

**Supplement Table S1.** Characteristics of participants and endometrial tissue biopsy samples in the study

Subject ID	Cycle Phase	Diagnosis	Age	Ethnicity
<i>No Endometriosis</i>				
<b>M182</b>	PE	Pipelle endometrial biopsy- normal volunteer	34	Caucasian
<b>598</b>	PE	Leiomyomata	33	Black
<b>562</b>	PE	Leiomyomata	50	Caucasian
<b>495</b>	PE	Leiomyomata	49	Caucasian
<b>641</b>	PE	Leiomyomata	43	Black
<b>715</b>	PE	Dysmenorrhea	32	Asian
<b>629</b>	ESE	Leiomyomata	46	Caucasian
<b>664</b>	ESE	Uterine prolapse; adenomyosis	44	Other
<b>650</b>	ESE	Leiomyomata	48	Caucasian
<b>320</b>	ESE	Pelvic pain and adhesive disease	27	Asian
<b>610</b>	MSE	Leiomyomata	49	Caucasian
<b>617</b>	MSE	Pelvic pain (no endometriosis at laparoscopy)	42	Caucasian
<b>626</b>	MSE	Uterine prolapse	42	Caucasian
<b>409</b>	MSE	Uterine prolapse	40	Asian
<b>442</b>	LSE	Leiomyomata; adenomyosis	43	Black
<b>449</b>	LSE	Leiomyomata	39	Caucasian
<b>462</b>	LSE	Leiomyomata	39	Asian
<b>648</b>	LSE	Leiomyomata	45	Caucasian
<i>Endometriosis*</i>				
<b>G26A</b>	PE	Severe endometriosis	31	Caucasian
<b>651</b>	PE	Severe endometriosis	37	Caucasian
<b>511</b>	PE	Severe endometriosis	42	Caucasian
<b>ST-70</b>	PE	Severe endometriosis	22	Caucasian
<b>575</b>	PE	Severe endometriosis	26	Unknown
<b>27A</b>	ESE	Severe endometriosis	22	Caucasian
<b>517</b>	ESE	Severe endometriosis	35	Asian
<b>607</b>	ESE	Severe endometriosis	24	Asian
<b>489</b>	ESE	Severe endometriosis	39	Asian
<b>33A</b>	MSE	Severe endometriosis	27	Caucasian
<b>635</b>	MSE	Severe endometriosis	39	Asian Indian
<b>7A</b>	MSE	Severe endometriosis	35	Unknown
<b>516</b>	MSE	Severe endometriosis	34	Asian
<b>678</b>	MSE	Severe endometriosis	44	Asian
<b>ST-85</b>	MSE	Severe endometriosis	34	Caucasian
<b>245</b>	LSE	Endometriosis, Pelvic prolapse	35	Caucasian
<b>259</b>	LSE	Minimal endometriosis	36	Caucasian
<b>260</b>	LSE	Severe endometriosis	44	Caucasian
<b>669</b>	LSE	Minimal endometriosis, enterocele, bilateral polycystic ovaries (PCOS)	38	Caucasian

\* The diagnosis of endometriosis was based on visualization of lesions found during laparoscopy and was also confirmed by histology. Endometrial staging was defined according to the revised American Fertility Society classification system (The American Fertility Society. Revised American Fertility Society classification of endometriosis: 1985. Fertil Steril 43:351–352).

**Supplement Table S2.** Oligonucleotide primers used for quantitative RT-PCR

<b>Gene Name</b>	<b>Forward Primer</b>	<b>Reverse Primer</b>	<b>PCR Product Size (bp)</b>
<i>18 S</i>	5'-TCTTAGCTGAGTGTCCCGCG-3'	5'-ATCATGGCCTCAGTTCCGA-3'	150
<i>BMP2</i>	5'-GACGCTCTTTCAATGGACGTG-3'	5'-AGCAGCAACGCTAGAAGACAGC-3'	105
<i>DKK1</i>	5'-GATCATAGCACCTTGGATGG-3'	5'-ACACAATCCTGAGGCACA-3'	120
<i>EGR1</i>	5'-AGCACCTTCAACCCTCA-3'	5'-AGTCGAGTGGTTTGGCT-3'	134
<i>IGFBP1</i>	5'-TTTACCTGCCAAACTGCAACAA-3'	5'-TCTTCCCATTCCAAGGGTAGAC-3'	111
<i>IL8</i>	5'-GCGCCAACACAGAAATTATTG-3'	5'-ACCACAGAGAATGAATTTTTTTATGA-3'	139
<i>KLF9</i>	5'-TGGCTGTGGGAAAGTCTATGG-3'	5'-CTCGTCTGAGCGGGAGAACT-3'	124
<i>PGR</i>	5'-CCT TTGGAAGGGCTACGAAGT-3'	5'-GAGCTCGACACAACCTCTTTTG-3'	110
<i>PGR-B</i>	5'-CGACCCAGGAGGTGGAGAT-3'	5'-GAGGGAAAAGGGAAGGAGGAG-3'	105
<i>PRL</i>	5'-TCAACAGCTGCCACACTTCTTC-3'	5'-CATTCCAGGATCGCAATATGC-3'	114
<i>WNT2</i>	5'-GAAAGGATGCCAGAGCC-3'	5'-TCCTGAGAGTACATGAGCC-3'	120
<i>WNT4</i>	5'-AGCAACTGGCTGTACCT -3'	5'-ACTTCCAGGTTCCGCTT-3'	122

**Supplement Table S3.** Top 100 genes regulated by cAME-treatment of HESC [Fold-change for cAME vs. vehicle; (+) positive-regulation; (-) negative-regulation]

	Gene Name	Fold-change	Regulated by FGR	Regulated by KLF9
<b>Top 50 up-regulated genes</b>				
<i>SST</i>	somatostatin	336.87		
<i>CGA</i>	glycoprotein hormones, alpha polypeptide	186.72		
<i>IGFBP1</i>	insulin-like growth factor binding protein 1	184.97		+
<i>IGF1</i>	insulin-like growth factor 1 (somatomedin C)	116.17	+	
<i>NPR3</i>	natriuretic peptide receptor C	109.99	+	
<i>RORB</i>	RAR-related orphan receptor B	103.46	+	
<i>P2RY14</i>	purinergic receptor P2Y, G-protein coupled, 14	96.85		
<i>C5orf23</i>	chromosome 5 open reading frame 23	86.84	+	
<i>AREG</i>	Amphiregulin	79.98		
<i>APCDD1</i>	adenomatosis polyposis coli down-regulated 1	75.42	+	
<i>CNR1</i>	cannabinoid receptor 1 (brain)	55.50	+	
<i>PDK4</i>	pyruvate dehydrogenase kinase, isozyme 4	48.95	+	
<i>CD83</i>	CD83 molecule	48.54		
<i>HSD11B1</i>	hydroxysteroid (11-beta) dehydrogenase 1	40.41		
<i>CCL8</i>	chemokine (C-C motif) ligand 8	38.95		
<i>MYOCD</i>	myocardin	38.01		
<i>DNER</i>	delta/notch-like EGF repeat containing	32.18		
<i>FKBP5</i>	FK506 binding protein 5	31.46		
<i>CHST7</i>	carbohydrate (N-acetylglucosamine 6-O) sulfotransferase 7	30.87	+	
<i>PI15</i>	peptidase inhibitor 15	30.39		
<i>MGP</i>	matrix Gla protein	27.76		
<i>ALDH1A3</i>	aldehyde dehydrogenase 1 family, member A3	26.92	+	
<i>INSL4</i>	insulin-like 4 (placenta)	26.84	+	
<i>ADAMTS3</i>	ADAM metallopeptidase with thrombospondin type 1 motif, 3	25.29	+	
<i>ZBTB16</i>	zinc finger and BTB domain containing 16	24.24	+	
<i>CHSY3</i>	chondroitin sulfate synthase 3	23.03		
<i>P4HA3</i>	prolyl 4-hydroxylase, alpha polypeptide III	20.06		
<i>MUMIL1</i>	melanoma associated antigen (mutated) 1-like 1	18.82		
<i>C7</i>	complement component 7	18.16		
<i>PTGER2</i>	prostaglandin E receptor 2 (subtype EP2), 53kDa	16.68		
<i>LOC129293</i>	hypothetical protein LOC129293	16.52		
<i>LOC647131</i>	hypothetical LOC647131	15.67		
<i>KYNU</i>	kynureninase (L-kynurenine hydrolase)	15.02		
<i>EDNRB</i>	endothelin receptor type B	13.89		
<i>PCSK1</i>	proprotein convertase subtilisin/kexin type 1	13.85		
<i>WNT4</i>	wingless-type MMTV integration site family, member 4	13.73	+	
<i>ADRA2C</i>	adrenergic, alpha-2C-, receptor	13.40		
<i>SCG2</i>	secretogranin II (chromogranin C)	13.36		
<i>FOXO1</i>	forkhead box O1	12.75		
<i>PRL</i>	prolactin	12.53		
<i>MAOA</i>	monoamine oxidase A	11.96	+	
<i>CSGALNACT1</i>	chondroitin sulfate N-acetylgalactosaminyl transferase 1	11.59	+	

