Supporting information

PALMD regulates aortic valve calcification via altered glycolysis and NF-κB-mediated inflammation

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This word file includes:

- Detailed Materials and Methods
- Figures S1-S19
- Tables S1-S5
- Unedited gels

Materials and Methods

Tissue dissection

The aortic valves obtained from CAVD patients undergoing aortic valve replacement surgery were stored in HBSS buffer (Hyclone, SC30588.01) and immediately transported to the laboratory. Non-calcified and calcified tissues were carefully dissected from the collected aortic valves as previously described (52). In brief, macroscopically non-calcified tissues were defined as transparent and pliable tissue, while calcified tissues were defined as solid, non-pliable, thickened, non-transparent tissue. After dissection, a portion of non-calcified and calcified tissues were sectioned for alizarin red staining to confirm the degree of calcification. The remaining non-calcified and calcified tissues were immediately frozen in liquid nitrogen and stored at -80 ºC for RNA extraction.

Isolation and culture of human valve interstitial cells (hVICs)

hVICs were isolated and characterized as previously described (23, 24, 51). In brief, non-calcified regions of aortic valve tissues from CAVD patients were carefully dissected. After incubation with 1 mg/ml trypsin (Gibco, 12605-010) for 10 min, the tissues were gently scraped to remove the valve endothelial layer, and then cut into small pieces. Subsequently, samples were washed in HBSS buffer (Hyclone, SC30588.01), and digested in 250 U/ml type II collagenase solution (Worthington, 47D17411A) at 37°C for 7 hrs. Obtained cells were re-suspended in growth media consisting of α-MEM supplemented with 10% FBS (Gibco, 16000-044), 100 U/mL of penicillin (HyClone, SH40003.01), and 100 mg/ml of streptomycin (Hyclone, SV30010), and seeded onto a 25 cm^2 flask coated with 0.25 $\mu g/cm^2$ type I collagen (Gibco, A1048301) at 37ºC with 5% CO_2. The media was changed every 2 to 3 days. Cells were passaged 2 to 4 times before each experiment. The purity of isolated hVICs was characterized by immunofluorescence staining of vimentin and smooth muscle protein 22 alpha (SM22α) as previously described (53). The NF-κB inhibitor SC75741 (Sigma, SML2382) was prepared in dimethyl sulfoxide (DMSO) according to the manufacturer's instructions, and used at the final concentration of 1 μM according to previous publication. The solvent DMSO served as a negative control (54).

Induction and detection of hVIC *in vitro* calcification

hVIC *in vitro* calcification was induced as previously reported (23, 24, 51). hVICs were seeded at the density of 1.0×10^5 cells/well in 6-well plates and incubated with growth media. To induce hVIC *in vitro* calcification, the cells were treated with control (1.0 mM Pi/1.8mM Ca) or calcifying media (50 μg/mL ascorbic acid/2.5 mM Pi/2.7 mM Ca) for up to 7 days. Pi was prepared as a combination of NaH_2PO_4/Na_2HPO_4, pH=7.4.

Calcium deposition was detected by alizarin red staining. Briefly, cells were washed twice with cold PBS, fixed with 4% paraformaldehyde (PFA) for 10 min, stained with 2% alizarin red (pH 4.2) for 10 min at room temperature, and photographed. Quantitative analysis of calcium deposition in hVICs was also performed. The cells were washed twice with cold PBS, decalcified with 0.6 M HCl at 4ºC overnight. The supernatants were then collected and used to quantify calcium using a calcium colorimetric assay (Sigma, MAK022-1KT). The cells were collected in lysis buffer (0.1 M NaOH and 0.1% SDS) for protein quantification using bicinchoninic acid

(BCA) protein assay kit (Thermo Fisher, 23235). Calcium content was normalized to total protein and expressed as μg/mg protein.

Real-time quantitative polymerase chain reaction (RT-qPCR)

Total RNA was extracted from hVICs using TaKaRa MiniBEST Universal RNA Extraction Kit (Takara, 9767) or from non-calcified regions and calcified regions of aortic valve leaflets from CAVD patients using Trizol (Invitrogen, 1596026). The genomic DNA contaminations from RNA samples were removed using DNase I. For gene expression analysis, RNA was quantified and reverse transcribed using PrimeScript™ RT Master Mix (Takara, RR036A). RT-qPCR was performed with SYBR Premix Ex Taq II (Takara, RR820A) in the QuantStudio 5 real-time system (Life technologies). Relative mRNA expression levels were calculated using the $2^{-\Delta\Delta CT}$ method and normalized; β-actin was used as a housekeeping gene. The control values were expressed as 1 to indicate a precise fold change value for each gene of interest. The primer sequences for the gene of interest examined are listed in **Table S3**.

Western blotting

hVICs were lysed in RIPA buffer (Beyotime Biotechnology, P0013B) containing 1 mM protease inhibitor phenylmethylsulfonyl fluoride (PMSF) (Beyotime Biotechnology, ST505). 10 μg protein samples were analyzed on SDS-Polyacrylamide gel, and transferred to PVDF membranes. The membranes were blocked with 5% BSA in Tris Buffered Saline-Tween-20 (TBST), and incubated with primary antibodies overnight at 4 °C. The primary antibodies used in the present study are summarized in **Table S4**. Subsequently, membranes were incubated with HRP-conjugated anti-mouse (1:10000, Cell Signaling Technology, 7076S) or anti-rabbit (1:10000, Cell Signaling Technology, 7074S) secondary antibodies for 1 hr at room temperature. The immune complexes were visualized by chemiluminescence Lumi-Light Western Blotting Substrate (Millipore, WBKLS0500), and imaged with Amersham Imager 600 from GE Healthcare.

siRNA-mediated gene silencing

hVICs were seeded at the density of 1.0×10^5 cells/well in 6-well plates and transfected with siRNAs using Lipofectamine RNAiMAX (Invitrogen, 13778) according to the manufacturer's instructions. A siRNA targeting PALMD (siPALMD) or PFKFB3 (siPFKFB3) was used at a concentration of 20 nM. Scrambled siRNA (siScrambled) at a concentration of 20 nM served as a negative control. All siRNAs were obtained from Guangzhou RiboBio Co., Ltd, China. siRNA-mediated knockdown efficiency was confirmed by RT-qPCR and Western blotting. For hVIC *in vitro* calcification experiments, cells were re-transfected every 4 days during the experiments in order to ensure the optimal knockdown efficiency. The siRNA sequences for PALMD and PFKFB3 are outlined in **Table S5**.

Adenovirus-mediated overexpression of PALMD

Recombinant adenoviruses expressing flag-tagged PALMD (Ad-PALMD) and adenoviruses containing empty plasmids (Ad-null) that served as negative controls were constructed and purchased from Hanheng Bioscience Incorporation, Shanghai, China. The schematic of plasmid construction are shown in **Figure S19.** In brief, full length human PALMD was amplified using PCR and subcloned into the pAdEasy-EF1-MCS-3flag-CMV-GFP. The PCR primer sequence was sense: 5’-CAAGCTGTGACCGGCGCCTACTCTGGTACCGAGCTCGGATCCGCCACC-3’ and antisense: 5’-GTCATCGTCATCCTTGTAGTCCTCGAGGATCACCTTTTTCCCAGC-3’. hVICs were seeded at the density of 1.0x10^5 cells/well in 6-well plates and infected with Ad-null or Ad-PALMD for 48 hrs at multiplicities of infection (MOI) of 100. The overexpression efficiency of PALMD was confirmed by RT-qPCR and Western blotting. For hVIC *in vitro* calcification assay, cells were re-infected every 4 days during the experiments.

Monocyte adhesion assay

hVICs were seeded in 96 well plates, and transfected with siScrambled or siPALMD at the final concentration of 20 nM in the presence of control or 10ng/ml TNFα for 48 hrs. THP-1 cells were labeled with 0.2 mg/L calcein-AM (Sigma, 17783) for 30 min at 37 °C according to the mansufacture’s instructions, and incubated with hVICs for 1 hr. The co-cultured cells were washed with pre-warmed 1× PBS and images were obtained under a fluorescence microscope. The data was expressed as number of THP1 cells adhered per field view.

Immunofluorescence staining

hVICs were seeded on glass coverslips and incubated with control medium (Ctr) or calcifying medium (Cal.) for up to 7 days. Cells were then fixed, permeabilized with 0.3% triton x-100 (Beyotime Biotechnology, P0013B), and incubated overnight at 4°C with anti-PALMD (1:500, I Proteintech, 16531-1-AP). After washing three times with PBS, cells were incubated with Alexa Fluor®594 anti-rabbit antibodies (1:1000, Invitrogen, A11012) at 37 °C for 1 hr in dark. Glass coverslips were then stained with DAPI and the fluorescence signal was detected under Leica DMRB fluorescence microscope (Leica SP8). Negative controls were carried out simultaneously by incubating with equivalent concentrations of normal rabbit IgG (Cell signaling technology, 2729s) instead of primary antibody.

Immunohistochemistry

Human aortic valve leaflets were fixed with 4% PFA for 24 hrs, dehydrated and embedded in paraffin wax before sectioning at 7 μm using standard procedures. Sections were deparaffinized and rehydrated. Alizarin red staining was used to detect calcium deposition in calcified aortic valves from CAVD patients. The stained sections were scanned with a digital pathology slide scanner (Leica Aperio CS2) to obtain light microscopy images. To examine the expression of PALMD, the rehydrated sections were subjected to Tris-EDTA Buffer (pH 9.0) for antigen retrieval for 10 min at 95 °C. Endogenous peroxidase activity and non-specific antibody binding were blocked before overnight incubation at 4 °C with anti-PALMD antibody (1:100, Proteintech, 16531-1-AP). The sections were then washed three times in PBS, and incubated with secondary antibody using ChemMate^{TM} EnVision^{TM} Detection Kit (Gene Tech, GK500710) following the manufacturer’s instructions. The sections were finally counterstained with hematoxylin and eosin, dehydrated, and mounted in neutral balsam (Solarbio, G8590). Negative controls were incubated with equal concentrations of normal rabbit IgG (Cell signaling technology, 2729s) instead of the primary antibody. Images were obtained with a digital pathology slide scanner (Leica Aperio CS2).

Detection of glucose uptake

hVICs were seeded at 8,000 cells per well in 96-well plates. Cells were then transfected with 25 nM scrambled siRNA or siPLAMD for 48 hrs. hVICs were then cultured with 300 μM fluorescent glucose analogue 2-(N-(7-Nitrobenz-2-oxa-1,3-diazol-4-yl)Amino)-2-Deoxyglucose (2-NBDG) (Life Technologies) for 20 min. Cells were washed twice with PBS. Fluorescence was quantified at 485 nm excitation and 535 nm emission on TECAN Spark® 10M multimode microplate reader and normalized against the total protein.

Seahorse Analysis

Glycolytic function or oxidative phosphorylation was examined as previously reported (23). hVICs were seeded into Seahorse XFe96 FluxPak cell culture microplates (102601-100, Agilent Technologies) at a density of $1.0\text{x}10^4$ cells/well. Cells were then infected with Ad-null and Ad-PALMD at an MOI of 100 for 48 hrs. On the day of analysis, cells were washed 3 times with Seahorse XF assay medium (103575-100, Agilent Technologies) supplemented with 1 mM pyruvate, 2 mM glutamine, and 10 mM glucose at 37°C, and then incubated in a CO_2-free incubator at 37˚C for 60 min. The microplates were then placed in a Seahorse XFe96 bioanalyzer (Agilent Technologies LDA UK Limited). Oxygen consumption rate (OCR) changes were measured in response to oligomycin (1 μM), FCCP (2 μM) and rotenone/antimycin A (0.5 μM) injection. The difference in OCR between FCCP and rotenone/antimycin A was considered maximal respiratory capacity. ATP-linked respiratory OCR was calculated from the difference between basal and oligomycin inhibited OCR. For the glycolytic rate assay, the microplates were placed in a Seahorse XFe96 bioanalyzer. After basal measurements were taken, rotenone/antimycin A was injected to a final concentration of 0.5 μM. The maximum in glycolytic proton efflux rate (glycoPER) measurements following the addition of rotenone/antimycin A was considered as the compensatory glycolysis. Seahorse results were normalized to cell total protein content. Normalized Seahorse data were analyzed using Wave (software for XFp Analyzer, Agilent), and statistical calculations and graphical representations were created using Prism (Graphpad) software.

RNA sequencing

hVICs were seeded at a density of $1.0\text{x}10^5$ cells/well in 6-well plates, and transfected with 20 nM siScrambled or siPALMD for 48 hrs. The cell samples were then sent to KangChen Biotech (Shanghai, People's Republic of China) for RNA sequencing. In brief, total RNA was extracted using Trizol (Invitrogen) according to the manufacturer's protocol. The concentration of total RNA was detected using a NanoDrop ND-1000 spectrophotometer (Thermo Scientific), and the integrity was examined by denaturing agarose gel electrophoresis. A total quantity of 1~2 μg total RNA was purified using oligo (dT) conjugated magnetic beads. RNA-seq libraries were constructed using KAPA Stranded RNA-Seq Library Prep Kit (Illumina), and monitored using an Agilent Bioanalyzer 2100. RNA sequencing was performed on an Illumina HiSeq 4000 by KangChen Biotech. The RNA-seq data reported in this paper is deposited in NCBI Gene Omnibus (http://www.ncbi.nlm.nih.gov/geo/) with the accession number of GEO: GSE165524 on Jan 26, 2021. Raw data are public available after Jan 24, 2024.

Supporting Figures

Figure S1

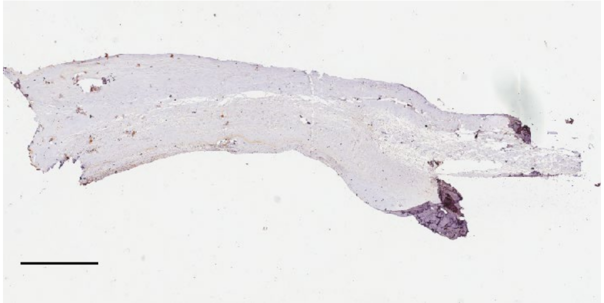

Figure S1. Negative control staining for PALMD immunohistochemistry in calcified human aortic valves. Equal amount of IgG used instead of Anti-PALMD served as negative controls for PALMD immunohistochemistry staining, and no positive staining was seen. Scale bar=800 µm.

Figure S2

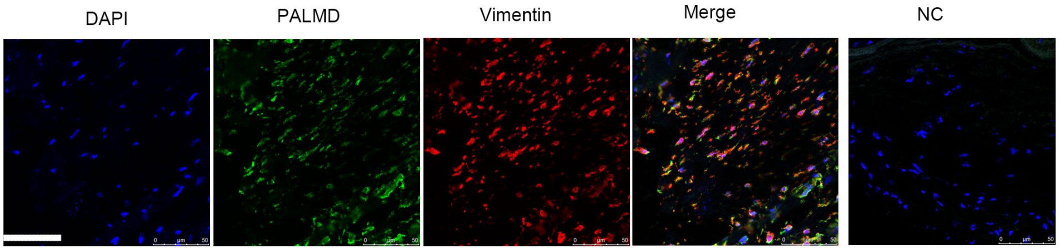

Figure S2. PALMD is co-localized with the VIC marker Vimentin in calcified human aortic valve tissues. Representative confocal images of double immunofluorescence staining for PALMD (Green) and Vimentin (Red) in calcified human aortic valve tissues. Scale bar=50 µm.

Figure S3

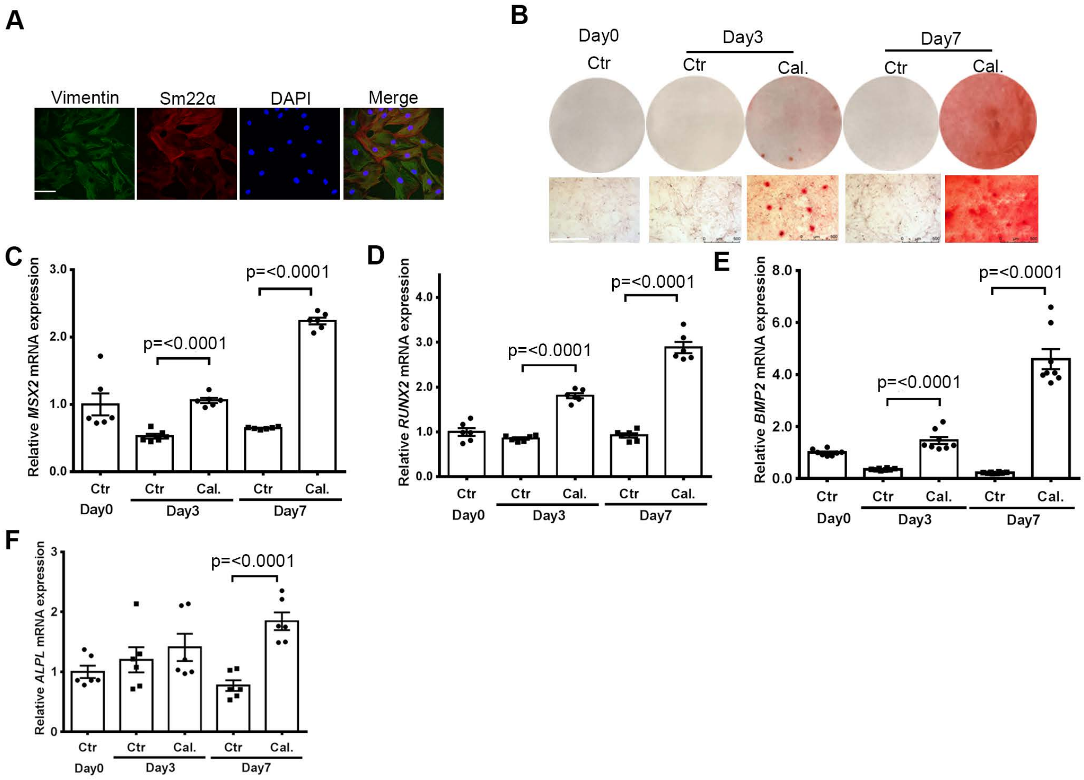

Figure S3. hVICs undergo osteogenic differentiation during the calcification process. hVICs were exposed to control (Ctr) or calcification media (Cal.) for up to 7 days. (A) Representative confocal images of double immunofluorescence staining for vimentin and alpha 22-smooth muscle actin (Sm22-α) in hVICs, scale bar=50μm. (B) Representative images of alizarin red staining for hVICs treated with control (Ctr) or calcification media (Cal.) for up to 7 days, scale bar=500μm. (C-F) RT-qPCR showing the osteogenic gene *MSX2*, *RUNX2*, *BMP2* and *ALPL* mRNA expression during hVIC *in vitro* calcification, n=6-8. Data are presented as mean ± SEM, and statistical significance was analyzed by a two-tailed unpaired Student's t-test.

