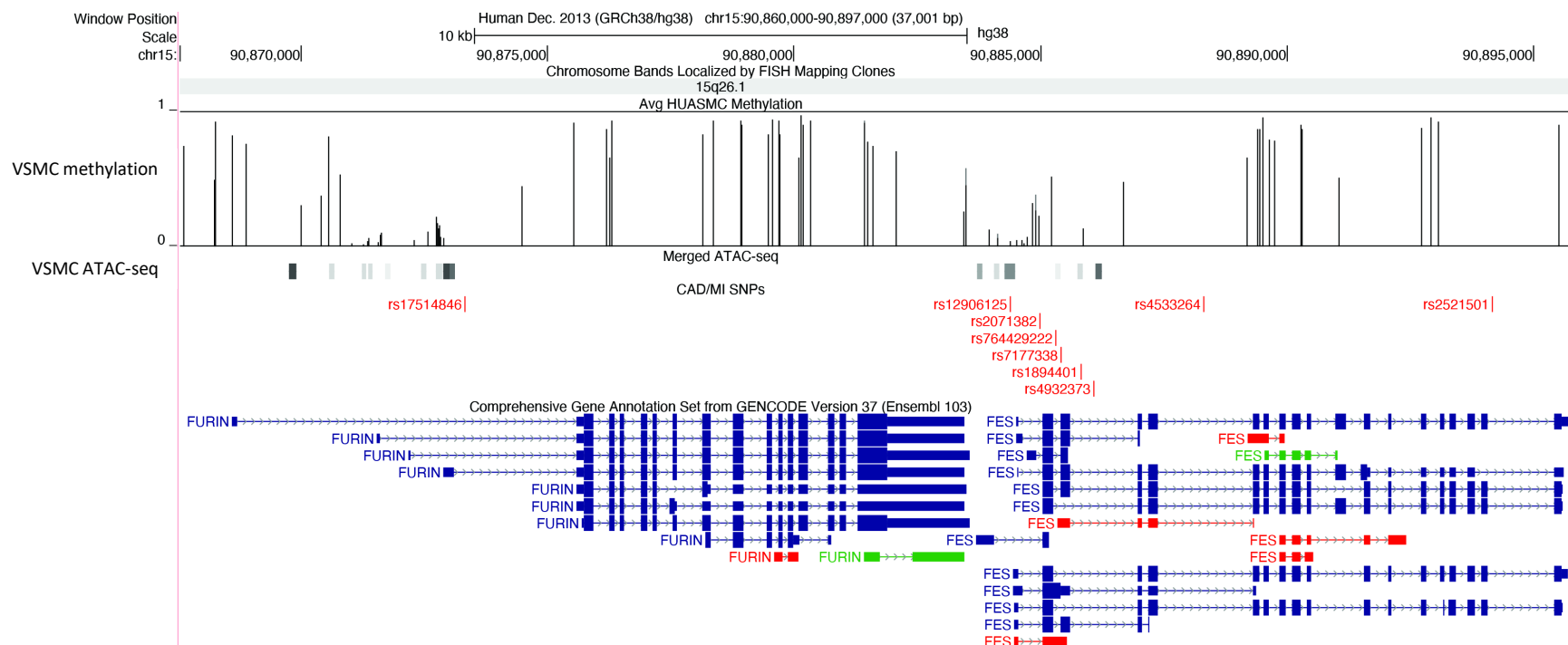
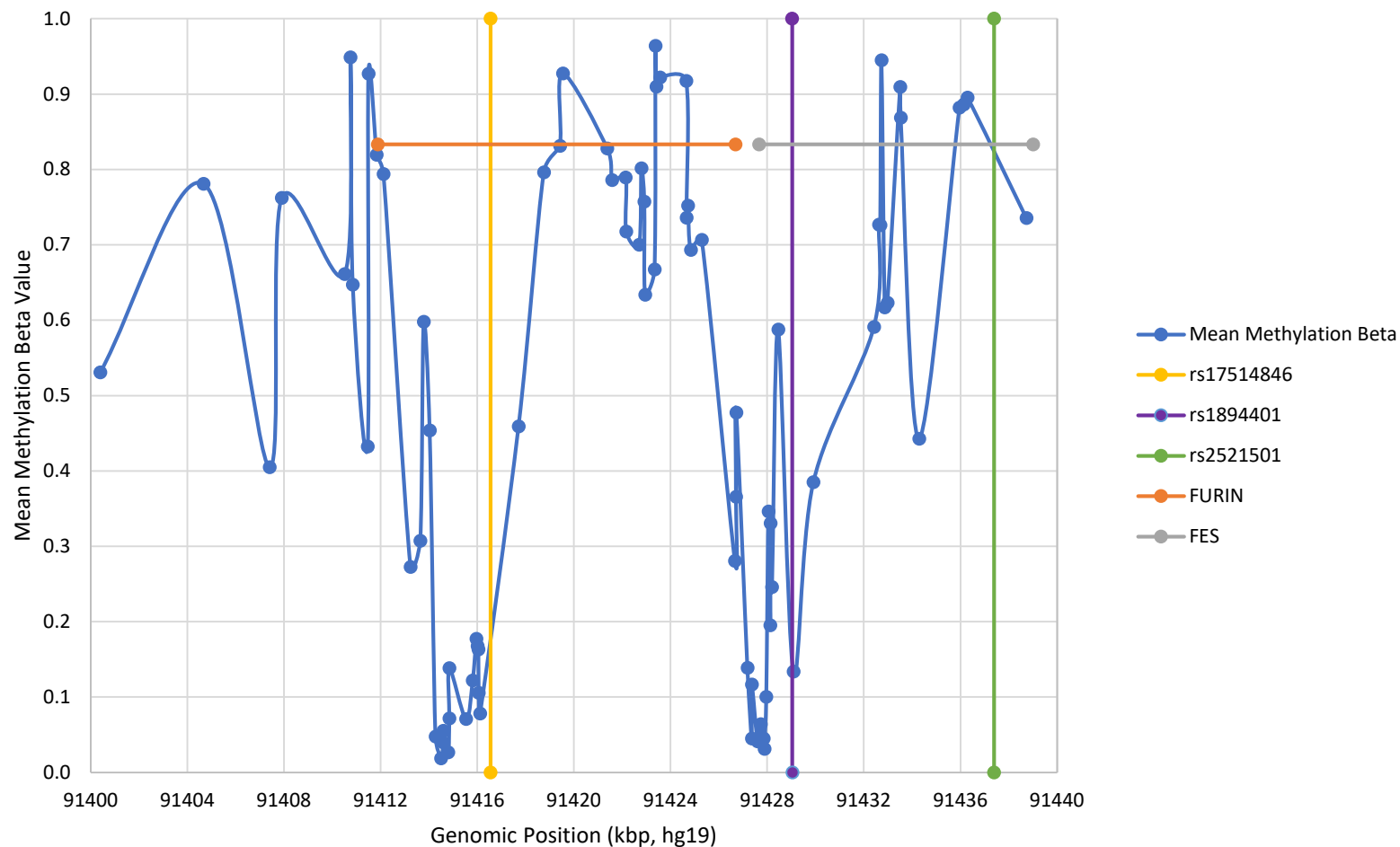


