

Evidences for KSHV-induced Mesenchymal-to-Endothelial Transition Transforming Oral Mesenchymal Stem Cell to Kaposi's Sarcoma

Supplementary Data

Fig. S1. Infectivity of KSHV in PDLSCs, GMSCs and DPSCs.

Fig. S2. Persistent KSHV infection in PDLSCs.

Fig. S3. Long-term cultured KSHV-infected PDLSCs preserve the potential of tubulogenesis and invasiveness.

Fig. S4. Expression of oral MSC-specific and endothelial markers in mock- and KSHV-infected MSCs in mouse kidney capsule implant.

Fig. S5. Gene expression profiling analysis of KSHV-infected oral MSCs.

Fig. S6. Top 20 significantly enriched Gene Ontology (GO) categories of molecular function and biological process in KSHV-infected PDLSC.

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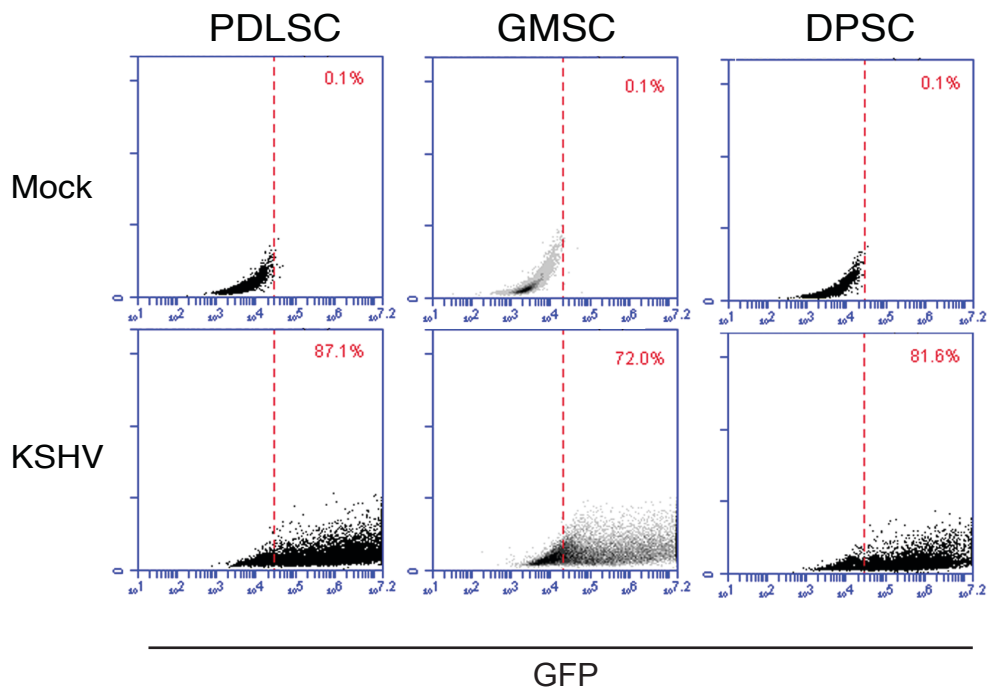
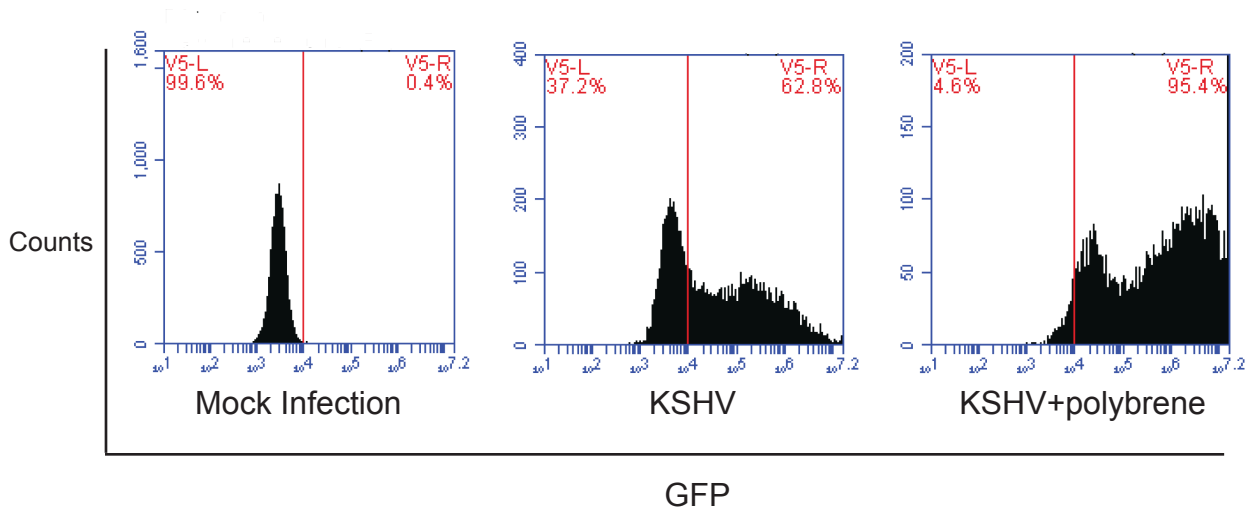
A**B**

Fig. S1. (A) Primary oral MSCs of different origins (PDLSCs, GMSCs and DPSCs) were infected with GFP-KSHV in an MOI of 50 (KSHV genome equivalent) in the presence of polybrene for 48 hours and analyzed by GFP fluorescence. The rates of KSHV infection were determined by flow cytometric analysis of GFP-expression cells. (B) Comparison of infectivity of KSHV to PDLSCs in the presence and absence of polybrene.

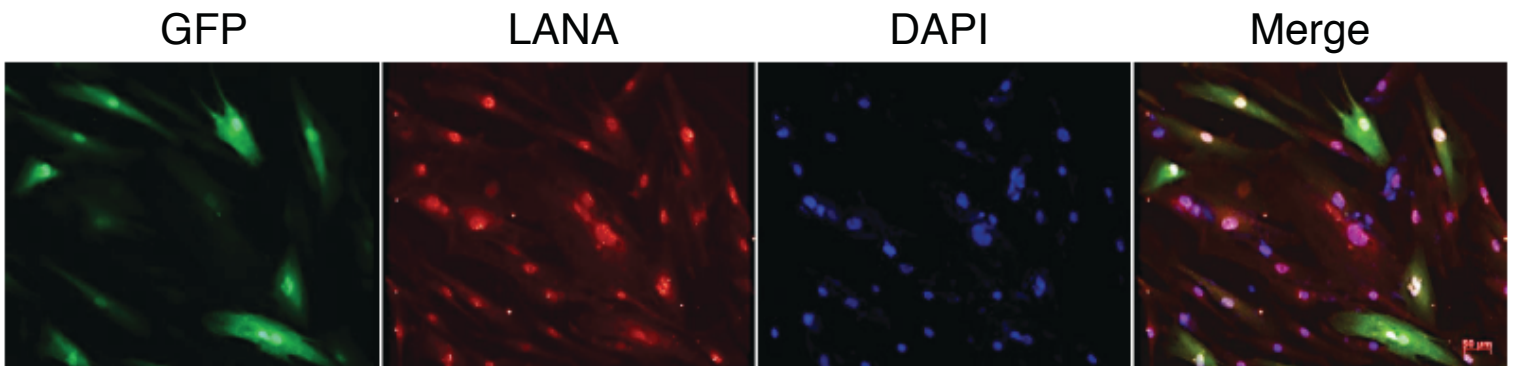


Fig. S2. Persistent KSHV infection in PDLSCs. Primary PDLSCs were infected with GFP-KSHV in an MOI of 50 (KSHV genome equivalent). Cells were cultured for four weeks with out any antibiotics selection. Cells were analyzed by GFP fluoresce and IFA with an anti-LANA antibody.