Figure S4

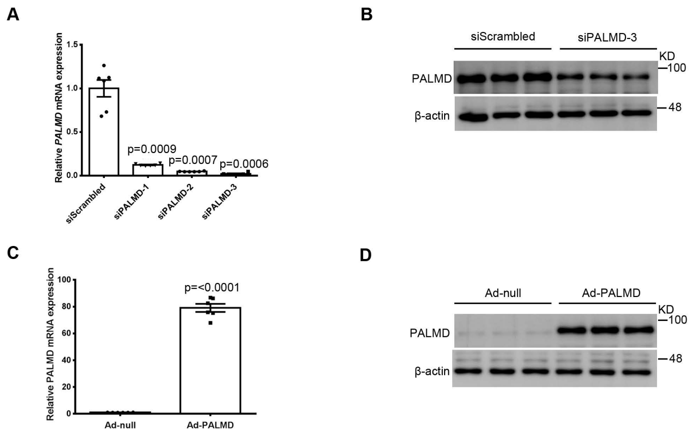

Figure S4. Confirmation of PALMD knockdown and overexpression efficiency in hVICs. hVICs were transfected with 20 nM scrambled siRNA (siScrambled) and PALMD siRNA (siPALMD) or infected with empty adenoviruses (Ad-null) and PALMD adenoviruses (Ad-PALMD) at an MOI of 100 for 48 hrs. (A) RT-qPCR showing *PALMD* mRNA expression in hVICs with PALMD depletinon, n=6. (B) Representative images of Western blotting for PALMD and β-actin protein expression in hVICs with PALMD depletion. (C) RT-qPCR showing *PALMD* mRNA expression in hVICs with PALMD overexpression, n=6. (D) Representative images of Western blotting for PALMD and β-actin protein expression in hVICs with PALMD overexpression. Data are presented as mean ± SEM, and statistical significance was analyzed by a two-tailed unpaired Student’s t-test or one-way ANOVA followed by Tukey's multiple comparisons test.

Figure S5

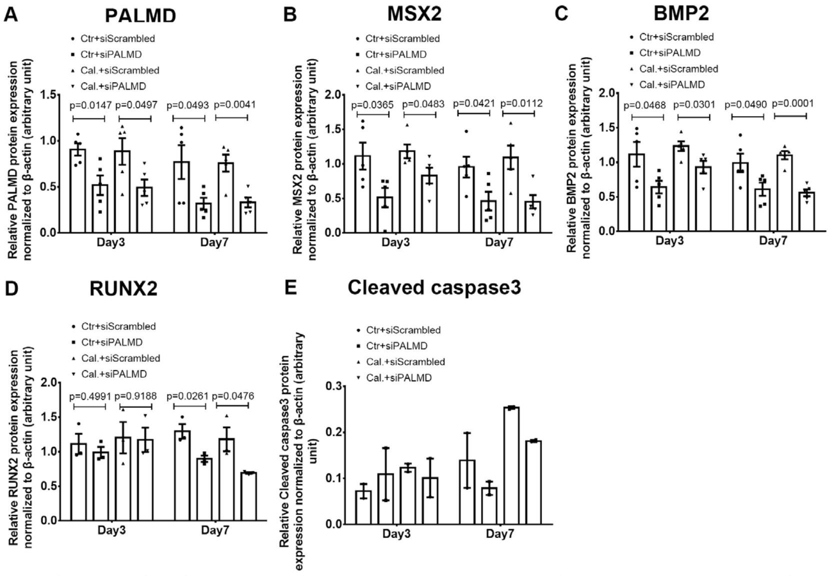

Figure S5. Semi-quantitative analysis of the western blotting data presented in Figure 2G. (A) PALMD, n=5. (B) MSX2, n=5. (C) BMP2, n=5. (D) RUNX2, n=3. (E) Cleaved caspase 3, n=2. Data are presented as mean ± SEM, and statistical significance was analyzed by a two-tailed unpaired Student’s t-test.

Figure S6

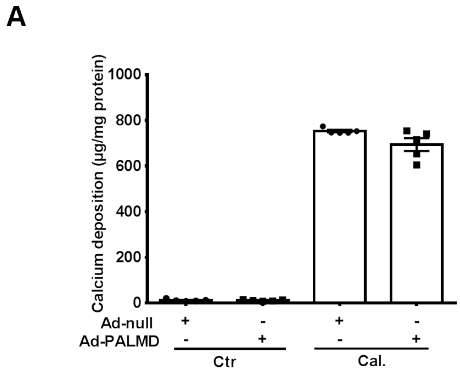

Figure S6. PALMD overexpression did not alter calcium deposition in hVICs at day 7. hVICs were infected with empty adenoviruses (Ad-null) or PALMD adenoviruses (Ad-PALMD) at an MOI of 100, and treated with control (Ctr) or calcification media (Cal.) for up to 7 days. Calcium quantitative assay showing calcium deposition in hVICs with PALMD overexpression at day 7, n=5. Data are presented as mean ± SEM, and statistical significance was analyzed by a two-tailed unpaired Student's t-test.

Figure S7

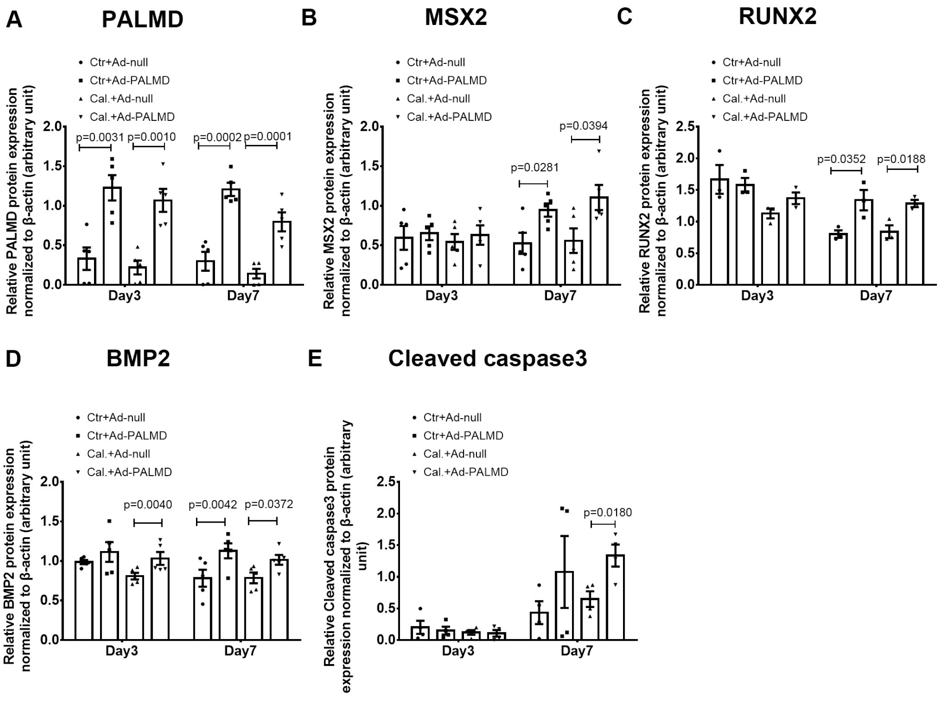

Figure S7. Semi-quantitative analysis of the western blotting data presented in Figure 2L. (A) PALMD, n=5. (B) MSX2, n=5. (C) RUNX2, n=3. (D) BMP2, n=5. (E) Cleaved caspase 3, n=4. Data are presented as mean ± SEM, and statistical significance was analyzed by a two-tailed unpaired Student's t-test.

Figure S8

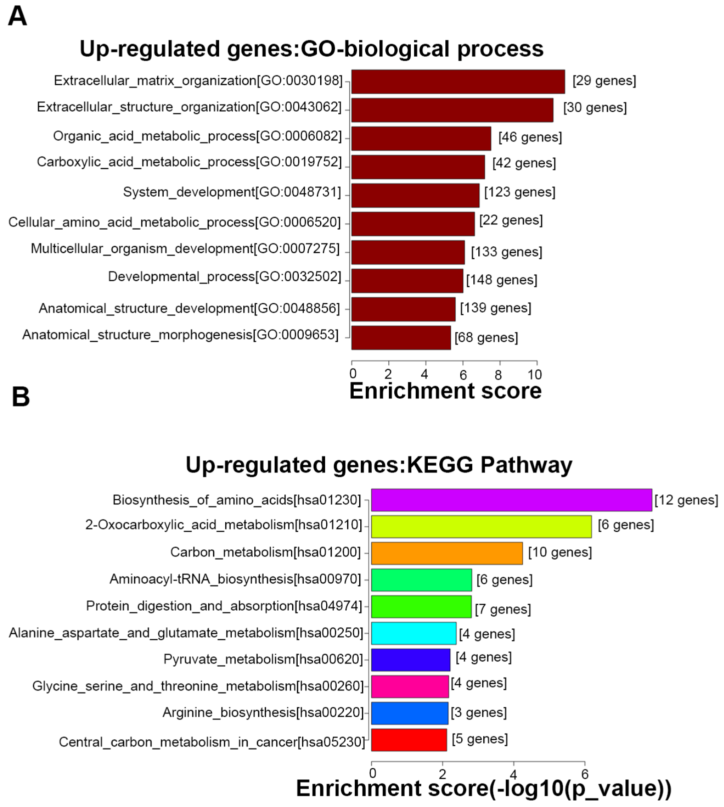

Figure S8. Gene ontology and KEGG pathway analysis of the up-regulated genes in PALMD depleted hVICs identified by RNA-Seq. hVICs were transfected with scrambled siRNA (siScrambled, 20 nM) or PALMD siRNA (siPALMD, 20 nM) for 48 hrs. (A) Up-regulated genes in hVICs with PALMD depletion are associated with biological processes, such as extracellular matrix and structural organization. (B) Up-regulated genes in hVICs with PALMD depletion are associated with multiple pathways, including biosynthesis of amino acids, and carbon metabolism.

Figure S9

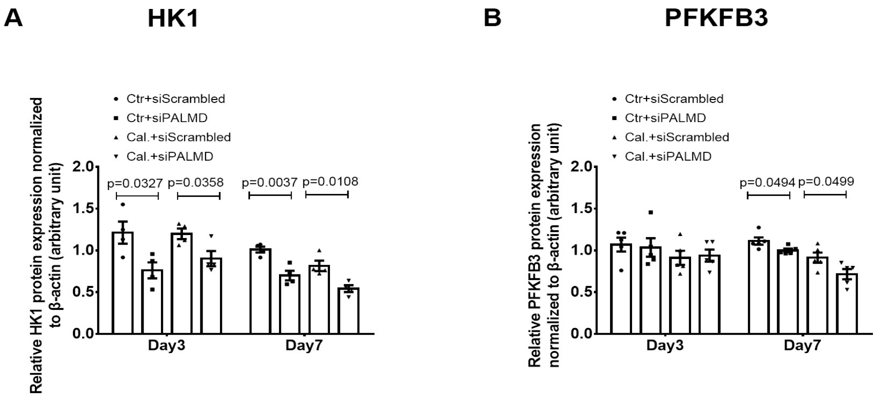

Figure S9. Semi-quantitative analysis of the western blotting data presented in Figure 4B. (A) HK1, n=4. (B) PFKFB3, n=5. Data are presented as mean ± SEM, and statistical significance was analyzed by a two-tailed unpaired Student's t-test.

Figure S10

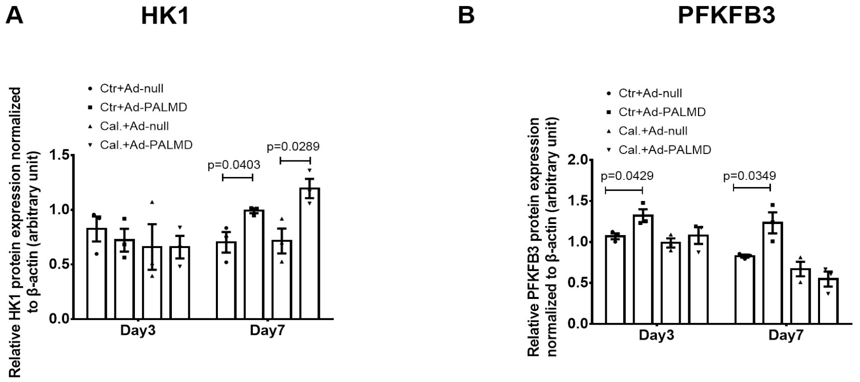

Figure S10. Semi-quantitative analysis of the western blotting data presented in Figure 4D. (A) HK1, n=3. (B) PFKFB3, n=3. Data are presented as mean ± SEM, and statistical significance was analyzed by a two-tailed unpaired Student's t-test.

Figure S11

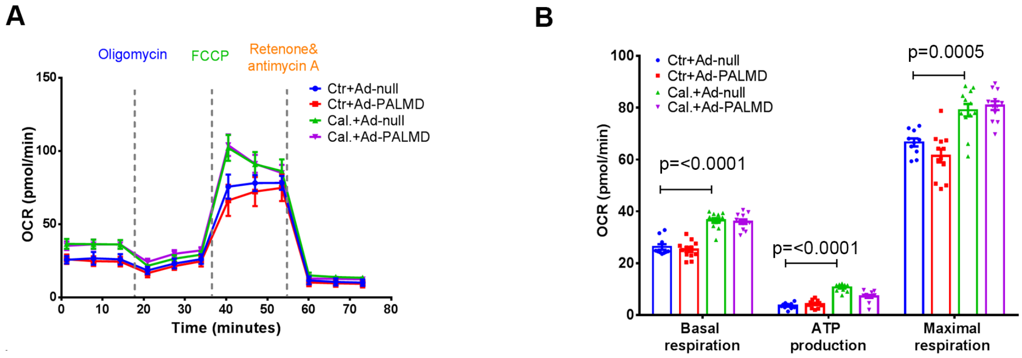

Figure S11. PALMD overexpression did not alter oxidative phosphorylation in hVICs. hVICs were infected with empty adenoviruses (Ad-null) or PALMD adenoviruses (Ad-PALMD) at an MOI of 100 for 48 hrs. (A-B) Oxygen consumption rate (OCR) in hVICs with PALMD overexpression in the presence of control (Ctr) or calcifying media for 48 hrs, n=12. Data are presented as mean ± SEM, and statistical significance was analyzed by a two-tailed unpaired Student's t-test.

Figure S12

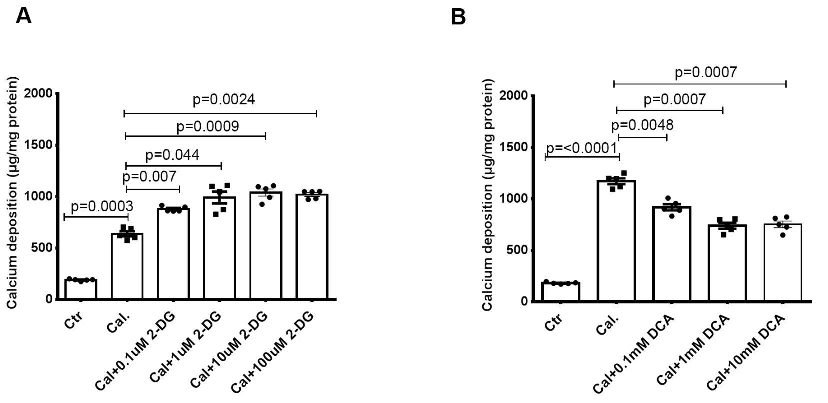

Figure S12. The glycolysis inhibitor 2-DG and DCA induced opposite effects on hVIC calcification. (A) hVICs were cultured with control (Ctr) or calcification media (Cal.) with or without 2-DG (0-100 μM) for 7 days. Calcium quantitative analysis showed 2-DG increased hVIC *in vitro* calcification, n=5. (B) hVICs were cultured with control (Ctr) or calcification media (Cal.) with or without DCA (0-100 mM) for 7 days. Calcium quantitative analysis showed DCA inhibited calcium deposition in hVICs at day 7, n=5. Data are presented as mean ± SEM, and statistical significance was analyzed by one-way ANOVA followed by Tukey's multiple comparisons test.