<i>PID1</i>	phosphotyrosine interaction domain containing 1	11.39		
<i>MFSD6</i>	major facilitator superfamily domain containing 6	11.04		
<i>LOC645638</i>	similar to WDNM1-like protein	10.21		
<i>IDI1</i>	inhibitor of DNA binding 1	10.12		+
<i>COL15A1</i>	collagen, type XV, alpha 1	10.05		
<i>FAM167A</i>	family with sequence similarity 167, member A	9.95		+
<i>LTBP1</i>	latent transforming growth factor beta binding protein 1	9.68		
<i>IMPA2</i>	inositol(myo)-1(or 4)-monophosphatase 2	9.67	+	
<b>Top 50 down-regulated genes</b>				
<i>KRTAP1-5</i>	keratin associated protein 1-5	143.17		
<i>CXCL3</i>	chemokine (C-X-C motif) ligand 3	58.15		
<i>MEST</i>	mesoderm specific transcript homolog (mouse)	51.05		
<i>KIT</i>	v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog	40.95		
<i>CDC20</i>	cell division cycle 20 homolog (S. cerevisiae)	35.86		
<i>ANLN</i>	anillin, actin binding protein	34.47		
<i>LYPD1</i>	LY6/PLAUR domain containing 1	30.68		
<i>HTR2B</i>	5-hydroxytryptamine (serotonin) receptor 2B	28.47		
<i>DLGAP5</i>	discs, large (Drosophila) homolog-associated protein 5	27.61		
<i>PRC1</i>	protein regulator of cytokinesis 1	26.49		-
<i>FAM176A</i>	family with sequence similarity 176, member A	24.96		
<i>RRM2</i>	ribonucleotide reductase M2 polypeptide	24.06		
<i>C21orf7</i>	chromosome 21 open reading frame 7	23.29		
<i>KIF20A</i>	kinesin family member 20A	22.11		
<i>KRT34</i>	keratin 34	21.39	-	
<i>FJX1</i>	four jointed box 1 (Drosophila)	21.13		
<i>SHCBP1</i>	SHC SH2-domain binding protein 1	20.48		
<i>SLIT2</i>	slit homolog 2 (Drosophila)	20.29		
<i>ASNS</i>	Asparagine synthetase	20.11		
<i>LOXL4</i>	lysyl oxidase-like 4	19.75		
<i>IL8</i>	interleukin 8	19.10	-	
<i>SCN9A</i>	sodium channel, voltage-gated, type IX, alpha subunit	18.02		
<i>CDC2</i>	Cell division cycle 2, G1 to S and G2 to M	17.77		
<i>CDKN3</i>	cyclin-dependent kinase inhibitor 3	17.59		
<i>PSAT1</i>	phosphoserine aminotransferase 1	17.55		
<i>APOBEC3B</i>	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3B	17.40		
<i>DDIT3/NR1H3</i>	DNA-damage-inducible transcript 3/nuclear receptor subfamily 1, group H, member 3	17.25	-	
<i>KRT19</i>	Keratin 19	17.09		
<i>HBD</i>	hemoglobin, delta	16.29		
<i>UHRF1</i>	ubiquitin-like with PHD and ring finger domains 1	16.19		-
<i>KIAA0101</i>	KIAA0101	15.84		
<i>CXCL2</i>	chemokine (C-X-C motif) ligand 2	15.58		
<i>DTL</i>	denticleless homolog (Drosophila)	15.51		
<i>OXTR</i>	oxytocin receptor	15.50		
<i>MLF1IP</i>	MLF1 interacting protein	15.44		
<i>AK5</i>	adenylate kinase 5	15.36		-
<i>OLR1</i>	oxidized low density lipoprotein (lectin-like) receptor 1	15.22		
<i>CEP55</i>	centrosomal protein 55kDa	15.13		
<i>SIPA1L2</i>	signal-induced proliferation-associated 1 like 2	14.12		

<i>ENC1</i>	ectodermal-neural cortex (with BTB-like domain)	14.00		
<i>LBH</i>	limb bud and heart development homolog (mouse)	13.98		
<i>FAM83D</i>	family with sequence similarity 83, member D	13.52		
<i>TPX2</i>	TPX2, microtubule-associated, homolog (Xenopus laevis)	13.07		
<i>NEIL3</i>	nei endonuclease VIII-like 3 (E. coli)	12.90		
<i>FAM84A</i>	Family with sequence similarity 84, member A	12.62		
<i>NUSAP1</i>	nucleolar and spindle associated protein 1	12.54		
<i>GINS1</i>	GINS complex subunit 1 (Psf1 homolog)	12.44		
<i>SLC38A4</i>	solute carrier family 38, member 4	12.41		
<i>DEPDC1</i>	DEP domain containing 1	12.19		
<i>DIAPH3</i>	diaphanous homolog 3 (Drosophila)	12.14		

**Supplement Table S4.** Top networks regulated with both *KLF9* and *PGR* knockdown identified through IPA (Total of 417 genes)\*

<b>ID</b>	<b>Molecules in Network</b>	<b>Score</b>	<b>Focus molecules</b>	<b>Top Functions</b>
<b>1</b>	ARNT, DUSP6, EGR1, EPOR, ERK, Estrogen Receptor, FJX1, G0S2, GDF15, hCG, HK2, HMGA2, IER3, INHBA, JUNB, MMP1 (includes EG:300339), NFkB (complex), NPR3, PDGF BB, PRDM2, PTHLH, SERPINB2, SLC4A4, SOAT1, STC1, STEAP1, TGM2, TIMP3, TM4SF1, TMEM158, TNFSF4, TNFSF13B, TRAF5, Vegf, VEGFC	39	29	Cellular Growth and Proliferation, Cell Death, Cellular Movement
<b>2</b>	AHR, Akt, ANXA1, Ap1, AREG/AREGB, CCL7, CNR1, Creb, CREM, CYR61, DIABLO, EREG, ERK1/2, FABP5, IGF1, IGFBP1, IL8, IL1B, Immunoglobulin, JUN, LDL, MAFF, Mapk, NPC1, NR4A2, PGR, PI3K (complex), PLIN2, PPP1R12A, RAB4B, SERPINE1, TNFAIP6, TNFRSF11B, TNFSF10, ZEB1	35	27	Cell Death, Cellular Growth and Proliferation, Cellular Movement
<b>3</b>	ACP5, AKAP7, ARL4C, ATP1B1, CD55, CD97, CDC37L1, CDKN1C, CRABP2, CXCL12, DHCR7, DHRS3, FSH, GEM, GK, GRK5, Hsp70, IER2, IFIH1, IFIT2, IFIT3, IFN Beta, IgG, Interferon alpha, Jnk, Lh, P38 MAPK, PAWR, PDXK, RAB27A, SLC16A6, TGFBR3, THBS1, TNPO1, TPM1 (includes EG:22003)	35	27	Cellular Development, Hematopoiesis, Nervous System Development and Function
<b>4</b>	ACTN1, APOE, APP, ATP1B1, CSRNP1, DIRAS3, FADD, FANCC, GLUL, Hsp90, HSP90AA1, IFI44L, IGF1R, INSR, NAMPT, NOS2, NR3C1, PAWR, PDLIM1, PHF17, PIK3R3, PPARG, PPP2CA, PRKCB, PRKCE, PSEN1, PTN, RPGR, SDPR, SGPL1, SLC40A1, STAT3, TIMP3, TNFRSF12A, TNFSF4	17	17	Cancer, Endocrine System Disorders, Gastrointestinal Disease
<b>5</b>	ADAM19, AKR1C1/AKR1C2, C11orf96, C13orf15, CD47, CDC25B, CDK1, Collagen type IV, Collagen(s), ETV5, FOXM1, GAS1, GLI1, HEY1, IMPA2, ITGA2, ITGAV, ITGB1, JUNB, LAMC2, Laminin, MMP2, MXI1, NR2F2, RPS6KB1, S100A4, SCD, SDC1, SLC2A1, TGFB1, TGFB2, THBS1, TMEM100, TNC, ZC3HAV1L	17	17	Cellular Movement, Nervous System Development and Function, Cancer
<b>6</b>	Actin, BAMBI, C19orf66, CTSD, DUSP4, FBLIM1, FERMT2, GADD45B, HBG1, HDAC1, HOXA5, HSP90B1, HSPA8, IFI35, IFNA2, MAD1L1, MTA2, NBN,	17	17	Cellular Assembly and Organization, DNA Replication, Recombination, and

