

Table S1 Differentiation protein expression involved in invasion and stemness

Gene name	U87			U118		
	Agg/Con ratio	Agg/Con P value	Expression	Agg/Con ratio	Agg/Con P value	Expression
PROCR	1.64339029	0.002590493	Up	1.542069014	0.001487405	Up
SLC25A22	1.684460012	0.001237498	Up	1.679189709	0.010561844	Up
ALDH1A3	1.666207324	0.022763125	Up	12.33089355	0.000199883	Up
HMGA2	2.734122498	0.004089914	Up	6.415397755	0.004453681	Up
ABCA1	1.822717988	0.002792701	Up	5.821167423	0.001473723	Up
ABCC4	1.642151438	0.021642199	Up	1.850064674	0.001539279	Up
YAP1	1.618440004	0.019292912	Up	1.683824399	0.020803378	Up
CHD1L	2.2706641	0.023733524	Up	3.531937176	0.001306488	Up
ALDH1A3	1.666207324	0.022763125	Up	12.33089355	0.000199883	Up
BCL2L12	1.875979596	0.011402308	Up	1.787983912	0.004826449	Up
CPA4	1.724904096	0.009107091	Up	1.724904096	0.009107091	Up
FMNL3	1.938707113	0.003569857	Up	1.521213265	0.011327822	Up
MAD1L1	3.909310763	0.013593438	Up	2.128446532	0.049159972	Up
AKAP12	1.612046539	0.000607309	Up	1.663916656	0.020692759	Up
EFNB2	2.292769715	0.040322356	Up	3.238374673	0.004184769	Up
LGR4	3.331164947	0.001778385	Up	3.38951925	0.02671365	Up
ALDH2	0.459492923	0.042712638	Down	0.514765935	0.011881771	Down
CDH13	1.724591559	0.028315429	Up	1.700706001	0.015546471	Up
TFPI2	4.510653521	0.005343053	Up	11.91634982	0.001598346	Up
ACP2	2.460589362	0.000467601	Up	2.460589362	0.000467601	Up
ADCY6	1.930759618	0.002655308	Up	1.611433749	0.003022489	Up
AGPAT5	2.113259514	0.009295051	Up	1.772299555	0.042227232	Up
ARHGAP15	3.530810397	0.021776376	Up	1.834796709	0.019972447	Up
DCUN1D3	2.098061453	0.000721579	Up	2.004772704	0.006440267	Up
ERP44	1.622378885	0.018466168	Up	1.60954367	0.043383631	Up
MRC2	1.501926877	0.019714605	Up	0.337649214	0.00529449	Down
PCDHGA9	1.986472628	0.001890832	Up	9.528483007	0.009568114	Up
SLC38A2	1.643606596	0.020262963	Up	2.625518759	0.000264924	Up
ANXA5	0.293085125	0.000472448	Down	0.425817687	0.004006131	Down
GBP1	0.286989675	0.001355958	Down	0.291345488	0.009519559	Down
LAMC1	0.517711463	0.048023484	Down	0.510026322	0.007799092	Down
PYGB	0.221578436	0.000112287	Down	0.322638967	0.00044365	Down
NCK1	0.617162452	0.00380581	Down	0.325194115	0.004493593	Down
PRDX2	0.206533566	1.08517E-05	Down	0.075807349	1.75031E-05	Down
MCM4	0.397207912	0.00282304	Down	0.578415801	0.007850114	Down
SOAT1	0.355221771	0.0001752	Down	0.648680302	0.033116151	Down
UBXN1	0.6155213	0.027240479	Down	0.494369153	0.002284093	Down
FMR1	0.352006215	0.000633397	Down	0.426777216	0.001415617	Down
CTBP1	0.639960219	0.021014772	Down	0.180271591	0.001145724	Down
NCAPH	0.558451077	0.003983147	Down	0.646013446	0.029448201	Down