Figure S13

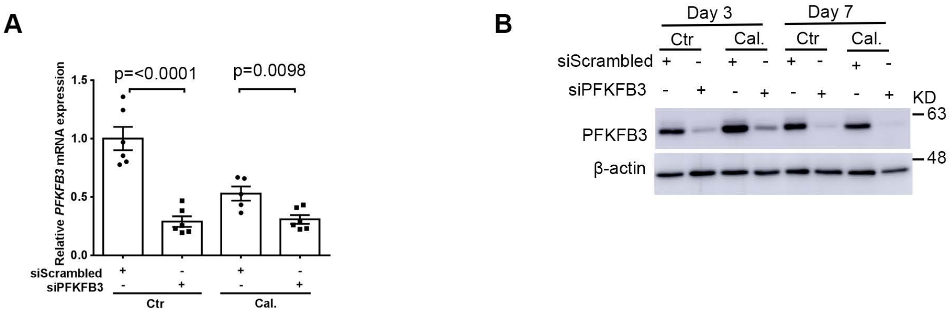

Figure S13. Validation of siRNA-mediated PFKFB3 knockdown efficiency in hVICs. hVICs were transfected with scrambled siRNA (siScrambled, 20 nM) or PFKFB3 siRNA (siPFKFB3, 20 nM) for 48 hrs. (A) RT-qPCR showing *PFKFB3* mRNA expression in hVICs, n=6. (B) Representative images of Western blotting for PFKFB3 and β-actin protein expression in hVICs. Data are presented as mean ± SEM, and statistical significance was analyzed by a two-tailed unpaired Student's t-test.

Figure S14

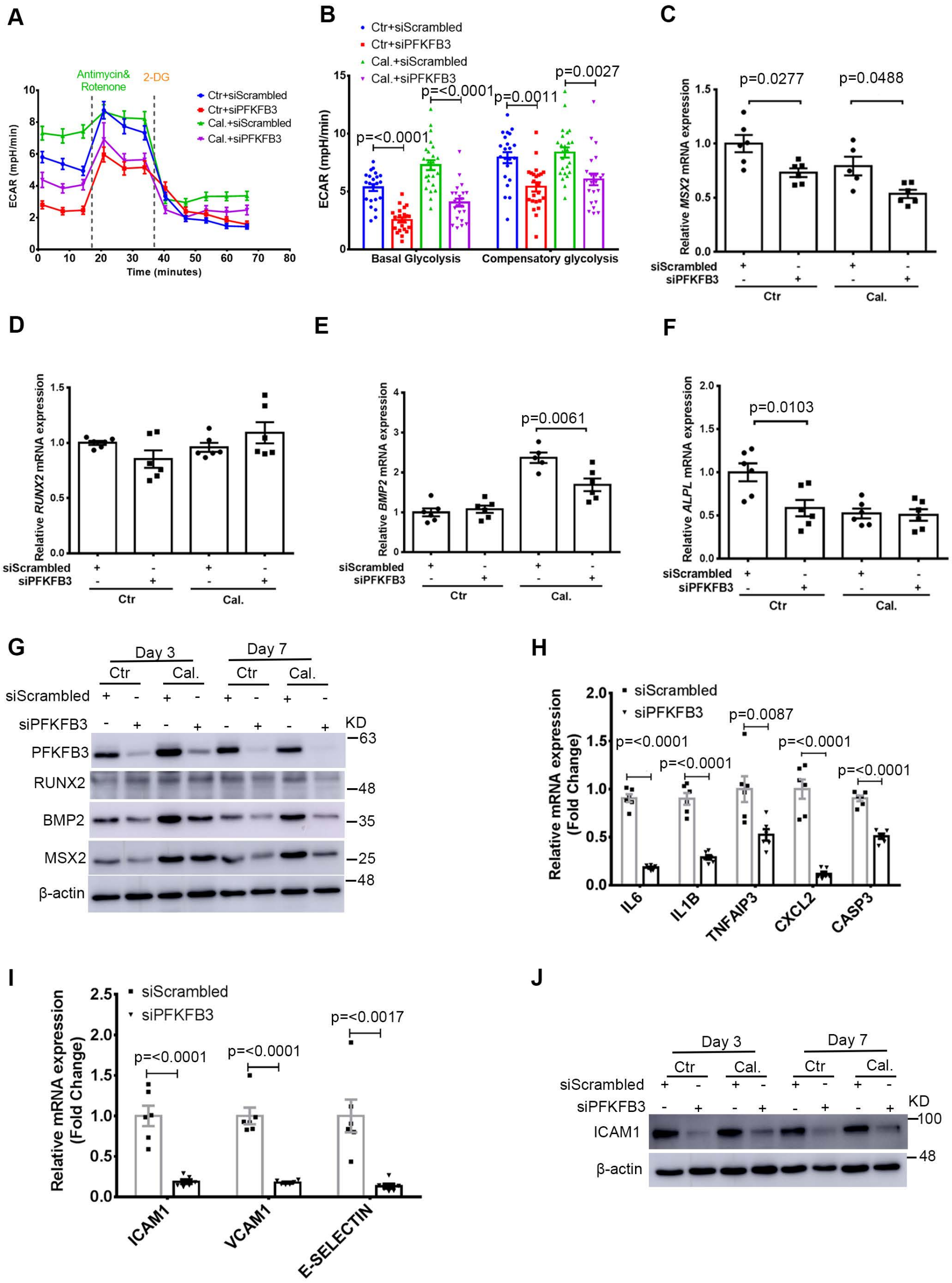

Figure S14. Inhibition of PFKFB3-mediated glycolysis attenuates hVIC osteogenic differentiation and inflammation. hVICs were transfected with scrambled siRNA (siScrambled, 20 nM) or PFKFB3 siRNA (siPFKFB3, 20 nM), and treated with control medium (Ctr) or calcifying medium (Cal.) for 48 hrs or for up to 7 days. (A-B) The glycolysis rate assay using the Seahorse in hVICs transfected with siScrambled or siPFKFB3 after 48 hrs, n=22. (C-F) RT-qPCR showing mRNA expression of the osteogenic gene *MSX2*, *RUNX2*, *BMP2* and *ALPL* in hVICs with depleted PFKFB3 at 48 hrs, n=6. (G) Representative images of Western blotting for RUNX2, BMP2, MSX2 and β-actin protein expression in hVICs with depleted PFKFB3 at day 3 and day 7. Please note that these western blotting samples were the same batch of sample preparation used in Figure S13-B. We reused the PFKFB3 western blotting image here to show more clealy that PFKFB3 was successfully supressed by siRNAs. (H) RT-qPCR showing mRNA expression of the inflammation-associated gene *IL6*, *IL1B*, *TNFAIP3*, *CXCL2*, and *CASP3* in hVICs with depleted PFKFB3 at 48 hrs, n=6. (I) RT-qPCR showing mRNA expression of the adhesion molecule ICAM1, VCAM1, and E-SELECTIN in hVICs with depleted PFKFB3 at 48 hrs, n=6. (J) Representative images of Western blotting for ICAM1 and β-actin protein expression in hVICs with depleted PFKFB3 at day 3 and day 7. Data are presented as mean ± SEM, and statistical significance was analyzed by a two-tailed unpaired Student's t-test or one-way ANOVA followed by Tukey's multiple comparisons test.

Figure S15

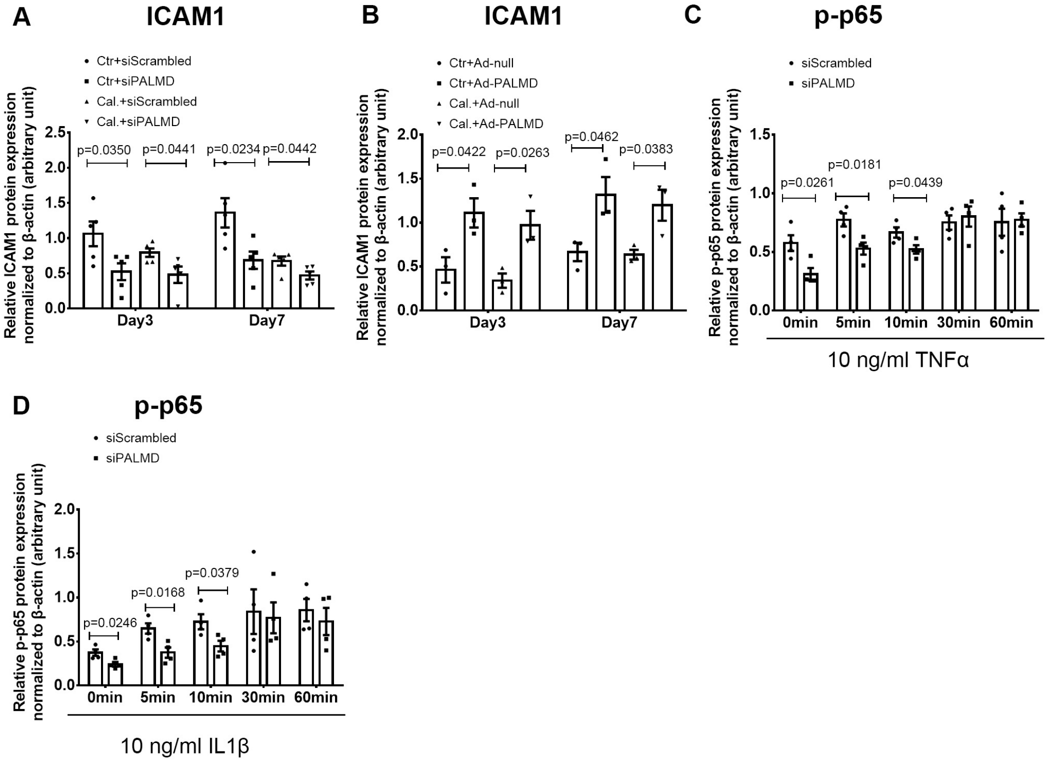

Figure S15 Semi-quantitative analysis of the western blotting data presented in Figure 5D, G, H and I. (A) ICAM1, n=5. (B) ICAM1, n=3. (C) p-p65, n=4. (D) p-p65, n=4. Data are presented as mean ± SEM, and statistical significance was analyzed by a two-tailed unpaired Student's t-test.

Figure S16

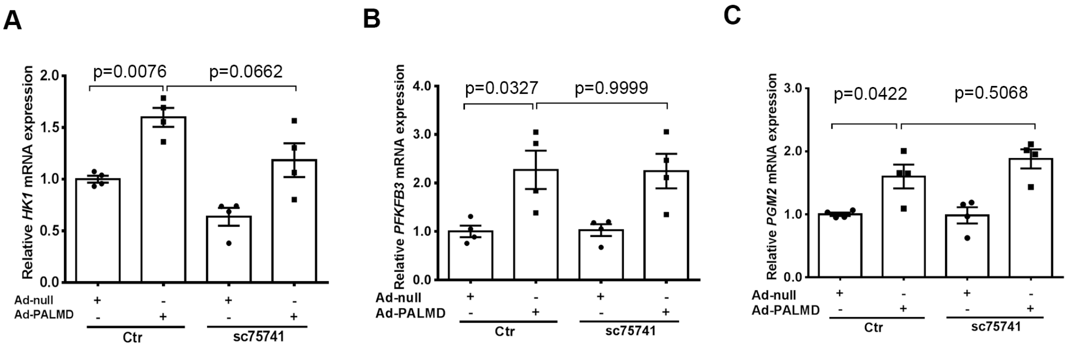

Figure S16. Inhibition of NF-κB did not alter PALMD overexpression-induced the glycolytic gene expression in hVICs. hVICs were infected with empty adenoviruses (Ad-null, MOI=100) or

PALMD adenoviruses (Ad-PALMD, MOI=100) and treated with 1μM the NF-κB inhibitor SC75741 for 48 hrs. (A-C) RT-qPCR showing mRNA expression of the key glycolytic gene *HK1*, *PFKFB3*, and *PGM2* in hVICs, n=4. Data are presented as mean ± SEM, and statistical significance was analyzed by one-way ANOVA followed by Tukey's multiple comparisons test.

Figure S17

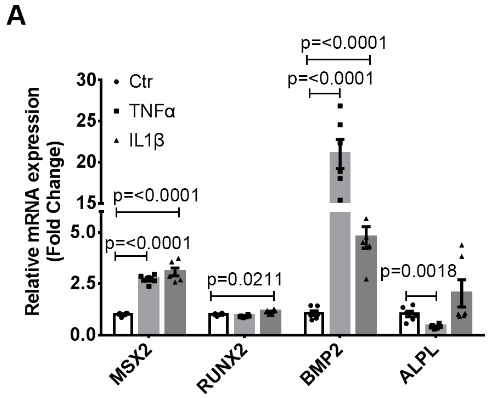

Figure S17. TNFα and IL1β treatment induces osteogenic gene expression in hVICs. hVICs were treated with 10 ng/ml TNFα or IL1β for 48 hrs. (A) RT-qPCR showing the osteogenic gene *MSX2*, *RUNX2*, *BMP2* and *ALPL* mRNA expression in hVICs, n=6. Data are presented as mean ± SEM, and statistical significance was analyzed by a two-tailed unpaired Student's t-test or one-way ANOVA followed by Tukey's multiple comparisons test.

Figure S18

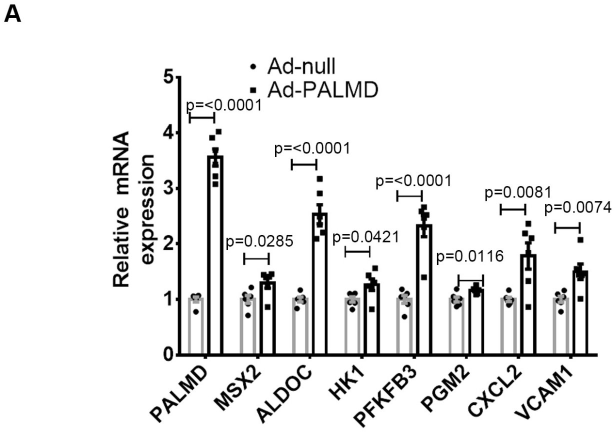

Figure S18. Adenovirus-mediated overexpression of PALMD regulates the osteogenic, glycolytic and inflammatory gene expression in hVICs. hVICs were transduced with Ad-PALMD at an MOI of 50 for 2 days, RT-qPCR was performed to examine mRNA expression of *PALMD*, *MSX2*, *ALDOC*, *HK1*, *PFKFB3*, *PGM2*, *CXCL2* and *VCAM1*, n=6. Data are presented as mean ± SEM, and statistical significance was analyzed by a two-tailed unpaired Student's t-test.

Figure S19

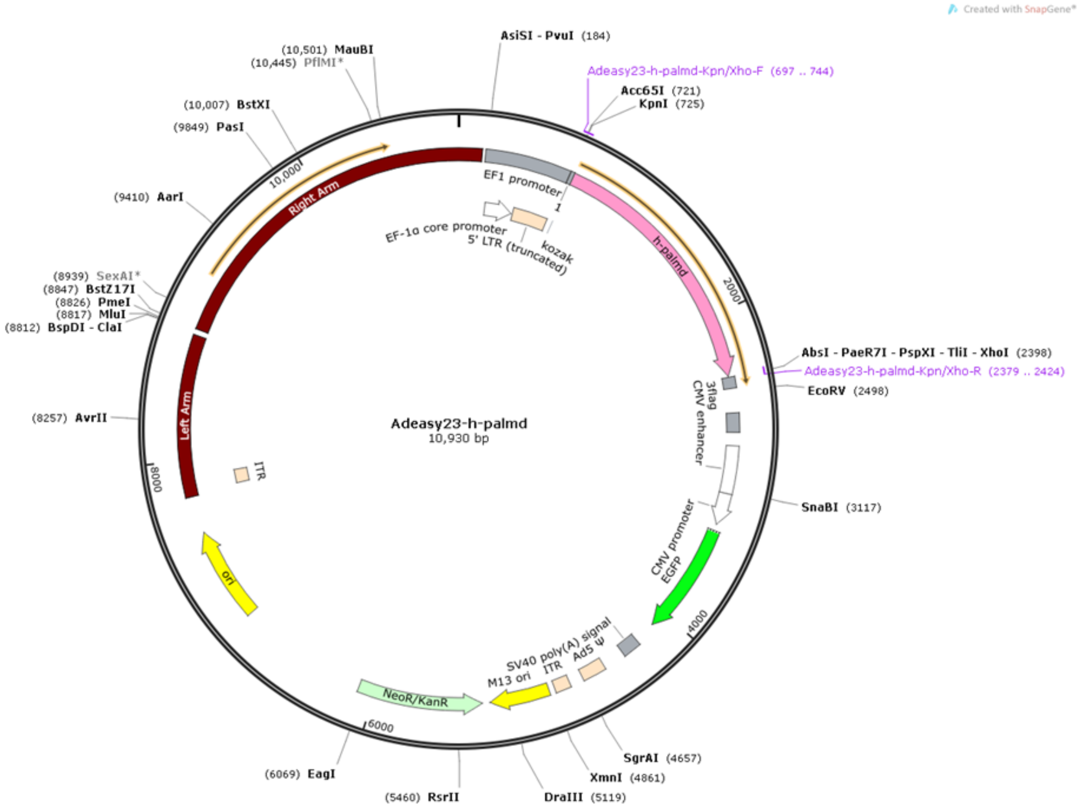

Figure S19. The schematic of plasmid construction for PALMD overexpressing adenovirus. Full length human PALMD was amplified using PCR and subcloned into the pAdEasy-EF1-MCS-3flag-CMV-GFP. The PCR primer sequence was sense: 5'-CAAGCTGTGACCGGCGCCTACTCTGGTACCGAGCTCGGATCCGCCACC-3' and antisense: 5'-GTCATCGTCATCCTTGTAGTCCTCGAGGATCACCTTTTTCCCAGC-3'.

Supporting Tables

Table S1. Spreadsheet of differentially expressed gene list regulated by PALMD in hVICs identified by RNA-Seq, see supplemental excel file.

