SUPPLEMENTAL MATERIAL

Expanded Materials & Methods

Cell isolation and culture. Umbilical cords were collected blind from normal pregnancies at UMass Memorial Medical Center; as such, these samples did not require Institutional Review Board approval. Two to three cords from were washed with phosphate-buffered saline (PBS) to remove excessive blood. For HUVEC isolation, the vein was cannulated at one end, perfused with 0.1% type 2 collagenase in PBS (Worthington Biochemical), then clamped at both ends, wrapped in aluminum foil and placed in a humidified incubator for 20 minutes at 37°C. Endothelial cells were collected by flushing collagenase solution containing detached cells with ECCM (EGM Endothelial Cell Growth Medium with SingleQuots Supplement, Lonza) into a 50 ml conical tube. Cells were centrifuged and re-suspended in ECCM, seeded in 0.2% gelatin-coated flasks and allowed to attach overnight in a humidified incubator (37°C, 5% CO_2). Medium was replaced the following day to remove erythrocytes and cells were grown to confluence (2-3 days). The same cords were used for HUAEC isolation by dissecting out arteries, which were washed twice with PBS and perfused with 0.05% Collagenase using a 20-gauge needle (Thermo Fisher) attached to a 20 ml syringe. Arteries were clamped on both ends, placed in a beaker containing PBS and incubated for 20 minutes in a 37°C water bath. Detached endothelial cells were collected by flushing the collagenase with ECCM followed by centrifugation. For passaging, cells were re-suspended in ECCM and grown for 2-3 days, or until ~80% confluence. HEK293T cells were grown in DMEM/10% Fetal Bovine Serum (FBS; GIBCO) and HeLa cells were grown in RPMI 1640/10% FBS (GIBCO). All media were supplemented with Penicillin-Streptomycin-Glutamine (GIBCO).

Chromatin Immunoprecipitation. $2x10^7$ HUAEC and HUVEC grown to ~80% confluence were used for each immunoprecipitation. Chromatin was cross-linked by adding 1:10 formaldehyde-containing solution (50 mM HEPES-KOH, pH 7.5, 100 mM NaCl, 1 mM EDTA, 0.5 mM EGTA, and 11% formaldehyde) for 10 minutes (histone modifications and transcription factors) or for 20 minutes (EP300) at room temperature, and quenched by adding 1:20 2.5 M glycine at room temperature for 5 minutes. Antibodies used were as follows: H3K27ac (Abcam, #ab4729), acetyl-CBP/EP300 (Cell Signaling, #4771), ERG (Abcam, #92513), NR2F2 (Perseus Proteomics, #PP-H7147-00). Cells were washed with ice-cold PBS, scraped into 50 ml canonical tubes and centrifuged. Cells were resuspended in 5 ml ice-cold lysis buffer (50 mM HEPES-KOH, pH 7.5, 140 mM NaCl, 1mM EDTA, 10% glycerol, 0.5% NP-40, 0.25% Triton X-100, and cOmplete protease inhibitors [Sigma]) for 5 min at 4°C. Nuclei were collected by centrifugation, resuspended in ice-cold wash buffer (10 mM Tis-HCl, pH 8.0, 200 mM NaCl, 1 mM EDTA, 0.5 mM EGTA, 0.1% Na-Deoxycholate, 20% N-lauroylsarcosine, cOmplete protease inhibitors) and rocked for 10 min at room temperature. Nuclei were centrifuged and resuspended in 2 ml ice-cold sonication buffer (10 mM Tis-HCl, pH 8.0, 100 mM NaCl, 1 mM EDTA, 0.5 mM EGTA, 0.1% Na-Deoxycholate, 0.5% N-lauroylsarcosine, and cOmplete protease inhibitors) followed by sonication with a Bioruptor (Diagenode) on high power mode and a 30 second on/off intervals for 25 minutes at 4°C. We confirmed shearing to 100-300 bp by gel electrophoresis. Sheared chromatin was treated with 1/10 of 10% Triton X-100 and centrifuged. Appropriate antibody (5 µg for histone modifications, 10 µg for transcription factors) was incubated with the resulting supernatant overnight at 4°C and 10% of chromatin was kept as input DNA control. In parallel, protein G Dynabeads (Invitrogen, #10004D) were washed and blocked overnight at 4°C with 1 ml blocking buffer (1% BSA in PBS), then washed and suspended in blocking buffer prior to incubation with chromatin/antibody mix for an additional 4 hours at 4°C. Immunoprecipitates were washed 5 times with 1 ml ice-cold wash buffer (50 mM HEPES-KOH, pH 7.5, 500 mM LiCl, 1 mM EDTA, 1% NP-40, 0.7% Na-deoxycholate). Chromatin was released from beads in 200 µl elution buffer (50 mM Tris-HCl, pH 8.0, 10 mM EDTA and 1% SDS) by shaking the tubes for 30 min at 65°C and cross-linking reversed by incubation at 65°C overnight. Following SDS dilution, RNA and protein were digested by sequential incubation in RNase A (Roche) and Proteinase K (Thermo Fisher). DNA was extracted using phenol-chloroform followed by ethanol precipitation and quantified using Qubit Fluorometric Quantitation assay (Life Technologies, #Q32854). For analysis of ac-EP300

and H3K27ac in HUAEC and HUVEC, we performed two replicates for each marker from separately isolated cell populations. For H3K27ac following NR2F2 knockdown, we performed ChIPon triplicate samples. For ERG and NR2F2, we generated ChIP material from two separate replicates. In all cases, ChIP with isotype control antibody was performed in parallel.