**Supplementary Figure 1. eQTL effects in VSMCs from SNPs associated with CAD, blood pressure/hypertension, AAA, or stroke**

**A.** Scatter plots of gene expression accounts by genotype of selected SNPs and genes as examples. **B.** Percentages of SNPs associated with CAD, blood pressure/hypertension (BP/HTN), abdominal aortic aneurysm (AAA), or stroke, that had eQTL effect on >1 gene, eQTL effect on just 1 gene, or no eQTL effect, in VSMCs.

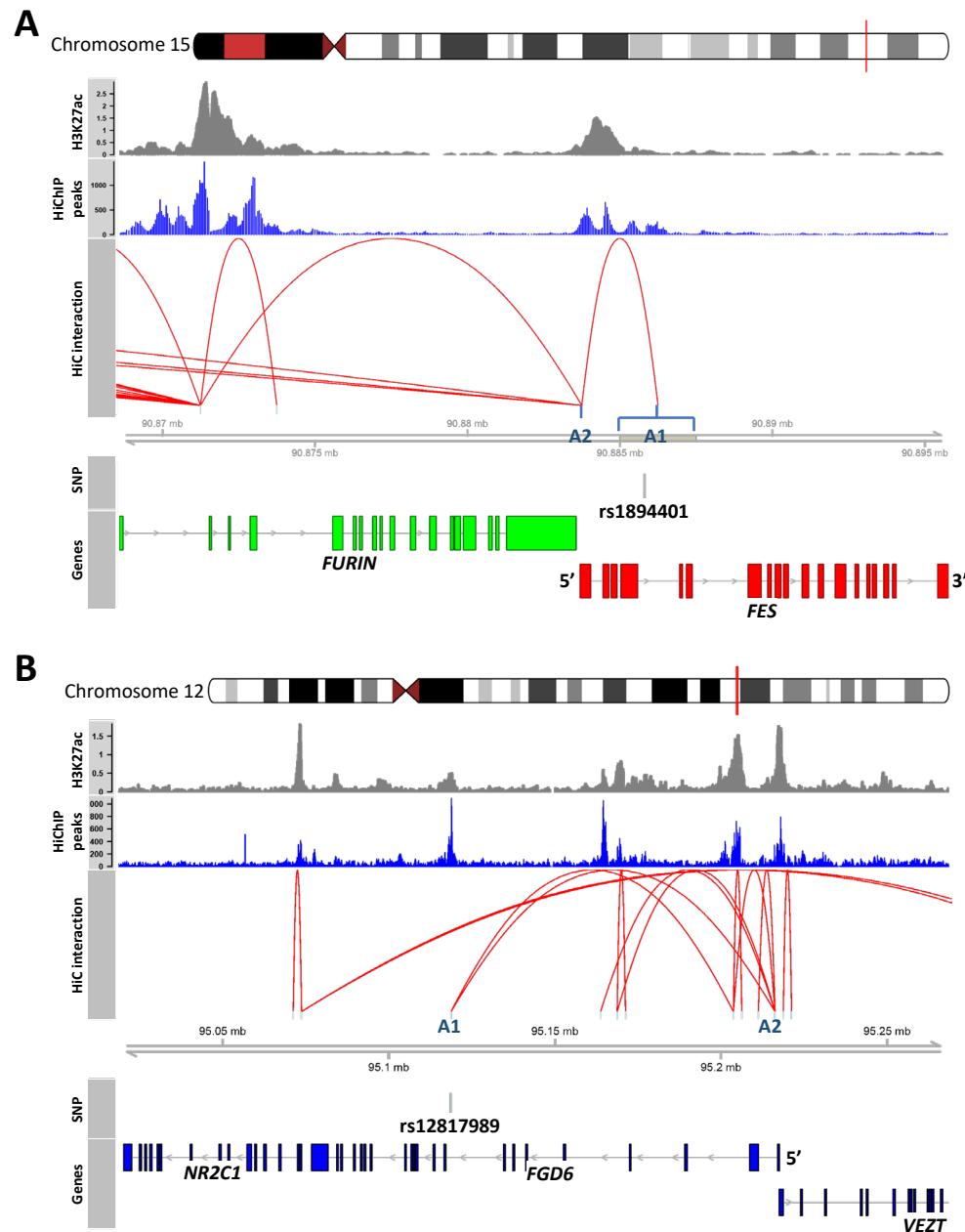


**Supplementary Figure 2. Representative results from ATAC-seq and DNA methylation analysis of vascular