Up-regulated genes (siPALMD vs siScrambled)

Annotation			DE	Statistic
Track_id	**Gene_Name**	**Gene_Type**	**log2FC**	**p_value**
ENSG00000137285.9_2	TUBB2B	protein_coding	2.899818176	0.000130175
ENSG00000143320.8_2	CRABP2	protein_coding	2.486792063	1.68441E-05
ENSG00000101255.10_3	TRIB3	protein_coding	2.27103235	3.14683E-05
ENSG00000123094.15_3	RASSF8	protein_coding	1.991436391	0.000104429
ENSG00000128165.8_2	ADM2	protein_coding	1.919405044	0.000344728
ENSG00000171951.4_3	SCG2	protein_coding	1.915956262	5.09743E-05

ENSG00000284461.1_1	RABGEF1	protein_coding	1.913210287	0.043133143
ENSG00000135069.13_2	PSAT1	protein_coding	1.863555524	1.00722E-05
ENSG00000100889.11_2	PCK2	protein_coding	1.778677992	9.49679E-06
ENSG00000089597.16_2	GANAB	protein_coding	1.727083853	2.45504E-05
ENSG00000130513.6_3	GDF15	protein_coding	1.666359898	4.4615E-06
ENSG00000169105.7_2	CHST14	protein_coding	1.660124342	2.41511E-06
ENSG00000197457.9_2	STMN3	protein_coding	1.632255467	6.19847E-06
ENSG00000128965.11_2	CHAC1	protein_coding	1.589281867	9.35048E-05
ENSG00000070669.16_3	ASNS	protein_coding	1.574849427	1.42747E-05
ENSG00000144827.8_2	ABHD10	protein_coding	1.544408981	0.001727832
ENSG00000130766.4_2	SESN2	protein_coding	1.52557269	2.45422E-05
ENSG00000166128.12_2	RAB8B	protein_coding	1.4978814	0.006946317
ENSG00000136010.13_2	ALDH1L2	protein_coding	1.353811083	2.63787E-05
ENSG00000123689.5_2	G0S2	protein_coding	1.350117205	0.001537314
ENSG00000176490.4_3	DIRAS1	protein_coding	1.3454103	5.15524E-05
ENSG00000078018.19_3	MAP2	protein_coding	1.343715663	0.003361034
ENSG00000204291.10_2	COL15A1	protein_coding	1.327581828	2.26541E-05
ENSG00000144476.5_3	ACKR3	protein_coding	1.326783258	1.02988E-06
ENSG00000167460.14_4	TPM4	protein_coding	1.325607756	0.001657832
ENSG00000164898.12_3	FMC1	protein_coding	1.296491547	0.001182677
ENSG00000145391.13_2	SETD7	protein_coding	1.248537893	1.92727E-05
ENSG00000139514.12_3	SLC7A1	protein_coding	1.244092067	3.96676E-05
ENSG00000186832.8_3	KRT16	protein_coding	1.233676669	5.43594E-05
ENSG00000112378.11_2	PERP	protein_coding	1.215476519	7.56121E-05
ENSG00000127083.7_2	OMD	protein_coding	1.214843139	9.46498E-05
ENSG00000146476.10_2	ARMT1	protein_coding	1.214643555	0.047171151
ENSG00000117758.13_3	STX12	protein_coding	1.213577149	2.14201E-05
ENSG00000099875.14_3	MKNK2	protein_coding	1.212132748	0.00041126
ENSG00000105281.12_3	SLC1A5	protein_coding	1.206207087	0.004944455
ENSG00000174807.3_2	CD248	protein_coding	1.20012413	9.14462E-05
ENSG00000204604.9_3	ZNF468	protein_coding	1.197397847	0.000584765
ENSG00000284194.1_1	SCO2	protein_coding	1.175906402	0.000653425
ENSG00000166123.13_3	GPT2	protein_coding	1.17275281	0.02271008
ENSG00000137166.14_2	FOXP4	protein_coding	1.169316984	9.00737E-06
ENSG00000060491.16_3	OGFR	protein_coding	1.155798663	3.98133E-05
ENSG00000092621.12_3	PHGDH	protein_coding	1.144694919	0.000259375
ENSG00000057019.15_3	DCBLD2	protein_coding	1.125257818	6.04191E-05
ENSG00000181218.5_2	HIST3H2A	protein_coding	1.124107658	0.000604281
ENSG00000104381.12_2	GDAP1	protein_coding	1.122780687	0.000267577
ENSG00000143537.13_3	ADAM15	protein_coding	1.122214427	0.000173118
ENSG00000185386.14_2	MAPK11	protein_coding	1.109235461	0.00039309
ENSG00000086062.12_2	B4GALT1	protein_coding	1.109035689	1.32908E-06
ENSG00000155254.12_2	MARVELD1	protein_coding	1.098045813	7.893E-06
ENSG00000156639.11_2	ZFAND3	protein_coding	1.093573823	1.84974E-05

ENSG00000165806.19_3	CASP7	protein_coding	1.089396662	0.000152882
ENSG00000135842.16_2	FAM129A	protein_coding	1.087878401	0.000249982
ENSG00000140367.11_3	UBE2Q2	protein_coding	1.081715886	0.000103416
ENSG00000181588.16_3	MEX3D	protein_coding	1.070335754	0.001064146
ENSG00000143367.15_3	TUFT1	protein_coding	1.066495282	0.030459787
ENSG00000116761.11_2	CTH	protein_coding	1.065968404	4.13255E-06
ENSG00000185567.6_2	AHNAK2	protein_coding	1.06388933	0.000297061
ENSG00000188223.9_4	AD000671.1	protein_coding	1.051654846	0.043554433
ENSG00000012963.14_3	UBR7	protein_coding	1.051269227	0.040651991
ENSG00000157613.10_3	CREB3L1	protein_coding	1.051059928	0.000335097
ENSG00000130635.15_3	COL5A1	protein_coding	1.050528974	0.000627994
ENSG00000153574.8_2	RPIA	protein_coding	1.047188517	0.00039141
ENSG00000179195.15_3	ZNF664	protein_coding	1.045882633	1.22872E-06
ENSG00000058091.16_3	CDK14	protein_coding	1.038873737	0.000121731
ENSG00000105327.17_3	BBC3	protein_coding	1.038646623	0.00056501
ENSG00000153879.8_2	CEBPG	protein_coding	1.029122015	5.74471E-05
ENSG00000117298.14_2	ECE1	protein_coding	1.026803911	7.06924E-06
ENSG00000176971.3_2	FIBIN	protein_coding	1.022825068	0.000135138
ENSG00000164932.12_2	CTHRC1	protein_coding	1.022782986	4.08327E-06
ENSG00000234444.9_3	ZNF736	protein_coding	1.016392773	0.007818677
ENSG00000144583.4_2	MARCH4	protein_coding	1.012325117	3.50535E-05
ENSG00000157693.14_2	TMEM268	protein_coding	1.006145136	0.004205411
ENSG00000173281.4_2	PPP1R3B	protein_coding	1.005801552	0.000509413
ENSG00000168542.14_3	COL3A1	protein_coding	1.003046823	0.000222432
ENSG00000183098.10_2	GPC6	protein_coding	1.002812418	6.11513E-05
ENSG00000177374.12_4	HIC1	protein_coding	0.995402478	0.000531916
ENSG00000169136.10_3	ATF5	protein_coding	0.99218785	0.002539038
ENSG00000171307.18_2	ZDHHC16	protein_coding	0.989031428	0.000327595
ENSG00000088256.8_2	GNA11	protein_coding	0.986128362	0.014528274
ENSG00000135048.13_4	TMEM2	protein_coding	0.983824899	0.005532864
ENSG00000049540.16_3	ELN	protein_coding	0.981933298	0.000898098
ENSG00000117899.10_4	MESD	protein_coding	0.979109761	0.000598695
ENSG00000029364.11_2	SLC39A9	protein_coding	0.977233133	0.007321663
ENSG00000114786.16_4	ABHD14A-ACY1	protein_coding	0.975064982	0.022947936
ENSG00000204439.3_2	C6orf47	protein_coding	0.966423274	0.00118198
ENSG00000104964.14_2	AES	protein_coding	0.963417149	5.36457E-05
ENSG00000104679.10_4	R3HCC1	protein_coding	0.963160949	0.004020215
ENSG00000146674.14_3	IGFBP3	protein_coding	0.957451455	5.11029E-05
ENSG00000037241.7_3	RPL26L1	protein_coding	0.953233679	0.001413679
ENSG00000123131.12_2	PRDX4	protein_coding	0.945532645	0.002902146
ENSG00000154930.14_2	ACSS1	protein_coding	0.943731339	4.49469E-05
ENSG00000181788.3_2	SIAH2	protein_coding	0.943468204	0.000154507
ENSG00000065911.11_2	MTHFD2	protein_coding	0.943353093	0.002820232
ENSG00000124702.17_2	KLHDC3	protein_coding	0.940552	5.33749E-05

ENSG00000106105.13_2	GARS	protein_coding	0.93968834	3.33649E-05
ENSG00000179292.4_2	TMEM151A	protein_coding	0.932852152	1.66736E-05
ENSG00000137573.13_3	SULF1	protein_coding	0.932739921	0.001944368
ENSG00000196975.15_2	ANXA4	protein_coding	0.932622022	7.48959E-06
ENSG00000143878.9_2	RHOB	protein_coding	0.929116526	0.00011057
ENSG00000197136.4_3	PCNX3	protein_coding	0.927549436	0.000962809
ENSG00000124098.9_2	FAM210B	protein_coding	0.92703612	0.000175179
ENSG00000080573.6_2	COL5A3	protein_coding	0.924610175	0.000933102
ENSG00000147883.10_2	CDKN2B	protein_coding	0.921496539	1.86994E-05
ENSG00000223496.2_3	EXOSC6	protein_coding	0.918154593	1.08556E-05
ENSG00000164106.7_2	SCRG1	protein_coding	0.916430855	0.000336665
ENSG00000161714.11_3	PLCD3	protein_coding	0.913571997	2.33326E-05
ENSG00000265972.5_2	TXNIP	protein_coding	0.912779326	0.00670096
ENSG00000168209.4_2	DDIT4	protein_coding	0.908396156	0.001528417
ENSG00000163815.5_3	CLEC3B	protein_coding	0.906787982	0.000402825
ENSG00000108639.7_3	SYNGR2	protein_coding	0.903419476	0.045145031
ENSG00000122203.14_2	KIAA1191	protein_coding	0.903268704	0.00029446
ENSG00000161920.9_2	MED11	protein_coding	0.900889164	8.55278E-05
ENSG00000172201.11_3	ID4	protein_coding	0.900564899	8.59211E-05
ENSG00000184939.15_2	ZFP90	protein_coding	0.898590575	0.021762109
ENSG00000154978.12_2	VOPP1	protein_coding	0.897541659	0.000355853
ENSG00000189184.11_2	PCDH18	protein_coding	0.897134274	0.000954867
ENSG00000127774.6_2	EMC6	protein_coding	0.890391945	2.55321E-05
ENSG00000115109.13_2	EPB41L5	protein_coding	0.890059111	0.008447819
ENSG00000186283.13_3	TOR3A	protein_coding	0.888055891	6.11211E-06
ENSG00000133169.5_2	BEX1	protein_coding	0.888047341	0.001649616
ENSG00000106819.11_2	ASPN	protein_coding	0.887485817	0.000147102
ENSG00000103257.8_2	SLC7A5	protein_coding	0.887460998	1.00338E-05
ENSG00000171700.13_2	RGS19	protein_coding	0.887384213	0.000662545
ENSG00000117862.11_3	TXNDC12	protein_coding	0.884794984	1.17431E-06
ENSG00000133110.14_2	POSTN	protein_coding	0.883108175	0.000553216
ENSG00000132613.14_2	MTSS1L	protein_coding	0.880345591	0.000110134
ENSG00000074416.13_4	MGLL	protein_coding	0.878831264	1.62905E-05
ENSG00000130956.13_2	HABP4	protein_coding	0.875907882	0.000247346
ENSG00000143816.7_2	WNT9A	protein_coding	0.875203844	0.000616902
ENSG00000123728.9_2	RAP2C	protein_coding	0.874816641	0.001073068
ENSG00000135480.15_3	KRT7	protein_coding	0.873824483	0.002822993
ENSG00000118898.15_3	PPL	protein_coding	0.872688153	0.034143248
ENSG00000188783.5_2	PRELP	protein_coding	0.86241938	1.56097E-05
ENSG00000106070.17_3	GRB10	protein_coding	0.860629934	6.23988E-05
ENSG00000100216.5_2	TOMM22	protein_coding	0.855410047	0.000389128
ENSG00000140044.12_2	JDP2	protein_coding	0.851519989	0.016702644
ENSG00000160200.17_2	CBS	protein_coding	0.847473843	0.019306549
ENSG00000163536.12_2	SERPINI1	protein_coding	0.842543985	0.000305106

ENSG00000005243.9_3	COPZ2	protein_coding	0.841848625	0.000189237
ENSG00000100360.14_3	IFT27	protein_coding	0.841009	0.042308072
ENSG00000068383.18_2	INPP5A	protein_coding	0.839038017	2.77248E-05
ENSG00000111801.15_3	BTN3A3	protein_coding	0.838706388	0.00130237
ENSG00000166224.16_3	SGPL1	protein_coding	0.838045528	9.48516E-05
ENSG00000031698.12_2	SARS	protein_coding	0.837279811	0.000208771
ENSG00000025772.7_2	TOMM34	protein_coding	0.832920182	7.99175E-06
ENSG00000101098.12_2	RIMS4	protein_coding	0.83056818	0.000959091
ENSG00000086827.8_3	ZW10	protein_coding	0.828657877	0.001271278
ENSG00000162755.13_2	KLHDC9	protein_coding	0.827772133	0.004452426
ENSG00000167969.12_2	ECI1	protein_coding	0.825274229	0.000185063
ENSG00000162104.9_2	ADCY9	protein_coding	0.822507529	0.000492651
ENSG00000198513.11_2	ATL1	protein_coding	0.819104873	0.001420734
ENSG00000154957.13_3	ZNF18	protein_coding	0.817501204	0.000923622
ENSG00000243646.9_3	IL10RB	protein_coding	0.814655957	0.047632318
ENSG00000187049.9_2	TMEM216	protein_coding	0.81352817	0.00069562
ENSG00000175395.15_2	ZNF25	protein_coding	0.813261321	4.72932E-05
ENSG00000012171.19_3	SEMA3B	protein_coding	0.812209123	0.008650354
ENSG00000105058.11_2	FAM32A	protein_coding	0.811078495	6.78649E-05
ENSG00000167994.11_3	RAB3IL1	protein_coding	0.810696203	0.002467132
ENSG00000155158.20_4	TTC39B	protein_coding	0.807156633	0.000499521
ENSG00000196670.13_3	ZFP62	protein_coding	0.806089289	0.013538525
ENSG00000119392.14_2	GLE1	protein_coding	0.80134323	0.001444391
ENSG00000124145.6_3	SDC4	protein_coding	0.80001216	7.87118E-06
ENSG00000171100.14_2	MTM1	protein_coding	0.798145883	1.7043E-05
ENSG00000204611.6_3	ZNF616	protein_coding	0.796471303	9.96431E-05
ENSG00000102225.15_3	CDK16	protein_coding	0.79185917	0.012637006
ENSG00000015676.17_2	NUDCD3	protein_coding	0.789522766	3.48755E-05
ENSG00000113721.13_2	PDGFRB	protein_coding	0.786117481	0.000453006
ENSG00000125869.9_2	LAMP5	protein_coding	0.785876382	0.001941671
ENSG00000146966.12_2	DENND2A	protein_coding	0.784690455	6.33387E-06
ENSG00000075643.5_3	MOCOS	protein_coding	0.782454685	5.43062E-05
ENSG00000148180.19_3	GSN	protein_coding	0.779893722	0.000120184
ENSG00000159792.9_2	PSKH1	protein_coding	0.775622607	4.90925E-05
ENSG00000121552.3_2	CSTA	protein_coding	0.774081845	0.004435745
ENSG00000128567.16_2	PODXL	protein_coding	0.772512795	7.51362E-05
ENSG00000196136.17_3	SERPINA3	protein_coding	0.771918272	0.002373732
ENSG00000144468.16_3	RHBDD1	protein_coding	0.769831446	0.000122155
ENSG00000170214.4_3	ADRA1B	protein_coding	0.765094728	0.001884441
ENSG00000154065.16_2	ANKRD29	protein_coding	0.764827607	1.59013E-05
ENSG00000109084.13_2	TMEM97	protein_coding	0.764745521	0.017912497
ENSG00000154175.16_3	ABI3BP	protein_coding	0.76244745	4.88079E-05
ENSG00000114631.10_3	PODXL2	protein_coding	0.760476535	0.001215234
ENSG00000132530.16_3	XAF1	protein_coding	0.759660979	0.000521657