	NR4A2, NUP153, POLD3, REST, RRM2, RUNX1T1, SATB1, SMARCA4, SMARCC1, SP110, ST6GALNAC5, TES, TP53, TRIM22, TSC22D3, UBE2L6, UHRF1			Repair, Cell Death
7	AKAP2/PALM2-AKAP2, ARRDC3, C9orf80, COL8A1, ETS2, GABPA, HRAS, ID2, INTS3, ITGB4, KIAA1199, KLF4, mir-135, MYB, MYC, MYCN, OBFC2A, ODC1, OXTR, PRDM5, PTGES, RNF144B, SAT1, SEMA3A, SHC4, SHMT2, SIK1, SKP2, SLC25A19, TAF1A, TAF1B, TAF1C, TCEAL1, TP73, ZNF217	17	17	Cell Death, Cancer, Gene Expression
8	ALDH1A3, BACE1, BCL3, BCL2A1, CASP1, COL1A2, DUSP10, EPHB2, FLI1, Gm-csf, GPR126, HOXA13, IGFBP2, IL24, KAT2B, KYNU, LAMA3, LAMB3, MYCN, NFKBIE, OAS1, PDK4, PLSCR1, PPARD, PPP1R3C, REL, RIPK2, SERPINB1, SERPINB9, SERPINE1, SLC1A2, TNF, TNFSF13B, VAPA, WNT5A	14	15	Dermatological Diseases and Conditions, Cancer, Genetic Disorder
9	ADAM17, Akt, ARNT, BID, CAV2, CKS2, EDN1, EPO, EPOR, ERBB2, ERBB4, ERRF1, ESR1, GRB2, HBEGF, HERC6, IFNG, IGFBP5, INSR, IRS1, IRS2, MAP2, MTA1, MX2, NR2F1, p85 (pik3r), PDE3B, PIK3R1, PLA2G16, PPT1, SHC1, SLC15A3, STAT5A, TFF3, TPM1 (includes EG:22003)	14	15	Cellular Movement, Cell Cycle, Tissue Development
10	26s Proteasome, AHR, ALG1, AR, ATAD2, CCND1, CCNT1, CDK9, ETV1, GPR37, H19, HEXIM1, IGF2, IGF2BP3, IGFBP1, IL2RB, KLF9, MAOA, MAT2A, MDFIC, NCOA3, PDE6B, PHOX2A, PI3K (complex), PIAS4, PSMD14, RAP1B, SLC22A4, SLC31A1, SP1, SP4, STUB1, TFF1, TGOLN2, ZBTB10	14	15	Gene Expression, Organ Morphology, Cell Death
11	AXIN1, BACH1, BCL2L1, CDC14B, CEBPB, CTNNB1, DAPK1, DBP, DIXDC1, ESR1, FBN1, FSH, GSK3B, HIF1A, Hsp70, IL10, ITPRIP, Lh, MAP3K4, MAPK8, MCL1, miR-21/miR-590-5p, NOX4, NQO1, PBK, PDE4B, PLK2, PTEN, SMAD3, SPRY1, TMSB15A, TNF, TP53, TP73, VCAN	9	11	Cell Death, Developmental Disorder, Cancer
12	AGTR1, ALG5, ATF4, CA9, CGA, CHEK2, DKK1, E2F4, EZH2, HDAC9, Hdac, Histone h3, Histone h4, HOXA9, HOXA11, HPSE, ID1, IGFBP1, MTA1,	7	10	Cancer, Hematological Disease, Cell Cycle

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	MYCN, MYT1, NCOA3, PHF1, RB1, RBBP4, RBL1, RNA polymerase II, RPS6, RRM2, SRPK2, SRPR, SUZ12, TP53INP1, WNT1, ZNF91			
<b>13</b>	ABCA1, C21orf7, CXCR7, FABP4, FADS1, FAM162A, HIC1, IL13, KAZN, KITLG, PAPPA, PPARG, RAB33A, RIN2, RQCD1, SPINT2, STAT6, TAL1, TCF3, TCF12	7	8	Cellular Development, Hematological System Development and Function, Hematopoiesis

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\* *siKP*-regulated genes (*siKP* vs. NT);  $\geq 1.5$  fold-change



**Supplement Table S5.** Top biological functions of differentially expressed KLF9+PGR targets in cAME-treated HESC identified through IPA (Total of 417 genes)\*

<b>Biological Functions</b>	<b>P-value</b>	<b>No. of Molecules</b>
<u>Diseases and disorders</u>		
Cancer	3.07E-14	158
Reproductive system disease	1.66E-12	114
Gastrointestinal disease	2.04E-07	69
Dermatological diseases and conditions	8.64E-07	61
Genetic disorder	8.64E-07	228
<u>Molecular and cellular functions</u>		
Cell death	7.21E-10	83
Cellular movement	1.23E-08	60
Cellular growth and proliferation	1.52E-08	100
Cellular development	1.06E-06	63
Gene expression	1.65E-05	71
<u>Physiological system development and function</u>		
Hematological system development and function	1.09E-05	29
Immune cell trafficking	1.09E-05	13
Organ morphology	2.69E-05	4
Tissue development	5.19E-05	50
Hematopoiesis	5.50E-05	25

\* *siKP*-regulated genes (*siKP* vs. NT);  $\geq 1.5$  fold-change

**Supplement Table S6.** Canonical Pathways identified using IPA with both *KLF9* and *PGR* knockdown (Total of 417 genes)

<b>Ingenuity Canonical Pathway</b>	<b>-log (P-value)</b>	<b>P-value</b>	<b>Ratio</b>	<b>Molecules</b>
Role of IL-17F in allergic inflammatory airway disease	3.312	4.88E-04	0.143	ATF4, CCL7, IGF1, IL8, IL1B, SIK1
Role of tissue factor in cancer	2.267	5.41E-03	0.074	CFL2, CYR61, EGR1, IL8, IL1B, MMP1, PIK3R3, VEGFC
Chondroitin sulfate biosynthesis	2.214	6.11E-03	0.106	CHST7, CHSY3, CSGALNACT1, UST, XYLT2
Inhibition of angiogenesis by TSP1	2.022	9.51E-03	0.121	CD47, JUN, SDC1, THBS1
HMGB1 signaling	2.016	9.64E-03	0.072	DIRAS3, IL8, JUN, PIK3R3, RHOU, SERPINE1, TNFRSF11B
Role of macrophages, fibroblasts and endothelial cells in rheumatoid arthritis	1.876	1.33E-03	0.045	ATF4, CXCL12, DKK1, IL8, IL1B, JUN, MMP1, PIK3R3, PLCL2, TNFRSF11B, TNFSF13B, TRAF5, VEGFC, WNT2
Pantothenate and CoA biosynthesis	1.866	1.36E-02	0.150	BCAT1, DPYD, ILVBL
Airway pathology in COPD	1.785	1.64E-02	0.250	IL8, MMP1
Aryl hydrocarbon receptor signaling	1.719	1.91E-02	0.057	AHR, ALDH1A3, ARNT, HSP90B1, IL1B, JUN, NR2F1, TGM2
Neuregulin signaling	1.669	2.14E-02	0.063	ADAM17, AREG/AREGB, EREG, ERF11, HSP90B1, PIK3R3
Role of osteoblasts, osteoclasts and chondrocytes in rheumatoid arthritis	1.665	2.16E-02	0.048	ACP5, ADAM17, DKK1, IGF1, IL1B, JUN, MMP1, PIK3R3, TNFRSF11B, TRAF5, WNT2
Hepatic fibrosis/ hepatic stellate cell activation	1.616	2.42E-02	0.057	BAMBI, IGF1, IL8, IL1B, MMP1, SERPINB2, TNFRSF11B, VEGFC
Glucocorticoid receptor signaling	1.522	3.01E-02	0.043	ANXA1, CDKN1C, HSP90B1, IL8, IL1B, JUN, MMP1, PGR, PIK3R3, PRKAB2, PRKAG2, SERPINE1, BCAT1, ILVBL
Valine, leucine and isoleucine biosynthesis	1.513	3.07E-02	0.182	BCAT1, ILVBL
Arginine and proline metabolism	1.481	3.3E-02	0.070	ALDH1A3, LAP3, MAOA, ODC1, SAT1
IGF-1 signaling	1.442	3.61E-02	0.059	CYR61, IGF1, IGFBP1, JUN, PIK3R3, PRKAG2
ILK signaling	1.434	3.68E-02	0.049	ATF4, CFL2, DIRAS3, FERMT2, JUN, PIK3R3, PPP1R12A, RHOU, VEGFC
Amyotrophic lateral sclerosis signaling	1.423	3.77E-02	0.060	CASP1, GLUL, IGF1, PIK3R3, SLC1A2, VEGFC
Role of pattern recognition receptors in recognition of bacteria and viruses	1.414	3.86E-02	0.065	CASP1, IFIH1, IL1B, OAS1, PIK3R3
Nitric oxide signaling in the cardiovascular system	1.392	4.05E-02	0.062	HSP90B1, PDE3B, PIK3R3, PRKAG2, VEGFC
TREM1 signaling	1.390	4.07E-02	0.075	CASP1, CCL7, IL8, IL1B,
cAMP-mediated signaling	1.387	4.10E-02	0.047	AKAP7, AKAP2, ATF4, CNR1, CREM, DUSP6, NPR3, PDE3B, PDE4B, RGS18
HIF1 $\alpha$ signaling	1.369	4.28E-02	0.058	ARNGT, JUN, MMP1, PIK3R3, SLC2A1, VEGFC
Semaphorin signaling in neurons	1.364	4.33E-02	0.077	CFL2, DIRAS3, RHOU, SEMA3A,
ATM signaling	1.364	4.33E-02	0.074	ATF4, GADD45B, JUN, NBN
Production of NO and ROS in macrophages	1.358	4.39E-02	0.049	DIRAS3, JUN, PIK3R3, PPP1R12A, PPP1R3C, RAP1B, RHOU, TNFRSF11B
Dopamine receptor signaling	1.350	4.46E-02	0.065	MAOA, PPP1R12A, PPP1R3C, PRKAG2, QDPR