smooth muscle cells**  
Shown in the figure are data in the genomic region containing the genetic variant rs1894401 and the *FES* gene.



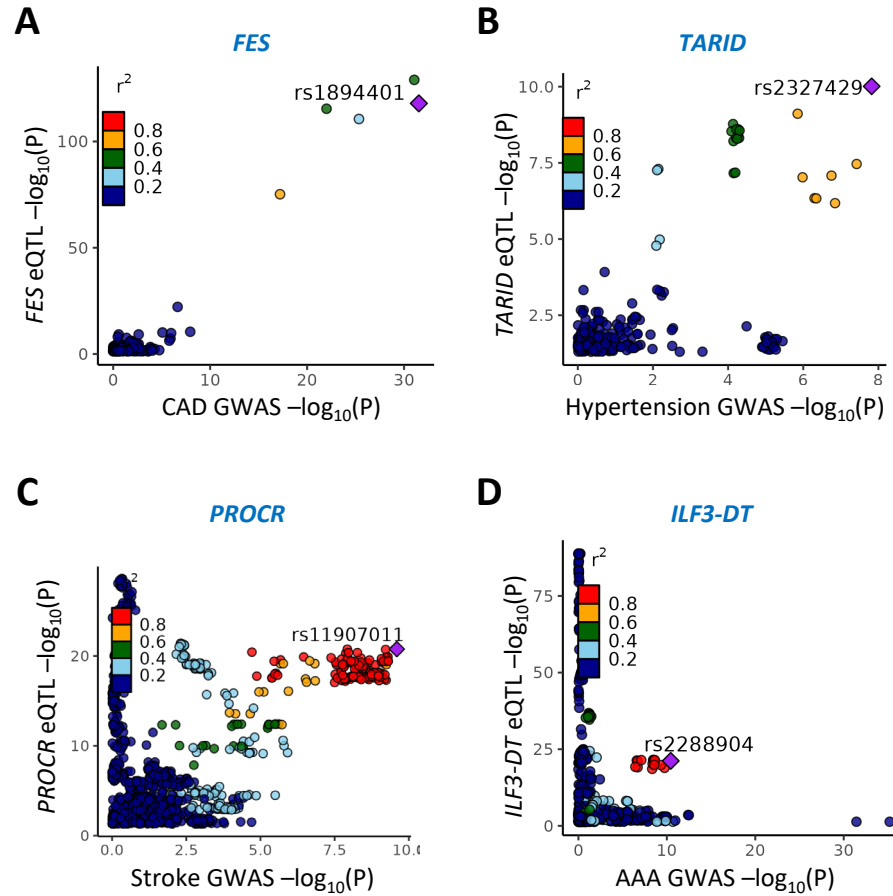
**Supplementary Figure 3. Relative levels of DNA methylation at CpG sites in the genomic region containing the genetic variant rs1894401 and the *FES* gene**

Each blue dot represents the mean beta value of a CpG site (calculated from 3 HUASMC and 1 HAO-SMC cell lines). Vertical lines indicate the position of CAD-associated SNPs and horizontal lines indicate the position of the *FURIN* and *FES* genes.