ENSG00000090861.15_3	AARS	protein_coding	0.755527201	0.000311136
ENSG00000196365.11_2	LONP1	protein_coding	0.755390519	0.002370729
ENSG00000100412.15_2	ACO2	protein_coding	0.7545623	0.000679268
ENSG00000169116.11_2	PARM1	protein_coding	0.754562071	1.43884E-05
ENSG00000132563.15_3	REEP2	protein_coding	0.75382181	0.037810813
ENSG00000187151.7_3	ANGPTL5	protein_coding	0.753502221	0.002663263
ENSG00000171160.17_2	MORN4	protein_coding	0.753231588	0.000831311
ENSG00000185585.19_3	OLFML2A	protein_coding	0.753103165	0.002463293
ENSG00000176438.12_2	SYNE3	protein_coding	0.752370193	3.03317E-05
ENSG00000174564.12_3	IL20RB	protein_coding	0.75142219	0.000898647
ENSG00000167779.7_2	IGFBP6	protein_coding	0.750067169	0.000788775
ENSG00000187840.4_2	EIF4EBP1	protein_coding	0.748374586	0.000333926
ENSG00000179954.15_3	SSC5D	protein_coding	0.747522928	1.91696E-05
ENSG00000107863.17_3	ARHGAP21	protein_coding	0.743952859	0.028015342
ENSG00000185963.13_2	BICD2	protein_coding	0.743553547	3.30489E-05
ENSG00000187325.4_2	TAF9B	protein_coding	0.742518246	0.000772236
ENSG00000102996.4_2	MMP15	protein_coding	0.741929652	0.000329449
ENSG00000183010.16_3	PYCR1	protein_coding	0.741790883	0.000324146
ENSG00000140265.12_2	ZSCAN29	protein_coding	0.740448481	0.000550805
ENSG00000177363.4_2	LRRN4CL	protein_coding	0.735303319	0.001048188
ENSG00000124523.15_3	SIRT5	protein_coding	0.732406925	6.23984E-05
ENSG00000158373.8_3	HIST1H2BD	protein_coding	0.732404034	0.002083634
ENSG00000133816.13_3	MICAL2	protein_coding	0.730957435	0.012234481
ENSG00000065833.8_2	ME1	protein_coding	0.730428454	0.000485356
ENSG00000107798.17_3	LIPA	protein_coding	0.730353899	2.16052E-05
ENSG00000060982.14_2	BCAT1	protein_coding	0.730168303	0.000253877
ENSG00000129009.12_3	ISLR	protein_coding	0.727602494	0.000376622
ENSG00000187239.16_2	FNBP1	protein_coding	0.725014739	2.50843E-06
ENSG00000074935.13_2	TUBE1	protein_coding	0.724459727	2.54254E-05
ENSG00000170624.13_2	SGCD	protein_coding	0.72434134	0.001339373
ENSG00000172845.14_2	SP3	protein_coding	0.722578157	0.000304159
ENSG00000115884.10_2	SDC1	protein_coding	0.716827048	0.000231197
ENSG00000129925.10_2	TMEM8A	protein_coding	0.716478491	9.48265E-06
ENSG00000175197.11_3	DDIT3	protein_coding	0.715990922	0.032597728
ENSG00000272325.1_3	NUDT3	protein_coding	0.714965116	0.004931558
ENSG00000154359.12_2	LONRF1	protein_coding	0.714415452	0.000212844
ENSG00000168672.3_2	FAM84B	protein_coding	0.712069014	0.000383281
ENSG00000148468.16_2	FAM171A1	protein_coding	0.709058584	8.95812E-05
ENSG00000164237.8_2	CMBL	protein_coding	0.707369474	0.000499888
ENSG00000138772.12_3	ANXA3	protein_coding	0.706908016	7.48217E-06
ENSG00000182400.14_3	TRAPPC6B	protein_coding	0.706556875	0.000208448
ENSG00000176953.12_4	NFATC2IP	protein_coding	0.705571602	0.044285498
ENSG00000187605.15_2	TET3	protein_coding	0.705503833	0.000630511
ENSG00000189060.5_2	H1F0	protein_coding	0.704342962	0.000173128

ENSG00000254692.1_4	AL136295.1	protein_coding	0.694169757	0.033241395
ENSG00000120053.10_2	GOT1	protein_coding	0.692799974	6.20954E-05
ENSG00000124249.6_3	KCNK15	protein_coding	0.692560251	0.005255664
ENSG00000256043.2_2	CTSO	protein_coding	0.691776045	4.51676E-05
ENSG00000115129.13_2	TP53I3	protein_coding	0.691256296	0.000226921
ENSG00000240303.7_3	ACAD11	protein_coding	0.690873867	0.000127334
ENSG00000107821.14_2	KAZALD1	protein_coding	0.689245823	0.000310545
ENSG00000171552.12_3	BCL2L1	protein_coding	0.688962322	0.000823731
ENSG00000014919.12_2	COX15	protein_coding	0.688843857	2.99887E-06
ENSG00000165312.6_2	OTUD1	protein_coding	0.687439416	0.001954855
ENSG00000189129.13_2	PLAC9	protein_coding	0.687183913	0.001019942
ENSG00000163071.10_2	SPATA18	protein_coding	0.686496844	0.000557557
ENSG00000042493.15_2	CAPG	protein_coding	0.686397019	2.18954E-06
ENSG00000070061.14_3	ELP1	protein_coding	0.685595791	0.000431272
ENSG00000103653.16_3	CSK	protein_coding	0.684759387	0.001246672
ENSG00000198121.13_3	LPAR1	protein_coding	0.684377889	0.000488404
ENSG00000102572.14_3	STK24	protein_coding	0.684036341	0.002296846
ENSG00000183479.8	TREX2	protein_coding	0.682045323	0.003815659
ENSG00000106823.12_3	ECM2	protein_coding	0.681335582	8.20616E-06
ENSG00000120820.12_2	GLT8D2	protein_coding	0.680011645	7.66562E-05
ENSG00000175390.13_3	EIF3F	protein_coding	0.678778612	0.001098454
ENSG00000182168.14_2	UNC5C	protein_coding	0.678085237	0.001729523
ENSG00000112936.18_2	C7	protein_coding	0.676976798	7.67511E-05
ENSG00000152779.13_3	SLC16A12	protein_coding	0.675657348	0.000244323
ENSG00000139899.10_2	CBLN3	protein_coding	0.674254076	0.000105193
ENSG00000021762.19_3	OSBPL5	protein_coding	0.673065816	0.000799217
ENSG00000150764.13_3	DIXDC1	protein_coding	0.672214544	0.000234375
ENSG00000117153.15_3	KLHL12	protein_coding	0.671710426	0.000434186
ENSG00000071282.11_2	LMCD1	protein_coding	0.67156883	0.014206351
ENSG00000185624.14_2	P4HB	protein_coding	0.671339915	0.001680288
ENSG00000033327.12_3	GAB2	protein_coding	0.670040198	0.002006645
ENSG00000177283.7_3	FZD8	protein_coding	0.668770439	0.000794403
ENSG00000011201.11_3	ANOS1	protein_coding	0.668353175	0.000509465
ENSG00000142046.14_3	TMEM91	protein_coding	0.668117453	0.038108078
ENSG00000179772.7_2	FOXS1	protein_coding	0.667876713	0.001733408
ENSG00000165698.15_3	SPACA9	protein_coding	0.66655589	0.004788478
ENSG00000204219.9_2	TCEA3	protein_coding	0.666186605	0.000611915
ENSG00000140931.19_3	CMTM3	protein_coding	0.664758289	0.007517401
ENSG00000267952.1_4	AC008878.1	protein_coding	0.663130819	0.031816198
ENSG00000167110.17_3	GOLGA2	protein_coding	0.662049849	7.56361E-05
ENSG00000047932.13_3	GOPC	protein_coding	0.661846517	0.001030043
ENSG00000168077.13_2	SCARA3	protein_coding	0.66102998	0.000151156
ENSG00000079156.16_2	OSBPL6	protein_coding	0.65898181	5.55389E-05
ENSG00000172992.11_2	DCAKD	protein_coding	0.658160955	0.000135485

ENSG00000144566.10_3	RAB5A	protein_coding	0.657909317	0.000404209
ENSG00000197930.12_3	ERO1A	protein_coding	0.656354531	0.000378686
ENSG00000154813.9_2	DPH3	protein_coding	0.654991308	0.00119591
ENSG00000198380.12_2	GFPT1	protein_coding	0.654413945	0.000268423
ENSG00000187955.11_2	COL14A1	protein_coding	0.654410578	0.001615857
ENSG00000166197.16_3	NOLC1	protein_coding	0.652695004	0.024007448
ENSG00000168495.12_3	POLR3D	protein_coding	0.651310251	0.000770357
ENSG00000143196.4_2	DPT	protein_coding	0.651099702	0.004063104
ENSG00000196182.10_2	STK40	protein_coding	0.650885632	0.000219445
ENSG00000130309.10_4	COLGALT1	protein_coding	0.650294782	0.000104285
ENSG00000111816.7_2	FRK	protein_coding	0.649720377	0.000375826
ENSG00000185437.13_3	SH3BGR	protein_coding	0.648541406	0.002623696
ENSG00000157227.12_2	MMP14	protein_coding	0.648343132	0.000906219
ENSG00000168994.13_2	PXDC1	protein_coding	0.646641245	0.002235544
ENSG00000103512.14_3	NOMO1	protein_coding	0.646381907	0.000117748
ENSG00000112769.18_3	LAMA4	protein_coding	0.646210538	0.000283336
ENSG00000184014.7_3	DENND5A	protein_coding	0.645173184	0.000455677
ENSG00000164402.13_4	SEPT8	protein_coding	0.644497064	0.000474279
ENSG00000247315.3_2	ZCCHC3	protein_coding	0.642904828	0.000359434
ENSG00000112759.16_2	SLC29A1	protein_coding	0.64261856	0.000642604
ENSG00000164253.13_4	WDR41	protein_coding	0.642336121	2.44294E-05
ENSG00000109436.7_3	TBC1D9	protein_coding	0.642170156	0.000287264
ENSG00000138757.14_2	G3BP2	protein_coding	0.641497567	0.017708485
ENSG00000155111.14_3	CDK19	protein_coding	0.641303161	0.001243923
ENSG00000197093.10_2	GAL3ST4	protein_coding	0.640270314	0.037501607
ENSG00000175906.4_2	ARL4D	protein_coding	0.637983074	0.006406003
ENSG00000076356.6_2	PLXNA2	protein_coding	0.637244628	0.000517655
ENSG00000111817.16_3	DSE	protein_coding	0.636877224	0.000867438
ENSG00000164823.9_2	OSGIN2	protein_coding	0.636627374	2.3539E-05
ENSG00000087303.17_3	NID2	protein_coding	0.636429797	0.000492726
ENSG00000077684.15_3	JADE1	protein_coding	0.634128355	0.030323512
ENSG00000114853.13_2	ZBTB47	protein_coding	0.633713865	0.001151219
ENSG00000250067.11_3	YJEFN3	protein_coding	0.633370073	0.009681573
ENSG00000166173.10_3	LARP6	protein_coding	0.631747454	0.001453858
ENSG00000063245.14_3	EPN1	protein_coding	0.631734256	0.000360583
ENSG00000138413.13_2	IDH1	protein_coding	0.631729511	0.00024937
ENSG00000143971.7_2	ETAA1	protein_coding	0.629233761	0.000622396
ENSG00000188811.13_3	NHLRC3	protein_coding	0.628933576	1.57168E-06
ENSG00000120656.11_2	TAF12	protein_coding	0.628922746	0.032073369
ENSG00000232859.9_3	LYRM9	protein_coding	0.627011609	4.18203E-05
ENSG00000186377.7_2	CYP4X1	protein_coding	0.626228105	0.002035288
ENSG00000117543.20_3	DPH5	protein_coding	0.625178112	0.007521113
ENSG00000111450.13_3	STX2	protein_coding	0.625103836	4.81636E-05
ENSG00000166797.10_2	FAM96A	protein_coding	0.624719322	0.001051689

ENSG00000136026.13_3	CKAP4	protein_coding	0.623842183	0.000162643
ENSG00000143387.12_2	CTSK	protein_coding	0.623617918	0.003975088
ENSG00000138061.11_3	CYP1B1	protein_coding	0.623410962	0.002023117
ENSG00000162976.12_2	PQLC3	protein_coding	0.621752424	0.022164316
ENSG00000138623.9_3	SEMA7A	protein_coding	0.621210859	0.000409678
ENSG00000196284.15_4	SUPT3H	protein_coding	0.61932536	0.001345464
ENSG00000101311.15_2	FERMT1	protein_coding	0.618976364	1.04802E-05
ENSG00000124786.9_2	SLC35B3	protein_coding	0.618903345	0.000254911
ENSG00000163393.12_2	SLC22A15	protein_coding	0.618676217	0.00061812
ENSG00000088280.18_3	ASAP3	protein_coding	0.618066148	0.000297523
ENSG00000185164.10	NOMO2	protein_coding	0.617034012	1.2137E-05
ENSG00000121057.12_3	AKAP1	protein_coding	0.616677797	0.02867769
ENSG00000066117.14_2	SMARCD1	protein_coding	0.613676928	0.013086878
ENSG00000133195.11_3	SLC39A11	protein_coding	0.612906215	0.000571065
ENSG00000145545.11_2	SRD5A1	protein_coding	0.610160877	0.003998333
ENSG00000165661.16_3	QSOX2	protein_coding	0.607604293	0.003454953
ENSG00000185483.11_2	ROR1	protein_coding	0.60686039	5.37881E-05
ENSG00000075239.13_2	ACAT1	protein_coding	0.606451811	3.98814E-05
ENSG00000001461.16_2	NIPAL3	protein_coding	0.606021006	4.76745E-05
ENSG00000186889.9_3	TMEM17	protein_coding	0.605909911	0.000400985
ENSG00000167074.14_2	TEF	protein_coding	0.605647496	0.000349639
ENSG00000119681.11_3	LTBP2	protein_coding	0.605458344	0.002992261
ENSG00000119699.7_2	TGFB3	protein_coding	0.603694406	0.000240679
ENSG00000196562.14_3	SULF2	protein_coding	0.603487681	0.003453815
ENSG00000205978.5_2	NYNRIN	protein_coding	0.603037344	0.000886138
ENSG00000133466.13_2	C1QTNF6	protein_coding	0.602703727	6.8759E-05
ENSG00000109089.7_2	CDR2L	protein_coding	0.601801389	0.000384239
ENSG00000138768.14_3	USO1	protein_coding	0.601628821	4.30603E-05
ENSG00000140105.17_3	WARS	protein_coding	0.601125977	0.009651498
ENSG00000100246.12_3	DNAL4	protein_coding	0.601112472	0.004352994
ENSG00000136628.17_2	EPRS	protein_coding	0.599818734	2.18691E-05
ENSG00000116584.17_3	ARHGEF2	protein_coding	0.59929021	0.002457169
ENSG00000165804.15_3	ZNF219	protein_coding	0.59924415	0.001704725
ENSG00000150281.6_2	CTF1	protein_coding	0.598972	0.002655804
ENSG00000263465.4_2	SRSF8	protein_coding	0.598888429	0.000348072
ENSG00000144231.10_3	POLR2D	protein_coding	0.59824761	0.002873071
ENSG00000102886.14_2	GDPD3	protein_coding	0.597717102	0.002258695
ENSG00000182809.10_2	CRIP2	protein_coding	0.597550602	0.000124975
ENSG00000175414.6_3	ARL10	protein_coding	0.597359878	9.88689E-06
ENSG00000174738.12_2	NR1D2	protein_coding	0.596696227	7.86148E-05
ENSG00000099377.13_3	HSD3B7	protein_coding	0.595607662	0.001758445
ENSG00000127528.5_2	KLF2	protein_coding	0.595405893	0.000293816
ENSG00000100138.13_2	SNU13	protein_coding	0.593950613	0.045611331
ENSG00000095383.19_2	TBC1D2	protein_coding	0.593935722	0.014098193

ENSG00000101052.12_2	IFT52	protein_coding	0.593031634	0.000544425
ENSG00000187098.14_3	MITF	protein_coding	0.590088576	0.039807887
ENSG00000134590.13_3	RTL8C	protein_coding	0.589935269	0.03727062
ENSG00000023608.4_3	SNAPC1	protein_coding	0.589720402	0.000327223
ENSG00000198538.10_3	ZNF28	protein_coding	0.589458653	0.008928998
ENSG00000126603.8_2	GLIS2	protein_coding	0.589170809	0.000550615
ENSG00000106080.10_2	FKBP14	protein_coding	0.589022868	0.00188278
ENSG00000106683.14_2	LIMK1	protein_coding	0.587837192	4.85274E-05
ENSG00000079150.17_2	FKBP7	protein_coding	0.587575008	0.00108472
ENSG00000157168.18_1	NRG1	protein_coding	0.586925922	0.003905507
ENSG00000183889.12_4	AC138969.1	protein_coding	0.586799825	0.013160193
ENSG00000196305.17_3	IARS	protein_coding	0.586742616	0.001246922
ENSG00000142871.16_3	CYR61	protein_coding	0.585057428	0.000397652

Down-regulated genes (siPALMD vs siScrambled)

Annotation			**DE**	**Statistic**
Track_id	**Gene_Name**	**Gene_Type**	**log2FC**	**p_value**
ENSG00000152952.11_2	PLOD2	protein_coding	-2.86293756	9.06264E-07
ENSG00000102158.19_2	MAGT1	protein_coding	-2.08821818	1.74435E-06
ENSG00000117152.13_2	RGS4	protein_coding	-2.0274694	0.027407324
ENSG00000139921.12_2	TMX1	protein_coding	-1.88016391	3.95532E-06
ENSG00000113369.8_2	ARRDC3	protein_coding	-1.86272291	7.13887E-06
ENSG00000136244.11_3	IL6	protein_coding	-1.69844461	0.000775013
ENSG00000158270.11_3	COLEC12	protein_coding	-1.66723856	7.84803E-08
ENSG00000143870.12_3	PDIA6	protein_coding	-1.66423617	3.68071E-05
ENSG00000186479.4_2	RGS7BP	protein_coding	-1.6238444	0.000194663
ENSG00000142166.12_3	IFNAR1	protein_coding	-1.59249996	1.12624E-06
ENSG00000139132.14_3	FGD4	protein_coding	-1.58784292	0.008591588
ENSG00000144959.9_3	NCEH1	protein_coding	-1.57724256	0.000268467
ENSG00000112902.11_3	SEMA5A	protein_coding	-1.51866446	8.04165E-05
ENSG00000186310.9_3	NAP1L3	protein_coding	-1.5152978	1.68852E-06
ENSG00000197632.8_3	SERPINB2	protein_coding	-1.49553388	0.002181303
ENSG00000163659.12_3	TIPARP	protein_coding	-1.45725787	0.00031039
ENSG00000141429.13_3	GALNT1	protein_coding	-1.45093121	0.006261528
ENSG00000099260.10_2	PALMD	protein_coding	-1.43530104	0.000118258
ENSG00000143815.14_3	LBR	protein_coding	-1.43034887	3.57094E-05
ENSG00000151422.12_3	FER	protein_coding	-1.42569959	0.002929752
ENSG00000141574.7_4	SECTM1	protein_coding	-1.39784903	0.000179999
ENSG00000111276.10_3	CDKN1B	protein_coding	-1.36592901	6.55204E-06
ENSG00000011426.10_3	ANLN	protein_coding	-1.35843995	2.10674E-05
ENSG00000214194.8_4	SMIM30	protein_coding	-1.35802116	0.00078282
ENSG00000115274.14_3	INO80B	protein_coding	-1.35454749	0.004075923
ENSG00000115738.9_2	ID2	protein_coding	-1.35367847	0.017192273