Cut&Run. Cut and Run was performed according to published protocols[35, 40] with the following modifications. $3x10^6$ cells were used per experiment. Cells were trypsinized, washed twice in ice-cold PBS, pelleted and re-suspended in 1 ml ice-cold Washing Buffer (20 mM HEPES, pH 7.5, 150 mM NaCl, 0.5 mM Spermidine, 0.1% BSA, and cOmplete protease inhibitors). 150 µl of Concanavalin A beads (Polysciences # 86057-3) were washed twice in 1ml and re-suspended in 200 µl binding buffer (20 mM HEPES-KOH, pH 7.9, 10 mM KCl, 1 mM $CaCl_2$ and 1mM $MnCl_2$) before they were added to cells. Bead-bound cells were incubated with 10 µg of HDAC1 antibody (Abcam, ab7028) in antibody buffer (20 mM HEPES, pH 7.5, 150 mM NaCl, 0.5 mM Spermidine, 0.1% BSA, 0.1% digitonin, 2 mM EDTA, and cOmplete protease inhibitors) overnight at 4°C. Protein A-micrococcal nuclease (pA-MN; kindly provided by Steven Henikoff, Seattle, WA, USA) was added to a final concentration of 700 ng/ml with gentle flicking to cells in 400 µl ice-cold digitonin buffer (antibody buffer minus EDTA). Chromatin cleavage was initiated by pA-MN in 150 µl ice-cold digitonin buffer with 3 µl of 100 mM $CaCl_2$ at 0°C for 30 minutes. Digestion was stopped with addition of 150 µl STOP buffer (340 mM NaCl, 20 mM EDTA, 4 mM EGTA, 0.02% digitonin, 50 µg/ml RNase A, 40 µg/ml glycogen, 10 pg/ml yeast spike-in DNA). Following RNA and protein digestion, DNA was purified using phenol/chloroform/isoamyl alcohol extraction followed by ethanol precipitation. HDAC1 Cut&Run was performed on two replicate sets of HUVEC.

ChIP-, RNA-seq and Cut&Run library construction. ChIP-Seq libraries were constructed using NEBNext ChIP-Seq Library Prep Master Mix Set for Illumina (New England Biolabs [NEB], #E6240) with 50-100 ng of ChIP DNA according to manufacturer's protocol. Cut&Run libraries were constructed using NEBNext® Ultra™ II DNA Library Prep Kit for Illumina (NEB, #E7645). For HUAEC versus HUVEC, total RNA from three separate cell isolations was sent to Beijing Genome Institute (BGI) for library construction and deep sequencing. For NR2F2 knockdown, RNA-seq libraries were constructed from triplicate experiments as described in the NEB Poly(A) mRNA magnetic isolation module (#E7490) and NEB RNA-Seq Library Prep Reagent Set for Illumina (#E6100), using mRNA isolated from 5 µg of total RNA with NEB magnetic Oligo $d(T)_{25}$ beads. In all cases, library quality and concentration were determined using an Agilent bioanalyzer (UMass Medical School Deep Sequencing Core). Deep sequencing of H3K27ac and p300 ChIP-Seq libraries and RNA-seq libraries from HUAEC and HUVEC was performed by BGI. All other deep sequencing was performed at the UMass Medical School Deep Sequencing Core.

Western Blotting and immunoprecipitation. Cell were lysed using RIPA buffer (150 mM NaCl, 1.0% NP-40 or 0.1% Triton X-100, 0.5% sodium deoxycholate, 0.1% SDS, 50 mM Tris-HCl, pH 8.0, and cOmplete protease inhibitors). Cell lysates containing equal amounts of protein (~30 µg) were separated by SDS-PAGE and transferred to Polyvinylidene difluoride (PVDF) membrane according to standard protocols. Membranes were incubated with 10 µg antibody overnight at 4°C, followed by washing and incubation with appropriate species-specific HRP-conjugated secondary antibody and detected by chemiluminescence using a Bio-Rad ChemiDoc Touch Imager or autoradiography films (Thermo Fisher, #34090). Antibodies used were those listed above, along with Histone 3 (H3, Fisher Scientific, #PIPA 516183) and Tubulin (TUBB, (Sigma-Aldrich, #T6074).

Co-immunoprecipitation. $4.0x10^7$ HUVEC were detached by trypsin, washed twice in ice-cold PBS. The nuclear fraction was extracted using NE-PER Nuclear and Cytoplasmic Extraction Reagents Kit (Pierce, #78833) following manufacturer's instructions. 50 µl of the nuclear extraction was retained at 4^oC as input and remainder used for immunoprecipitation using indicated antibodies (see above) or an

isotype control. Immunoprecipitations were performed overnight at 4°C in 2 ml safe-lock Eppendorf tubes in 1.5 ml IP buffer (50 mM Tris, pH 7.4, 150 mM NaCl, 1 mM EDTA, 0.1% Triton X-100 and cOmplete protease inhibitors). In parallel, 50 µl protein G magnetic beads per IP were washed twice and blocked overnight at 4°C with 1 ml blocking buffer (1% BSA in PBS). Beads were washed twice, suspended in 250 µl blocking buffer, then incubated with nuclear-antibody complexes for 4 hours at 4°C. Bead/protein-antibody complexes were washed 3 times with IP buffer and eluted in sample buffer for SDS-PAGE. Western blotting was carried out as described above, with the exception, Clean-Blot (ThermoFisher, #21230) was used at 1:400 dilution as an alternative to HRP-conjugated secondary antibody.

