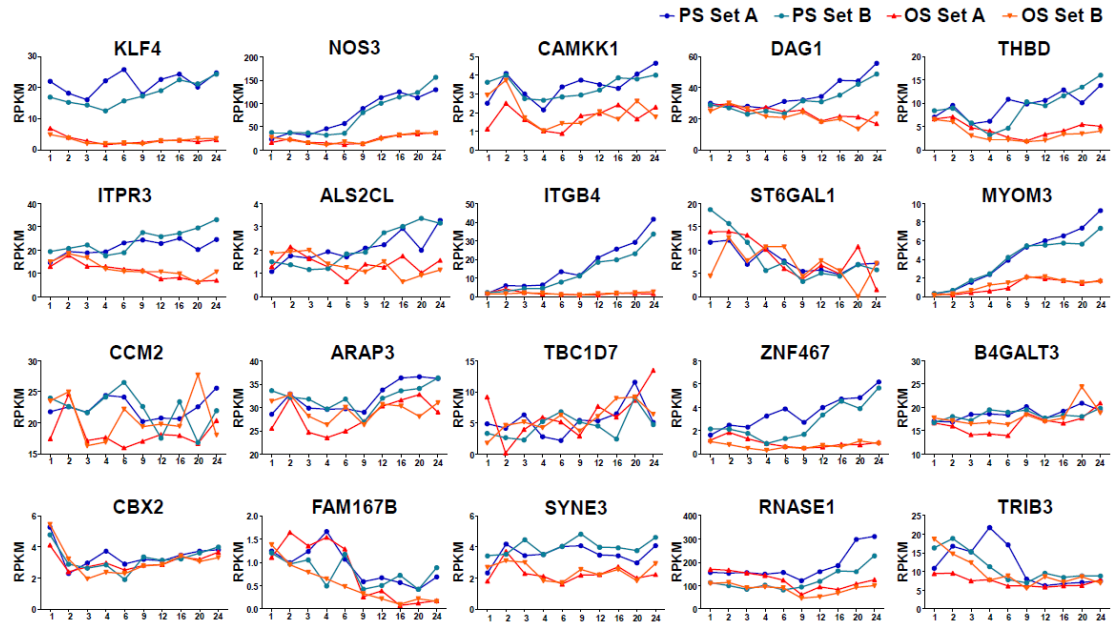


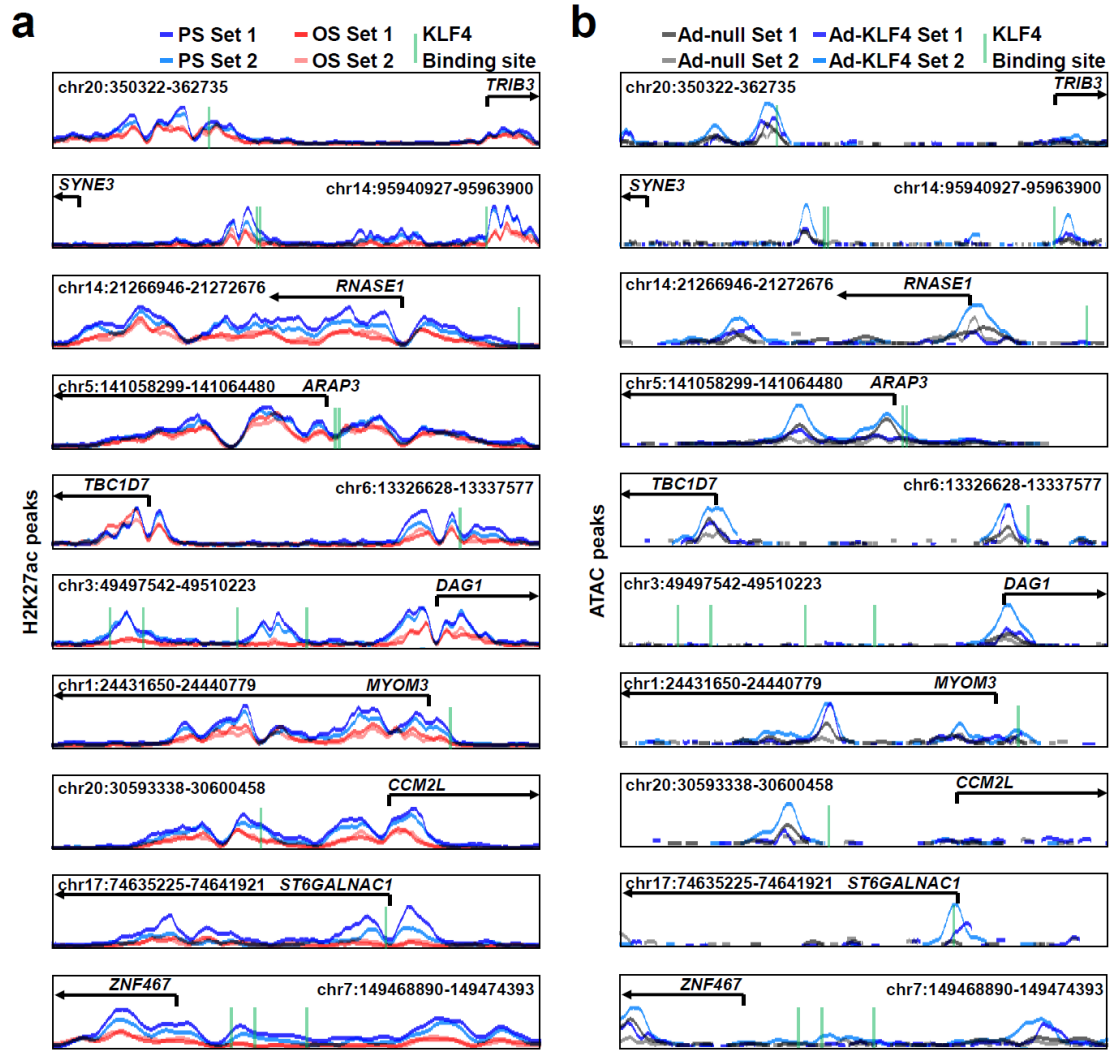
Supplement Material

Supplementary Figure I



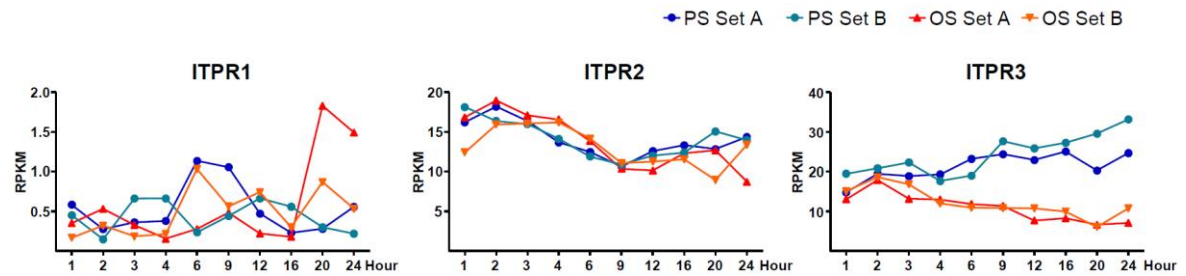
Supplementary Figure I. RNA-sequencing analysis of identified 18 genes under shear stress. HUVECs were exposed to OS or PS for the 10 time-point as indicated. RNA samples collected at each time-point underwent RNA-seq analysis. mRNA levels of identified 18 genes represented by reads per kilobase million mapped reads (RPKM). Each time-point under OS or PS includes two biological repeats.

Supplementary Figure II



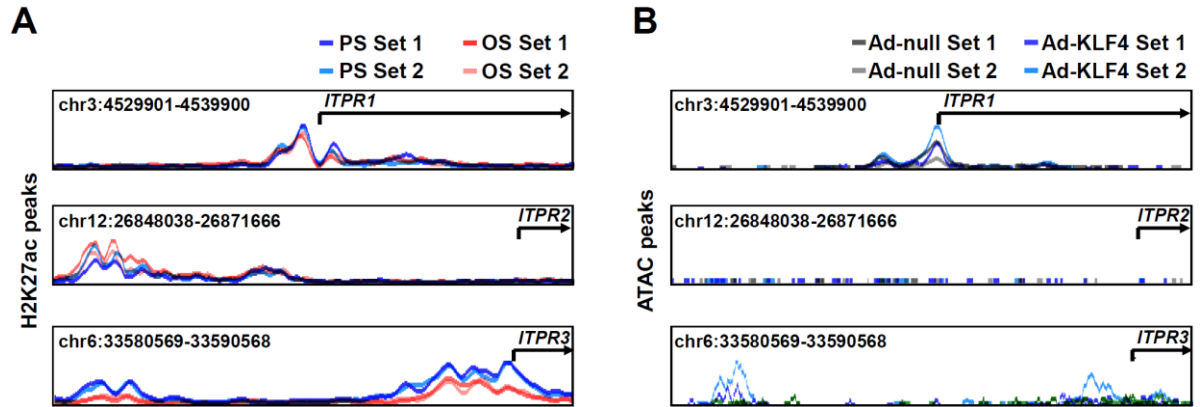
Supplementary Figure II. PS-induced genes via KLF4-dependent chromatin remodeling. (a) Normalized PS (blue)- or OS (red)-induced H3K27ac enrichment in the promoter regions of *TRIB3*, *SYNE3*, *RNASE1*, *ARAP3*, *TBC1D7*, *DAG1*, *MYOM3*, *CCM2L*, *ST6GALNAC1*, and *ZNF467*. The putative KLF4 binding sites in the respective promoter regions are illustrated in green. (b) HUVECs were infected with Ad-null or Ad-KLF4 for 24 hr in two biological repeats. ATAC-seq was performed to evaluate the chromatin accessibility. Lines in gray (from Ad-null-infected ECs) and blue (from Ad-KLF4-infected ECs) represent ATAC signals in the same loci as those in (a).