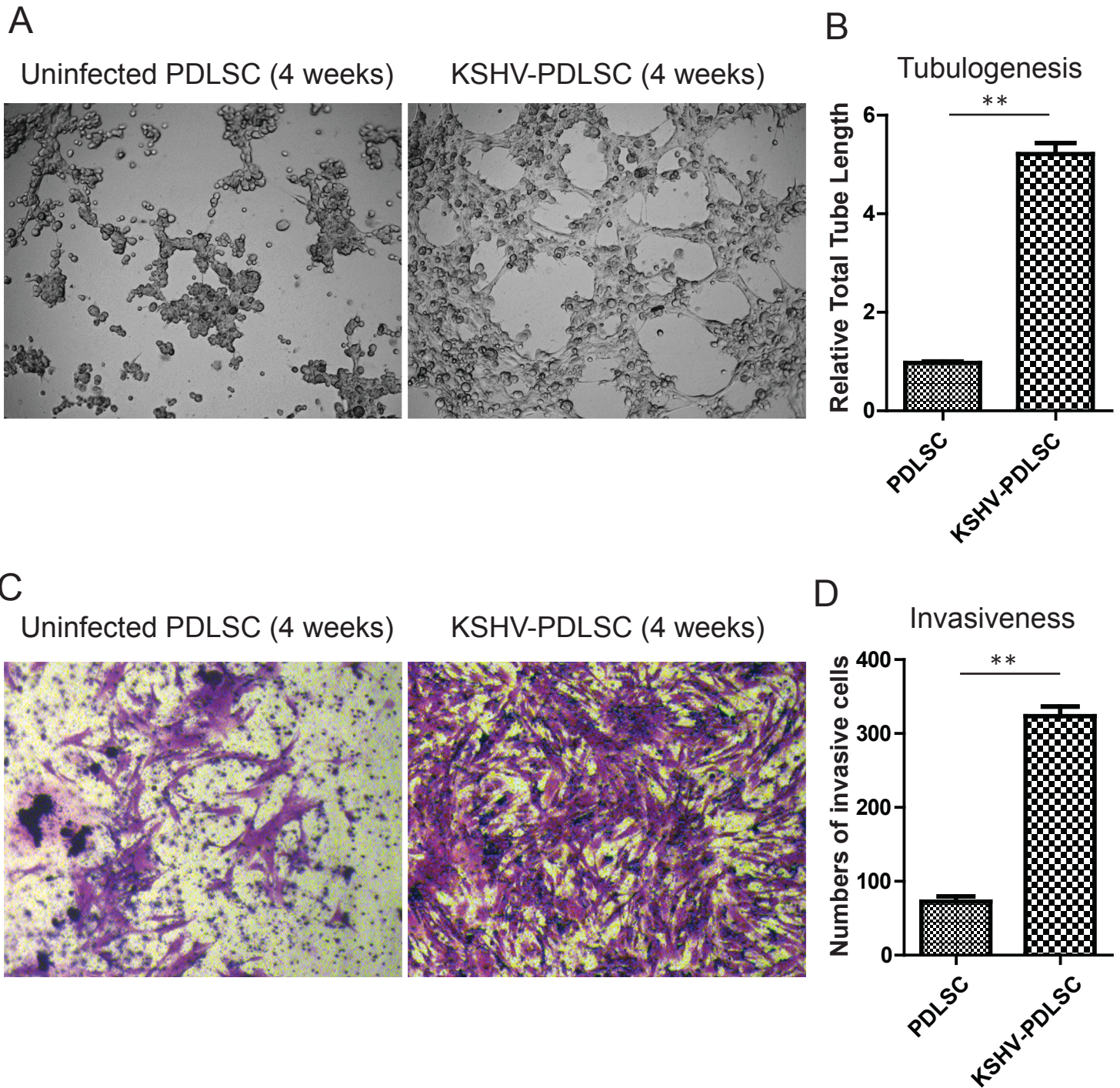


Fig. S3. Long-term cultured KSHV-infected PDLSCs preserve the potential of tubulogenesis and invasiveness. Primary PDLSCs were infected with GFP-KSHV in an MOI of 50 (KSHV genome equivalent). Cells were cultured without any antibiotics selection in cytokine-free medium for four weeks. Mock- and virally infected PDLSCs were loaded on the top of Matrigel and the ability of the cells in formation of capillary-like tubules was analyzed under a microscope (A). Quantification of tubulogenesis was performed by calculating the average length of the capillary-like tubules (B). Cells were subjected to Transwell migration assay to assess cell invasion ability. PDLSCs or KSHV-PDLSCs were seeded in the upper chamber of Transwell in serum-free MEM. MEM containing 10% FBS was used as a stimulus for chemotaxis in the lower chamber. Cells migrated to the lower chamber were stained with crystal violet (C). Quantification of invasiveness was performed by counting the invasive cell numbers from 5 different fields (D).

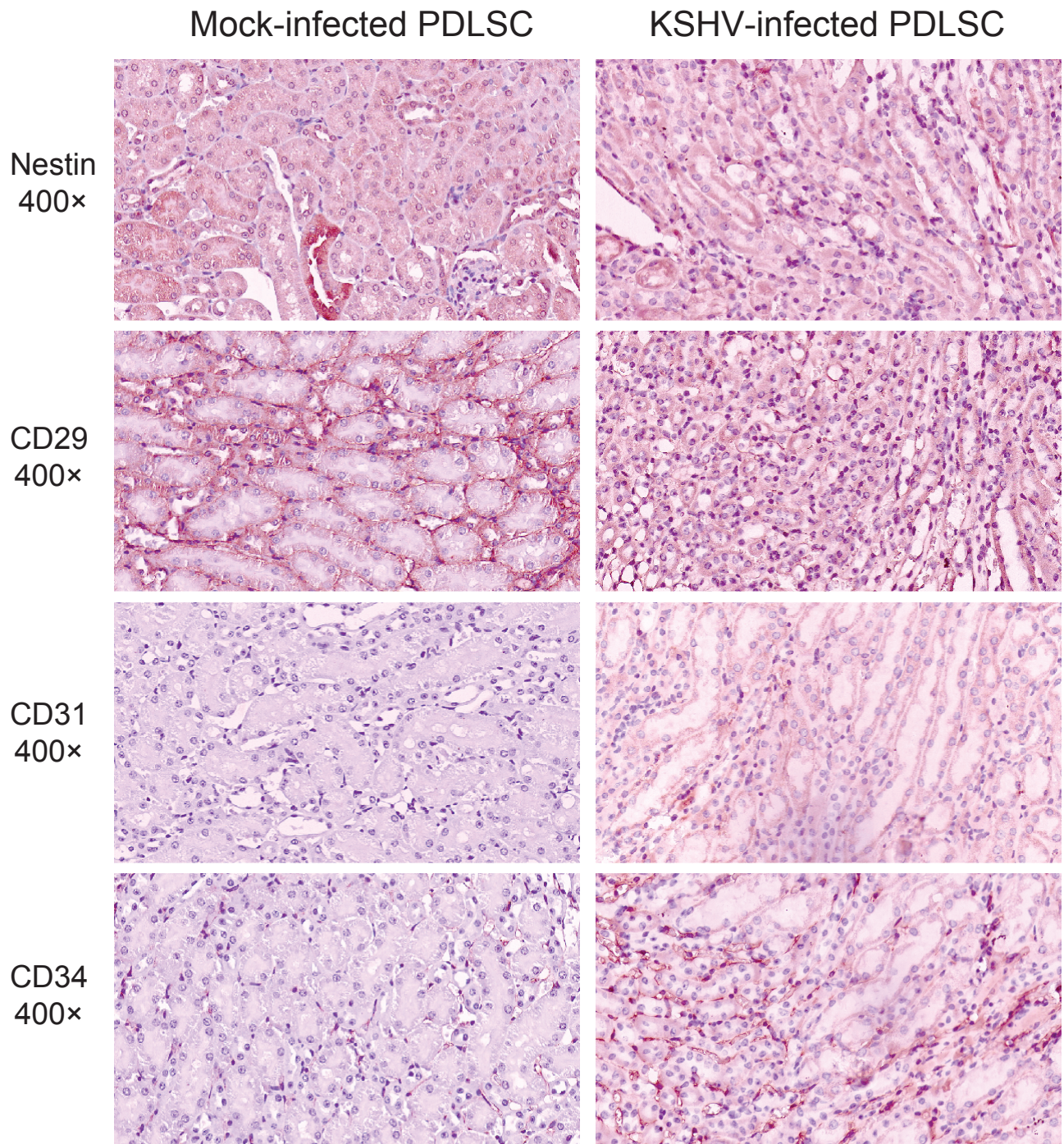


Fig. S4. Expression of oral MSC-specific and endothelial markers in mock- and KSHV-infected MSCs. Sections of kidney capsule implantation of mock- and KSHV-infected PDLSCs were subjected to immunohistochemical analyses with antibodies against neural crest-derived stem marker Nestin, oral MSC marker CD29, endothelial marker CD31 and hematopoietic/endothelial progenitor marker CD34.