Lentivirus production and transduction. HEK293T cells (ATCC) were transfected with lentiviral vector expressing an open reading frame or shRNA of interest, along with psPAX2 (Addgene, # 12260) and pMD2.G (Addgene, #12259) according to Qiagen effectene transfection reagent kit protocol (Qiagen, #301427). Viral supernatants were harvested 72 hours post-transfection, filtered, concentrated using a Lenti-X concentrator (Clontech, #631231) and aliquots stored at -80°C. Viral titers were determined by colony formation assays. HUVEC and HUAEC were transduced at MOI=25 using standard protocols. When appropriate, puromycin selection (2 µg/ml) was applied 48 hours post-infection. RNA or protein was harvested for downstream applications at 72 hours post-infection (hpi). For reporter assays, luciferase was measured at 72 hpi using the dual-luciferase reporter assay system (Promega) and Glomax plate reader (Promega).

Plasmid Constructs. For recombination-based cloning, we constructed a lentiviral plasmid with an attR4-attR3 gateway cassette, which was synthesized as pDestR4-R3v2 (Genewiz). The attR4-attR3 cassette was removed from pDestR4-R3v2 by digestion with SbfI and XhoI and cloned into 7TFC[41] (Addgene, #24307) digested with SbfI and SalI, to give pLenti-R4-R3-DEST2. To generate a minimal promoter/firefly luciferase (Fluc) entry plasmid (pME-minP:luc2), we PCR-amplified from pGL4.26 using primers containing attB1 and attB2 sites, F: GGGGACAAGTTTGTACAAAAAAGCAGGCTAGACACTAGAGGGTATATAATGGA, and R: GGGGACCACTTTGTACAAGAAAGCTGGGTGACTCTAGAATTATTACACGGCGA and cloned the resulting fragment in a BP reaction into pDONR221 (ThermoFisher). A constitutive TK-Renilla luciferase (Rluc) cassette was amplified from pRL-TK using primers with attB2-TK F: GGGGACAGCTTTCTTGTACAAAGTGGAAATGAGTCTTCGGACCTCGCG , and attB3-rLuc R: GGGGACAACTTTGTATAATAAAGTTGCTCATCAATGTATCTTATCATGTCTGCTCG , followed by BP cloning into pDONR P2-P3 (p3E-TK:rLuc). Enhancer fragments were synthesized (Integrated DNA technologies [IDT]) or amplified from human genomic DNA using Phusion polymerase (NEB, #M0530S) and BP cloned into pDONRP4-P1R (Thermo Fisher). Enhancer fragments from IDT bear a deletion of 9 adenines found in wild type sequence to facilitate fragment synthesis. Comparison of wild type enhancer activity with and without these adenines showed no difference (data not shown). To generate reporter constructs, LR reactions were performed using the appropriate p5E enhancer construct, along with pME-minP:luc2, p3E-SV40:rLuc, and pLenti-R4-R3-DEST2. For the TP1 reporter, we used p5E-tp1[5] (Addgene plasmid, #73585). NR2F2 coding sequences were PCR-amplified from cDNA using the following attB1- and attB2-containing primers, F: GGGG ACA AGT TTG TAC AAA AAA GCA GGC TCT CCGCCACC ATGGCAATGGTAGTCAGCACGT, and R: GGGG AC CAC TTT GTA CAA GAA AGC TGG GTG TTATTGAATTGCCATATACGGCC and BP cloned into pDONR221. Expression constructs were generated by LR reaction with p5E-CMVSP6, pME-NR2F2, p3E-SV40-puromycin, and pLenti-R4-R3-DEST2. All plasmids were sequence-verified and are available at Addgene.

Expression analysis. Total RNA was isolated using the RNeasy Mini Kit (Qiagen) and used for cDNA synthesis using SuperScript III First-Strand Synthesis SuperMix for qRT-PCR (ThermoFisher, #11752-

50). Resulting cDNA was diluted 1:20 prior to qPCR using primers for indicated transcripts (Online Table I). nCounter Analysis was performed using 100 ng of total RNA and a custom codeset (see Major Resources Table) according to manufacturer's protocols (Nanostring technologies).