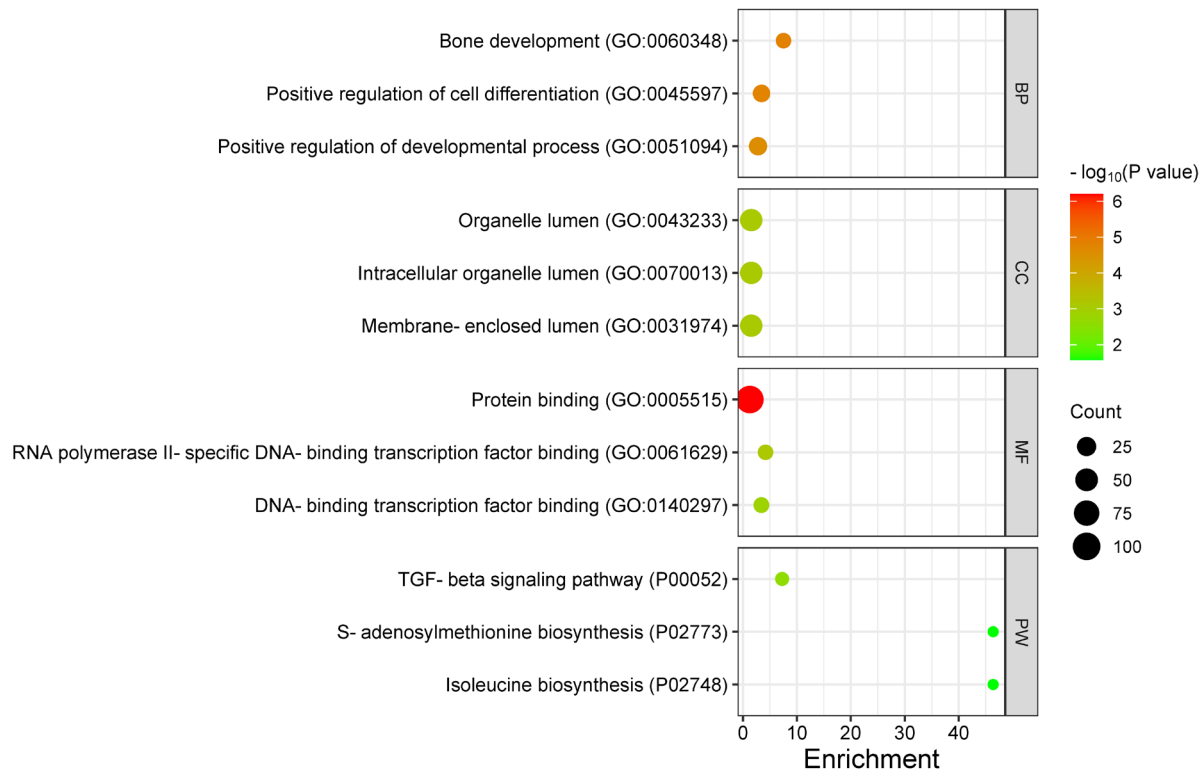
**Supplementary Figure 4. Representative results from vascular smooth muscle cell H3K27ac HiChIP-seq analysis**

- A.** Figure shows that the CAD-associated variant rs1894401 is in an anchor (A1) and the *FES* gene 5'-region is in a linked anchor (A2).
- B.** Figure shows that the CAD-associated variant rs12817989 is an anchor (A1) and the *FGD6* gene 5'-region in a linked anchor (A2).



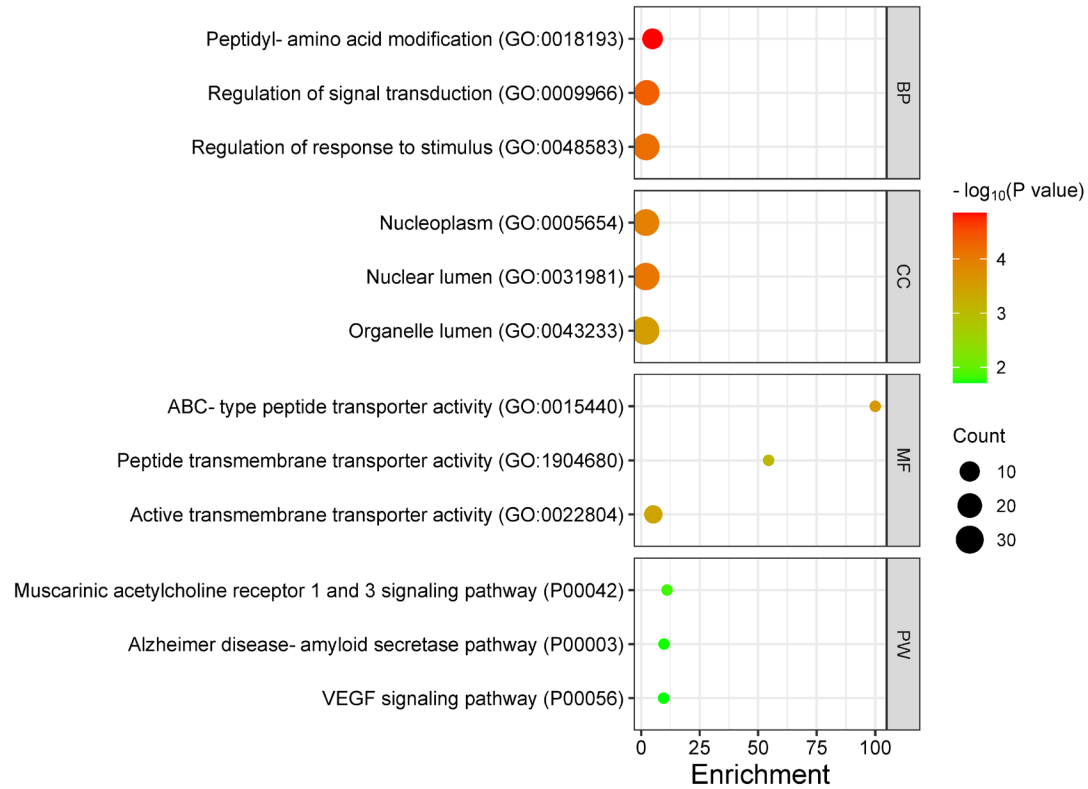
**Supplementary Figure 5. Representative results of colocalization analyses**