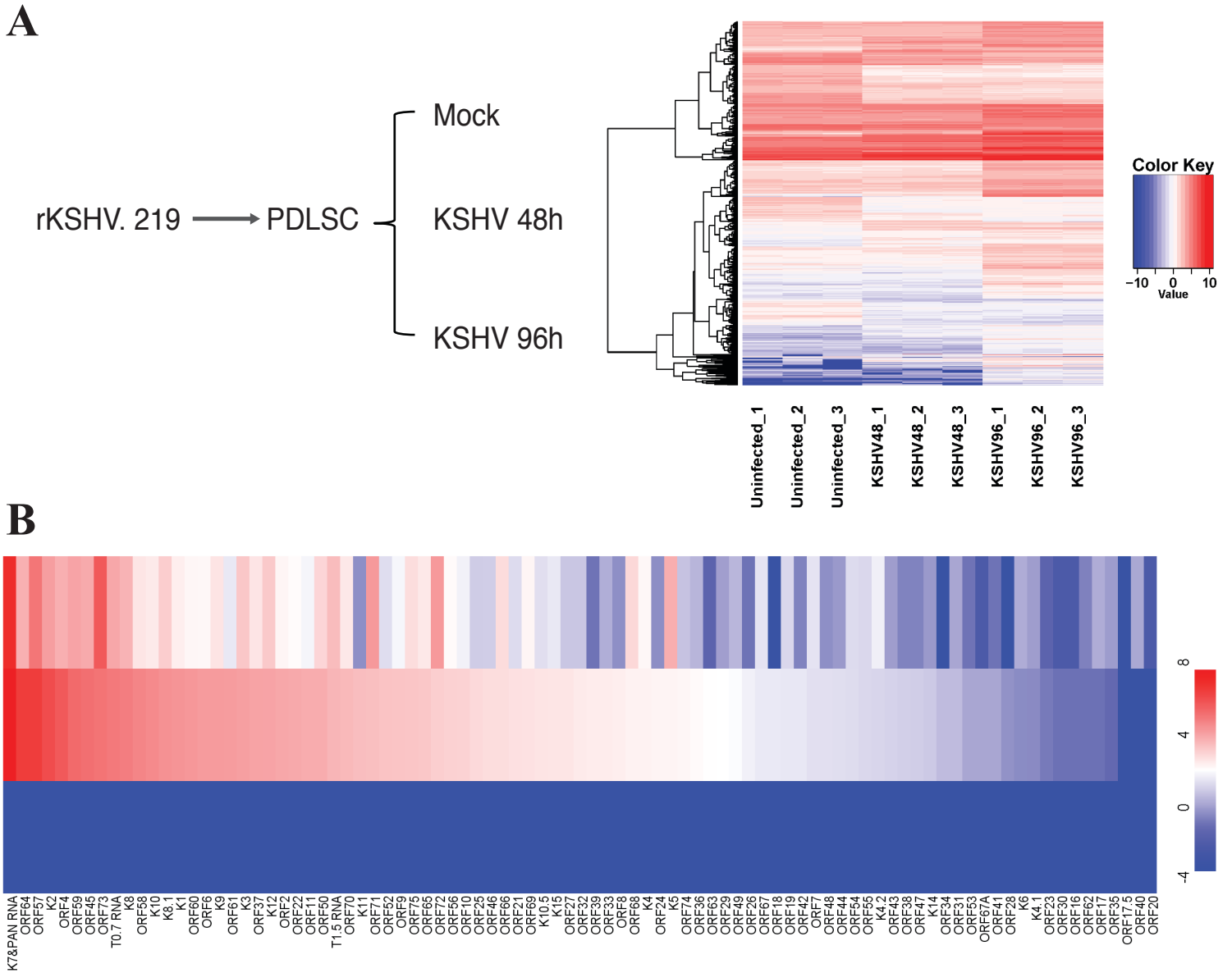
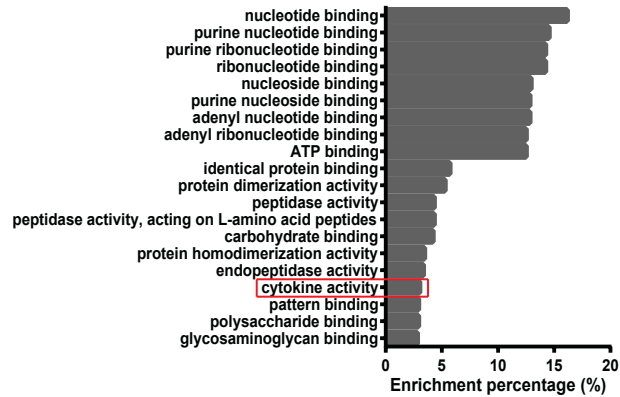


Fig. S5. Gene expression profiling analysis of KSHV-infected oral MSCs. PDLSCs (p2) were infected with rKSHV.219 in an MOI of 50 (viral genomic DNA equivalent). RNA was isolated from mock- and KSHV-infected PDLSCs (48 or 96 hour post-infection) and subjected to RNA-seq analysis. Clean reads were mapped to human reference genome (version hg19/GRCh37) and KSHV reference genome (version CQ994935.1). Differentially expressed cellular (A) and viral genes (B) were shown in heatmap.