Interferon signaling	1.324	4.74E-02	0.088	IFII35, IFIT3, OAS1
Role of IL-17A in arthritis	1.313	4.86E-02	0.067	CCL7, IL8, MMP1, PIK3R3
Ceramide signaling	1.310	4.90E-02	0.061	DIABLO, JUN, PIK3R3, S1PR2, TNFRSF11B
LPS/IL-1 mediated inhibition of RXR function	1.307	4.93E-02	0.045	ALDH1A3, CHST7, FABP4, FABP5, IL1B, JUN, MAOA, TNFRSF11B, UST
PPAR $\alpha$ /RXR $\alpha$ activation	1.304	4.97E-02	0.048	GK, HSP90B1, IL1B, JUN, PLCL2, PRKAB2, PRKAG2, TGFB3, JUN, PDE3B, PDE4B, PIK3R3, PRKAG2, RAP1B, RXFP1
Relaxin signaling	1.295	5.07E-02	0.049	JUN, PDE3B, PDE4B, PIK3R3, PRKAG2, RAP1B, RXFP1
Cardiac $\beta$ -adrenergic signaling	1.281	5.24E-02	0.051	AKAP7, AKAP2, PDE3B, PDE4B, PPP1R12A, PP1R3C, PRKAG2
Sphingosine-1-phosphate signaling	1.267	5.40E-02	0.052	CASP1, DIRAS3, PIK3R3, PLCL2, RHOU, S1PR2
Glioma invasiveness signaling	1.242	5.73E-02	0.068	DIRAS3, PIK3R3, RHOU, TIMP3
IL-17A signaling in fibroblast	1.228	5.92E-02	0.077	CCL7, JUN, MMP1,
Estrogen-dependent breast cancer signaling	1.197	6.35E-02	0.062	ATF4, IGF1, JUN, PIK3R3
TR/RXR activation	1.180	6.61E-02	0.056	AKR1C1, KLF9, PDE3B, PIK3R3, SLC2A1
RAR activation	1.178	6.64E-02	0.046	ALDH1A3, CRABP2, JUN, MMP1, NR2F1, PIK3R3, PNPLA4, PRKAG2
Valine, leucine and isoleucine degradation	1.176	6.67E-02	0.066	ALDH1A3, AOX1, BCAT1, MCEE
Androgen and estrogen metabolism	1.176	6.67E-02	0.056	AKR1C1, ARSG, CSGALNACT1, HSD17B6
CDK5 signaling	1.145	7.15E-02	0.056	EGR1, LAMB1, PPP1R12A, PPP1R3C, PRKAG2
Hypoxia signaling in the cardiovascular system	1.134	7.34E-02	0.061	ARNT, ATF4, HSP90B1, JUN
Atherosclerosis signaling	1.112	7.72E-02	0.049	CXCL12, IL8, IL1B, MMP1, TNFRSF12A
PPAR signaling	1.096	8.01E-02	0.050	HSP90B1, IL1B, JUN, NR2F1
Neurotrophin/TRK signaling	1.094	8.05E-02	0.056	ATF4, JUN, PIK3R3, SPRY1
B cell activating factor signaling	1.089	8.15E-02	0.068	JUN, TNFSF13B, TRAF5,
G-protein coupled receptor signaling	1.083	8.26E-02	0.035	ATF4, CD97, CNR1, DUSP6, GPR37, GPR126, GPR89A/GPR89B, LPHN3, NPR3, OXTR, PDE3B, PDE4B, PIK3R3, PRKAG2, PTHLH, RGS18, RXFP1, S1PR2
p53 signaling	1.049	8.93E-02	0.053	GADD45B, JUN, PIK3R3, THBS1, TP53INP1
IL-6 signaling	1.034	9.24E-02	0.051	IL8, IL1B, JUN, TNFAIP6, TNFRSF11B
Renal cell carcinoma signaling	1.020	9.55E-02	0.056	ARNT, JUN, PIK3R3, SLC2A1
Chemokine signaling	1.020	9.55E-02	0.059	CCL7, CXCL12, JUN, PPP1R12A
Polyamine regulation in colon cancer	1.003	9.92E-02	0.083	ODC1, SAT1
Fructose and mannose metabolism	0.993	1.02E-01	0.067	GMDS, HK2, TSTA3
Cellular effects of sildenafil (Viagra)	0.985	1.04E-01	0.047	GPR37, PDE3B, PDE4B, PLCL2, PPP1R12A, PRKAG2,
OX40 signaling pathway	0.950	1.12E-01	0.049	JUN, TNFSF4, TRAF5
Cholecystokinin/gastrin-mediated signaling	0.949	1.13E-01	0.050	CREM, DIRAS3, IL1B, JUN, RHOU
Bile acid biosynthesis	0.929	1.18E-01	0.060	AKR1C1/AKR1C2, ALDH1A3, SOAT1
Leptin signaling in obesity	0.920	1.20E-01	0.052	PDE3B, PIK3R3, PLCL2, PRKAG2,
Synaptic long-term potentiation	0.909	1.23E-01	0.048	ATF4, PPP1R12A, PPP1R3C, PRKAG2,