MGME1	0.269693781	0.008006855	Down	0.269693781	0.008006855	Down
C20orf27	0.32973774	7.36427E-05	Down	0.461172556	0.022721122	Down
GOLT1B	1.690862825	0.002939111	Up	1.98004382	0.003098555	Up
ITGA2	1.884077767	0.001543564	Up	1.653649489	0.022124598	Up
CD40	1.642376519	0.001185476	Up	2.525318085	0.009518257	Up
TRIM22	2.350875526	0.023421135	Up	3.394343249	0.013234349	Up
PAPPA	2.66044296	0.00248275	Up	10.27873008	0.004473294	Up
ITGB3	1.604448471	0.00613092	Up	39.6232232	4.0914E-06	Up
PTPRE	1.558311858	0.00433624	Up	5.008937909	0.003726418	Up
ADCK5	2.211913924	0.010047887	Up	2.510016256	0.038427767	Up
ANO6	1.662055729	0.005545972	Up	1.662055729	0.005545972	Up
GALNT7	1.716855183	0.012206614	Up	1.716855183	0.012206614	Up
GTPBP2	2.678059277	0.002723563	Up	1.601133177	0.008240658	Up
IFITM2	3.26574891	0.001002159	Up	1.801622723	0.015511851	Up
MTCH2	1.653421953	0.002304593	Up	2.138163911	0.003573504	Up
MTFR1	1.82304682	0.045720925	Up	1.82304682	0.045720925	Up
MYL9	2.869622154	0.000657681	Up	2.976227587	0.000429837	Up
SHC1	1.606537062	0.00246315	Up	2.119041389	0.014227499	Up
SIRT6	2.842612983	0.005148005	Up	1.529280061	0.00245528	Up
TRIM21	0.468608681	0.003418182	Down	0.587910127	0.010807495	Down
PTPRG	0.552503419	0.023411176	Down	0.509613649	0.00376942	Down
GSTM2	0.274882336	0.001269599	Down	0.558932731	0.027224447	Down
VEPH1	0.579214294	0.028336165	Down	0.542508803	0.009766722	Down
CUL5	0.558596177	0.002057316	Down	0.634696292	0.018025087	Down
EHD2	0.442362897	0.002535756	Down	0.480175315	0.003943868	Down

Table S11 GSEA analysis of the hallmark according to differentiation expression genes

	Hallmark	ES	NES	pvalue	p.adjust
U87	AGING	0.653644837	1.95956208	7.22E-06	4.60E-05
	FRIDMAN_SENESCENCE_UP	0.654627235	1.857033052	0.000531685	0.002764764
	SENESCENCE_INFLAMMATORY_GENES	0.627150418	1.844277137	0.000351987	0.002287919
	EPITHELIAL_MESENCHYMAL_TRANSITION	0.725035096	2.356584605	1.00E-10	2.55E-09
	G2M_CHECKPOINT	-0.607274428	-2.274846425	1.00E-10	2.55E-09
	ATR_SUPPRESSED_TARGETS	-0.696105192	-1.954468031	0.000283709	0.002287919
	E2F_TARGETS	0.653644837	1.95956208	7.22E-06	4.60E-05
	SASP_COPPE	0.795242572	2.147799142	2.32E-07	6.04E-06
	MITOTIC_SPINDLE	-0.516380681	-1.940309268	4.28E-07	3.12E-06
	MYC_TARGETS_V1	-0.395562368	-1.476387655	0.002777726	0.010317266
	APOPTOSIS	0.602377972	1.901542905	8.46E-06	4.79E-05
	TNFA_SIGNALING_VIA_NFKB	0.601006037	1.956063655	2.25E-07	2.30E-06
	P53_PATHWAY	0.545122092	1.77420474	5.10E-05	0.000236324
	COMPLEMENT	0.501566773	1.617132782	0.001450824	0.005691694
	COAGULATION	0.644665104	1.944786264	1.27E-05	6.49E-05
	DUY_CISG_UP	0.604562267	1.961069616	5.03E-07	6.53E-06
	HYPOXIA	0.635268159	2.048469026	1.76E-08	2.24E-07
	UV_RESPONSE_DN	0.50254338	1.566128925	0.002989288	0.010889549
	INFLAMMATORY_RESPONSE	0.612688606	1.962149625	2.92E-07	2.48E-06
U118	G2M_CHECKPOINT	-0.448870134	-1.429109502	0.006665003	0.028326264
	TNFA_SIGNALING_VIA_NFKB	0.574879845	1.910784555	2.63E-07	1.34E-05
	P53_PATHWAY	0.535963403	1.776692157	5.70E-06	9.69E-05
	UV_RESPONSE_DN	-0.524412753	-1.608459916	0.001789167	0.013035359
	DUY_CISG_UP	0.635605387	2.103660013	1.00E-10	2.60E-09
	HALLMARK_INFLAMMATORY_RESPONSE	0.559753293	1.846275672	1.44E-06	3.68E-05
	COMPLEMENT	0.45754483	1.51354693	0.002108431	0.013441249
	XENOBIOTIC_METABOLISM	0.482555119	1.586900596	0.000534472	0.004543011
	INFLAMMATORY_RESPONSE	0.586791351	1.814374429	0.000283057	0.003679735
	HEMATOPOIETIC_STEM_CELL_UP	-0.41641134	-1.36606057	0.009225004	0.039975019
	SENESCENCE_INFLAMMATORY_GENES	0.56916797	1.720450393	0.000984155	0.008529342
	IL6_JAK_STAT3_SIGNALING	0.533406577	1.564943426	0.005871441	0.027222136
	INTERFERON_GAMMA_RESPONSE	0.443228294	1.472394967	0.004295787	0.024342794
	KRAS_SIGNALING_UP	0.481487591	1.583812104	0.000329111	0.003356927
	REGULATION_OF_MITOTIC_CELL_CYCLE	-0.547423946	-1.679394785	0.000778731	0.020247017
	MITOTIC_SPINDLE	-0.493053817	-1.641861505	2.03E-05	0.000680125
	PROTEIN_SECRETION	-0.495291908	-1.53513565	0.009711427	0.041273567
	HEDGEHOG_SIGNALING	-0.63712589	-1.701050161	0.002179613	0.013895035