Supplementary Figure III



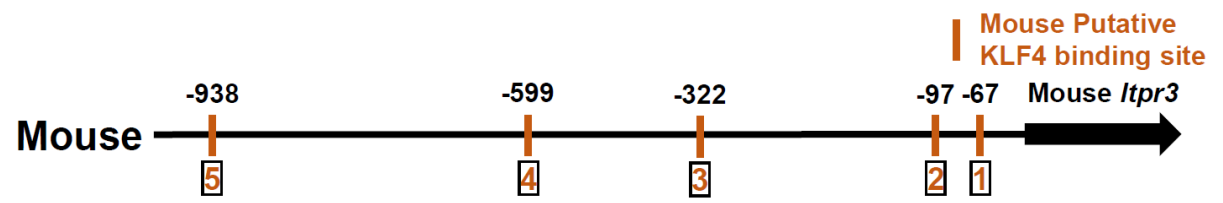
Supplementary Figure III. RNA-seq data demonstrating PS upregulation of ITPR3 in ECs. HUVECs were exposed to OS or PS for the indicated times. RNA samples were collected and underwent RNA-seq analysis. mRNA levels of ITPR1, ITPR2, and ITPR3 are represented as reads per kilobase million mapped reads (RPKM). Two biologic repeats were performed for each group. The conclusions were made by comparing the averaged values from the two sets of data.

Supplementary Figure IV



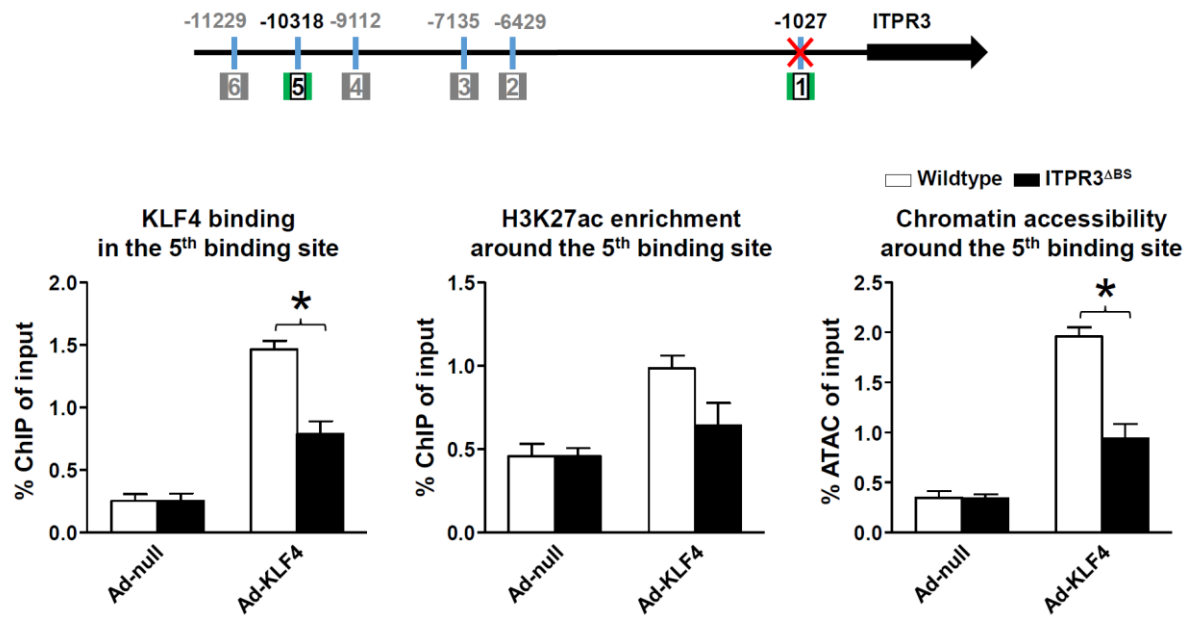
Supplementary Figure IV. PS and KLF4 increase H3K27ac enrichment and chromatin accessibility in the *ITPR3* promoter. (A) Normalized PS (blue)- or OS (red)-induced H3K27ac enrichments in the promoter region of the *ITPR1*, *ITPR2*, and *ITPR3* gene. (B) HUVECs were infected with Ad-null or Ad-KLF4 for 24 hr in two biological repeats. ATAC-seq was performed to evaluate the chromatin accessibility. Lines in gray (Ad-null-infected ECs) and blue (Ad-KLF4-infected ECs) represent ATAC signals in the *loci* identical to those in (A). Two biologic repeats were performed for each group. The conclusions were made by comparing the averaged values from the two sets of data.