				RAP1B
LXR/RXR activation	0.904	1.25E-01	0.048	CCL7, IL1B, SCD, TNFRSF11B
IL-17A signaling in gastric cells	0.877	1.33E-01	0.080	IL8, JUN
Pentose and glucuronate interconversions	0.877	1.33E-01	0.061	CSGALNACT1, UCHL3
Protein kinase A signaling	0.862	1.37E-01	0.036	AKAP7, AKAP2, ATF4, CREM, PDE3B, PDE4B, PLCL2, PPP1R12A, PPP1R3C, PRKAG2, RAP1B
Corticotrophin releasing hormone signaling	0.859	1.38E-01	0.043	ATF4, CNR1, JUN, PRKAG2, RAP1B
Type 2 diabetes mellitus signaling	0.812	1.54E-01	0.040	PIK3R3, PKM2, PRKAB2, PRKAG2, TNFRSF11B
Lymphotoxin $\beta$ receptor signaling	0.799	1.59E-01	0.054	DIABLO, PIK3R3, TRAF5
NRF2-mediated oxidative stress response	0.794	1.61E-01	0.037	AOX1, ATF4, BACH1, JUN, JUNB, MAFF, PIK3R3
Glioblastoma multiforme signaling	0.788	1.63E-01	0.038	DIRAS3, IGF1, PIK3R3, PLCL2, RHOU, WNT2
Propanoate metabolism	0.782	1.65E-01	0.054	ALDH1A3, MCEE, SUCLA2
VEGF signaling	0.764	1.72E-01	0.044	ARNT, EIF1AX, PIK3R3, VEGFC
Bladder cancer signaling	0.752	1.77E-01	0.044	IL8, MMP1, THBS1, VEGFC
ERK/MAPK signaling	0.751	1.77E-01	0.035	ATF4, DUSP6, PIK3R3, PPP1R12A, PPP1R3C, PRKAG2, RAP1B,
Serotonin receptor signaling	0.750	1.78E-01	0.061	MAOA, QDPR
Starch and sucrose metabolism	0.750	1.78E-01	0.045	CSGALNACT1, HK2, UCHL3
P2Y purigenic receptor signaling pathway	0.746	1.79E-01	0.040	ATF4, JUN, PIK3R3, PLCL2, PRKAG2
Axonal guidance signaling	0.740	1.82E-01	0.031	ADAM17, ADAM19, CFL2, CXCL12, EPHA5, IGF1, PIK3R3, PRKAG2, RAP1B, SEMA3A, SEMA5A, VEGFC, WNT2
Retinoic acid mediated apoptosis signaling	0.735	1.84E-01	0.049	CRABP2, PARP9, TNFSF10,
Xenobiotic metabolism signaling	0.735	1.84E-01	0.034	AHR, ALDH1A3, ARNT, CHST7, HSP90B1, IL1B, MAOA, PIK3R3, UST
CXCR4 signaling	0.723	1.89E-01	0.038	CXCL12, DIRAS3, EGR1, JUN, PIK3R3, RHOU
Complement system	0.707	1.96E-01	0.061	CD55, MASP1
Insulin receptor signaling	0.706	1.97E-01	0.040	PDE3B, PIK3R3, PPP1R12A, PPP1R3C, PRKAG2
Activation of IRF by cytosolic pattern recognition receptors	0.705	1.97E-01	0.048	IFIH1, IFIT2, JUN,
PXR/RXR activation	0.691	2.04E-01	0.047	IGFBP1, PRKAG2, SCD
Assembly of RNA polymerase I complex	0.683	2.08E-01	0.083	TAF1A
CD40 signaling	0.677	2.1E-01	0.044	JUN, PIK3R3, TRAF5
Oncostatin M signaling	0.668	2.15E-01	0.059	MMP1, TIMP3
NF- $\kappa$ B signaling	0.664	2.17E-01	0.035	IL1B, PIK3R3, TGFBR3, TNFRSF11B, TNFSF13B, TRAF5
Tyrosine metabolism	0.663	2.17E-01	0.045	ALDH1A3, AOX1, MAOA
Nitrogen metabolism	0.649	2.24E-01	0.057	GLUL, TGM2,
Aminoacyl-tRNA biosynthesis	0.649	2.24E-01	0.057	ERAS2, NARS2
Ovarian cancer signaling	0.640	2.29E-01	0.036	CGA, PIK3R3, PRKAG2, VEGFC, WNT2
Glutamate metabolism	0.631	2.34E-01	0.056	EARS2, GLUL
Colorectal cancer metastasis signaling	0.616	2.42E-01	0.033	DIRAS3, JUN, MMP1, PIK3R3, PRKAG2, RHOU, VEGFC,

				WNT2
Notch signaling	0.614	2.43E-01	0.049	ADAM17, HEY1,
Phenylalanine metabolism	0.614	2.43E-01	0.054	ALDH1A3, MAOA
Erythropoietin signaling	0.612	2.44E-01	0.041	EPOR, JUN, PIK3R3
Melatonin signaling	0.612	2.44E-01	0.044	PLCL2, PRKAG2, RORB
Glycine, serine and threonine metabolism	0.612	2.44E-01	0.044	MAOA, PLCL2, SHMT2
Neuropathic pain signaling in dorsal horn neurons	0.608	2.46E-01	0.039	GPR37, PIK3R3, PLCL2, PRKAG2,
Lysine biosynthesis	0.606	2.48E-01	0.091	TGM2
Acute phase response signaling	0.601	2.50E-01	0.035	CRABP2, IL1B, JUN, PIK3R3, SERPINE1, TNFRSF11B
Docosahexaenoic acid (DHA) signaling	0.597	2.53E-01	0.050	IL1B, PIK3R3
April mediated signaling	0.597	2.53E-01	0.048	JUN, TRAF5
Inositol phosphate metabolism	0.581	2.62E-01	0.036	GRK5, IMPA2, INPP5A, PIK3R3, PLCL2
Aminosugars metabolism	0.577	2.65E-01	0.043	HK2, PDE3B, PDE4B
Folate biosynthesis	0.574	2.67E-01	0.077	QDPR
Hepatic cholestasis	0.573	2.67E-01	0.035	IL8, IL1B, JUN, PRKAG2, TNFRSR11B
Ephrin receptor signaling	0.573	2.68E-01	0.031	ATF4, CFL2, CXCL12, EPHA5, RAP1B, VEGFC
Rac signaling	0.571	2.69E-01	0.034	CFL2, JUN, NOX4, PIK3R3,
IL-8 signaling	0.566	2.72E-01	0.034	DIRAS3, IL8, NOX4, PIK3R3, RHOU, VEGFC
IL-17 signaling	0.555	2.79E-01	0.041	IL8, JUN, PIK3R3
Communication between innate and adaptive immune cells	0.555	2.79E-01	0.032	IL8, IL1B, TNFSF13B
mTOR signaling	0.532	2.94E-01	0.032	DIRAS3, PIK3R3, PRKAB2, PRKAG2, RHOU, VEGFC
TGF- $\beta$ signaling	0.449	3.56E-01	0.034	INHBA, JUN, SERPINE1
Rank signaling in osteoclasts	0.424	3.77E-01	0.033	JUN, PIK3R3, TRAF5
HGF signaling	0.332	4.65E-01	0.029	JUN, PIK3R3, RAP1B

**Supplement Table S7.** List of KLF9+PGR- regulated genes in cAME-treated HESC that are associated with uterine pathologies<sup>a,b</sup>

Functions Annotation	Molecules	P-value	No. of Molecules
1. Endometriosis	<b>AHR</b> , ALDH1A3, <b>ATF4</b> , ATP1B1, BCAT1, C13orf15, <b>CASP1</b> , CAV2, CYR61, DKK1, <b>EGR1</b> , <b>EPOR</b> , ERFF1, FBN1, <b>G0S2</b> , <b>HMGA2</b> , IGFBP1, <b>IL8</b> , <b>INHBA</b> , JUN, <b>JUNB</b> , <b>KIAA1199</b> , MAOA, MMP1 (includes EG:300339), <b>PBK</b> , PGR, <b>PLK2</b> , PRDM2, RAP1B, <b>REL</b> , SAT1, <b>STC1</b> , <b>TNFSF13B</b> , VEGFC	1.58E-09	34
2. Uterine cancer	<b>AHR</b> , ANXA1, ARNT, C16orf45, <b>CD97</b> , <b>CRABP2</b> , <b>CXCL12</b> , CYR61, DIXDC1, DKK1, <b>EPOR</b> , <b>ETV5</b> , FBN1, HSP90B1, <b>IFI44L</b> , <b>IFIH1</b> , <b>IFIT3</b> , IGF1, <b>IL8</b> , JUN, KLF9, <b>LPCAT2</b> , MAOA, MASP1, MRV11, ODC1, PDK4, PGR, PIK3R3, SDPR, TIMP3, <b>TPBG</b> , <b>TPM1</b> (includes EG:22003), ZEB1	1.64E-06	34
3. Uterine leiomyoma	<b>AHR</b> , ARNT, <b>CD97</b> , <b>CRABP2</b> , CYR61, FBN1, <b>IFI44L</b> , <b>IFIH1</b> , <b>IFIT3</b> , JUN, MAOA, MRV11, PDK4, PIK3R3, SDPR, <b>TPBG</b> , ZEB1	1.13E-04	17
4. Adenomyosis	CDKN1C, <b>KCNE4</b> , LGMN, MRV11, RHOU, THBS1	2.68E-03	6

<sup>a</sup> Bold indicates up-regulation with *KLF9* and *PGR* knockdown (From 417 genes).