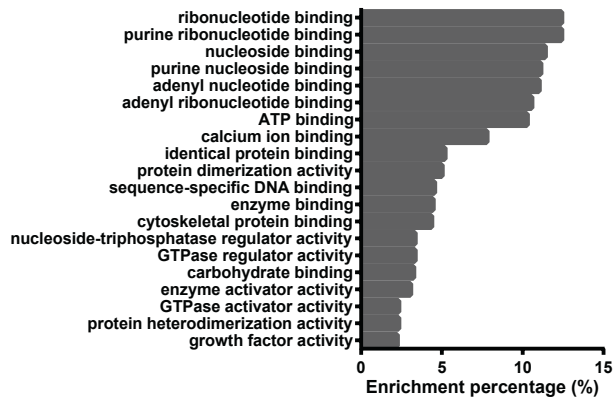
A

GO Enrichment of Molecular Function for PDLSC DEG



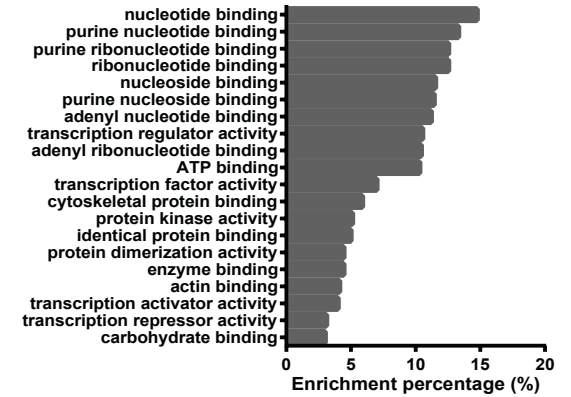
B

GO Enrichment of Molecular Function for HDMEC DEG



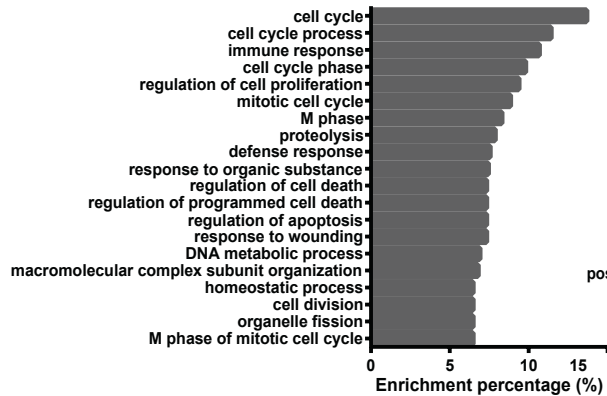
C

GO Enrichment of Molecular Function for HMVEC DEG



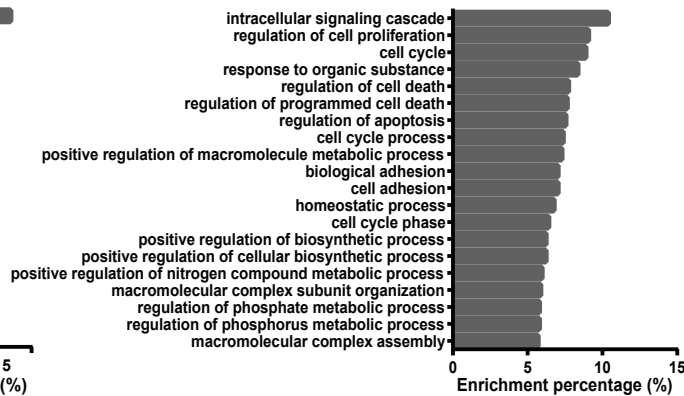
D

GO Enrichment of Biological Process for PDLSC DEG



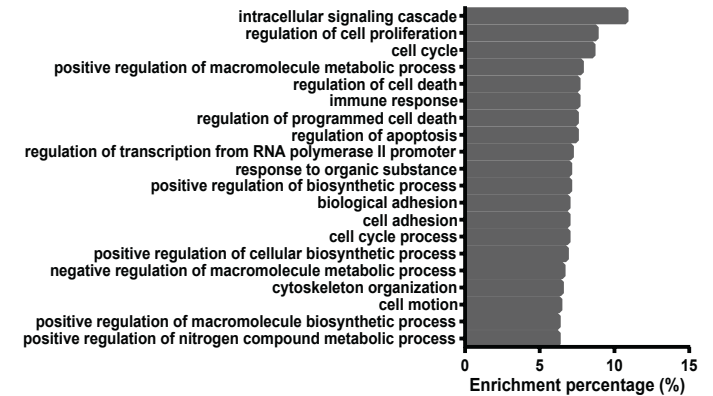
E

GO Enrichment of Biological Process for HDMEC DEG



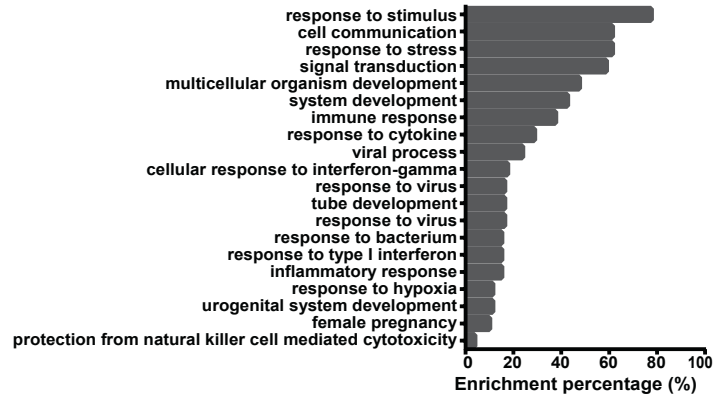
F

GO Enrichment of Biological Process for HMVEC DEG



G

GO Enrichment of Biological Process for 80 consistent DEGs between PDLSC and KS



H

GO Enrichment of Biological Process for 134 consistent DEGs between EC and KS

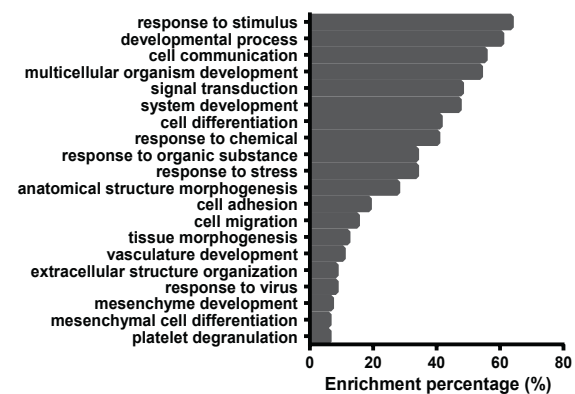


Fig. S6. Top 20 significantly enriched Gene Ontology (GO) categories of molecular function and biological process in KSHV-infected PDLSC (A, D), HDMEC (B, E) and HMVEC (C, F), as well as biological process in consistent DEGs of KS and PDLSC or endothelial cells (G, H).

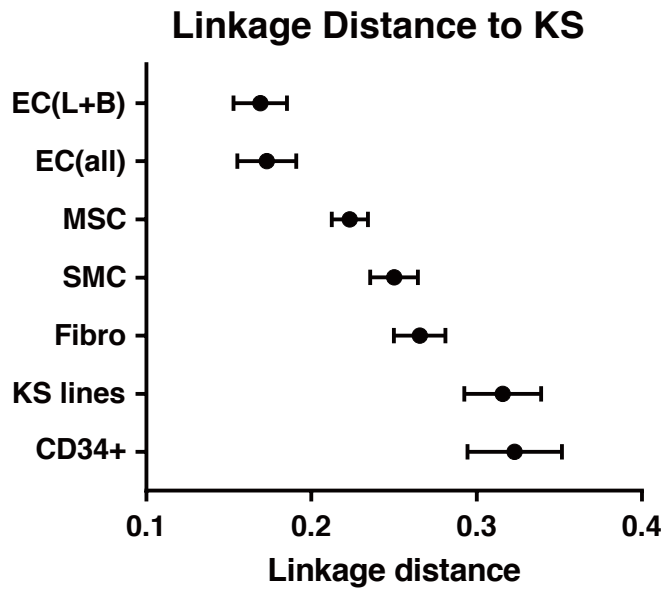


Fig. S7. The average linkage distance between Kaposi's sarcoma (KS) and each cell group was re-calculated from the published data (52) by Pearson correlation coefficient and then subtracted by 1. EC (L+B): endothelial cells (LECs+BECs).

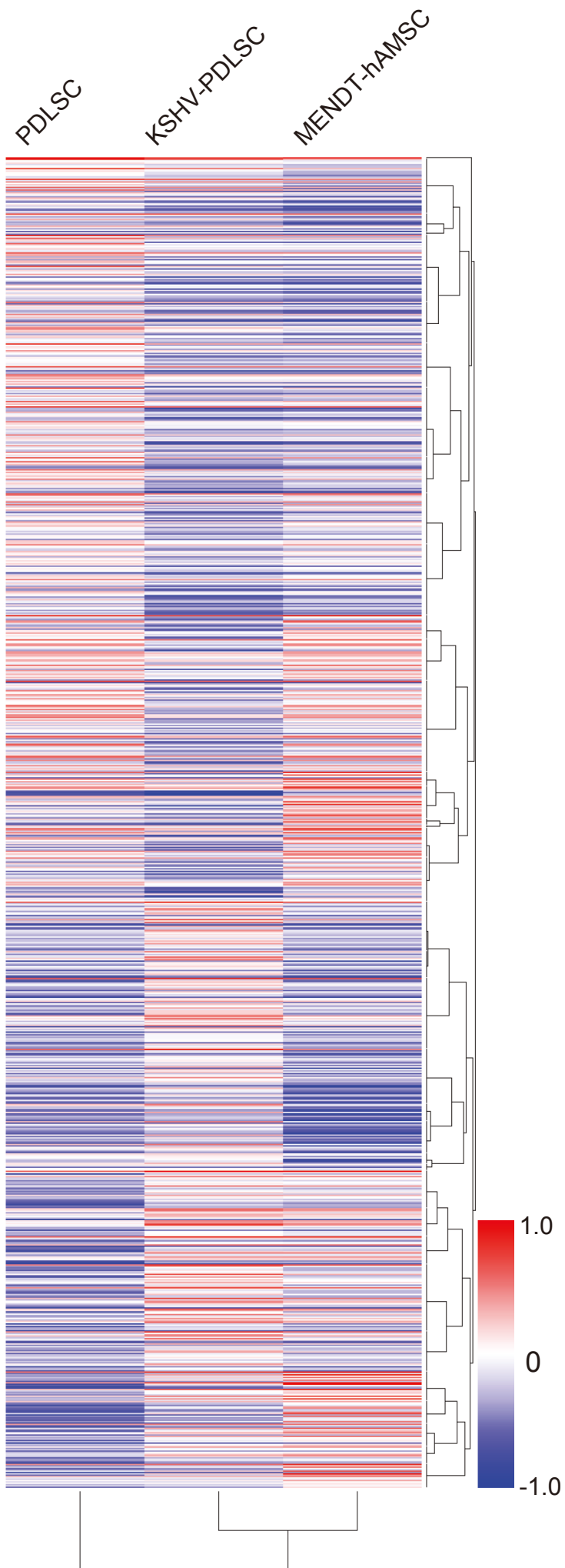


Fig. S8. Relationship of KSHV-infected MSC and an MENDT model (induced hAMSC) in gene expression profile. Mock- and KSHV-infected PDLSCs were normalized and subjected to a comparison with hAMSCs that have been induced for endothelial differentiation. Unsupervised clustering of samples (X-axis) and genes (Y-axis) were performed by average linkage method.