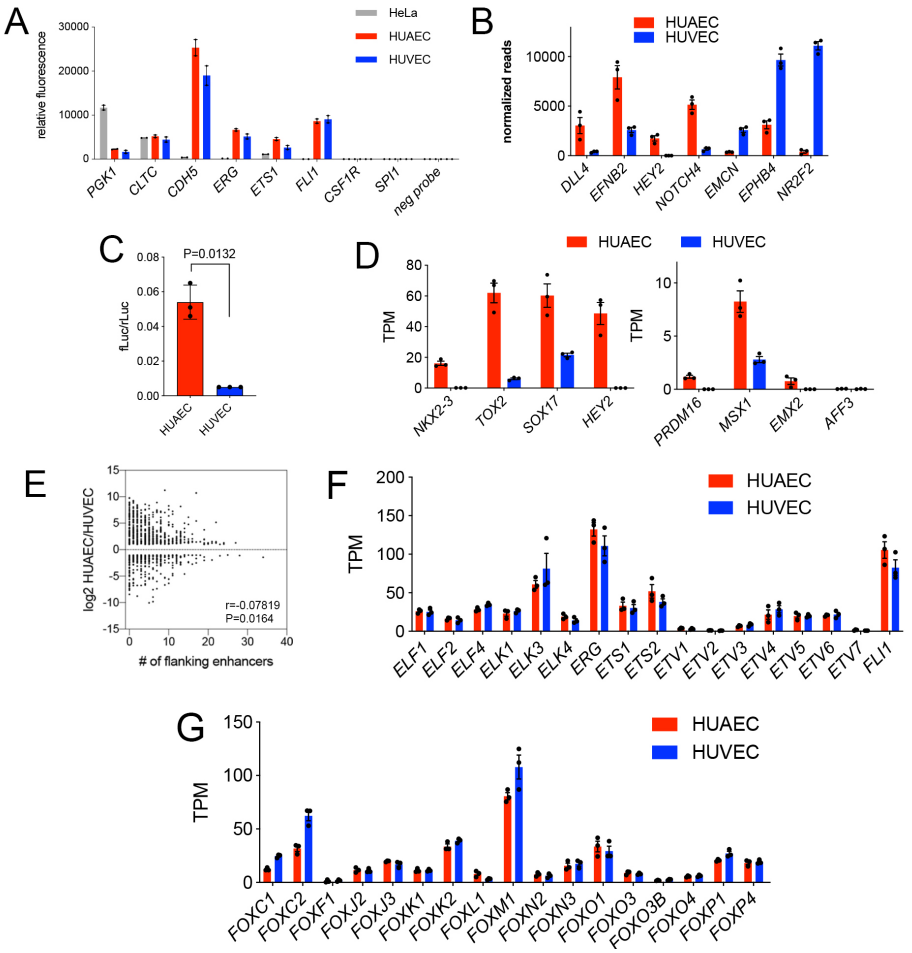
Computational analysis. For RNA-seq, the following pipeline was run using the DolphinNext platform (https://github.com/UMMS-Biocore/dolphinnext). Paired end reads were mapped to hg19 using STAR[42] to generate BAM files, which were subsequently used for transcript quantification using RSEM[43]. Differential expression analysis was performed using gene-mapped expected count files from the RSEM output using DESeq2 through the DEBrowser interface[44, 45]. Both HUAEC/HUVEC and NR2F2 knockdown datasets were filtered with the Low count filtering method by filtering features with counts per million of less than 1 (HUAEC/HUVEC) or 5 (NR2F2 knockdown) in at least 3 samples. Median ratio normalization was used for both datasets[46]. Dispersion was estimated using a parametric fit and hypothesis testing performed using the likelihood ratio test. p-values obtained by the Wald test were adjusted for multiple testing using the Benjamini and Hochberg method [47]. For comparison of HUAEC versus HUVEC, artery genes (338) were defined as those with $\log_2$ fold change >= 1 and adjusted p-value<=0.01; vein genes (210) were defined as $\log_2$ fold change <=-1 and adj.p<=0.01. The same parameters (log2 fold-change <=-1 or >=1, adj.p<=0.01) were used to identify NR2F2-regulated genes in HUVEC. For NR2F2 knockdown RNA-seq, Gene ontology Biological process (GO BP) terms were obtained through the DEBrowser interface. We used an FDR cut-off at <=0.01, which is somewhat below the standard accepted cutoff (0.05), since it reduced the number of differentially expressed genes that exhibited very low expression. A list of genes associated with the top 10 GO BP terms (all cell-cycle related) was obtained by cross-referencing with tables from ENSEMBL bioMart and used to color-code panel 2A. For all ChIP-Seq and Cut&Run samples, single or paired end reads were mapped to hg19 using Bowtie2[48] and binding sites were identified using MACS[49]. For NR2F2, ERG, and HDAC1, replicate elements from two separate ChIP-Seq experiments for each factor were combined using bedtools[50] into single bed files for each factor. Only significantly called features shared in replicate samples were considered as true binding sites.

To identify regions of the genome that exhibited differential occupancy in HUAEC and HUVEC, we used the DiffBind package from Bioconductor[51, 52]. As input files, we used called peaks from MACS analysis of HUAEC and HUVEC H3K27ac and p300 ChIP-Seq as bed files, as well as .bam files for mapped reads from both ChIP and input samples; all replicates were included in this analysis. The resulting output table was filtered (FDR<=0.01; adjusted according to Benjamini and Hochberg method as noted above; 0.01 was chosen to limit features with differential occupancy but low read density) to identify elements that were preferentially enriched for both marks in HUAEC ($\log_2$ fold change >=1) and HUVEC ($\log_2$ fold change <=-1). A set of "Common" H3K27ac/p300 elements was identified from each replicate ChIP-Seq dataset as described elsewhere[53] then merged and depleted of HUAEC- and HUVEC-enriched elements identified above. All elements were filtered to remove centromeric or heterochromatic regions and then divided into separate annotation files based on their localization to transcriptional start sites (TSS). Only final filtered files were used for subsequent analysis and are provided here. All manipulations of genomic features, including analysis to determine number of flanking elements, was performed using bedtools[50]. For enhancers, "concordance" was restricted to overlapping features; for TSS, overlap at 2kb up or downstream was considered concordant. Concordance to HMVEC and Th1 DNAse hypersensitivity sites was performed using identified hotspot bed files downloaded from GEO (GSM736523,GSM736592). Venn diagrams were generated using Intervene[54]. To assess correlation of enhancer number and expression in HUAEC/HUVEC RNA-seq, Pearson correlation was performed; absence of outliers in the dataset was confirmed using Grubbs' method. "Flanking enhancers" in all cases were those located within 250kb up and downstream of the TSS. Over-represented motifs in artery or vein elements were identified using 300 bp of sequence up and downstream of EP300 peaks and the MEME-ChIP package [55, 56]. The top motifs from this analysis are shown in Online Figures 5 and 6. Density plots and heat maps were generated using ChIPpeakAnno[57] or deepTools[58] by binning reads from replicate or single ChIP-Seq samples from indicated factor onto bed files for indicated class of regulatory element.