ENSG00000181751.9_2	C5orf30	protein_coding	-1.34544334	2.1097E-06
ENSG00000131747.14_2	TOP2A	protein_coding	-1.30091112	9.2955E-05
ENSG00000125965.8_2	GDF5	protein_coding	-1.2970864	3.50586E-05
ENSG00000061676.14_2	NCKAP1	protein_coding	-1.27408742	1.33571E-05
ENSG00000160307.9_2	S100B	protein_coding	-1.26704701	0.000220472
ENSG00000118971.7_3	CCND2	protein_coding	-1.26059061	0.000101254
ENSG00000013297.10_3	CLDN11	protein_coding	-1.25785862	0.001107445
ENSG00000198431.15_3	TXNRD1	protein_coding	-1.24742927	0.012937492
ENSG00000189067.12_3	LITAF	protein_coding	-1.23616667	0.023633326
ENSG00000112308.12_2	C6orf62	protein_coding	-1.23457405	2.31249E-06
ENSG00000118503.14_3	TNFAIP3	protein_coding	-1.23240368	0.000257499
ENSG00000152133.14_2	GPATCH11	protein_coding	-1.21260144	1.22198E-05
ENSG00000163293.11_3	NIPAL1	protein_coding	-1.2011278	0.000875546
ENSG00000172399.5_2	MYOZ2	protein_coding	-1.19039619	0.001235901
ENSG00000073737.16_3	DHRS9	protein_coding	-1.18605999	6.17671E-05
ENSG00000116962.14_2	NID1	protein_coding	-1.1812164	4.20219E-06
ENSG00000072952.18_3	MRVI1	protein_coding	-1.18075381	6.06286E-05
ENSG00000170113.15_4	NIPA1	protein_coding	-1.16924895	0.000819731
ENSG00000131389.16_2	SLC6A6	protein_coding	-1.16722432	8.71241E-05
ENSG00000153956.15_2	CACNA2D1	protein_coding	-1.16449806	0.000277177
ENSG00000125148.6_2	MT2A	protein_coding	-1.1634358	0.000205598
ENSG00000151474.21_3	FRMD4A	protein_coding	-1.15822575	3.69983E-05
ENSG00000181019.12_2	NQO1	protein_coding	-1.15573727	2.67418E-05
ENSG00000100697.14_2	DICER1	protein_coding	-1.15359065	0.001129352
ENSG00000164466.12_3	SFXN1	protein_coding	-1.15205179	2.38969E-05
ENSG00000065485.19_3	PDIA5	protein_coding	-1.13520706	7.54764E-05
ENSG00000154734.14_4	ADAMTS1	protein_coding	-1.13501299	2.52605E-05
ENSG00000140961.12_3	OSGIN1	protein_coding	-1.1286728	0.000547102
ENSG00000175274.18_4	TP53I11	protein_coding	-1.12771611	0.010114457
ENSG00000164114.18_3	MAP9	protein_coding	-1.11753402	1.2487E-05
ENSG00000137033.11_2	IL33	protein_coding	-1.1162228	0.001948578
ENSG00000068305.17_3	MEF2A	protein_coding	-1.10942011	0.000464964
ENSG00000134291.11_2	TMEM106C	protein_coding	-1.10507248	0.002643005
ENSG00000134333.13_3	LDHA	protein_coding	-1.10266491	0.001379304
ENSG00000123975.4_2	CKS2	protein_coding	-1.10065233	0.006507842
ENSG00000004864.13_2	SLC25A13	protein_coding	-1.09879013	8.68314E-06
ENSG00000113739.10_2	STC2	protein_coding	-1.09366138	3.75772E-05
ENSG00000064393.15_2	HIPK2	protein_coding	-1.0929059	0.000110888
ENSG00000123485.11_3	HJURP	protein_coding	-1.09103671	0.001097712
ENSG00000119950.20_4	MXI1	protein_coding	-1.0888804	0.044756437
ENSG00000116717.11_2	GADD45A	protein_coding	-1.08577922	0.00031651
ENSG00000164687.10_2	FABP5	protein_coding	-1.08391292	0.000621137
ENSG00000182985.17_3	CADM1	protein_coding	-1.07498677	0.001038704
ENSG00000071967.11_2	CYBRD1	protein_coding	-1.07488533	0.000174383

ENSG00000024526.16_3	DEPDC1	protein_coding	-1.06423137	0.000626322
ENSG00000167695.14_2	FAM57A	protein_coding	-1.0582906	0.03164808
ENSG00000154310.16_3	TNIK	protein_coding	-1.05412651	2.74547E-05
ENSG00000145675.14_2	PIK3R1	protein_coding	-1.05278813	0.009457626
ENSG00000170266.15_3	GLB1	protein_coding	-1.05274509	0.003053027
ENSG00000112984.11_3	KIF20A	protein_coding	-1.04703477	0.000304117
ENSG00000139734.17_3	DIAPH3	protein_coding	-1.04452656	8.87327E-06
ENSG00000158164.6_2	TMSB15A	protein_coding	-1.04111076	0.006699008
ENSG00000068489.12_3	PRR11	protein_coding	-1.04080942	0.000351373
ENSG00000141526.16_3	SLC16A3	protein_coding	-1.03762665	0.000251439
ENSG00000117399.13_2	CDC20	protein_coding	-1.03523083	0.000421673
ENSG00000198743.6_3	SLC5A3	protein_coding	-1.03421395	0.000682204
ENSG00000104368.17_3	PLAT	protein_coding	-1.02795009	0.000515857
ENSG00000170571.11_2	EMB	protein_coding	-1.02267524	3.83644E-05
ENSG00000081041.8_2	CXCL2	protein_coding	-1.01547238	0.005343847
ENSG00000165757.8_3	JCAD	protein_coding	-1.01369898	8.46998E-05
ENSG00000118777.10_3	ABCG2	protein_coding	-1.01280635	0.000799986
ENSG00000125538.11_3	IL1B	protein_coding	-1.01093546	0.000196716
ENSG00000082153.17_3	BZW1	protein_coding	-1.01070953	0.014577908
ENSG00000157600.11_2	TMEM164	protein_coding	-0.98823306	0.049425926
ENSG00000090889.11_2	KIF4A	protein_coding	-0.98604573	0.000160786
ENSG00000082482.13_3	KCNK2	protein_coding	-0.98157733	0.002454842
ENSG00000198961.9_2	PJA2	protein_coding	-0.97583946	7.63521E-05
ENSG00000067955.13_3	CBFB	protein_coding	-0.97221492	0.025073195
ENSG00000196616.13_2	ADH1B	protein_coding	-0.97023537	0.000537074
ENSG00000134668.12_3	SPOCD1	protein_coding	-0.96832988	0.000183787
ENSG00000106853.18_3	PTGR1	protein_coding	-0.96282207	0.000408145
ENSG00000107159.12_2	CA9	protein_coding	-0.95863966	0.000293369
ENSG00000164761.8_2	TNFRSF11B	protein_coding	-0.957875	0.000128008
ENSG00000198642.6_3	KLHL9	protein_coding	-0.9562934	9.44497E-05
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ENSG00000118705.16_3	RPN2	protein_coding	-0.94622231	5.33155E-05
ENSG00000274810.4_3	NPHP3-ACAD11	protein_coding	-0.94551795	0.000456829
ENSG00000196083.9_3	IL1RAP	protein_coding	-0.9451511	0.031842836
ENSG00000163814.7_3	CDCP1	protein_coding	-0.94296554	1.70082E-05
ENSG00000112144.15_2	ICK	protein_coding	-0.94270161	5.93777E-05
ENSG00000132718.8_2	SYT11	protein_coding	-0.93908095	7.14515E-06
ENSG00000108602.17_3	ALDH3A1	protein_coding	-0.93903495	0.00059009
ENSG00000139531.12_2	SUOX	protein_coding	-0.93290382	0.005839977
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ENSG00000184254.16_3	ALDH1A3	protein_coding	-0.92839702	0.000377707
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ENSG00000133983.14_3	COX16	protein_coding	-0.90830103	0.003099215
ENSG00000176170.13_2	SPHK1	protein_coding	-0.90496521	0.0291286
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ENSG00000135914.5_2	HTR2B	protein_coding	-0.89622302	0.00045987
ENSG00000271793.1_4	AL589666.1	protein_coding	-0.89580105	0.001192966
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ENSG00000174720.15_3	LARP7	protein_coding	-0.88000451	0.001133888
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Table S2. Clinical characteristics of CAVD patients for the isolation of hVICs.

Characteristics	CAVD (n=38)
Age, years	55.03±11.6
Male, %	97
Smoking, %	18
Hypertension, %	32
Diabetes mellitus, %	13
Bicuspid aortic valves, %	18
BMI, kg/m^2	24.94±3.6
triglycerides, mmol/L	1.65±1.36
LDL, mmol/L	3.12±0.84
HDL, mmol/L	1.13+0.41
Cholesterol, μmol/L	4.82±1.09
Statins, %	43
Beta-blocker, %	62
ACEI/ARB, %	46

CAVD indicates calcific aortic valve disease; BMI, body mass index; LDL, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol; ACEI/ARB, Angiotensin Converting Enzyme Inhibitors/Angiotensin Receptor Blockers. Values are presented as mean±SD when appropriate.

Table S3. Primer sequences for RT-qPCR.

Gene of interest	Primer sequences used for RT-qPCR (5'-3')
human-β-actin-F	CATGTACGTTGCTATCCAGGC
human-β-actin-R	CTCCTTAATGTCACGCACGAT
human-GAPDH-F	GAGTCAACGGATTTGGTCGT
human-GAPDH-R	GACAAGCTTCCCGTTCTCAG
human-BMP2-F	TTCGGCCTGAAACAGAGACC
human-BMP2-R	CCTGAGTGCCTGCGATACAG
human-PALMD-F	ACAGAAGCGTCTGAAAATAGAGG
human-PALMD-R	TCCTTCGTTGAGATTTGCAGTTC
human-MSX2-F	TGGATGCAGGAACCCGG
human-MSX2-R	AGGGCTCATATGTCTTGGCG
human-ALPL-F	ACTGGTACTCAGACAACGAGAT
human-ALPL-R	ACGTCAATGTCCCTGATGTTATG
human-RUNX-F	GCCTTCCACTCTCAGTAAGAAGA
human-RUNX-R	GCCTGGGGTCTGAAAAAGGG
human-HIF1A-F	GAACGTCGAAAAGAAAAGTCTCG
human-HIF1A-R	CCTTATCAAGATGCGAACTCACA
human-SLC2A1-F	GGCCAAGAGTGTGCTAAAGAA
human-SLC2A1-R	ACAGCGTTGATGCCAGACAG
human-PFKFB3-F	AGCCCGGATTACAAAGACTGC
human-PFKFB3-R	GGTAGCTGGCTTCATAGCAAC
human-HK1-F	CACATGGAGTCCGAGGTTTATG
human-HK1-R	CGTGAATCCCACAGGTAACTTC
human-PDK4-F	GGAAGCATTGATCCTAACTGTGA
human-PDK4-R	GGTGAGAAGGAACATACACGATG
human-PFKP-F	GCATGGGTATCTACGTGGGG
human-PFKP-R	CTCTGCGATGTTTGAGCCTC
human-PGK1-F	GAACAAGGTTAAAGCCGAGCC
human-PGK1-R	GTGGCAGATTGACTCCTACCA
human-ENO1-F	GCCGTGAACGAGAAGTCCTG
human-ENO1-R	ACGCCTGAAGAGACTCGGT
human-LDHA-F	ATGGCAACTCTAAAGGATCAGC
human-LDHA-R	CCAACCCCAACAACTGTAATCT
human-PGM2-F	GAGCTGCTATGGGACCTGGA
human-PGM2-R	GCTCGGGCGTCAAAACTGA
human-PKM-F	AAGGGTGTGAACCTTCCTGG
human-PKM-R	GCTCGACCCCAAACTTCAGA
human-ALDOC-F	GCCAAATTGGGGTGGAAAACA
human-ALDOC-R	TTCACACGGTCATCAGCACTG
human-HK2-F	GAGCCACCACTCACCCTACT
human-HK2-R	CCAGGCATTCGGCAATGTG
human-TPI1-F	ACTGCCTATATCGACTTCGCC
human-TPI1-R	AAGCCCCATTAGTCACTTTGTAG

human-TUBB2B-F	GGCACGATGGATTCGGTTAGG
human-TUBB2B-R	ACACGAAATTGTCTGGTCTGAAG
human-CRABP2-F	ATCGGAAAACTTCGAGGAATTGC
human-CRABP2-R	AGGCTCTTACAGGGCCTCC
human-TRIB3-F	AAGCGGTTGGAGTTGGATGAC
human-TRIB3-R	CACGATCTGGAGCAGTAGGTG
human-RASSF8-F	AGTTCAGAGGATTGTTTGTGGAG
human-RASSF8-R	CACATCACTAGCATACTGCCC
human-ADM2-F	CTGAGCCCCATCTGAAGCC
human-ADM2-R	CAGCACTGCGTGTAGACCAG
human-SCG2-F	ACCAGACCTCAGGTTGGAAAA
human-SCG2-R	AAGTGGCTTTCATCGCCATTT
human-RABGEF1-F	ATGTGGATCAATCGGATCTCCT
human-RABGEF1-R	GCTTTGTGGTACTCTTCCCTCC
human-PSAT1-F	TGCCGCACTCAGTGTTGTTAG
human-PSAT1-R	GCAATTCCCGCACAAGATTCT
human-PCK2-F	GGCTGAGAATACTGCCACACT
human-PCK2-R	ACCGTCTTGCTCTCTACTCGT
human-GANAB-F	TGGGGATTACCCTTGCTGTG
human-GANAB-R	CCGTATGCTTCTCTGTCGCT
human-PLOD2-F	CATGGACACAGGATAATGGCTG
human-PLOD2-R	AGGGGTTGGTTGCTCAATAAAAA
human-MAGT1-F	ATCGTTTGCGACGTTCCCTC
human-MAGT1-R	ACGGAGTAATTTCTCGGTGGG
human-RGS4-F	ACATCGGCTAGGTTTCCTGC
human-RGS4-R	GTTGTGGGAAGAATTGTGTTCAC
human-TMX1-F	TTGCGAAAGTAGATGTCACAGAG
human-TMX1-R	CTGATAGCGCCTAAATTCACCAT
human-ARRDC3-F	TGTATTCTAGTGGGGATACCGTC
human-ARRDC3-R	TCGCATGTCCTCTTGCATGAA
human-IL6-F	ACTCACCTCTTCAGAACGAATTG
human-IL6-R	CCATCTTTGGAAGGTTCAGGTTG
human-COLEC12-F	AATCCTTCGGTTACAAGCGGT
human-COLEC12-R	ACTGTGATTGTTAGCAAGGCAC
human-PDIA6-F	GGACACTGCAAAAACCTAGAGC
human-PDIA6-R	CCAGAACCTGATTGACTGTAGCA
human-RGS7BP-F	CCTGGACGACTGCAAGATG
human-RGS7BP-R	ATGGCAGCCAATTTTTGGTGT
human-IFNAR1-F	ATTTACACCATTTCGCAAAGCTC
human-IFNAR1-R	TCCAAAGCCCACATAACACTATC
human-IL1B-F	AGCTACGAATCTCCGACCAC
human-IL1B-R	CGTTATCCCATGTGTCGAAGAA
human-TNFAIP3-F	TCCTCAGGCTTTGTATTTGAGC
human-TNFAIP3-R	TGTGTATCGGTGCATGGTTTTA

human-CASP3-F	CATGGAAGCGAATCAATGGACT
human-CASP3-R	CTGTACCAGACCGAGATGTCA
human-CXCL2-F	AAGTGTGAAGGTGAAGTCCC
human-CXCL2-R	CCATTTTTCAGCATCTTTTC
human-CARD10-F	CTGTGGGAGCGAATCGAGG
human-CARD10-R	CAGCGCAAGATGTCCATCA
human-CXCL12-F	ATTCTCAACACTCCAAACTGTGC
human-CXCL12-R	ACTTTAGCTTCGGGTCAATGC
human-CXCL8-F	ACTGAGAGTGATTGAGAGTGGAC
human-CXCL8-R	AACCCTCTGCACCCAGTTTTC
human-PGK1-F	GAACAAGGTTAAAGCCGAGCC
human-PGK1-R	GTGGCAGATTGACTCCTACCA
human-TNF-α-F	GAGGCCAAGCCCTGGTATG
human-TNF-α-R	CGGGCCGATTGATCTCAGC
human-PFKFB3 -F	CAACTCCCCAACCGTGATTGT
human-PFKFB3 -R	TGAGGTAGCGAGTCAGCTTCT
human-ICAM-1 -F	TTGGGCATAGAGACCCCGTT
human-ICAM-1 -R	GCACATTGCTCAGTTCATACACC
human-VCAM-1-F	TTTGACAGGCTGGAGATAGACT
human-VCAM-1-R	TCAATGTGTAATTTAGCTCGGCA
human-E-selectin-F	CAGCAAAGGTACACACACCTG
human-E-selectin-R	CAGACCCACACATTGTTGACTT

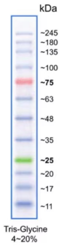
Table S4. Source of primary and secondary antibodies used in the present study

Antibodies	Source	Catlogue no.	Dilution
Cleaved Caspase-3	CST, Rabbit	9664s	1:2000 in 5%BSA
Caspase-3	CST, Rabbit	9662s	1:2000 in 5%BSA
Vimentin	Abcam, Mouse	ab8978	1:500 in for immunnofluorescence
SM22-α	Abcam, Rabbit	ab209484	1:500 in for immunnofluorescence
β-actin	SantaCruze, Mouse	SC81178	1:2000 in 5%BSA
p65	CST, Rabbit	8242s	1:2000 in 5%BSA
p-p65	Abcam, Rabbit	ab183559	1:2000 in 5%BSA
RUNX2	Abcam, Rabbit	ab23981	1:2000 in 5%BSA
PALMD	Proteintech, Rabbit	16531-1-AP	1:2000 in 5%BSA
Hexokinase 1	Abcam, Rabbit	ab150423	1:5000 in 5%BSA
PFKFB3	Abcam, Rabbit	ab181861	1:5000 in 5%BSA
BMP2	Abcam, Rabbit	ab214821	1:2000 in 5%BSA
MSX2	Abcam, Rabbit	ab223692	1:2000 in 5%BSA
BIP	Proteintech, Rabbit	11587-1-AP	1:2000 in 5%BSA
CD2AP	Proteintech, Rabbit	24122-1-AP	1:2000 in 5%BSA
MYH10	Proteintech, Rabbit	19673-1-AP	1:2000 in 5%BSA
MYH9	Proteintech, Rabbit	11128-1-AP	1:2000 in 5%BSA
FLAG	Proteintech, Mouse	66008-3-Ig	4μg used for immunoprecipitation
ICAM1	CST, Rabbit	67836T	1:2000 in 5%BSA
GAPDH	Proteintech, Rabbit	10494-1-AP	1:2000 in 5%BSA
Ant-mouse IgG HRP	CST	7076s	1:10000 in 5%BSA
Ant-rabbit IgG HRP	CST	7074s	1:10000 in 5%BSA

Table S5. Sequences of PALMD and PFKFB3 siRNA

siRNA	Sequence (5′-3′)
PALMD siRNA 1	GACUGAGGAUCCAUCCUUA
PALMD siRNA 2	GAUCCAGGUUCUAGAACAA
PALMD siRNA 3	GAUCCAAGAUCUUGAAAAA
PFKFB3 siRNA	AGUUGUAGGAGCUGUACUG

Unedited gels



The protein ladder used in this study was obtained from Absin, Shanghai, China (abs923-500μl). The image on the left is provided by the supplier, and shows the SDS-PAGE band profile of the Spectra Multicolor Broad Range of this protein ladder. All the maker lanes around the bands of interest are labelled according to this protein ladder for the whole unedited gels.