<sup>b</sup> Identified through IPA

**Supplement Table S8A.** Summary of GSEA of *siKP* vs. NT gene sets, with FDR  $\leq 0.25$

	GO	Functional Processes	Gene	FDR
<b>Enriched in <i>siKP</i></b>	Biological process	Defense response	RSAD, IL8, MX2, MX1, TNFAIP6, NOX4, INHBA, CD97, CLEC1A, NMI, HRH1, CXCL2, IRAK2, IL1RAP, LY96, FOSL1, CEBPB, BCL10, GNLY, TCIRG1, GPR68, TGFB1, CBARA1, FAIM3, CEBPG, BNIP3, IL1A, SCG2, LILRB5, APOBEC3G, CCR6, PRF1, CYSLTR1, NFATC3, STAB1, C5, MST1R, MLF2, BNIP3L, PRDX5, TLR3, MBL2, CCL4, AGER, PLA2G7, LYST, KLRG1, MNDA, CD19, CCR7, S100A7, CXCL10, OR2H2, CHST2, KNG1, XCR1, DEFB127, DEFB103A, TRAT1, EREG, NCF2, CX3CR1, TACR1, IL17C, TNFRSF1A	0.235
		Response to biotic stimulus	RSAD2, ERN1, ISG20, IFI44, CXCL12, IRF7, FOSL1, BCL10, BANF1, BNIP3, DNAJB2, APOBEC3G, TRIM22, TP53, SPACA3, HSPA1L, POLA1, CCL18, IFNGR2, STAB1, DNAJB1, BCL3, BNIP3L, DUOX2, TLR3, CCL4, HSPE1, DNAJA1, TNF, CD24, S100A7, DERL3, DEFB127, DEFB103A, DNAJC4, CCL8, APOBEC3F, IFNGR1, TOR1A, AMFR, HSPA1B, DERL2, IFNAR2, CCDC130, CCL22, HBXIP	0.237
		Negative regulation of MAP kinase activity	DUSP6, RGS4, SPRED2, SPRED1, DUSP2	0.249
	Molecular function	Chemokine activity	IL8, CCL7, CXCL12, CXCL2, CKLF, CCL18, C5, CCL4, CXCL3, XCL2, CXCL10, CCL17, CCL2, CCL8	0.154
		G protein coupled receptor binding	IL8, CCL7, CXCL12, CXCL2, CKLF, REEP1, CCL18, C5, CCL4, CXCL3, XCL2, CXCL10, CCL17, CCL2, CCL8,	0.158
		Cytokine activity	TNFRSF11B, IL8, CCL7, GDF15, INHBA, CXCL12, CXCL2, SDCBP, SPRED2, MIF, SPRED1, CSF1, IL1RN, SCG2, CKLF, YARS, SECTM1, GH1, CCL18, C5, IL7, CCL4, CXCL3	0.209
<b>Diminished in <i>siKP</i></b>	Cellular compartment	Proteinaceous extracellular matrix	MUC5AC, APLP1, OPTC, TFPI2, COL7A1, COL3A1, COL9A1, COL1A2, COL5A2, ODAM, EFEMP1, ECM1, LAMC1, COL16A1, TNXB, DSPP, COL10A1,	<0.001

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	COL9A3, COL8A1, FMOD, MGP, MATN3, COL5A1, EFEMP2, SNTB2, LAMB2, COL6A3, LTBP2, ADAMTS5, SGCB, ERBB2IP, FBN1, FBLN2, POSTN, CTGF, COL18A1, FBLN1, COL4A2, FBLN5, NID2, MMP10, COL15A1, LAMB1	
Extracellular matrix	MUC5AC, APLP1, OPTC, TFPI2, COL7A1, COL3A1, COL9A1, COL1A2, COL5A2, ODAM, EFEMP1, ECM1, LAMC1, COL16A1, TNXB, DSPP, COL10A1, COL9A3, COL8A1, FMOD, MGP, MATN3, COL5A1, EFEMP2, SNTB2, LAMB2, COL6A3, LTBP2, ADAMTS5, SGCB, ERBB2IP, FBN1, FBLN2, POSTN, CTGF, COL18A1, FBLN1, COL4A2, FBLN5, NID2, MMP10, COL15A1, LAMB1	<0.001
Extracellular matrix part	MUC5AC, APLP1, COL7A1, COL3A1, COL9A1, COL1A2, COL5A2, ODAM, LAMC1, COL16A1, TNXB, COL10A1, COL9A3, COL8A1, COL5A1, EFEMP2, SNTB2, LAMB2, COL6A3, SGCB, ERBB2IP, FBN1, COL18A1, COL4A2, NID2, COL15A1, LAMB1	<0.001
Collagen	COL7A1, COL3A1, COL9A1, COL1A2, COL5A2, COL16A1, TNXB, COL10A1, COL9A3, COL8A1, COL5A1, COL6A3, COL18A1, COL4A2, COL15A1	<0.001
Basement membrane	LAMC1, EFEMP2, SNTB2, LAMB2, SGCB, ERBB2IP, FBN1, COL4A2, NID2, LAMB1	<0.001
Actin filament	TSC1, AMOT, MYO6, ACTA1, PALLD, ACTC1	<0.001
Cell matrix junction	VCL, SORBS1, ERBB2IP, NEXN	0.016
Actin cytoskeleton	MYL6, MYL9, MTSS1, MYH9, AMPH, CORO1A, TSC1, DCTN2, EPB49, KALRN, ARPC4, IPP, AMOT, MYO6, ACTR1A, ACTR2, TPM3, ACTA1, SPTBN1, CASK, ABRA, MYH10, VASP, MYOM1, ACTR3, KLHL2, VILL, CLIC4, FLNA, CORO1C, SORBS1, GSN, FLNB, PALLD, SMTN, ARPC5, CDC42EP3, TPM1, PDLIM5, ACTC1	0.025
Basal lamina	LAMC1, SNTB2, LAMB2, SGCB, LAMB1	0.044
Extracellular region part	COL9A1, COL1A2, COL5A2, PGCP, LGALS3BP, WNT5A, TCN2, IL5RA, IL15, VTN, CRLF1, FLT1,	0.061

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	ODAM, EFEMP1, ECM1, LAMC1, NUCB1, GPX3, FSTL3, DKK3, COL16A1, NOG, TNXB, DSPP, MMP2, FGF9, COL10A1, COL9A3, COL8A1, CDH13, FMOD, GPC1, PSAP, MGP, MATN3, COL5A1, EFEMP2, SNTB2, LAMB2, COL6A3, LTBP2, ADAMTS5, SGCB, ERBB2IP, INSL4, FBN1, FBLN2, REN, POSTN, CTGF, COL18A1, FBLN1, SST, LOXL2, NUCB2, PTN, COL4A2, IGFBP1, FBLN5, NID2, MMP3, MMP10, TGFBI, HTRA1, PCSK5, COL15A1, LAMB1	
Lamellipodium	WASF2, DBNL, ABI1, TESC, TSC1, ITGB1BP1, APBB2, FGD3, AMOT, PDPN, ALS2, FAP, FGD6	0.100
Extracellular region	COL9A1, COL1A2, COL5A2, FRZB, PGCP, LPL, LGALS3BP, WNT5A, TCN2, IL5RA, IL15, VTN, CRLF1, EGFL7, FLT1, APP, ODAM, EFEMP1, ECM1, LAMC1, NUCB1, GPX3, FSTL3, DKK3, COL16A1, NOG, TNXB, DSPP, MMP2, FGF9, COL10A1, COL9A3, COL8A1, SERPINF1, CDH13, GSN, AGGF1, FMOD, GPC1, PSAP, MGP, MATN3, COL5A1, EFEMP2, CLEC11A, SNTB2, LAMB2, COL6A3, LTBP2, ADAMTS5, GLA, SGCB, ERBB2IP, INSL4, INHBB, FBN1, FBLN2, REN, POSTN, IFI30, CTGF, COL18A1, FBLN1, SST, LOXL2, NUCB2, PLTP, PTN, COL4A2, IGFBP1, FBLN5, NID2, MMP3, MMP10, RNASET2, TGFBI, HTRA1, PCSK5, COL15A1, PPT1, LAMB1, PAPPA	0.099
DNA-directed RNA polymerase complex	SFRS2IP, PPARGC1A, POLR3G, POLR2D, HCLS1, POLR2A, C19ORF2	0.092
Leading edge	DBNL, MYH9, ABI1, TESC, TSC1, ITGB1BP1, APBB2, FGD3, AMOT, TLN1, MYO6, CDC42BPG, CDK6, PDPN, ALS2, FAP, FDG6, CDC42BPA, MYO5A	0.094
Basolateral plasma membrane	PTPRC, TJP1, STX2, SLC4A11, VCL, SORBS1, ERBB2IP, NEXN	0.090
ER golgi intermediate compartment	NUCB1, P4HB, TMED10, ANPEP, PDIA6, ERGIC3, NUCB2, FN1	0.090