Scatter plots showing colocalization of GWAS signals with VSMC eQTL signals at selected representative loci associated with CAD (A), hypertension (B), stroke (C), or AAA (D).



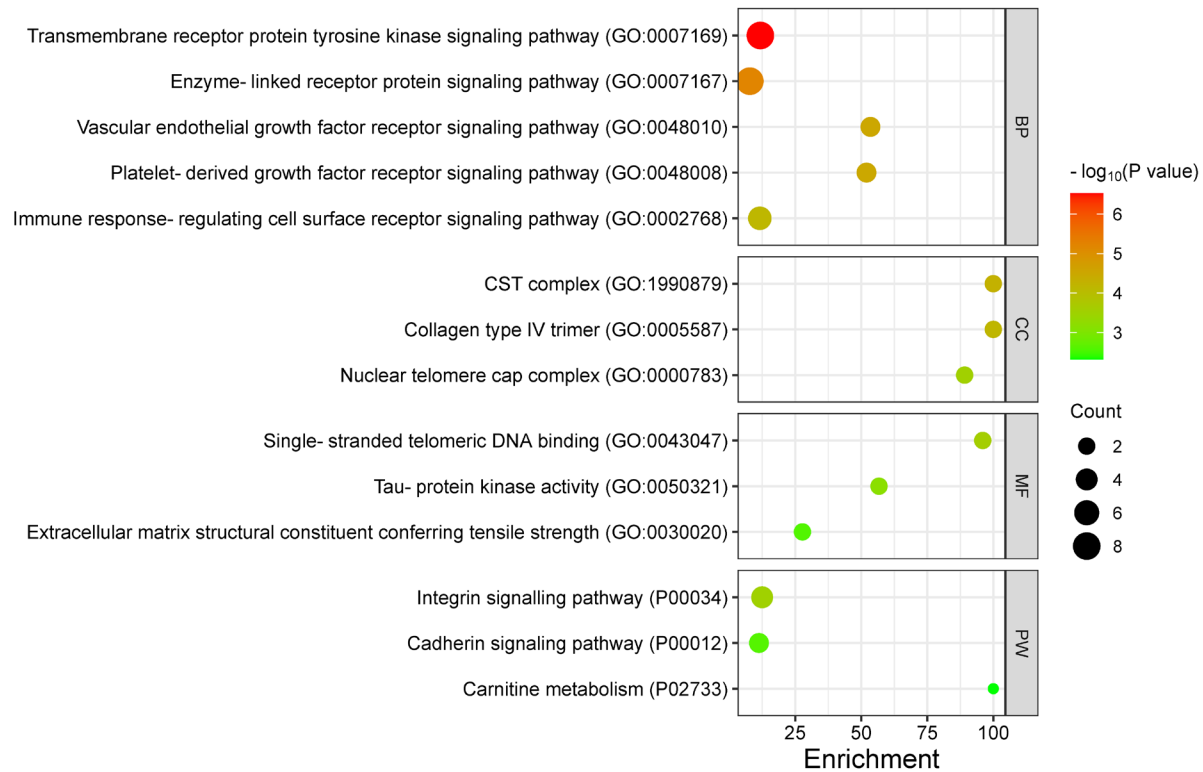
**Supplementary Figure 6. Gene ontology enrichment of CAD candidate causal genes**

BP: biological processes; CC: cellular component; MF: molecular function; PW: pathway.  
TGF: transforming growth factor.