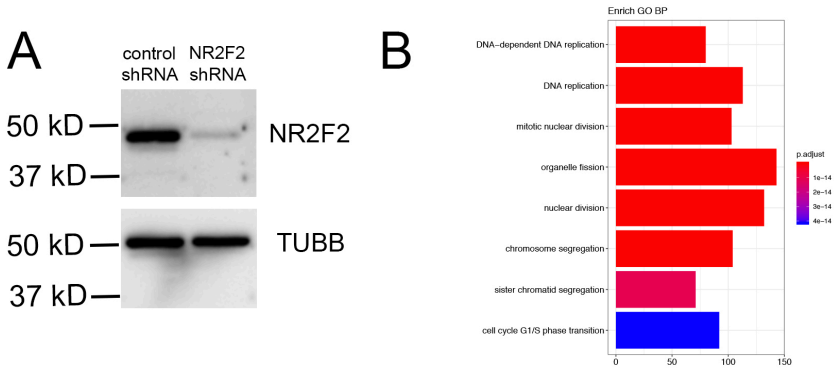
Heatmaps and density plots shown in figure panels represent average normalized read depth from replicate or single samples, as indicated in respective figure legends. Differential H3K27ac occupancy (control versus NR2F2 knockdown in HUVEC) was determined by binning mapped reads from triplicate ChIP-Seq samples into artery, vein, and common elements identified by DiffBind above. Significantly up- and down-regulated elements were identified using EdgeR and defined as $\log_2$ fold-change averaged reads >=1, or <=-1, respectively (FDR<=0.05; adjusted according to Benjamini and Hochberg method as noted above; since the features used for this analysis had already been determined using a more stringent FDR described above, we used the standard FDR cut-off in this case). Data were visualized at specific loci by uploading tracks to the UCSC genome browser. All datasets are publicly available through the Gene Expression Omnibus (GEO; GSE128382).

Other statistical analysis.
R (version 3.6.1) was used for all statistical analysis [59]. We used the Shapiro-Wilk test to check the normality of data distribution [60]. When the assumption of normality was not met, non-parametric Wilcoxon signed rank-sum test was performed (Figure 4B, gene *EFNB2*). Otherwise, paired Student's t-test was used. For experiments with more than two groups, Levene's test indicated that the assumption of homogeneity of variances was met. Therefore, One-way analysis of variance (ANOVA; Figures 3H, 5D, 5H) with Completely Randomized Design was performed to test whether there are significant overall treatment effects. In all cases there was a significant overall treatment effect and Tukey's multiple comparison test was performed to compare different groups.