Table S1. Common DEGs in KSHV-PDLSC vs. PDLSC and KS signature

Function Cluster		Gene symbol	KSHV- MSC vs. MSC	KS vs. skin	KSHV- HDMEC vs. HDMEC	KSHV- HMVEC vs. HMVEC	KSHV- LEC vs. LEC	KSHV- BEC vs. BEC
Mesenchymal to Endothelial Transition		BGN	↓↓	↑↑	—	↓	↓↓	↓
		DSP	↑↑	↓↓	—	↓	↓↓	—
		EDNRA	↑↑	↑↑	—	—	↓	—
		FGF2	↑	↑↑	—	—	—	↓↓
		MMP11	↑	↑↑	—	—	↓	↑
		PDPN	↑↑	↑↑	↓↓	↑↑	↑	↑
		PROX1	↑↑	↑↑	↑	↓	↓↓	↑
		PGF	↑↑	↑↑	↓	↑	↓	—
		PML	↑↑	↑↑	—	—	↓	—
		TGFB3	↑↑	↑↑	—	—	—	—
		TGFBR2	↑↑	↑↑	—	—	↓	—
Vessel development		ANGPTL2	↑↑	↑↑	—	↑	↓	↑↑
		VCAM1	↑↑	↑↑	—	—	—	↓
		WARS	↑↑	↑↑	↑	—	↓	—
Immune response	Chemotaxis	CCL5	↑↑	↑↑	—	—	↑	↑↑
		CCL8	↑↑	↑↑	—	—	↑	—
		CXCL10	↑↑	↑↑	—	↑↑	—	—
		SHC3	↑↑	↓↓	—	—	—	—
		STAT1	↑↑	↑↑	↑↑	—	—	—
	Inflammation	APOL2	↑↑	↑↑	—	—	↓	—
		APOL3	↑↑	↑↑	—	—	—	↓
		CFH	↑↑	↑↑	—	—	—	—
		FN1	↑↑	↑↑	—	↓↓	↓↓	↓
		IFI16	↑↑	↑↑	—	↑↑	↑	—
		IL-1RN	↑↑	↓↓	—	—	—	—
		LY96	↑↑	↑↑	—	—	—	↑
		NT5E	↑↑	↑↑	↓	↑	↓	—
	PLA2G4C	↑↑	↑↑	—	—	—	—	
	Other genes involved in	FCGRT	↑↑	↑↑	—	—	—	—
GBP1		↑↑	↑↑	↑↑	↑↑	—	↓↓	
GCH1		↑↑	↑↑	—	↑	↑↑	—	

immune response	HLA-A	↑↑	↑↑	—	—	—	—
	HLA-B	↑↑	↑↑	↑	↑	—	—
	HLA-C	↑↑	↑↑	↑	↑	—	—
	HLA-E	↑↑	↑↑	—	—	—	—
	HLA-F	↑↑	↑↑	—	—	—	—
	HLA-G	↑↑	↑↑	—	—	—	—
	IFI35	↑↑	↑↑	—	↑↑	—	—
	IFITM1	↑↑	↑↑	—	↑↑	↑	—
	IFITM3	↑↑	↑↑	—	—	—	—
	ISG15	↑↑	↑↑	—	↑↑	↑↑	↑
	ISG20	↑↑	↑↑	—	—	—	↓↓
	NOD2	↑↑	↓↓	↑↑	—	—	—
	PSMB9	↑↑	↑↑	↑	↑↑	↑	↑
	SP110	↑↑	↑↑	—	↑↑	—	↓
	SPON2	↑↑	↑↑	—	—	—	—
	TACC3	↓↓	↑↑	↓	↓	—	↓↓
	TIMP1	↑↑	↑↑	—	—	↑↑	↑↑
	TNFSF10	↑↑	↑↑	↑↑	—	↓↓	—
	TRIM25	↑↑	↓↓	—	—	—	—
	TRIM38	↑↑	↑↑	—	↑	↑	↑
Cell proliferation	CCND1	↑↑	↓↓	—	—	↑↑	↑↑
	DHCR24	↓↓	↓↓	—	—	—	—
	IGF1	↑↑	↑↑	—	—	↓↓	—
	KLF4	↑↑	↓↓	↓↓	↓	↓	—
	MCM5	↓↓	↑↑	↓	—	↓	↓
	MCM6	↓↓	↑↑	↓	—	↓	↓
	TOB1	↑↑	↓↓	—	—	↓↓	↑
Signal Transduction	CD36	↑↑	↑↑	↑↑	↓	↓↓	↑
	DAPK2	↑↑	↓↓	—	—	↓	—
	DUSP6	↑↑	↑↑	—	—	↓	↓
	FAM129A	↓↓	↑↑	—	—	↓	—
	GDF5	↑↑	↓↓	—	—	↓↓	—
	GPSM2	↓↓	↓↓	↓↓	↓	—	—
	LGALS9	↑↑	↑↑	—	↑↑	↓	—
	RGS2	↑↑	↓↓	—	—	—	—

	SRGAP3	↑↑	↓↓	—	—	—	—
	TBC1D1	↓↓	↑↑	—	—	—	—
Metabolism	BACE2	↑↑	↑↑	—	—	↓	—
	EHF	↑↑	↓↓	↑	—	—	—
	KLHL3	↑↑	↑↑	—	—	↓	—
	PBXIP1	↑↑	↑↑	—	—	↓	↑↑
	TIMP3	↑↑	↑↑	↑↑	—	↓↓	—
	UBE2L6	↑↑	↑↑	—	↑↑	↓	—
	UBE2S	↓↓	↑↑	↓	↓	—	↓
	Cell adhesion	C1ORF38	↑↑	↑↑	—	—	↑
CLCA2		↑↑	↓↓	↓↓	—	↑	↑
PCDH17		↑↑	↑↑	↑	↑↑	↓	—
PODXL		↑↑	↑↑	↓	↑	↑↑	↑↑
Others	ADD3	↑↑	↑↑	↑	—	↓↓	—
	AKAP12	↑↑	↑↑	—	↑	↓	—
	AKR1B1	↑↑	↑↑	↓↓	—	—	—
	ALDH3A1	↑↑	↓↓	—	—	↑	↑↑
	AVPI1	↑↑	↓↓	—	—	—	—
	BTN3A3	↑↑	↑↑	—	—	↓	—
	ChGn	↑↑	↑↑	—	—	↓	—
	COTL1	↓↓	↑↑	—	—	↓↓	↓
	CPA4	↓↓	↓↓	—	—	↓↓	—
	CYP2E1	↑↑	↓↓	—	—	—	—
	DTNA	↑↑	↓↓	—	—	↓↓	—
	DTYMK	↓↓	↑↑	↓	—	—	—
	EPS8L2	↑↑	↓↓	—	—	↓↓	—
	GABBR2	↑↑	↑↑	↓↓	↓	↓	↓
	GCAT	↓↓	↓↓	—	—	↑	↑
	GOLM1	↑↑	↑↑	—	—	↑↑	—
	HSPA4L	↑↑	↓↓	—	↑↑	—	—
	KCTD12	↑↑	↑↑	—	↓	↓↓	↓
	KPNA2	↓↓	↑↑	—	—	—	↓
	KRT10	↓↓	↓↓	—	—	↑	—
LAP3	↑↑	↑↑	—	↑	↓	—	
LGMN	↑↑	↑↑	—	—	↓	↑	

MDK	↑↑	↑↑	-	-	↓	-
OLFML1	↑↑	↑↑	-	-	↓	-
PAM	↑↑	↑↑	-	-	↓	↑
RPLP0P2	↑↑	↓↓	-	-	-	-
SLC9A7	↑↑	↓↓	-	-	↓↓	↑
STOM	↑↑	↑↑	↑↑	-	↑↑	↑
TAGLN2	↓↓	↑↑	-	-	↑	-
TM4SF1	↑↑	↑↑	-	↑↑	-	↑
TMEM140	↑↑	↑↑	↑↑	↑	-	↑↑
TPP1	↑↑	↑↑	-	-	↓	-

↑↑: \log_2 (Fold change) > 1;

↑: $0.5 \leq \log_2$ (Fold change) ≤ 1 ;

-: No significant change;

↓↓: \log_2 (Fold change) < -1;

↓: $-1 \leq \log_2$ (Fold change) ≤ -0.5 .