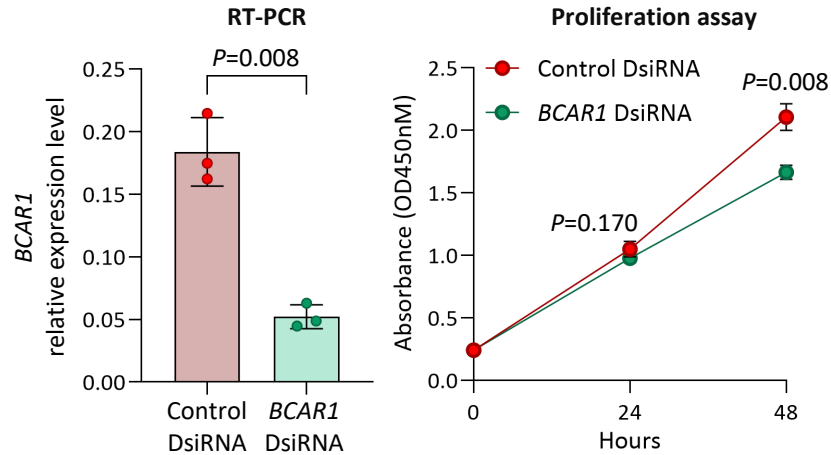
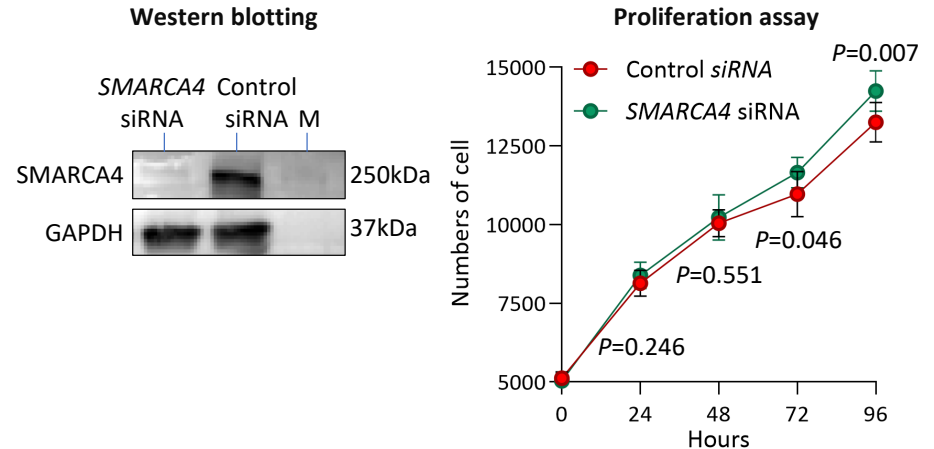
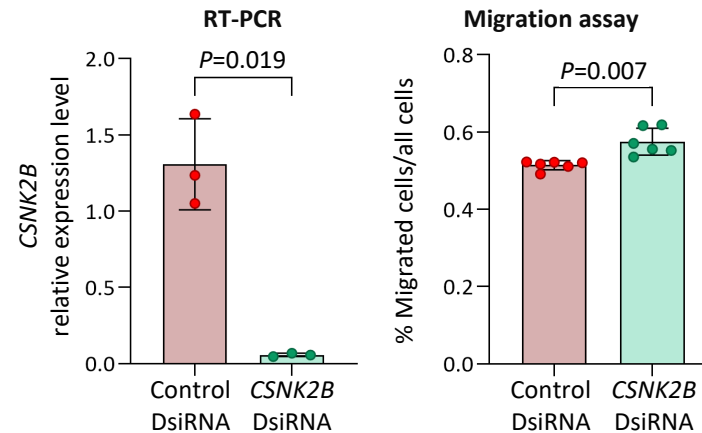
**Supplementary Figure 7. Gene ontology enrichment of hypertension candidate causal genes**

BP: biological processes; CC: cellular component; MF: molecular function; PW: pathway;  
VEGF: vascular endothelial growth factor.



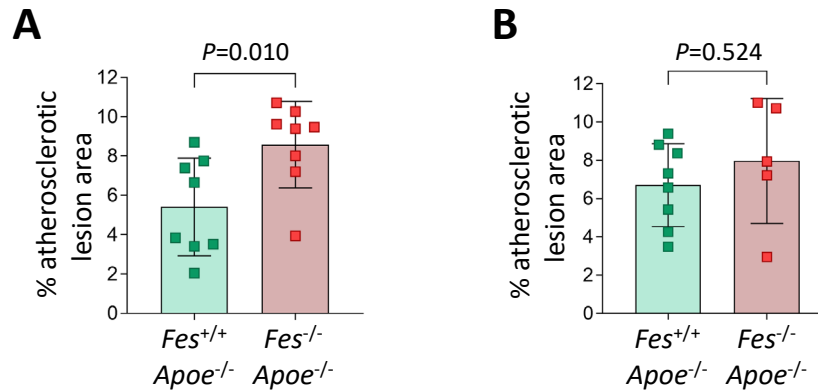
**Supplementary Figure 8. Gene ontology enrichment of AAA candidate causal genes**  
 BP: biological processes; CC: cellular component; MF: molecular function; PW: pathway.