GSE 1007 36	UV_RESPONSE_DN	-0.465941857	-1.510069557	0.00378118	0.019284017
	APICAL_JUNCTION	-0.469537413	-1.557875894	0.000470281	0.004796863
	P53_PATHWAY	0.362576594	1.515562676	0.000146685	0.00249364
	HYPOXIA	0.348673959	1.468438956	0.00105447	0.008962997
	COMPLEMENT	0.312097867	1.316262671	0.009393509	0.041273567

Table S12 Common elements of differential expression genes with SASP expression according to proteome, mRNA and miRNA sequence analysis

U87 mRNA sequence

1)	Common elements in SASP and mRNA DEGs
DEGs	IL6, CXCL3, CCL26, FGF2, MMP7, TIMP3, NOS1, COLQ, COL11A2, COL5A1, LAMB3, CDK10, CDK8, ATM, CDC25C, ITGBL1, ITGA4
Total	17
2)	Common elements in SASP and mRNA transcript DEGs
DEGs	IL7, OCLN, MMP2, MMP19, TIMP2, EGFR, COL1A2, LAMA3, LAMB1, LAMB2, CDK19, CDK13, MSH6, ITGA7
Total	14
3)	Common elements in SASP, mRNA DEGs and mRNA transcript DEGs
DEGs	CXCL2, CXCL8, CCL2, CCL3, CCL5, CSF3, HGF, NGF, IGFBP3, IGFBP4, IGFBP5, IGFBP6, IGFBP7, MMP14, MMP15, TIMP1, CTSB, ICAM1, NOS3, FN1, IGFBP1, COL5A2, COL17A1, COL6A3, COL5A3, COL3A1, COL15A1, COL4A6, COL6A1, LAMC2, FAT2, LAMA4, CDKN2D, CDKN3, CDK5R2, CDKL2, CDK16, CCNB1, CCNB2, CDKN1A, CDC25A, CDC25B, PDGFRB, ITGB2-AS1, ITGB3
Total	45

U118 mRNA sequence

1)	Common elements in SASP and mRNA DEGs
DEGs	OCLN, MMP10, MMP15, COL24A1, CDKN1B, CDKN1C, CCNB1, CCNB2, CCNB1IP1, MSH2, ITGB2-AS1, ITGB8
Total	12
2)	Common elements in SASP and mRNA transcript DEGs
DEGs	CXCL3, HGF, IGFBP7, MMP2, MMP14, CTSB, TNFRSF1A, COL6A3, COL5A1, CDK16, ITGB1
Total	11
3)	Common elements in SASP, mRNA DEGs and mRNA transcript DEGs
DEGs	IL6, CXCL2, CXCL5, CXCL8, CXCL10, CXCL11, CXCL12, CCL2, CCL3, CCL4, CCL5, CCL26, CSF2, CSF3, EREG, NGF, IGFBP3, IGFBP4, IGFBP5, IGFBP6, MMP1, MMP3, MMP7, MMP9, MMP12, MMP19, TIMP3, TIMP4, ICAM1, TNFRSF11B, FAS, EGFR, NOS3, FN1, COL5A2, COLQ, COL5A3, COL15A1, COL4A6, COL6A1, COL11A1, COL9A2, COL1A2, COL4A2, COL27A1, COL16A1, FAT2, LAMA4, LAMB3, LAMC1, NTN4, FAT4, DCHS2, LAMA3, LAMB1, LAMA2, NTNG1, LAMB2, LAMA5, MEGF9, CDKN2C, CDK10, CDK5R2, CDK18, CDK5R1, CDK11A, CDK17, CCNT2, CDK19, CDKL1, CDKAL1, CDK11B, CDK13, CDKN1A, ATM, ATR, CDC25B, CDC25C, MSH6, MSH5, EXO1, ITGA6, ITGB3, ITGBL1, ITGA4, ITGAD, ITGAX, ITGA11, ITGA7, ITGA10, ITGAM, ITGA8, ITGA9-AS1
Total	93