Table S2. Consistently regulated genes between KSHV-PDLSC vs. PDLSC and MEndT hAMSC vs. hAMSC

Function Cluster		Gene symbol	KSHV-MSC vs. MSC	MEndT hAMSC vs. hAMSC	KS vs. Skin	Function Cluster	Gene symbol	KSHV-MSC vs. MSC	MEndT hAMSC vs. hAMSC	KS vs. Skin
Differentiation	Endothelial related	ANGPTL1	↑↑	↑↑	↑	Immune response	BTN3A1	↑↑	↑↑	↑↑
		EDNRA	↑↑	↑↑	↑↑		BTN3A3	↑↑	↑↑	↑↑
		FGF5	↑↑	↑↑	↑		CD55	↓↓	↓↓	↓↓
		FGF7	↑↑	↑↑	↑		C1R	↑↑	↑↑	—
		PDPN	↑↑	↑↑	↑↑		C1S	↑↑	↑↑	—
		PROX1	↑↑	↑↑	↑↑		CFH	↑↑	↑↑	↑↑
		TGFB3	↑↑	↑↑	↑↑		COTL1	↓↓	↓↓	↑↑
		PTGS2	↑↑	↑↑	↑		EPHA3	↑↑	↑↑	↑↑
		SLC40A1	↑↑	↑↑	—		IFI44	↑↑	↑↑	↑
		SRPX2	↑↑	↑↑	↑		IFI44L	↑↑	↑↑	↑↑
	WARS	↑↑	↑↑	↑↑	IFITM1		↑↑	↑↑	↑↑	
	Mesenchymal related	ACTA2	↓↓	↓↓	↓↓		IFITM3	↑↑	↑↑	↑↑
		CMKLR1	↑↑	↑↑	—		IGDCC4	↑↑	↑↑	—
		CNN1	↓↓	↓↓	↓↓		PSMB8	↑↑	↑↑	↑
		DACT1	↓↓	↓↓	↓		SAMHD1	↑↑	↑↑	↑↑
		DDIT3	↓↓	↓↓	↓		TAPBPL	↑↑	↑↑	↑
		EFEMP1	↑↑	↑↑	↓↓		TLR3	↑↑	↑↑	—
		EGFL6	↑↑	↑↑	↓↓		TNFAIP3	↑↑	↑↑	—
		ETV1	↑↑	↑↑	↑		TNFAIP6	↑↑	↑↑	↓
		NBEA	↓↓	↓↓	↓↓		TNFRSF10D	↓↓	↓↓	↓↓
SVIL		↑↑	↑↑	↓↓	ACSL4	↓↓	↓↓	—		
TAGLN	↓↓	↓↓	↓	APOD	↑↑	↑↑	↑			
TPM1	↓↓	↓↓	↓↓	APOE	↑↑	↑↑	↑			

Other genes involved in differentiation	ADAMTSL4	↑↑	↑↑	—	Metabolic	APOL1	↑↑	↑↑	↑↑	
	CRABP2	↑↑	↑↑	↓↓		CHST7	↑↑	↑↑	↑↑	
	DCN	↑↑	↑↑	↓		ENO1	↓↓	↓↓	↓	
	DIAPH3	↓↓	↓↓	↓↓		PDK4	↑↑	↑↑	—	
	IGF1	↑↑	↑↑	↑↑		PLA2G4A	↑↑	↑↑	↓↓	
	OXTR	↓↓	↓↓	↓↓		PTGIS	↓↓	↓↓	↓↓	
	TSHZ2	↑↑	↑↑	—		SMOX	↑↑	↑↑	↑	
	TXNIP	↑↑	↑↑	↓↓		TCN2	↑↑	↑↑	—	
Signal transduction	AKAP12	↑↑	↑↑	↑↑		Others	COL21A1	↑↑	↑↑	—
	ARHGAP20	↑↑	↑↑	—			CORO2B	↑↑	↑↑	↓
	BST2	↑↑	↑↑	↑↑	CPA4		↓↓	↓↓	↓↓	
	CHI3L1	↑↑	↑↑	↓↓	GADD45A		↓↓	↓↓	↓	
	CHI3L2	↑↑	↑↑	↓↓	KCNJ2		↑↑	↑↑	—	
	FAM129A	↓↓	↓↓	↑↑	MAMDC2		↑↑	↑↑	—	
	FAM180A	↑↑	↑↑	—	MME		↑↑	↑↑	↓	
	FIBIN	↑↑	↑↑	—	PARP14		↑↑	↑↑	—	
	FOS	↑↑	↑↑	↑↑	PLAT		↑↑	↑↑	↑	
	F10	↑↑	↑↑	↓↓	SDK1		↑↑	↑↑	—	
	GGH	↓↓	↓↓	↓	SLC1A3		↑↑	↑↑	↓	
	HSPA4L	↑↑	↓↓	↓↓	SLC38A4		↓↓	↓↓	↓	
	PCDHB14	↑↑	↑↑	—	SPON1		↑↑	↑↑	↑	
	PMEPA1	↓↓	↓↓	↑↑	STOM		↑↑	↑↑	↑↑	
				TRANK1	↑↑	↑↑	—			

↑↑: \log_2 (Fold change) > 1;

↑: $0.5 \leq \log_2$ (Fold change) ≤ 1 ;

—: No significant change;

↓↓: \log_2 (Fold change) < -1;

↓: $-1 \leq \log_2$ (Fold change) ≤ -0.5 .

DEGs present both in KSHV-infected MSC and KS signature were marked as red.

Table S3. Common DEGs in KSHV-HDMEC vs. HDMEC and KS signature

Function Cluster		Gene symbol	KSHV- HDMEC vs. HDMEC	KSHV- HMVEC vs. HMVEC	KSHV- LEC vs. LEC	KSHV -BEC vs. BEC	KS vs. skin	KSHV- MSC vs. MSC
Endothelial-mesenchymal transition		COL15A1	↑↑	↑↑	—	↑	↑↑	—
		COL5A1	↓↓	↓	—	↓	↑↑	↓
		EZR	↓↓	—	—	↓	↓↓	↓
		LMO2	↑↑	—	—	—	↑↑	—
		S100A4	↓↓	—	—	↑	↑↑	—
		SEMA3C	↓↓	↓↓	↓↓	—	↓↓	↑
		TGFA	↑↑	↓	↓	—	↓↓	—
Vessel development		ADORA2B	↓↓	—	↓↓	↓↓	↓↓	—
		ANGPT2	↑↑	↑↑	↑↑	↑	↑↑	↑
		FGFR2	↓↓	—	↑	↑↑	↓↓	—
		LYVE1	↑↑	↑↑	—	—	↑↑	—
		PGF1	↓	↑	↓	—	↑↑	↑↑
Immune response	Chemotaxis	STAT1	↑↑	—	—	—	↑↑	↑↑
	Inflammation	A2M	↑↑	↑↑	—	↑↑	↑↑	—
		MGLL	↓↓	—	—	↓	↑↑	—
	Other genes involved in immune response	CBLB	↑↑	—	—	↑↑	↑↑	—
		GBP1	↑↑	↑↑	—	↓↓	↑↑	↑↑
		GIMAP5	↑↑	—	—	↑	↑↑	—
		HLX	↑↑	↑↑	↑↑	↑↑	↑↑	—
		MICAL2	↓↓	↓	—	↓	↑↑	↓
		NOD2	↑↑	—	—	—	↓↓	↑↑
		PTGER4	↓↓	—	—	↓↓	↑↑	—
TNFSF10	↑↑	—	↓↓	—	↑↑	↑↑		
Cell proliferation		KLF4	↓↓	↓	↓	—	↓↓	↑↑
		MYCN	↑↑	—	↓	—	↓↓	—
		TBX5	↓↓	—	—	—	↓↓	—
Metabolism		CD36	↑↑	↓	↓↓	↑	↑↑	↑↑
		EFS	↑↑	—	—	—	↓↓	—
		EGFR	↓↓	↓↓	↓	↓	↓↓	↑
		EPS8	↓↓	—	—	—	↑↑	—
		GPSM2	↓↓	↓	—	—	↓↓	↓↓