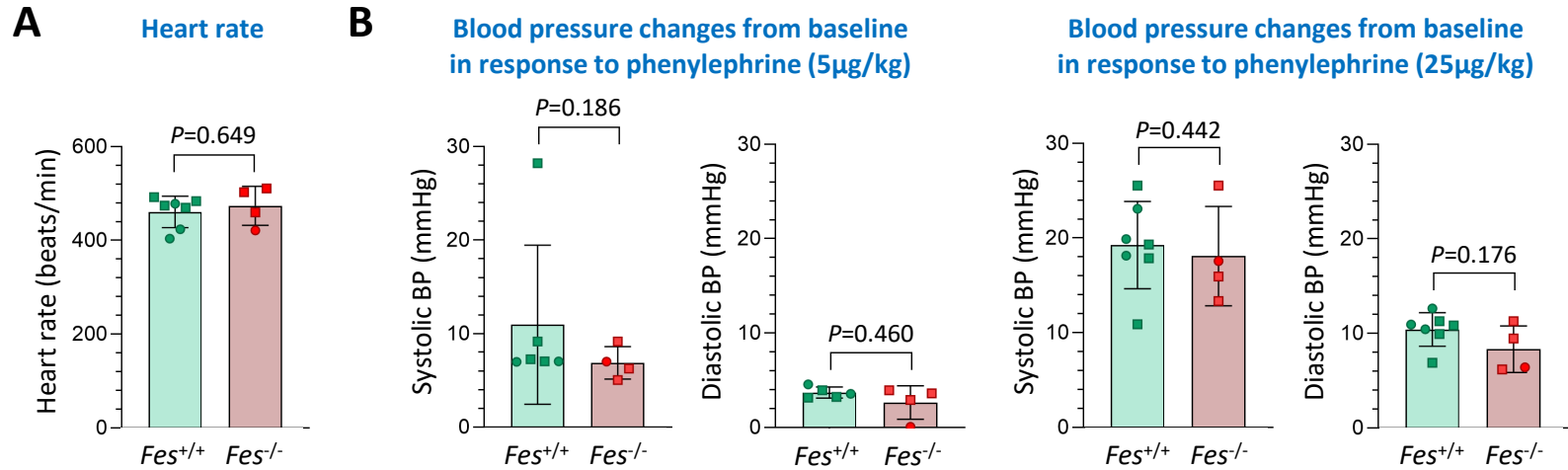
**A***BCAR1***B***SMARCA4***C***CSNK2B*

**Supplementary Figure 9. *BCAR1* Knockdown decreases VSMC proliferation, *SMARCA4* Knockdown increases VSMC proliferation, whilst *CSNK2B* knockdown promotes VSMC migration**

**A.** Results of *BCAR1* reverse transcriptase polymerase chain reaction (RT-PCR, left, n=3 technical replicates) and proliferation assay (right, n=3 technical replicates) of VSMCs transfected with either *BCAR1* DsiRNA or control DsiRNA. **B.** Results of Western blotting (left) and proliferation assay (right, n=8 technical replicates) of VSMCs transfected with either *SMARCA4* siRNA or control siRNA. Western blot image shown is a representative from 3 experiments. M, molecular weight marker. **C.** Results of *CSNK2B* RT-PCR (left, n=3 technical replicates) and migration assay (right, n=6 technical replicates) of VSMCs transfected with either *CSNK2B* DsiRNA or control DsiRNA. **A-C.** Charts show mean  $\pm$  standard deviation (error bars);  $P$ -values are from two-sided t-test; source data are provided as a Source Data file.