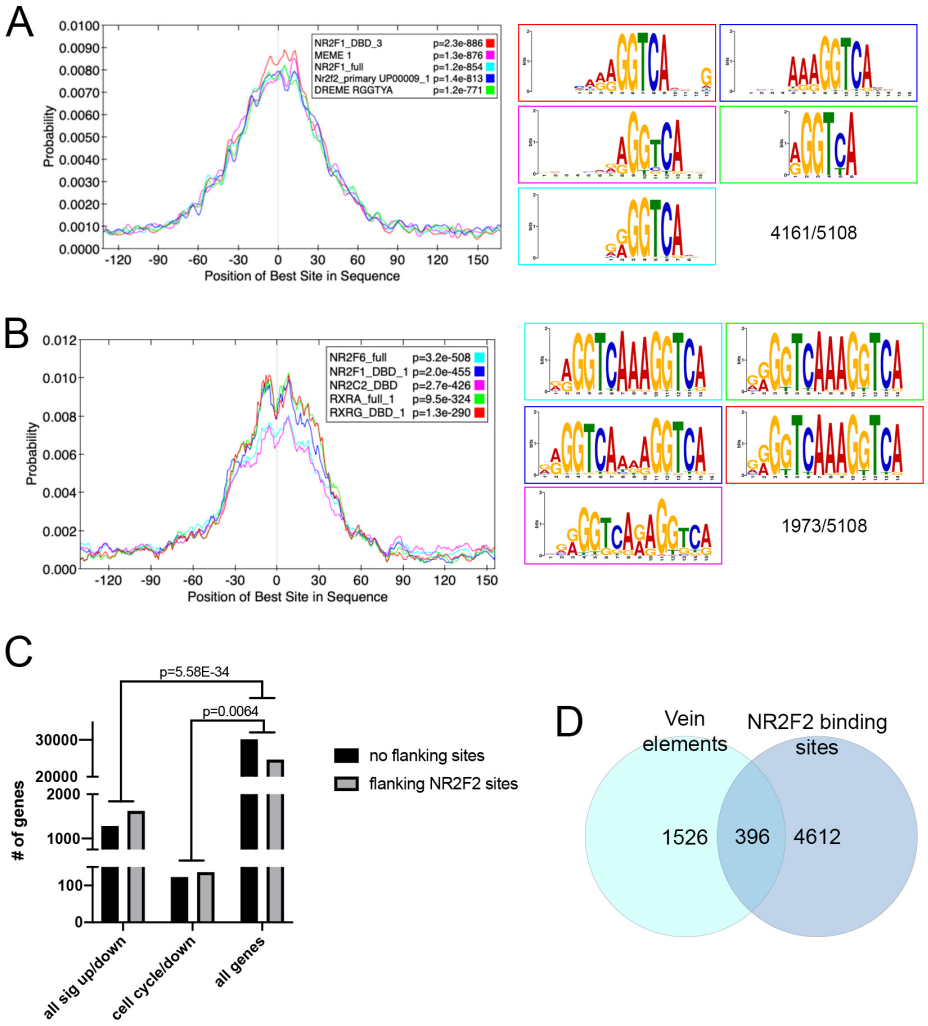
Supplemental Figures and Figure Legends



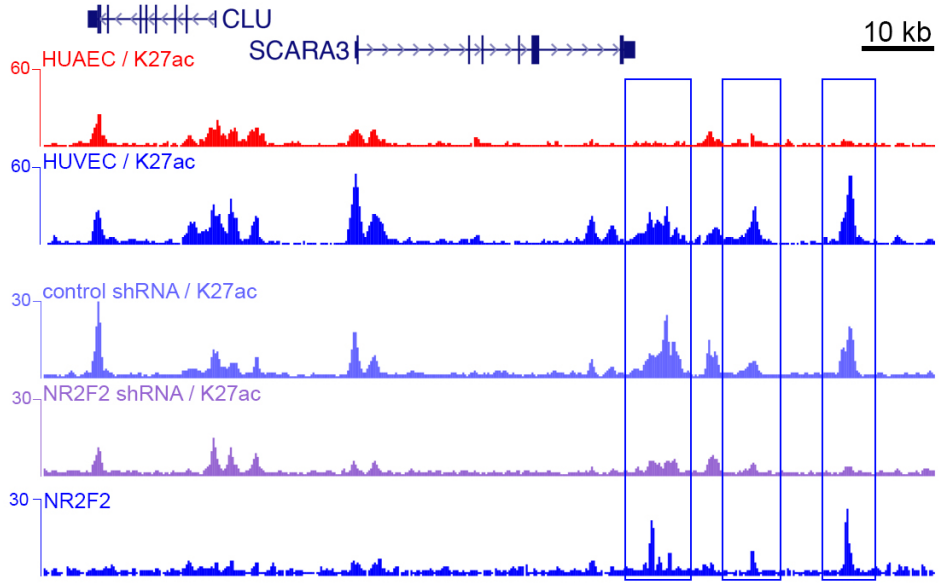
Online Figure I. Quantification of selected gene from RNA-seq. A, Nanostring quantification in indicated cell types. **B,** Median ratio normalized read number from RNA-seq of triplicate samples for indicated cells and genes. Differential expression between HUAEC and HUVEC for all genes in this plot was statistically significant (see Online Table I). **C,** Luciferase reporter assay using the Notch responsive TP1 promoter driving firefly luciferase. **D**, Average expression (TPM - transcripts per million) of indicated artery transcription factors in HUAEC and HUVEC as assessed by RNA-Seq. All but *EMX2* and *AFF3* are significantly enriched in HUAEC (see Online Table I). **E,** Scatter plot showing relationship between fold-enrichment in HUAEC or HUVEC and number of flanking common enhancers. r and P values from Pearson Correlation are shown. **F, G,** Average expression (TPM) in triplicate HUAEC or HUVEC RNA-Seq samples for **F,** ETS transcription factors and **G,** Forkhead transcription factors. Genes expressed below 1 TPM were not considered.



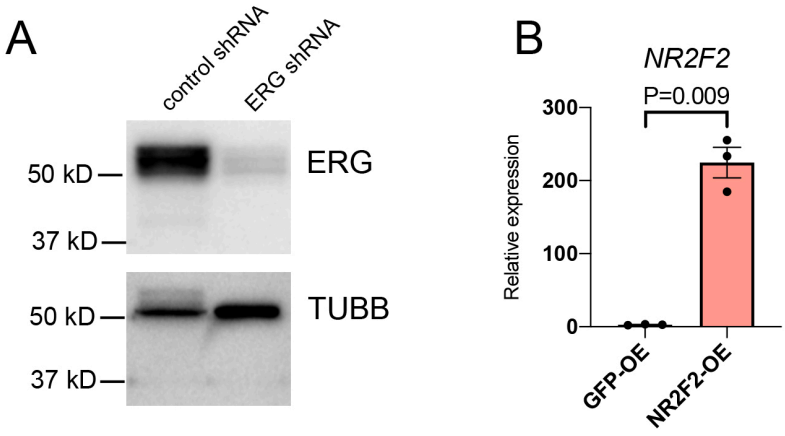
Online Figure II. A, Western analysis to detect NR2F2 in HUVEC expressing a control or NR2F2 shRNA. Blot was probed with a TUBB antibody as a loading control. **B,** Top Biological Process Gene Ontology terms associated with all genes regulated by NR2F2 (log2 fold change control shRNA/NR2F2 shRNA <=-1 or >=1, adjP<=0.01).