	RAB38	↓↓	—	—	↓	↓↓	—
	RASGRP3	↑↑	↑↑	—	↑↑	↑↑	↑
	RGS4	↓↓	↓↓	↓↓	↓↓	↑↑	↑
	RIPK4	↓↓	—	—	↓	↓↓	—
	STK32B	↓↓	↑	—	↓	↑↑	—
Metabolism	BTRC	↑↑	—	—	↑↑	↓↓	—
	CSGALNACT1	↑↑	—	—	—	↑↑	↑↑
	MAOA	↑↑	↓	↑	↓↓	↓↓	—
	TIMP3	↑↑	—	↓↓	—	↑↑	↑↑
Cell adhesion	CLCA2	↓↓	—	↑	↑	↓↓	↑↑
	COL6A3	↓↓	—	—	—	↑↑	—
	MPZL2	↓↓	↑	—	↓	↓↓	—
	VCAN	↓↓	—	↓	↓	↑↑	↑
Cytoskeleton	ANK3	↓↓	—	↓	—	↓↓	—
	EPB41L3	↓↓	↓	—	—	↑↑	↑
	KIF1A	↑↑	—	↑↑	—	↓↓	—
	SEMA6A	↑↑	—	↑	—	↑↑	—
Others	AKR1B1	↓↓	—	—	—	↑↑	↑↑
	ASTN2	↑↑	—	↑	↑	↓↓	—
	BDH1	↓↓	—	—	↑↑	↓↓	—
	BIN1	↓↓	↓	↓	—	↑↑	—
	CD200	↑↑	—	—	—	↑↑	—
	COPS8	↓↓	—	—	—	↑↑	—
	ELOVL6	↓↓	—	↑	↑	↓↓	—
	ETV5	↓↓	↑	—	↓	↓↓	↑
	GABBR2	↓↓	↓	↓	↓	↑↑	↑↑
	GAD2	↓↓	—	—	↑	↓↓	—
	GPR37	↓↓	—	—	↓	↓↓	—
	HPCAL1	↓↓	—	↑	—	↑↑	—
	IRX5	↓↓	—	—	—	↓↓	—
	KCNJ13	↑↑	—	—	—	↓↓	—
	KIAA1045	↑↑	—	—	↓	↓↓	—
	KLK11	↓↓	—	—	—	↓↓	—
	LIMD1	↓↓	—	↓	—	↓↓	—
	NAGA	↓↓	—	—	↑	↑↑	—

NES	↓↓↓	—	—	—	↑↑	↓
OLFM1	↑↑	—	—	↑	↑↑	—
RAMP2	↑↑	—	—	↑↑	↑↑	—
RAMP3	↑↑	↓	↓	—	↑↑	—
REEP1	↑↑	—	↓	—	↑↑	—
RTEL1	↓↓↓	—	—	↓	↑↑	—
SEPP1	↑↑	—	↓	—	↑↑	↑↑
SEP6	↑↑	—	—	—	↑↑	—
SLC15A1	↓↓↓	—	—	↑	↓↓↓	—
STOM	↑↑	—	↑↑	↑	↑↑	↑↑
TMEM140	↑↑	↑↑	—	↑↑	↑↑	↑↑
ZNF185	↓↓↓	—	—	—	↓↓↓	↓

↑↑: \log_2 (Fold change) > 1;

↑: $0.5 \leq \log_2$ (Fold change) ≤ 1 ;

—: No significant change;

↓↓: \log_2 (Fold change) < -1;

↓: $-1 \leq \log_2$ (Fold change) ≤ -0.5 .

Table S4. Common DEGs in KSHV-HMVEC vs. HMVEC and KS signature

Function Cluster	Gene symbol	KSHV- HDMEC vs. HDMEC	KSHV- HMVEC vs. HMVEC	KSHV- LEC vs. LEC	KSHV- BEC vs. BEC	KS vs. skin	KSHV- MSC vs. MSC	
Endothelial-mesenchymal transition	COL15A1	↑↑	↑↑	—	↑	↑↑	—	
	GJA4	↑	↓↓	↓↓	—	↑↑	—	
	HEY1	↑	↓↓	—	↑↑	↑↑	—	
	NRP1	—	↑↑	↑↑	—	↑↑	↑	
	SEMA3C	↓↓	↓↓	↓↓	—	↓↓	↑	
Vessel development	ANGPT2	↑↑	↑↑	↑↑	↑	↑↑	↑	
	ANGPTL2	—	↑↑	↓	↑↑	↑↑	↑↑	
	LYVE1	↑↑	↑↑	—	—	↑↑	—	
	PGF1	↓	↑↑	↓	—	↑↑	↑↑	
	PTPRM	—	↑↑	—	—	↑↑	—	
Immune Response	Chemotaxis	CXCL10	—	↑↑	—	—	↑↑	↑↑
		CXCR4	↓	↑↑	—	—	↑↑	—
		GRK5	—	↑↑	—	↑	↑↑	↑
	Inflammation	A2M	↑↑	↑↑	—	↑↑	↑↑	—
		FN1	—	↓↓	↓↓	↓	↑↑	↑↑
		IFI16	—	↑↑	↑	—	↑↑	↑↑
		TLR2	↑	↑↑	—	—	↑↑	↑
	Other genes involved in immune response	GBP1	↑↑	↑↑	—	↓↓	↑↑	↑↑
		HLX	↑↑	↑↑	↑↑	↑↑	↑↑	—
		HOXB7	—	↑↑	↑↑	—	↑↑	—
		IFI35	—	↑↑	—	—	↑↑	↑↑
		IFITM1	—	↑↑	↑	—	↑↑	↑↑
		ISG15	—	↑↑	↑↑	↑	↑↑	↑↑
		PSMB9	↑	↑↑	↑	↑	↑↑	↑↑
SP110	—	↑↑	—	↓	↑↑	↑		
Cell proliferation	HYAL1	—	↓↓	↓	—	↓↓	—	
Signal transduction	EGFR	↓↓	↓↓	↓	↓	↓↓	↑	
	GUCY1A3	—	↓↓	↓	—	↑↑	—	
	LGALS9	—	↑↑	—	—	↑↑	↑↑	
	RASGRP3	↑↑	↑↑	—	↑↑	↑↑	↑	
	RGS4	↓↓	↓↓	↓↓	↓↓	↑↑	↑	

	TRIB2	—	↓↓	↓	—	↑↑	—
Metabolism	NR2F1	—	↓↓	↓	↓↓	↑↑	—
	PCSK6	↑	↑↑	—	↑↑	↑↑	—
	UBE2L6	—	↑↑	↓	—	↑↑	↑↑
	PCDH12	—	↑↑	—	—	↑↑	—
Cell adhesion	PCDH17	↑	↑↑	↓	—	↑↑	↑↑
	DIAPH2	—	↑↑	↑↑	↑	↑↑	—
Cytoskeleton	CA2	↓	↑↑	↑↑	↑↑	↓↓	—
Others	HSPA4L	—	↑↑	—	—	↓↓	↑↑
	LXN	—	↑↑	—	—	↑↑	↓
	PPAP2C	—	↓↓	—	↑	↓↓	—
	TACSTD2	—	↓↓	↑	↑	↓↓	—
	TM4SF1	—	↑↑	—	↑	↑↑	↑↑
	ZNF117	—	↑↑	—	—	↓↓	—

↑↑: \log_2 (Fold change) > 1;

↑: $0.5 \leq \log_2$ (Fold change) ≤ 1 ;

—: No significant change;

↓↓: \log_2 (Fold change) < -1;

↓: $-1 \leq \log_2$ (Fold change) ≤ -0.5 .

Table S5. Common DEGs in KSHV-LEC vs. LEC and KS signature

Function Cluster	Gene symbol	KSHV- HDMEC vs. HDMEC	KSHV- HMVEC vs. HMVEC	KSHV- LEC vs. LEC	KSHV- BEC vs. BEC	KS vs. skin	KSHV- MSC vs. MSC
Endothelial-mesenchymal transition	GJA4	↑	↓↓	↓↓	—	↑↑	—
	NRP1	—	↑↑	↑↑	—	↑↑	↑
	SEMA3C	↓↓	↓↓	↓↓	—	↓↓	↑
	TGFB1I1	—	—	↓↓	↓	↑↑	↓
Vessel development	ADORA2B	↓↓	—	↓↓	↓↓	↓↓	—
	ANGPT2	↑↑	↑↑	↑↑	↑	↑↑	↑
	LOC100131909	—	—	↓↓	↓↓	↓↓	—
Immune response	AZGP1	—	—	↑↑	↑	↓↓	—
	AZGP1P1	—	—	↑↑	↑	↓↓	—
	CBLB	↑↑	—	↑↑	↑↑	↑↑	—
	CD47	↑	—	↑↑	—	↑↑	↑
	GCH1	—	↑	↑↑	—	↑↑	↑↑
	HLX	↑↑	↑↑	↑↑	↑↑	↑↑	—
	HOXB7	—	↑↑	↑↑	—	↑↑	—
	ISG15	—	↑↑	↑↑	↑	↑↑	↑↑
	TIMP1	—	—	↑↑	↑↑	↑↑	↑↑
Cell proliferation	CCND1	—	—	↑↑	↑↑	↓↓	↑↑
	DERL2	—	—	↑↑	—	↑↑	—
	SSR1	—	—	↑↑	—	↑↑	—
Signal transduction	ARL4C	↓	↓	↓↓	↓	↑↑	—
	ATP6V0E1	—	—	↑↑	↑	↑↑	↑
	DGKD	—	—	↑↑	↑	↑↑	—
	ECE1	—	—	↑↑	—	↑↑	↑
	FLNA	—	—	↑↑	↓	↑↑	↓
	IQGAP2	—	—	↓↓	—	↑↑	—
	JAK1	—	↑	↑↑	↑	↑↑	—
	RGS4	↓↓	↓↓	↓↓	↓↓	↑↑	↑
Metabolism	B3GAT3	—	—	↑↑	—	↑↑	↑
	CST3	—	—	↑↑	↑	↑↑	↑
	IMPA2	—	—	↓↓	—	↓↓	↑
	ITGB3	↑	↑	↑↑	↑	↑↑	—
	UBE2J1	—	—	↑↑	↑↑	↑↑	—