Supplementary Figure V



Supplementary Figure V. Putative KLF4 binding sites in the mouse *Itpr3* promoter.

Supplementary Figure VI



Supplementary Figure VI. Crosstalk between KLF4 binding sites in the *ITPR3* promoter. Wildtype or *ITPR3*^{ABS} HUVECs were infected with Ad-null or Ad-KLF4. Twenty-four hr post infection, cells were harvested for KLF4-ChIP-, H3K27ac-ChIP-, or ATAC- qPCR to assess KLF4 binding, H3K27ac enrichment, and chromatin accessibility of the 5th binding site.

Supplementary Table I. KLF4 binding sites in the human ITPR3 promoter

Sites	Distance to TSS (bp)	Location	Binding Sequence
Site 1	-1027	chr6:33,587,107-33,587,115	GGGTGTGGC
Site 2	-6429	chr6:33,581,705-33,581,713	CCCCACCCA
Site 3	-7135	chr6:33,580,999-33,581,007	CCGCACCCA
Site 4	-9112	chr6:33,579,022-33,579,030	GGGTGCGGC
Site 5	-10318	chr6:33,577,816-33,577,824	CCCCTCCA
Site 6	-11229	chr6:33,576,905-33,576,913	GGGTGGGGT

Supplementary Table II. Primers used for qPCR

Gene symbol	Forward 5'-3'	Reverse 5'-3'
<i>For gene expression (Human genes)</i>		
NOS3	TGATGGCGAAGCGAGTGAAG	ACTCATCCATACACAGGACCC
KLF4	CCCACATGAAGCGACTTCCC	CAGGTCCAGGAGATCGTTGAA
ITGB4	CTTCACCTGCAGCTCTTTCC	TCTCCTACCGCACACAGGA
ZNF467	CCTGCACGGAATGCGAGAA	GGGGCAGTGAATGAGGAG
ST6GALNAC1	AGAAAGGTCTCTACAGTCCCTG	TGTGTGTTGAGGGCATTGTTC
CCM2L	AGGGAAGAAGGGCTTTGTATCC	ATAAAGGGGCATCGAGTGCAG
FAM167B	CTGCACCGACTGAAGATGGAC	CTGATGTTTCATGCGCGTGA
MYOM3	AGATTAGGAGATGCGCCATTG	GTGCGGACGAGGACTTTGG
ALS2CL	TGGCTGACAGGAAACACTTG	CTGCTCGAGTTCCTGGATGT
CBX2	AGAAGGAACATGAGAAGGAGGT	GAGGGACAGACTGTTGGCAG
THBD	GCATTTGCATGGTTTGTGAG	ACACAGGCAAATCCTTGCT
DAG1	AAGTGACTTGGTCCCAGAGC	AGGAGGAGCGAACACCTG
TBC1D7	GTTGCCAAAAGCGTTTGAACA	CATCCCGCAAAGCACCTCTT
CAMKK1	CCACCCGTTCTACCAGCTC	AATTTGGGAAGCTGTGGTGT
B4GALT3	GCTCCCGAACAGCCATCATT	TCCACATCGTGCAAGAACAGG
ARAP3	TCAATGGGAGGAGTCTGATGT	CTCTGTGCGGAACACGAACA
RNASE1	ACTGTAACCAAATGATGAGGCG	GTACCTGGAGCCGTTTGTCA