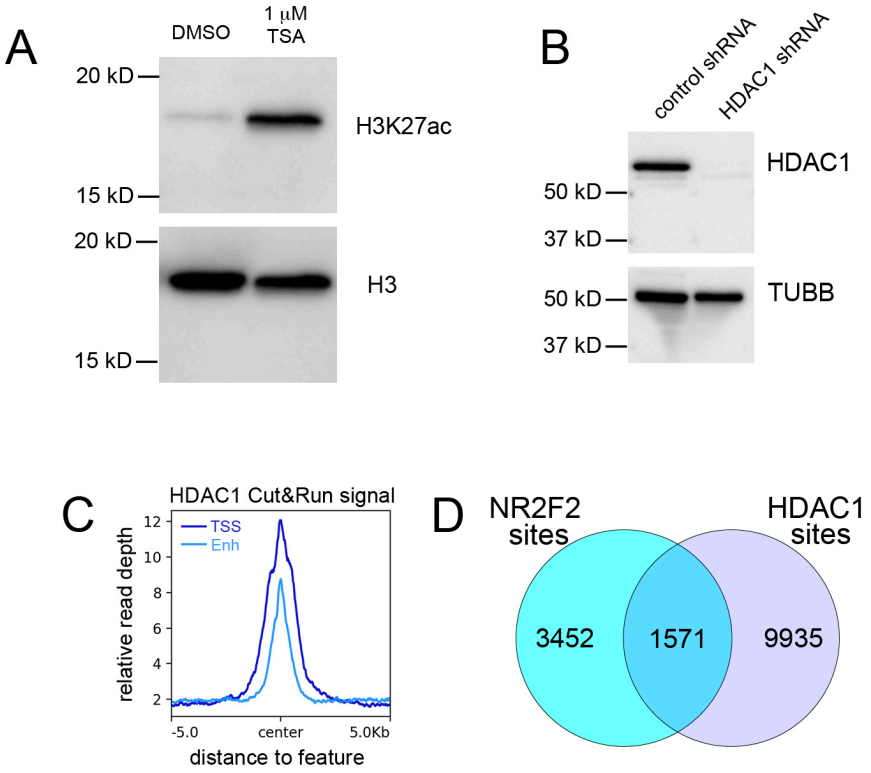
Online Figure III. Validation of NR2F2 ChIP-Seq. A, B, Motif probability graph outputs from CentriMO showing motifs enriched in sequence elements isolated by NR2F2 ChIP-Seq in replicate samples. Color of boxes outlining indicated motifs matches motif legend in the graph. **A,** shows matches with half-sites; number of elements bearing half-sites in all bound sites is shown at bottom right. **B**, Matches with direct repeat motifs; number of elements bearing direct repeats in all bound sites is shown at bottom right. **C,** Graph showing number of genes of indicated class (x-axis) regulated by NR2F2 or all genes with number of those with or without flanking NR2F2 binding sites (+/- 250kb flanking TSS). Hypergeometric test, p-values are indicated on the graph. **D,** Venn diagram showing intersection of vein-specific active regulatory elements (TSS and enhancers) with all NR2F2 binding sites. Note that total number of intersected elements is not equal to each individual dataset since a single feature from one set can intersect with multiple features from the other. In this case, intersected features are collapsed into the larger feature.



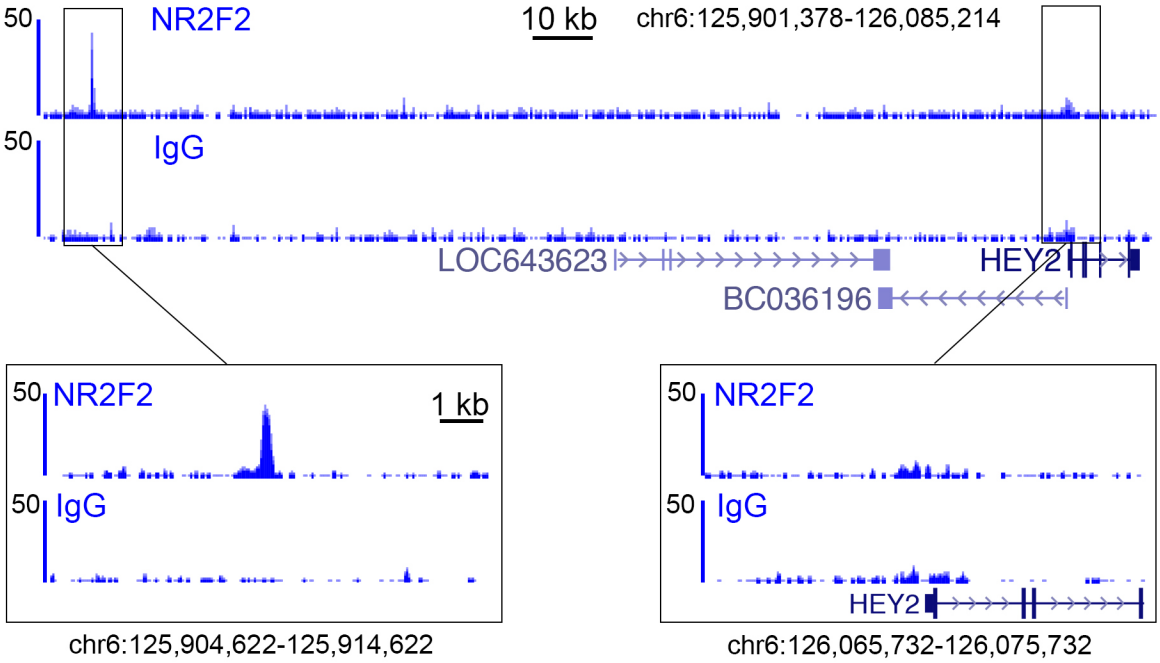
Online Figure IV. CLU is a target of NR2F2. *CLU* loci showing mapped reads for K27ac ChIP-Seq in HUAEC and HUVEC, and in HUVEC expressing control or NR2F2 shRNA, as well as NR2F2 and ERG ChIP-Seq from HUVEC. Blue boxes denote vein-specific enhancers bound by both ERG and NR2F2 (called as significant binding in replicate samples) and showing significantly reduced (log2FC<-1, FDR<0.05) K27ac occupancy following NR2F2 knockdown.



Online Figure V. Confirmation of ERG knockdown and NR2F2 overexpression. A, Immunoblot of ERG and TUBB in HUAEC expressing control or ERG shRNAs. **B,** qRT-PCR to detect NR2F2 transcript in HUAEC transduced with lentiviral constructs expressing green fluorescent protein (GFP) or NR2F2. n=3, Student's t-test, P value is shown, error bars denote S.E.M.