Cell adhesion	LOXL2	—	—	↑↑	↓↓	↑↑	↓
	NID1	↑	—	↓↓	—	↑↑	—
	PODXL	↓	↑	↑↑	↑↑	↑↑	↑↑
Cytoskeleton	DIAPH2	—	↑↑	↑↑	↑	↑↑	—
	KIF1A	↑↑	—	↑↑	—	↓↓	—
Others	C21ORF7	—	—	↑↑	↑↑	↑↑	—
	CA2	↓	↑↑	↑↑	↑↑	↓↓	—
	CNNM2	—	—	↑↑	—	↓↓	↑
	GOLM1	—	—	↑↑	—	↑↑	↑↑
	GPR116	—	—	↑↑	↑	↑↑	—
	HEG1	—	—	↓↓	↑	↑↑	—
	IGSF3	—	—	↓↓	↑	↓↓	—
	KCNIP1	—	—	↓↓	—	↓↓	—
	KIAA1462	—	—	↓↓	—	↑↑	↑
	LOC283398	—	—	↑↑	—	↓↓	—
	NCR2	—	—	↑↑	↓	↓↓	—
	PLLP	—	↓	↓↓	—	↓↓	—
	PLVAP	—	—	↑↑	↑↑	↑↑	—
	RNF115	—	—	↑↑	↑	↑↑	—
	SLC39A14	—	—	↑↑	—	↑↑	—
	SNX10	—	—	↓↓	—	↑↑	—
	STOM	↑↑	—	↑↑	↑	↑↑	↑↑
	SUCLG2	↓	—	↑↑	—	↓↓	—
	TBCD	—	—	↑↑	—	↑↑	—
	TFPI	—	↓	↓↓	↓	↑↑	↑
THSD7A	↑	—	↓↓	—	↑↑	—	
XPNPEP1	—	—	↓↓	—	↑↑	—	

↑↑: \log_2 (Fold change) > 1;

↑: $0.5 \leq \log_2$ (Fold change) ≤ 1 ;

—: No significant change;

↓↓: \log_2 (Fold change) < -1;

↓: $-1 \leq \log_2$ (Fold change) ≤ -0.5 .

Table S6. Common DEGs in KSHV-BEC vs. BEC and KS signature

Function Cluster		Gene symbol	KSHV- HDMEC vs. HDMEC	KSHV- HMVEC vs. HMVEC	KSHV- LEC vs. LEC	KSHV- BEC vs. BEC	KS vs. skin	KSHV- MSC vs. MSC
Vessel development		ADORA2B	↓↓	—	↓↓	↓↓	↓↓	—
		ANGPTL2	—	↑	↓	↑↑	↑↑	↑↑
		FGFR2	↓↓	—	↑	↑↑	↓↓	—
		HEY1	↑	↓↓	—	↑↑	↑↑	—
		LOC100131909	—	—	↓↓	↓↓	↓↓	—
		VCAM1	—	—	—	↓↓	↑↑	↑↑
Immune Response	Chemotaxis	CCL5	—	—	↑	↑↑	↑↑	↑↑
		CYBA	—	—	—	↑↑	↑↑	↑
	Inflammation	A2M	↑↑	↑↑	—	↑↑	↑↑	—
		TNFRSF4	—	↓	↓	↑↑	↑↑	—
	Other genes involved in immune response	CBLB	↑↑	—	—	↑↑	↑↑	—
		GBP1	↑↑	↑↑	—	↓↓	↑↑	↑↑
		HLX	↑↑	↑↑	↑↑	↑↑	↑↑	—
		ISG20	—	—	—	↓↓	↑↑	↑↑
		PTGER4	↓↓	—	—	↓↓	↑↑	—
		TACC3	↓	↓	—	↓↓	↑↑	↓↓
TAPBP	—	—	—	↑↑	↑↑	↑		
TIMP1	—	—	↑↑	↑↑	↑↑	↑↑		
Cell proliferation		CCND1	—	—	↑↑	↑↑	↓↓	↑↑
Signal transduction		APP	—	—	—	↑↑	↑↑	↑
		CCDC88A	↓	—	—	↑↑	↑↑	—
		HPGD	—	—	—	↓↓	↓↓	—
		RASGRP3	↑↑	↑↑	—	↑↑	↑↑	↑
		RGS4	↓↓	↓↓	↓↓	↓↓	↑↑	↑
		SIK1	—	—	↑	↓↓	↓↓	—
	SPRY1	↑	↑	↓	↑↑	↑↑	↑	
Metabolism		BTRC	↑↑	—	—	↑↑	↓↓	—
		MAOA	↑↑	↓	↑	↓↓	↓↓	—
		MEF2C	—	↑	—	↑↑	↑↑	—
		MGAT2	↓	—	—	↑↑	↑↑	—
		NR2F1	—	↓↓	↓	↓↓	↑↑	—

	PBXIP1	—	—	↓	↑↑	↑↑	↑↑
	PCSK6	↑	↑↑	—	↑↑	↑↑	—
	PTPRN2	—	—	↓	↑↑	↑↑	↑
	UBE2J1	—	—	↑↑	↑↑	↑↑	—
Cell adhesion	COL6A1	—	↑	↑	↑↑	↑↑	↑
	LOXL2	—	—	↑↑	↓↓	↑↑	↓
	PARVB	—	—	↓	↓↓	↑↑	↓
	PCDHGA12	—	—	—	↑↑	↑↑	—
	PCDHGC3	—	—	—	↑↑	↑↑	—
	PCDHGC4	—	—	—	↑↑	↑↑	—
	PCDHGC5	—	—	—	↑↑	↑↑	↑
	PODXL	↓	↑	↑↑	↑↑	↑↑	↑↑
	ZYX	—	↓	—	↓↓	↑↑	—
Others	ALDH3A1	—	—	↑	↑↑	↓↓	↑↑
	ASPA	—	—	—	↑↑	↓↓	↑
	BDH1	↓↓	—	—	↑↑	↓↓	—
	C21ORF7	—	—	↑↑	↑↑	↑↑	—
	CA2	↓	↑↑	↑↑	↑↑	↓↓	—
	CYB5R2	—	—	—	↑↑	↓↓	—
	CYP3A43	—	—	↑	↓↓	↓↓	—
	GOLGA8A	—	—	—	↑↑	↓↓	↑
	GOLGA8B	—	—	—	↑↑	↓↓	—
	GPR126	—	↓	—	↓↓	↓↓	—
	HIP1R	—	—	—	↓↓	↓↓	—
	LZTS1	—	—	↑	↑↑	↓↓	—
	METRN	↓	—	—	↑↑	↑↑	↑
	MTERF	—	—	—	↓↓	↓↓	—
	NOL3	—	—	↑	↑↑	↓↓	—
	PLVAP	—	—	↑↑	↑↑	↑↑	—
	RAMP2	↑↑	—	—	↑↑	↑↑	—
	RTN1	—	—	—	↑↑	↑↑	—
	SDPR	—	—	—	↓↓	↑↑	↑
	SEP6	↑↑	—	—	↑↑	↑↑	—
	SLC38A7	—	—	↓	↑↑	↑↑	—
	TLL2	—	—	—	↓↓	↓↓	—
TMEM140	—	↑↑	—	↑↑	↑↑	↑↑	

	TMEM204	—	—	—	↑↑	↑↑	—
	TTC39A	—	—	—	↓↓	↓↓	—

↑↑: \log_2 (Fold change) > 1;

↑: $0.5 \leq \log_2$ (Fold change) ≤ 1 ;

—: No significant change;

↓↓: \log_2 (Fold change) < -1;

↓: $-1 \leq \log_2$ (Fold change) ≤ -0.5 .