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	RNA polymerase complex	SFRS2IP, PPARGC1A, POLR3G, POLR2D, HCLS1, POLR2A, C19ORF2	0.103
	Nuclear DNA-directed RNA polymerase complex	SFRS2IP, PPARGC1A, POLR3G, POLR2D, HCLS1, POLR2A, C19ORF2	0.098
	Lytic vacuole	TOM1L1, NAGLU, RAMP2, DNASE2, SLC17A5, ANKRD27, CTSF, NPC2, TPP1, GLA, IFI30, GALC, PPT1	0.099
	Microtubule associated complex	KIF5B, MAP1A, KIF3C, KIF15, ATG4D, DCTN2, ACTR1A, KIF5C, EML2, MAP4, KIFAP3, KIF1B, KIF23, DYNC1LI2, MAP1B, MAP2	0.095
	Lysosome	TOM1L1, NAGLU, RAMP2, DNASE2, SLC17A5, ANKRD27, CTSF, NPC2, TPP1, GLA, IFI30, GALC, PPT1	0.119
	Myofibril	DES, TPM3, ACTA1, ABRA, MYOM1, TTN, VCL, TPM1	0.234
	Vacuole	TOM1L1, NAGLU, RAMP2, DNASE2, SLC17A5, ANKRD27, CTSF, NPC2, TPP1, GLA, IFI30, GALC, PPT1	0.227
Molecular function	Oxidoreductase activity acting on the aldehyde or oxo group of donors	ADH5, ALDH3A1, ALDH2, ALDH9A1, PDHA2, GAPDHS, PDHB, ALDH6A1, ALDH1A1, AOX1, ALDH1A3	0.025
	Structural constituent of muscle	TCAP, MYOM1, TTN, SMTN, TPM1, ACTC1, ASPH	0.026
	Extracellular matrix structural constituent	KAL1, OPTC, TFPI2, LAMC1, DSPP, MGP, MATN3, EFEMP2, FBN1, FBLN2, COL4A2, LAMB1	0.021
	Oxidoreductase activity acting on the aldehyde or oxo group of donors NAD or NADP as acceptor	ALDH4A1, ADH5, ALDH3A1, ALDH2, ALDH9A1, GAPDHS, ALDH6A1, ALDH1A1, ALDH1A3	0.034
	Peptidase activity	ACE2, SENP1, ATG4D, MMP24, CTSO, CASP9, USP12, KLKB1, SENP2, CAPN11, USP5, MAP1D, F11, IDE, AEBP1, METAP2, NPEPPS, CTSS, USP9X, USP7, RCE1, CTSH, CTSK, PGCP, TPP2, BLMH, MME, LNPEP, CFI, ADAMTS2, CORIN, F10, MMP2, CTSD, MMP12, CPE, FAP, TRHDE, DPP4, ANPEP, CFD, TPP1, C1S, LGMN, CTSB, REN, PDIA3, USP53, MMP3, MASP1, GGH, HTRA1, CASP6,	0.120

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Integrin binding	PAPPA COL4A3, ADAM9, ADAM11, THY1, SYK, ICAM4, ADAM23, COL16A1, TNXB, ADAMST5, ERBB2IP, FBLN5, TGFB1	0.125
Exopeptidase activity	CPD, ACE2, MAP1D, AEBP1, METAP2, NPEPPS, PGCP, BLMH, LNPEP, CPE, TRHDE, DPP4, ANPEP, TPP1, GGH	0.157
Protein N-terminus binding	GTF2H3, APTX, TSC1, SMARCE1, ERCC4, NCOA1, GTF2H2, NFE2, ZWINT, CSNK2A2, SMARCA4, GLRX, NCOA3, NBN, PGR	0.181
Sulfotransferase activity	CHST13, TPST1, HS6ST1, UST, CHST7	0.212
Endopeptidase activity	SENPI1, ATG4D, MMP24, CTSO, CASP9, KLKB1, CAPN11, USP5, F11, IDE, CTSS, USP9X, USP7, RCE1, CTSH, STCK, TPP2, BLMH, CFI, ADAMTS2, CORIN, F10, MMP2, CTSD, MMP12, FAP, CFD, C1S, LGMN, CTSB, REN, PDIA3, MMP3, MASP1, HTRA1,	0.205
Intramolecular oxidoreductase activity	ERP29, P4HB, PDIA6, PDIA3, PDIA5, GNPDA1	0.190
Metallopeptidase activity	MAP1D, IDE, METAP2, RCE1, PGCP, MME, LNPEP, ADAMTS2, MMP2, MMP12, FAP, ANPEP, MMP3, PAPPA	0.197
Hydrolase activity hydrolyzing <i>o</i> glycosyl compounds	NAGA, MANBA, NAGLU, PARG, MAN2B1, FUCA1, GLA, GLB1, GUSB, HEXB, MAN1A2	0.218
Unfolded protein binding	TAPBP, DNAJA3, TOR1B, PPIC, NAP1L4, LRPAP1, AIPL1, HSPA2, RP2, MKKS, PPIB, SCG5, CLGN	0.209

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**Supplement Table S8B.** Summary of GSEA result in *siKLF9* vs. NT with FDR  $\leq 0.25$ .

	GO	Functional Processes	Gene	FDR
<b>Enriched in <i>siKLF9</i></b>	Biological process	Microtubule cytoskeleton organization and biogenesis	TTK, PRC1, MAP1S, STMN1, PAFAH1B1, MAPT, NUSAP1, KIF23, SMC3, MID1IP1, RCC1, RAN, KIF2C, TUBG1	0.008
		Meiotic recombination	RAD51L1, RAD51L3, LIG3, SYCP1, SPO11, RAD50, MSH5	0.111
		Mitosis	TTK, CCNA2, ANLN, UBE2C, MAD2L1, BUB1B, TGFB1, NEK2, BUB1, CETN1, SSSCA1, ZW10, ESPL1, NUSAP1, PLK1, KIF25, GML, CENPE, SMC3, ANAPC11, CDC16, BIRC5, BRSK1, SMC4, RCC1, RAN, NUMA1, KIF2C, NOLC1, CD28, CDC23, TPX2, DCTN2, CDC27	0.250
		M phase of mitotic cell cycle	TTK, CCNA2, ANLN, UBE2C, MAD2L1, BUB1B, TGFB1, NEK2, BUB1, CETN1, SSSCA1, ZW10, ESPL1, NUSAP1, PLK1, KIF25, GML, CENPE, SMC3, ANAPC11, CDC16, BIRC5, BRSK1, SMC4, RCC1, RAN, NUMA1, KIF2C, NOLC1, CD28, CDC23, TPX2, DCTN2, CDC27	0.238
		M phase	TTK, CCNA2, ANLN, UBE2C, MAD2L1, BUB1B, TGFB1, NEK2, RAD51L1, RAD51L3, BUB1, CETN1, SSSCA1, ZW10, TAF1L, LIG3, ESPL1, NUSAP1, SYCP1, SPO11, RAD50, PLK1, KIF25, GML, CENPE, SMC3, MSH5, ANAPC11, CDC16, BIRC5, SC65, BRSK1, SMC4, DUSP13, RCC1, RAN, NUMA1, KIF2C, NOLC1, CD28, CDC23, TPX2, DCTN2, CDC27	0.219
		Positive regulation of transcription	EGR1, CREBBP, NCOA6, GLIS2, MKL2, MAML2, FOXE1, TBX5, TGFB1, NUFIP1, CAMKK2, ESRRG, SMARCC1, PRPF6, ILF3, SPI1, THRAP3, NFATC2, BCL10, SMARCD1, RXRA, MED12, TFAP2B, GATA4, PCBD2, SCAP, TCF3, RSF1, NPAS2, NUP62, ARID1A, SMARCD3, ATF7IP, BCL3, SMAD3, YWHAH, UTF1, CDK7, ELF1, IRF4, HMGA1, GLI2, CRTCL1, CTCF, GTF2H1, ATF4	0.223

	Cell cycle process	TTK, CDKN3, PRC1, CCNA2, ANLN, UBE2C, MAD2L1, BUB1B, TGFB1, NEK2, STMN1, MDM4, RAD51L1, RAD51L3, BUB1, CETN1, PAFAH1B1, SSSCA1, ZW10, TAF1L, LIG3, MAP3K11, ESPL1, , NUSAP1, SYCP1, APBB2, KATNA1, SAC3D1, SPO11, RAD50, MYH10, POLD1, KIF23, PLK1, KIF25, GML, CENPE, CENPF, SMC3, MSH5, ANAPC11, CDC16, RACGAP1, CDC7, SKP2, BIRC5, SC65, BRSK1, SMC4, DUSP13, RCC1, RAN, NUMA1, BCAT1, KIF2C, TUBG1, NOLC1, CD28, CDC23, TPX2, NPM1	0.248
Cellular compartment	Spindle	TTK, PRC1, CDC20, KIF4A, BUB1, CETN1, PAFAH1B1, ZW10, KATNA1, SAC3D1, KIF23, CENPF, SMC3, CDC16, BIRC5, NUMA1, TUBG1, TPX2, CDC27	0.250
	Spindle pole	BUB1, CETN1, ZW10, KATNA1, CENPF, SMC3, NUMA1, TUBG1, TPX2	0.181
	Spindle microtubule	PRC1, KIF4A, PAFAH1B1, ZW10, CDC16, BIRC5, NUMA1, TUBG1, CDC27	0.233
	Microtubule cytoskeleton	TOP2A, TTK, MAP1B, PRC1, CDC20, PXN, NIN, CROCC, PKHD1, EML1, NEK2, MAP1S, KIF4A, CEP57, BUB1, CETN1, MAP2, PAFAH1B1, ZW10, MAPT, MAP3K11, ESPL1, CEP63, CDK5RAP2, KATNA1, SAC3D1, KIF23, KLC2, CENPF, SMC3, CDC16, THAP6, MAP4, BIRC5	0.185
	Cytoskeletal part	TOP2A, TTK, MAP1B, LMNB1, TNNC1, PRC1, ANLN, CDC20, PXN, TCHP, NIN, CROCC, EML1, NEK2, MAP1S, MYO18B, KIF4A, CEP57, BUB1, CETN1, MAP2, PAFAH1B1, ZW10, MAPT, MAP3K11, ESPL1, CEP63, CDK5RAP2, SHROOM1, KATNA1, SAC3D1, MYH10, TPM4, TNNT2, LLGL1, KIF23, PLK1, DRD2, KIF25, KLC2, CENPF, SMC3, CDC16, MAP4, BIRC5, ACTN2, MYO1C, CEP290, CAPG, NUMA1, MYH6, ARPC2, KIF2C, TUBG1, LASP1, KIF5A, LCK, VIM, TPX2, NPM1, IQGAP1, STAU1, DCTN2, CDC27, GYS2, TNNI3, KRT2,	0.168