Figure 1 I

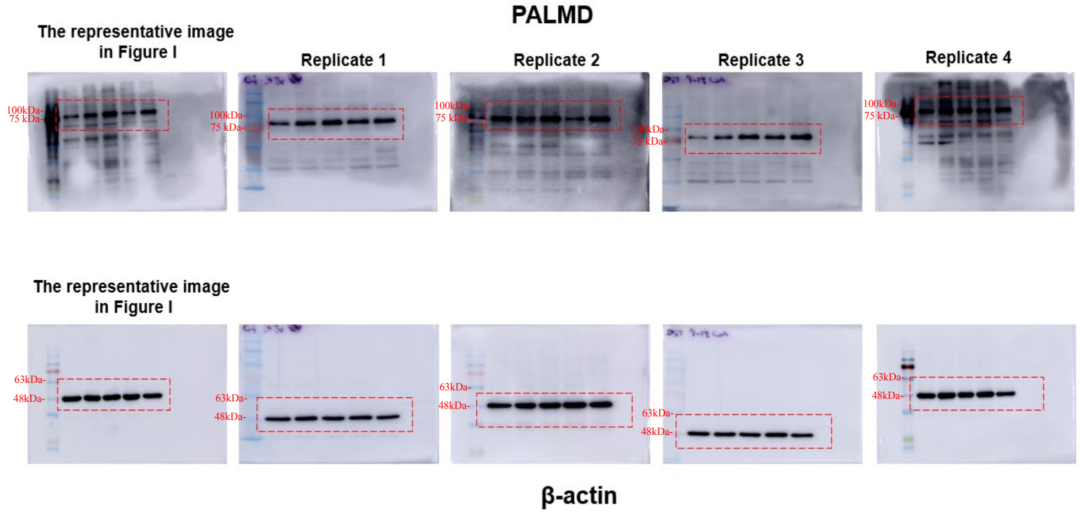
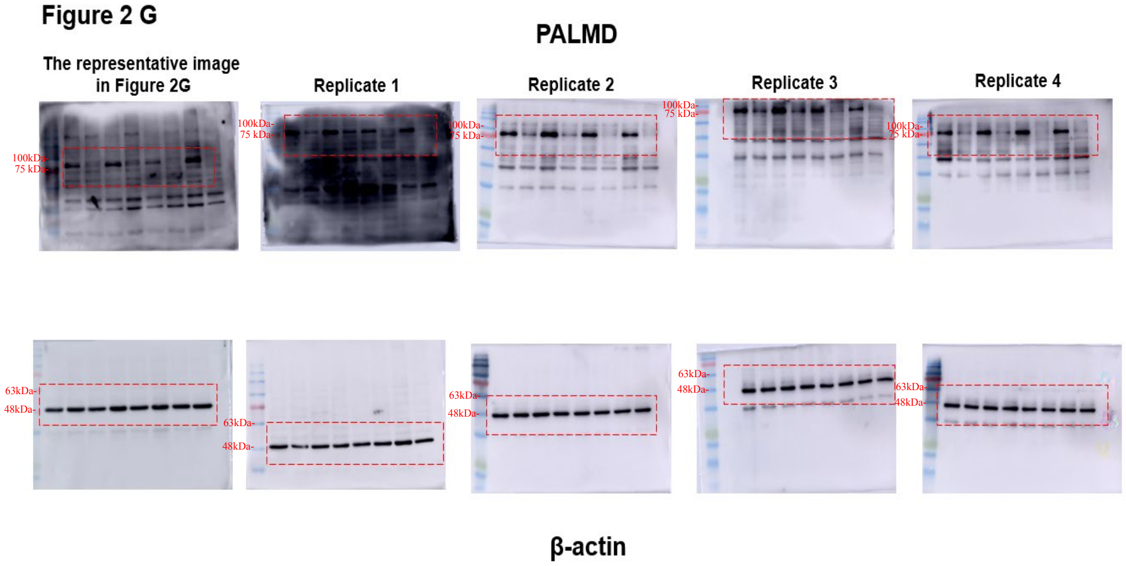


Figure 2 G



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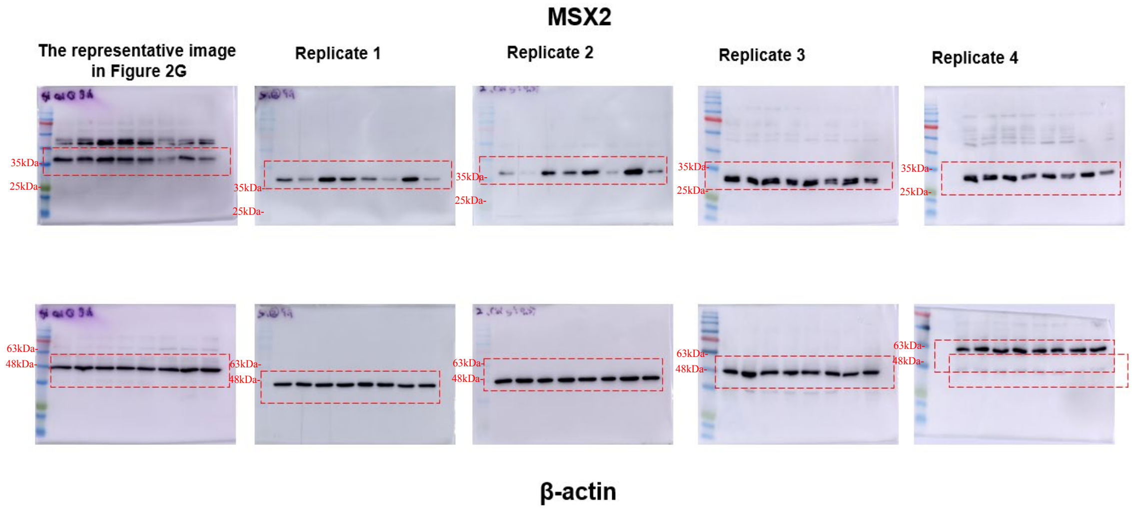

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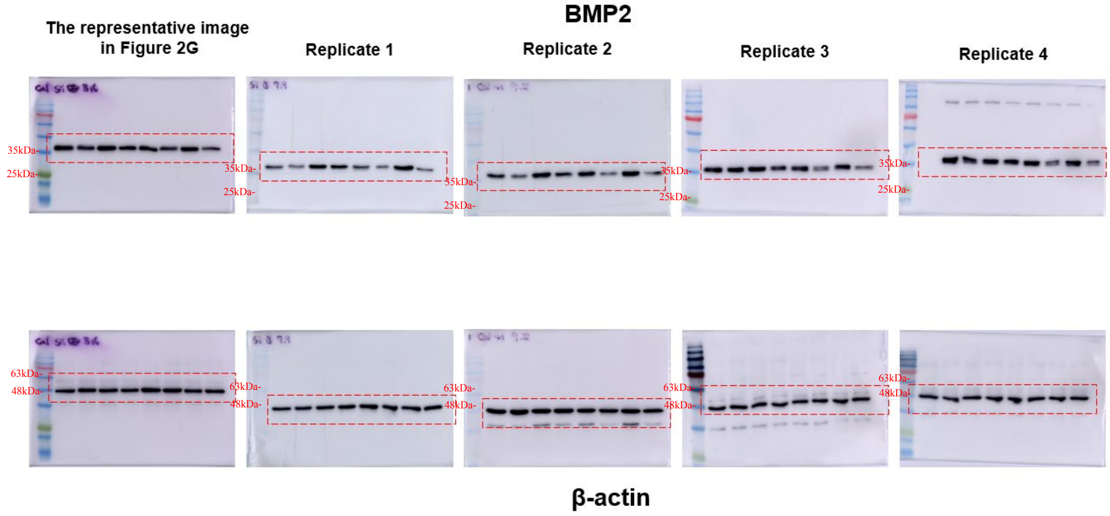

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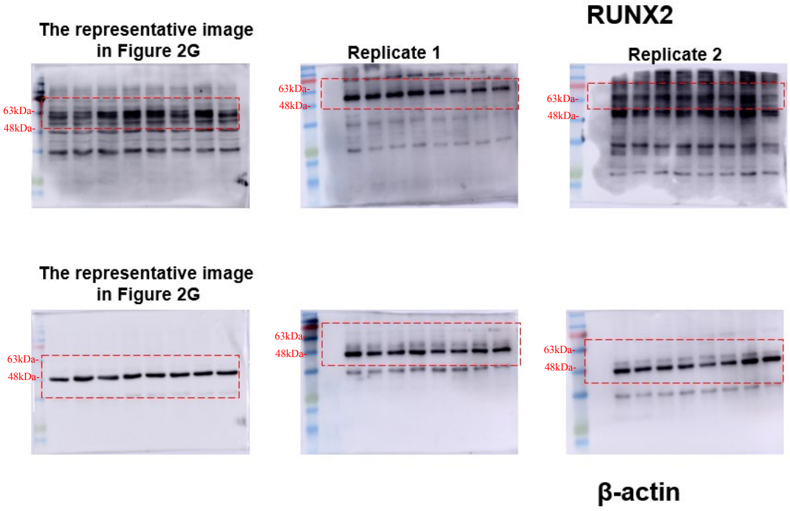

Figure 2 G

Cleaved-caspase3

The representative image in Figure 2G

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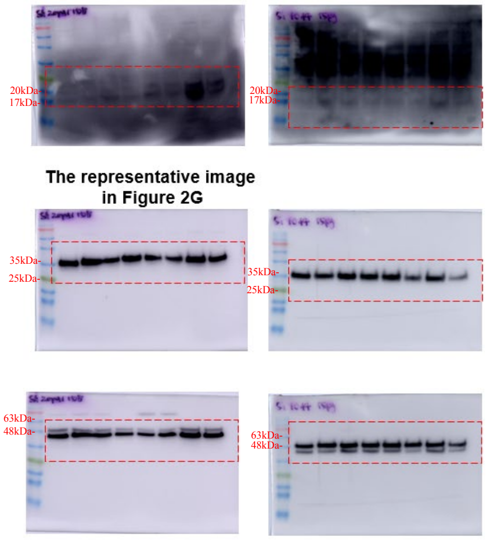


Caspase3

β-actin

Figure 2 L

PALMD

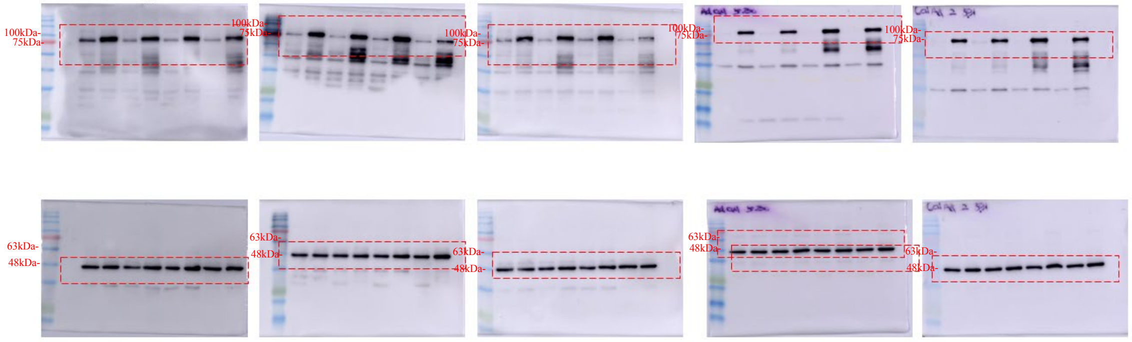
The representative image in Figure 2L

Replicate 1

Replicate 2

Replicate 3

Replicate 4



β-actin

Figure 2 L

MSX2

The representative image in Figure 2L

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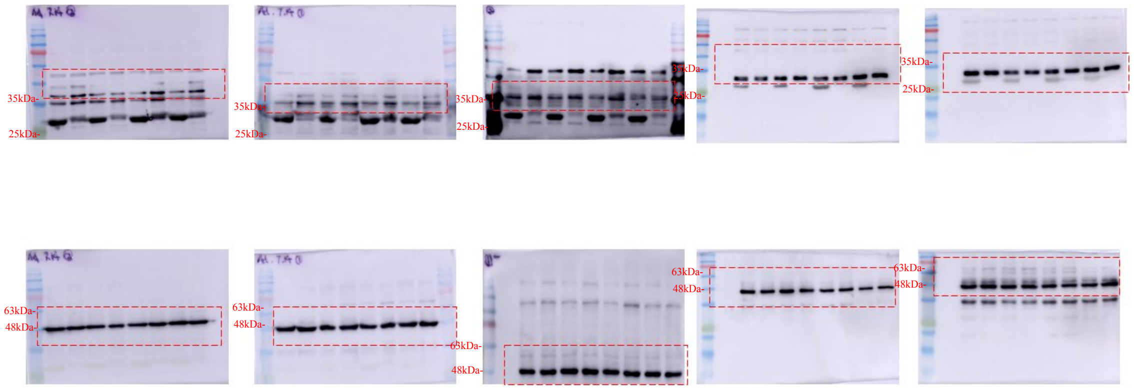
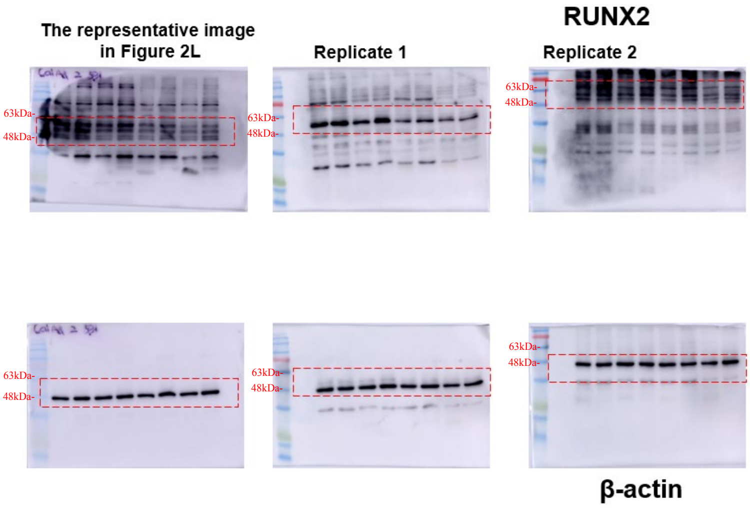


β-actin

Figure 2 L



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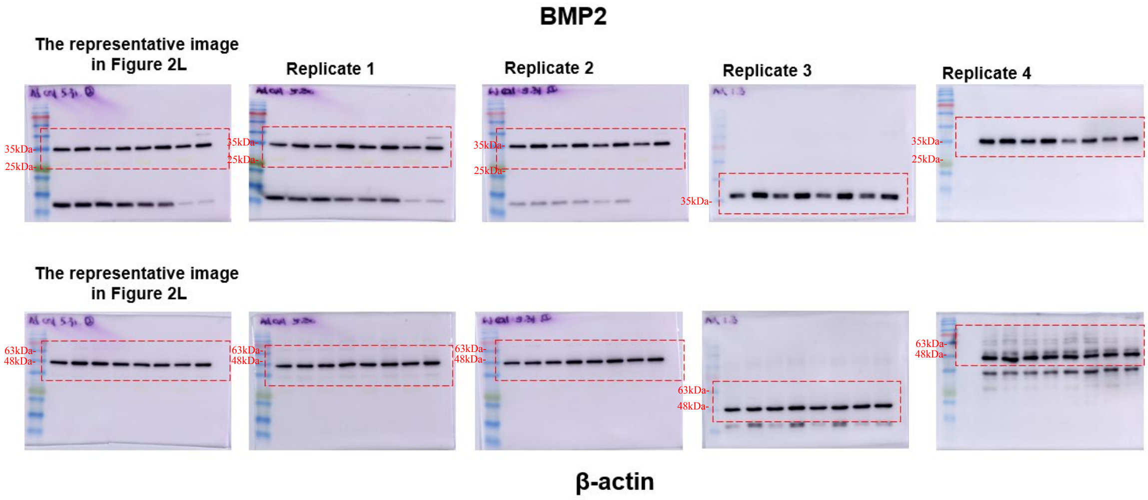