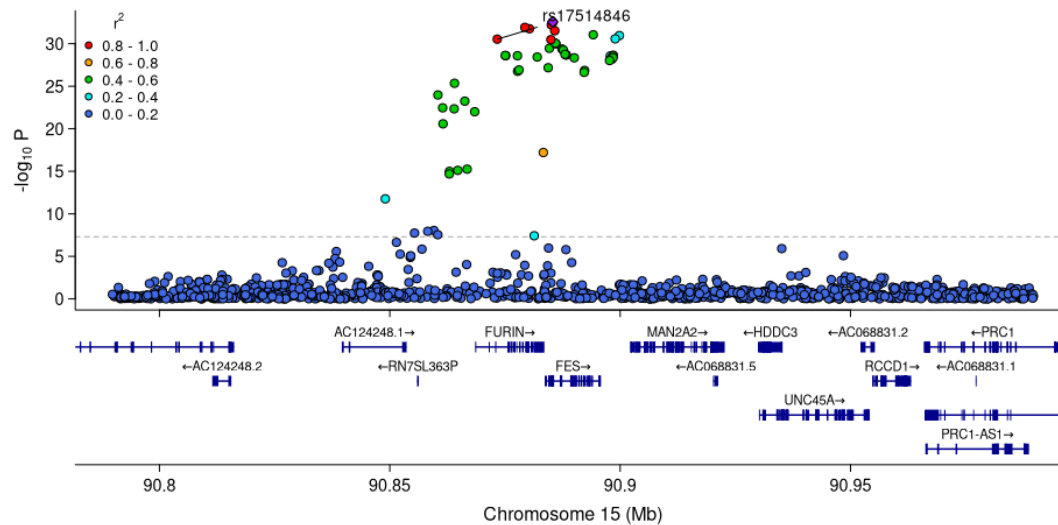


**Supplementary Figure 10. Atherosclerotic lesions in male and female mice with and without *Fes* knockout**  
**A.** Results of en face Oil-red-O staining of aortae of male mice. **B.** Results of en face Oil-red-O staining of aortae of female mice. Columns and error bars show mean  $\pm$  standard deviation; *P*-values are from two-sided Mann-Whitney test; *n*=8 mice/group in A and *n*=5-8 mice/group in B.



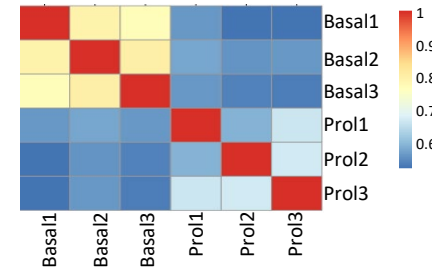
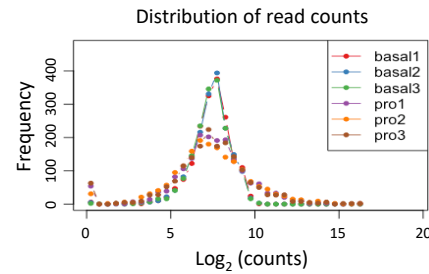
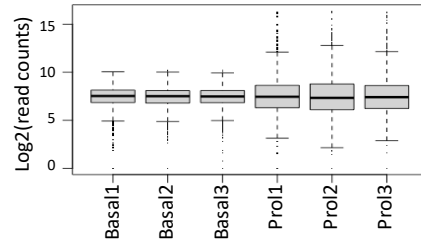
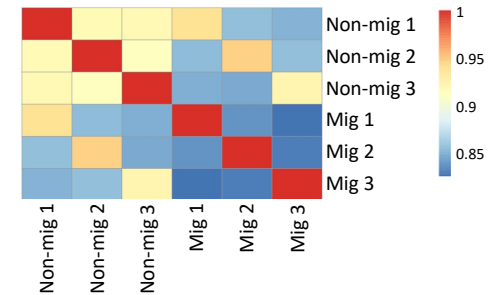
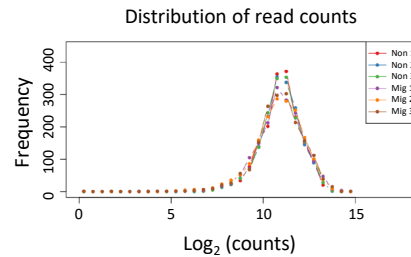
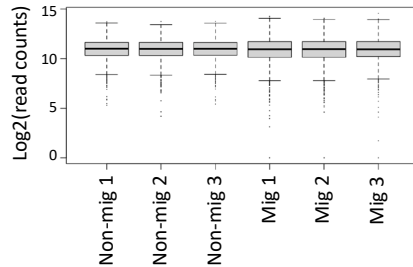
**Supplementary Figure 11. Baseline heart rates, and blood pressure changes from baseline in response to phenylephrine treatment, of  $Fes^{+/+}$  mice and  $Fes^{-/-}$  mice**

Square symbols represent values from male mice whilst circle symbols represent values from female mice; columns and error bars show mean  $\pm$  standard deviation;  $P$ -values are from two-sided Mann-Whitney test;  $n=4-7$  mice per group.



### Supplementary Figure 12. Locus zoom plot of a coronary artery disease-associated locus on chromosome 15

The purple diamond symbol indicates the tagging single nucleotide polymorphism (SNP) rs17514846 that has been reported to be associated with coronary artery disease in genome-wide association studies (PMID: 29212778, 26343387). Each colored circle represents a SNP; the different colors indicate the different degrees of linkage disequilibrium ( $r^2$ ) with the tagging SNP as shown in the legend. The Y-axis shows  $-\log_{10}$  transformed P values for association with coronary artery disease.

**A****B**

### Supplementary Figure 13. Distributions and corrections of data from pooled CRISPR screen experiments

**A.** Data from vascular smooth muscle cell proliferation experiments. Left and middle panels: the baseline cell samples have similar distributions, as do the proliferated cell samples. Right panel: data of baseline cell samples have high corrections (indicating high reproductivity), as do data of proliferated cell samples. **B.** Data from vascular smooth muscle cell migration experiments. Left and middle panels: data of non-migrated (Non-mig) cell samples have similar distributions, as do data of migrated (Mig) cell samples. Right panel: data of non-migrated cell samples have high corrections (indicating high reproductivity), as do data of migrated cell samples.