SYNE3	CTGCACAACGTGGACAACC	CACTGCATCGTACTCAGCCTT
TRIB3	TACCTGCAAGGTGTACCCC	GGTCCGAGTGAAAAAGGCGTA
ITPR3	GAGGCAGTCACGGAACCTTCT	GTCAATGGCTTCATCAGCAC
b-Actin	GAGCACAGAGCCTCGCCTTT	TCATCATCCATGGTGAGCTGG
<i>For gene expression (Mouse genes)</i>		
Nos3	GGCTGGGTTTAGGGCTGTG	CTGAGGGTGTCTAGGTGATG
Klf4	GTGCCCCGACTAACCGTTG	GTCGTTGAACTCCTCGGTCT
Itgb4	GCAGACGAAGTTCGACAG	GGCCACCTTCAGTTCATGGA
Zfp467	TCCTGCTCAGGGCATGAGA	TCCGAATCATCCATTCTCCC
St6galnac1	TGACTGTGTTGGCATTGCTCT	CTCCTGTTTCTTCAGGTCTTTG
Ccm2l	TGTCCCCATCCGAAGACT	GGATAAAGAGGCATAGAGTGCAG
Fam167b	CGGCTGCACAGACTGAAAGT	TGATGTTTCATGCGCGTGAGT
Myom3	CTCTGGCTGGAACGTGGAAAT	CCTTCTCGTTGAAGATGAGGTG
Als2cl	TCTCAACGACTCTTGCTCGAA	CTCTGTACATAACCACAACCG
Cbx2	GGCTGGTCCCTCAAACACAA	CCCTGGGTCTCTTGCTCT
Thbd	CTCTCCGCACTAGCCAAGC	GGAGCGCACTGTCATCAAATG
Dag1	CTTGAGGCGTCCATGCACT	GGCAATTAAATCCGTTGGAATGC
Tbc1d7	GGATCAGCCGATGCTTCGT	GTGACTCAGCAGCCTACTGTC
Camkk1	TGGCCCACTTGGAAAGAAGC	GGAGAACTTTCTAGCCGAGAGG
B4galt3	ATGATGTATCTGTCAGTGGGG	GGACCCACTAAGAAGGGTGAT
Arap3	AGGCCCTGATAAGCAAAGG	CACAGCGATGTCCAGGTCC
Rnase1	CTGCAACCAAATGATGAAACGC	CCTTCAGGTGGCAGTCAGTG
Syne3	TGGAGGCAAGGCTTCGAGA	TTCTGGAACCAGCGGTAAAC

Trib3	GCAAAGCGGCTGATGTCTG	AGAGTCGTGGAATGGGTATCTG
Itp3	GGGCGCAGAACAACGAGAT	GAAGTTTTGCAGGTCACGGTT
<i>For ChIP-qPCR or ATAC-qPCR</i>		
KLF4 promoter	GGCGCAGGTTTCGGTCG	GCTGACCCCACCAGTCTTCG
NOS3 promoter	CCGAACACCAAATCTCCAACC	AGCCCTGCCAAGAATGATGC
VCAM1 promoter	AGAACAGGAGCTGATAATGCTGT	AAGGCAATGAAGGAGCCTAGT
SELE promoter	AGGCCAGAACCCCACTTGTA	TTCTTTAGCAGCTATTCTCTCTTGC
<i>ITPR3 promoter</i>		
ITPR3 -1027	GAGGTGGATTCCCTGGGTGTG	ACCGTGAGGATGAAGAGGGA
ITPR3 -6429	GCTTATGGCATGGGGAAGGA	CCTGACTCAGTGTAGCAGCC
ITPR3 -7135	ACTGTGACTGTGAAGGTGCC	TTACTAGGTGCCCCCTCCTC
ITPR3 -9112	AGGGCCTTAGTCCTGCCAA	GACAGAGGTGAAAAGCATGACG
ITPR3 -10318	GACAGGGAGTGGGCTTCAAA	GAGCCACAGGAAGGGATTGG
ITPR3 -11229	CTCCATGATGGCTGCTCTCC	AAACCAGCCAGGTGCTCTC
ITPR3 Pol II	GGCACCTATCTTAGGCGTT	TACTTTCTGTTCTGTTCCCCG