Online Figure VI. Validation of HDAC inhibition and knockdown. A, Western analysis to detect global levels of H3K27ac and total histone 3 (H3) in HUVEC treated with DMSO or 1 □M TSA for 24 hours. **B,** Western analysis to detect HDAC1 and TUBB (loading control) in HUVEC expressing a control or HDAC1 shRNA for 3 days. **C,** Density plot showing mapped reads from HDAC1 Cut&Run plotted against all detected enhancers or all known TSS. **D,** Venn diagram showing intersection of NR2F2 sites detected by ChIP-Seq with HDAC1 sites detected by Cut&Run. Note that total number of intersected elements is not equal to each individual dataset since a single feature from one set can intersect with multiple features from the other. In this case, intersected features are collapsed into the larger feature.



Online Figure VII. NR2F2 binds at a distal upstream enhancer in *HEY2*, but not at the promoter. UCSC Browser tracks showing mapped read density for ChIP-Seq using NR2F2 antibody, or IgG as control, in HUVEC. Boxed regions indicate zoomed-in view of upstream enhancer at -161 kb (left) and promoter (right). Given coordinates refer to hg19.

Supplemental Tables.

Online Tables I-IV are available as separate downloadable Excel spreadsheet files.

Online Table descriptions.

Online Table I. Integrated HUAEC/HUVEC and NR2F2 knockdown RNAseq, including associated genomic features.

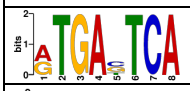
Online Table II. Diffbind Output from HUAEC/HUVEC H3K27ac and acEP300 ChIP-Seq analysis.

Online Table III. Integrated annotation for all active regulatory elements in HUAEC and HUVEC.

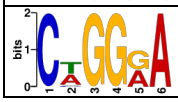
Online Table IV. Output from Genomic Regions Enrichment of Annotations Tool (GREAT) for all HUAEC and HUVEC enhancers.

Additional Online Tables are otherwise shown below.

Online Table V. Over-represented sequence motifs in HUVEC-enriched elements

	DREME		TOMTOM		
Motif	Proportion with motif	p-val	TF match	q-value	Note
	0.059	1.1×10^{-32}	FOSL2	5.47×10^{-05}	Also over-represented in artery elements
	0.0649	7×10^{-23}	Nuclear receptor half-site	0.002	can be bound by NR2F2
	0.011	3.7×10^{-7}	GATA2	0.002	
	0.28	1×10^{-81}	ERG	0.023	Also over-represented in artery elements
	0.013	2.4×10^{-8}	TEAD4	0.03	
	0.38	4×10^{-43}	FOXC2 FOXC1	0.065 0.08	Also over-represented in artery elements
	0.026		No statistically significant TF match		
	0.186	9.1×10^{-29}			Also over-represented in artery elements

Online Table VI. Over-represented sequence motifs in HUAEC-enriched elements

	DREME		TOMTOM		
	Proportion with motif	p-val	TF match	q-value (FDR)	Note
	0.077	6.5×10^{-43}	FOSL2, JUNB	2.3×10^{-4}	Also over-represented in vein elements
	0.198	7×10^{-83}	ERG	0.026	Also over-represented in vein elements
	0.069	7×10^{-11}	FOXC1	0.078	Also over-represented in vein elements
	0.088	9×10^{-54}	No statistically significant TF match		Encompasses possible ETS sites (GGAA)
	0.147	1.9×10^{-24}			
	0.02	1.1×10^{-23}			Encompasses possible ETS sites (GGAA)
	0.38	1.6×10^{-28}			Encompasses possible ETS sites (GGAA)

Online Table VII. Top 10 Biological Process Gene Ontology terms associated with all NR2F2-regulated genes

ID	Description	Gene Ratio	pvalue	p.adjust	qvalue
GO:0006261	DNA-dependent DNA replication	80/2479	6.06E-32	3.67E-28	3.25E-28
GO:0006260	DNA replication	113/2479	1.31E-31	3.98E-28	3.52E-28
GO:0140014	mitotic nuclear division	103/2479	1.00E-23	1.88E-20	1.66E-20
GO:0048285	organelle fission	143/2479	1.24E-23	1.88E-20	1.66E-20
GO:0000280	nuclear division	132/2479	1.33E-22	1.61E-19	1.43E-19
GO:0007059	chromosome segregation	104/2479	8.36E-20	8.44E-17	7.47E-17
GO:0000819	sister chromatid segregation	71/2479	1.24E-17	1.08E-14	9.53E-15
GO:0044843	cell cycle G1/S phase transition	92/2479	5.47E-17	4.14E-14	3.66E-14
GO:0098813	nuclear chromosome segregation	86/2479	1.32E-16	8.27E-14	7.32E-14
GO:0000082	G1/S transition of mitotic cell cycle	87/2479	1.49E-16	8.27E-14	7.32E-14

Online Data Files I-V are available as separate text or .xlsx files.

Online Data file descriptions

Online Data File I. Bed file to visualize artery, vein, or common transcriptional start sites (TSS) on hg19. Hash-tagged lines will be ignored upon upload to the UCSC Genome Browser.

Online Data File II. Bed file to visualize artery, vein, or common enhancers on hg19. Hash-tagged lines will be ignored upon upload to the UCSC Genome Browser.

Online Data File III. MACS output for NR2F2 ChIP-Seq in HUVEC. Worksheet with binding sites in replicate samples is included.

Online Data File IV. MACS output for ERG ChIP-Seq in HUVEC. Worksheet with binding sites in replicate samples is included.

Online Data File V. MACS output for HDAC1 Cut&Run in HUVEC. Worksheet with binding sites in replicate samples is included.