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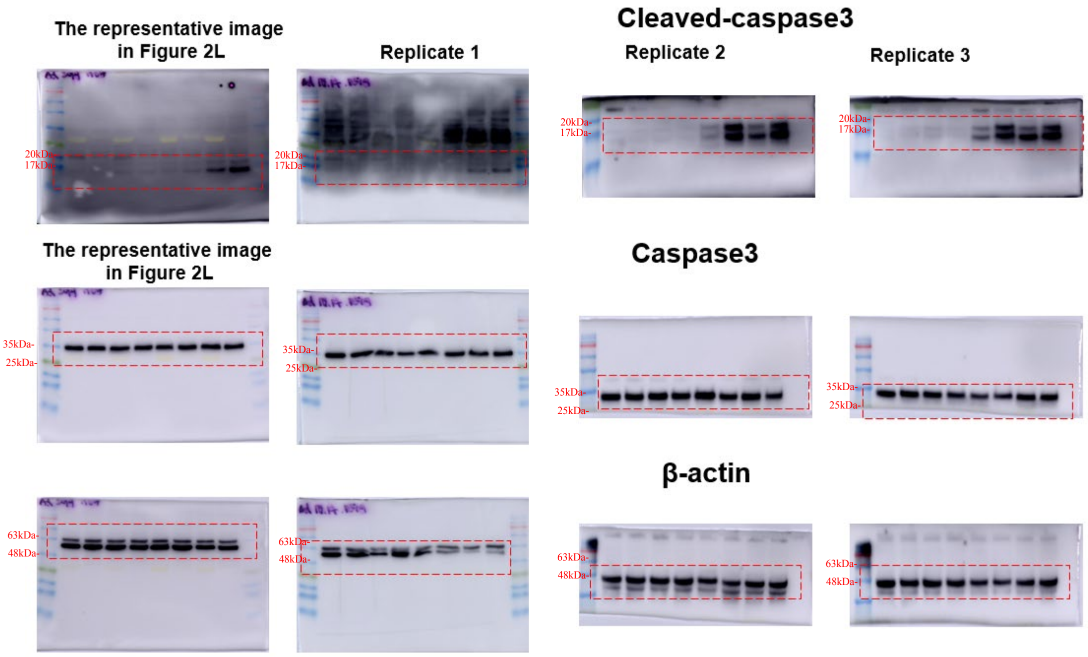

Figure 4 B

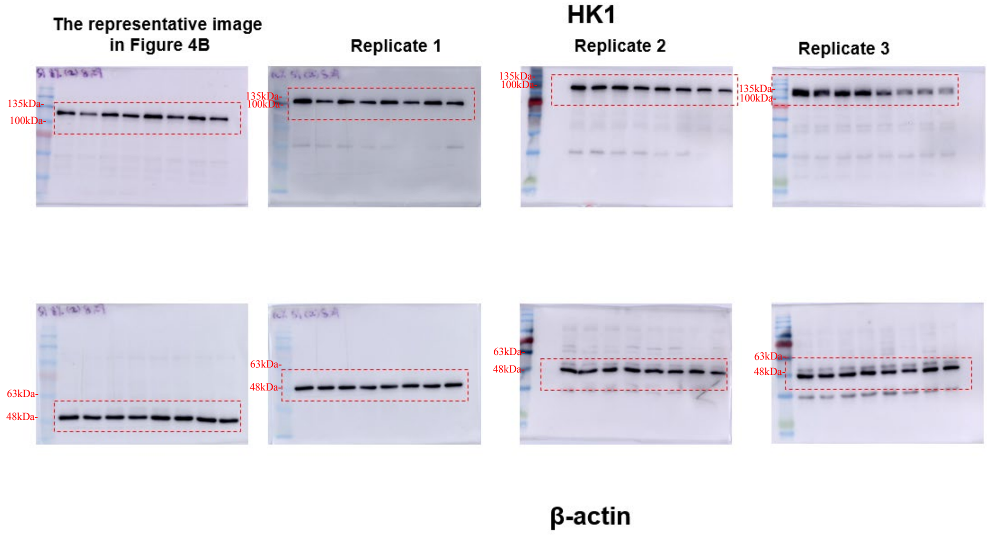

Figure 4 B

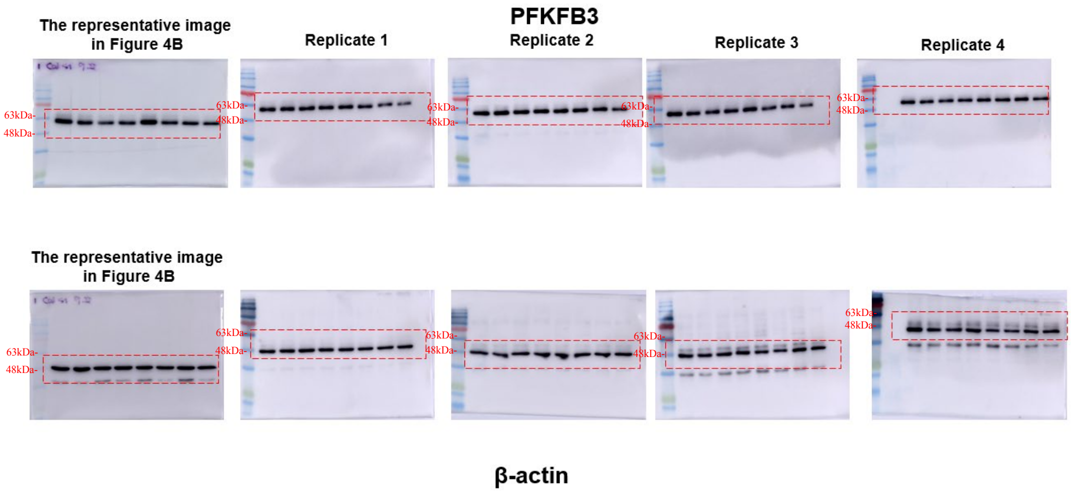

Figure 4 D

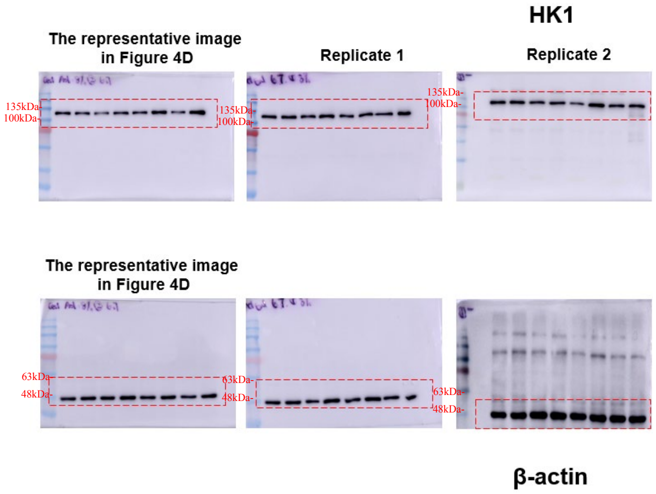

Figure 4 D

PFKFB3

The representative image in Figure 4D

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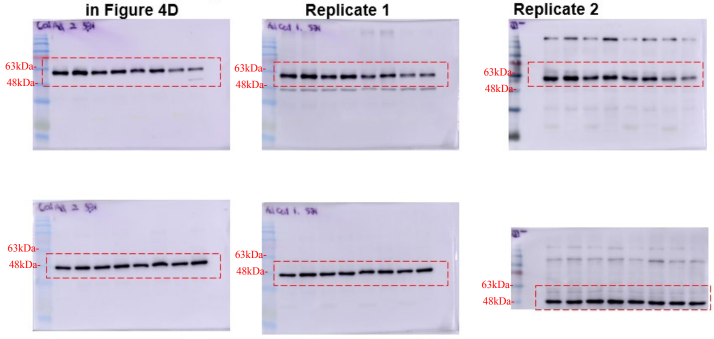
Replicate 2



β-actin

Figure 5 D

ICAM1

The representative image in Figure 5D

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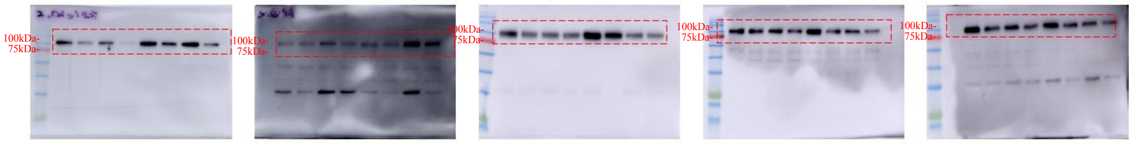
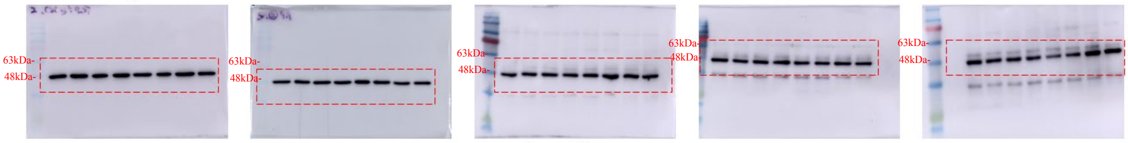
Replicate 3

Replicate 4



The representative image in Figure 5D



β-actin

Figure 5 G

ICAM1

The representative image in Figure 5G

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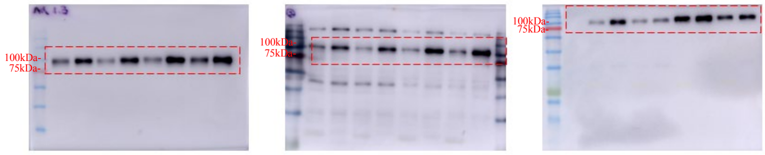
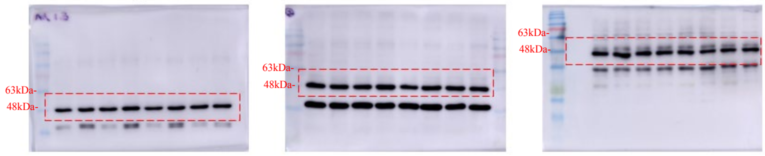


The representative image in Figure 5G



β-actin

Figure 5 H

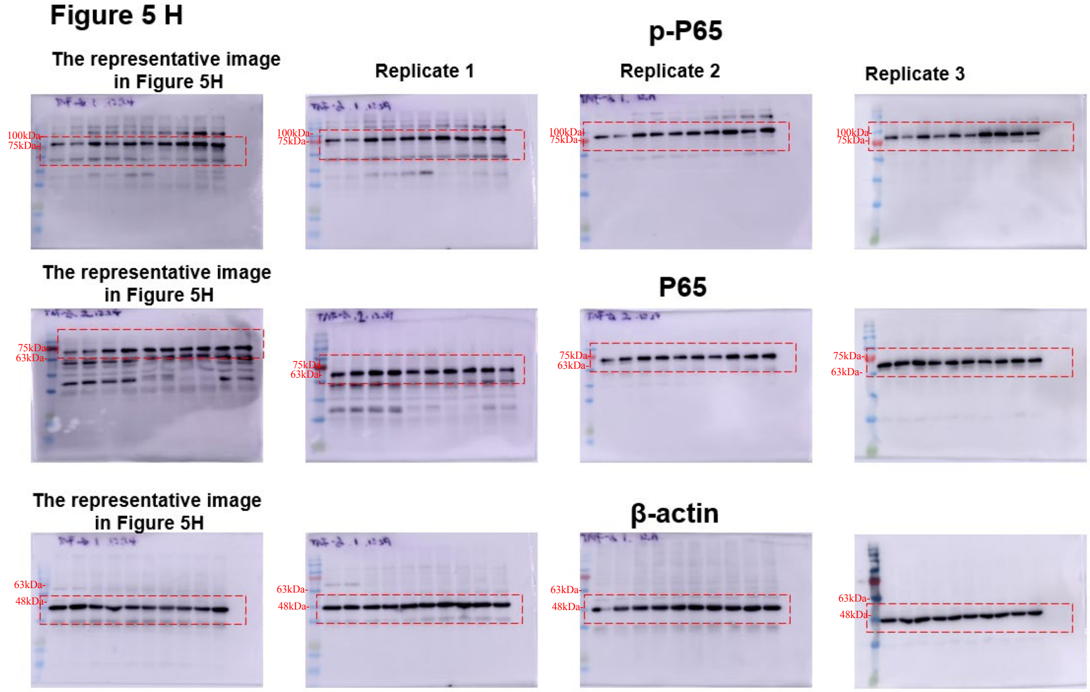


Figure 5 I

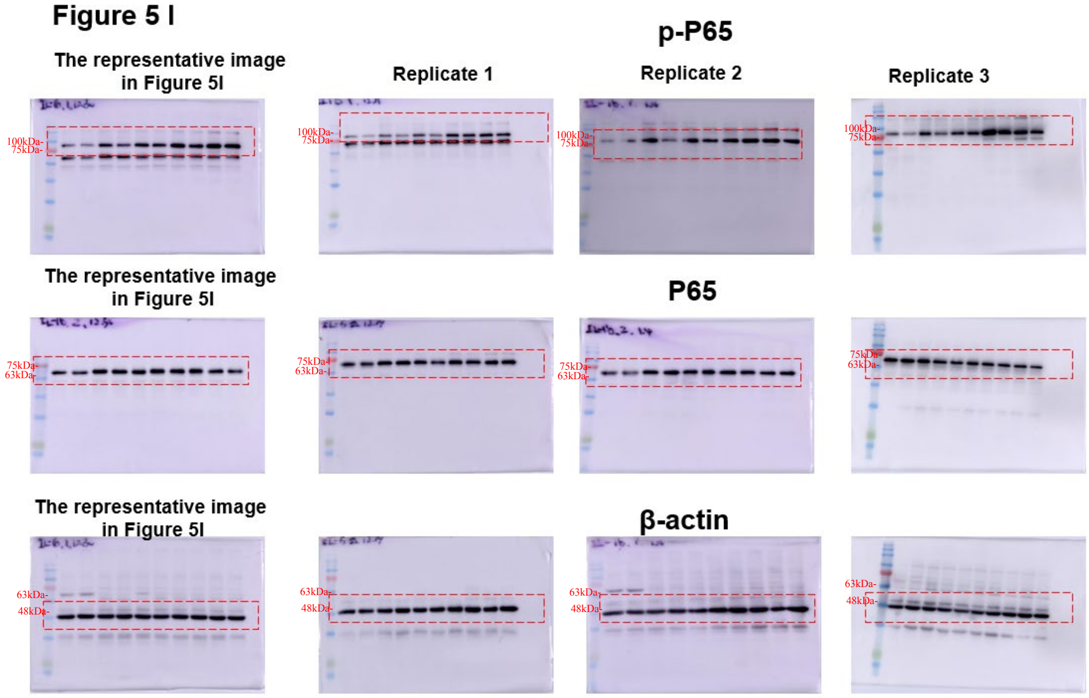
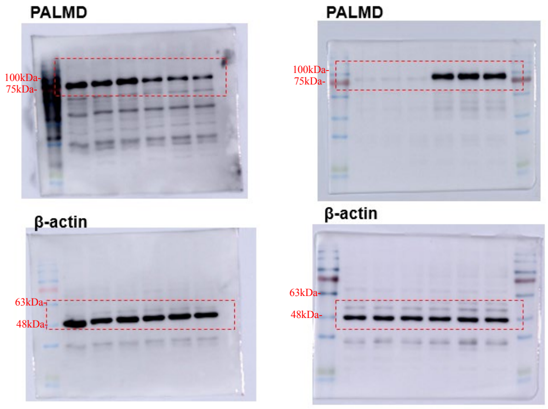
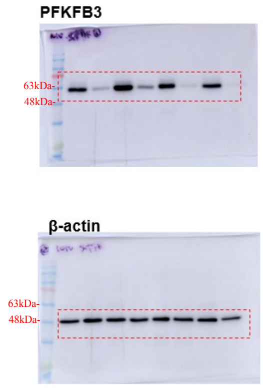


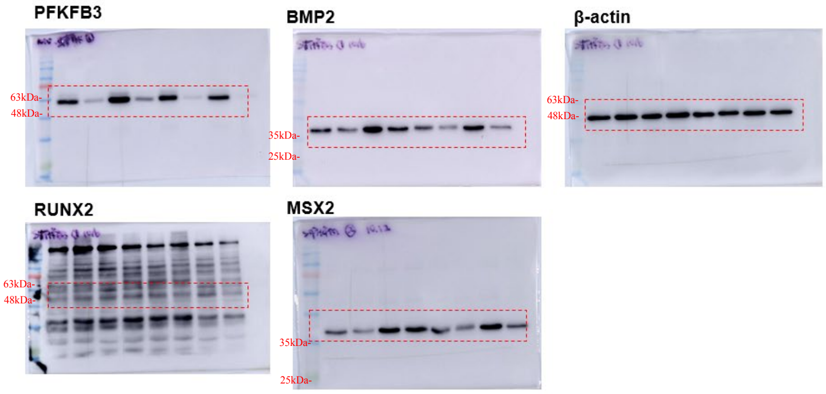
Figure S4



Supplementary Figure S13



Supplementary Figure S14G



Supplementary Figure S14J