			MEFV, CACNA1C, SPTA1, BMF, SPTBN1, SPTBN2, CD2AP, MYO9B	
		Microtubule	PRC1, MAP1S, KIF4A, CEP57, PAFAH1B1, ZW10, MAPT, MAP3K11, CDC16, BIRC5, NUMA1, TUBG1	0.163
		Pore complex	C7, NUP107, KPNB1, NUP214, TMEM48, SNUPN, TPR, NXT1, NUTF2, NUP62, NUP153, NUP88, RANGAP1	0.220
		Cytoskeleton	TOP2A, TTK, MAP1B, LMNB1, TNNC1, PRC1, CDC42EP3, WASF2, ANLN, IQGAP2, TUBB, UTRN, CDC20, PXN, TCHP, NIN, CROCC, PKHD1, EML1, FLNB, NEK2, MAP1S, TUBB2C, WASL, DAG1, ANXA1, HSPB1, MYO18B, KIF4A, EPB41LL4B, MCF2, CEP57, BUB1, CETN1, MAP2, PAFAH1B1, ZW10, MAPT, MAP3K11, ESPL1, DYNLL2, MYOM1, CEP63, CDK5RAP2, EDA, SHROOM1, KATNA1, SAC3D1, SORBS2, MYH10, TPM4, TNNT2, LLGL1, KIF23, PLK1, DRD2, KIF25, KLC2, CENPF, SMC3, CTTNBP2NL, CDC16, THAP6, MAP4, BIRC5, ACTN2, FSCN2, CLIC5, MYO1C, CEP290, CAPG, PTPN21, NUMA1, WASF1, MYH6, ARPC2, KIF2C, TUBG1, LASP1, TGM1, EPB42, KIF5A, SYNPO, DDX20, LCK, FSCN1, VIM, PPL, TPX2, NPM1, IQGAP1, STAU1, DNAH9, DCTN2, CDC27, GYS2, LOR, VASP, TNNI3, KRT2, MEFV, CACNA1C, SPTA1, BMF, SPTBN1, CPTBN2, CD2AP	0.201
	Molecular function	DNA polymerase activity	POLE2, REV3L, POLG, TEP1, POLI, POLD1, POLQ, DKC1	0.243
		Nucleotidyltransferase activity	UGP2, THG1L, PRIM1, POLE2, REV3L, POLG, TEP1, POLI, POLD1, USP14, POLQ, DKC1, UAP1	0.243
<b>Diminished in <i>siKLF9</i></b>	Biological process	Positive regulation of protein amino acid phosphorylation	CCND3, IL5, IL3, BMP4, IL29, CCND2, LYN, HCLS1	0.043
		Jak stat cascade	SOCS2, STAT5B, IL29, STAT2, LYN, STAT1, SOCS3, HCLS1	0.171

**Supplement Table S8C.** Summary of GSEA result in *siPGR* vs. NT with FDR  $\leq 0.25$ .

	GO	Functional Processes	Gene	FDR
<b>Diminished in <i>siPGR</i></b>	Cellular compartment	Proteinaceous extracellular matrix	MATN3, COL5A2, COL4A5, EFEMP1, TFPI2, EFEMP2, COL8A1, SNTB2, COL10A1, SGCB, COL9A1, LAMC1, DSPP, COL15A1, POSTN, MATN1, PI3, FBLN2, COL6A3, FBN1, ECM1, MMP10, COL7A1, COL9A3, ERBB2IP, FBLN1, FBLN5, COL5A1, LTBP2, ADAMTS5, NID2, COL18A1, CTGF, COL4A2, LAMB1	0.002
		Extracellular matrix	SOD1, MATN3, COL5A2, COL4A5, EFEMP1, TFPI2, EFEMP2, COL8A1, SNTB2, COL10A1, SGCB, COL9A1, LAMC1, DSPP, COL15A1, POSTN, MATN1, PI3, FBLN2, COL6A3, FBN1, ECM1, MMP10, COL7A1, COL9A3, ERBB2IP, FBLN1, FBLN5, COL5A1, LTBP2, ADAMTS5, NID2, COL18A1, CTGF, COL4A2, LAMB1	0.006
		Extracellular matrix part	LAMB2, COL5A2, COL4A5, EFEMP2, COL8A1, SNTB2, COL10A1, SGCB, COL9A1, LAMC1, COL15A1, COL6A3, FBN1, COL7A1, COL9A3, ERBB2IP, COL5A1, NID2, COL18A1, COL4A2, LAMB1	0.065
		Collagen	COL4A3, COL5A3, COL3A1, COL1A2, COL5A2, COL4A5, COL8A1, COL10A1, COL9A1, COL15A1, COL6A3, COL7A1, COL9A3, COL5A1, COL18A1, COL4A2	0.051
		Basement membrane	LAMB2, COL4A5, EFEMP2, SNTB2, SGCB, LAMC1, FBN1, COL7A1, ERBB2IP, NID2, COL4A2, LAMB1	0.250
		Extracellular region	IDE, PGC, SOD1, SFN, ANGPTL1, MATN3, CFHR1, APOA5, COL5A2, COL4A5, MMP7, EFEMP1, GHRL, APP, TFPI2, MATN4, NUCB1, REG3A, PNLIPRP2, PNOC, IL3, FGF17, EFEMP2, PGCP, IGFALS, EDN1, ACE2, OSM, HPX, VTN, PTN, COL8A1, SNTB2, CDH13, COL10A1, CTF1, APOD, FSTL3, EGFL7, SGCB, COL9A1, CXCL9, GPHA2, MIA, IL27, FRZB, LAMC1, RNASE6, MMP9, DSPP, MMP2, FGF18,	0.240

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		PSAP, LALBA, SST, INHBC, PLA2G4B, WNT5A, COL15A1, TCN2, POSTN, MATN1, PI3, PLA2G2D, LGALS3BP, FBLN2, CLEC11A, GLA, IL16, COL6A3, FBN1, IGFBP1, NUCB2, EFNA5, IL15, ECM1, PLTP, LPL, MMP10, AGGF1, COL7A1, WFDC2, COL9A3, SCG2, NOG, MMP3, ERBB2IP, LOXL2, REN, FBLN1, INSL4, FBLN5, COL5A1, SPINT2, LTBP2, HTRA1, ADAMTS5, CRLF1, NID2, TGFBI, COL18A1, IFI30, CTGF, PTX3, RNASET2, COL4A2, FLT1, LAMB1, INHBB, PPT1, PAPP	
Molecular function	Structural constituent of muscle	SMTN, MYL9, TPM1, ACTC1, ASPH	0.111
	Intramolecular oxidoreductase activity	P4HB, PDIA6, PDIA3, GNPDA1, PDIA5	0.250
	Oxidoreductase activity GO 0016705	TYR, RGLN1, P4HA2, P4HB, PLOD2, SC5DL, NOS3, PLOD3, PTGS1, ASPH	0.225
	Isomerase activity	GNE, TOP2A, GLCE, PGM5, P4HB, PDIA6, PDIA3, GNPDA1, PDIA5,	0.233
	Peptidase activity	CAPN9, IDE, KEL, USP9X, RCE1, ACR, USP12, METAP2, MAP1D, TRHDE, PGCP, ACE2, FURIN, USP7, GZMB, PROC, MMP12, CTSH, MME, LGMN, ANPEP, BLMH, USP9Y, MMP9, MMP2, TPP1, F11, CFD, ADAMTS2, ATG4D, CAPN11, CTSB, DPEP1, FAP, C1S, PDIA3, CTSD, MASP1, MMP3, REN, DPP4, GGH, HTRA1, F10, CASP6, USP53, PAPP	0.210

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