GSE100736 mRNA sequence

1)	Common elements in SASP and mRNA DEGs
DEGs	IL7, CXCL14, CCL2, CCL26, OCLN, MIF, EREG, EGF, IGFBP2, IGFBP3, IGFBP4, IGFBP5, IGFBP6, MMP2, MMP14, MMP15, TIMP3, CTSB, TNFRSF11B, COL5A2, COL17A1, COL6A3, COL3A1, COL15A1, COL4A6, COL6A1, COL11A1, LAMA4, LAMA3, NTNG1, CDKN2D, CDKN2C, CDKN1C, CDKN2A, CDKN2B, PDGFRB, ITGBL1, ITGA4, ITGB8, ITGA7, ITGA9-AS1
Total	41

Proteome detection

1)	Common elements in SASP and U87 differentially expressed proteins
DEPs	IGFBP5, MMP15, COL16A1
Total	3
2)	Common elements in SASP and U118 differentially expressed proteins
DEGs	FGF2, HGF, IGFBP3, IGFBP4, MMP2, MMP3, TIMP1, TIMP3, CTSB, EGFR, COL5A2, COL6A3, COL5A1, COL6A1, COL1A2, LAMA4, NTN4, NTNG1, LAMB2, ATM, PDGFRB, ITGB8, ITGAX, ITGA11, ITGA7
Total	25
3)	Common elements in SASP, U87 and U118 differentially expressed proteins
DEGs	IGFBP7, FAS, FN1, LAMC1, MSH2, MSH6, ITGA6, ITGB3, ITGA4, ITGA8
Total	10

U87 miRNA sequence

1)	Common elements in SASP and U87 DE-miRNA targets genes
DE_miRNA target_genes	IL15, CXCL14, CCL5, CSF3, AREG, IGFBP2, IGFBP3, IGFBP4, IGFBP7, MMP2, MMP15, TIMP2, TIMP3, ICAM1, ICAM3, TNFRSF1A, TNFRSF11B, EGFR, FN1, IGFN1, COL5A2, COL6A3, COL5A3, COL3A1, COL15A1, COL4A6, COL5A1, COL11A1, COL1A2, COL4A2, COL27A1, LAMA4, LAMC1, LAMA3, LAMA5, MEGF9, CDKN2D, CDKN2C, CDKN1B, CDK5R2, CDK16, CDK8, CDK18, CDK5R1, CDK11A, CDK17, CDK11B, CDK13, CDKN2A, MYC, ATM, CDC25A, CDC25B, MSH5, ITGA6, ITGA11, ITGA8
Total	57

U118 miRNA sequence

1)	Common elements in SASP and U118 DE-miRNA targets genes
DE_miRNA target_genes	COL5A2, COL3A1, COL6A3, IGFBP2, ITGA4, CDC25B, FN1, IGFBP5, CDK5R2, COL16A1, COL9A2, CDK11B, CDK11A, COL11A1, NTNG1, ITGA10, CDK18, LAMC1, IGFN1, LAMC2, LAMB3, ITGA8, CXCL12, COL17A1, FAS, CDKN1C, ATM, CDKN1B, TNFRSF1A, MMP13, ITGA7, CDK17, NTN4, NOS1, MMP14, COL4A2, CCNB1IP1, CDKL1, ITGA11, RAD51, ITGAX, ITGAM, MMP15, MMP2, CDK10, CCL5, IGFBP4, CDK5R1, CSF3, CCL16, TIMP2, LAMA3, MSH6, MSH2, ITGA6, ICAM3, ICAM1, COL5A3, CDKN2D, TIMP3, COLQ, LAMB2, CSF2RB, CDC25A, EREG, CXCL2, CXCL5, IL13, FAT2, PDGFRB, CDKAL1, CXCL14, CDK13, IGFBP3,

	ITGB8, EGFR, IL6, LAMA5, COL6A1, MIF, COL15A1, COL5A1, COL27A1, MEGF9, DCHS2, FGF2, EGF, OCLN, IL15, FAT4, TNFRSF11B, CDKN2A, CDKN2B, MYC, ATR, COL4A6, CDK16, TIMP1, COL11A2, MSH5, CDK19, CDKN1A, LAMA2, LAMA4, CTSB, COL1A2, LAMB1, NOS3
Total	108

Table S13 Primary antibodies used for immunofluorescence staining

Antigens	Manufacturer	Catalogue numbers	Application
CD133	Proteintech	18470-1-AP	1:300
Nestin	Proteintech	19483-1-AP	1:300
Sox2	abcam	ab171380	1:200
Klf4	Proteintech	11880-1-AP	1:100
HIF1A	abcam	ab179483	1:500
HIF2A	NOVUS	NB100-132SS	1:200

Table S14 Primary antibodies used for western blotting

Antigens	Manufacturer	Catalogue numbers	Application
CD133	Proteintech	18470-1-AP	1:2000
CD15	NOVUS	NB100-1831	2ug/ml
Nestin	Proteintech	19483-1-AP	1:1000
Sox2	abcam	ab171380	1:1000
Klf4	Proteintech	11880-1-AP	1:2000
HIF1A	abcam	ab179483	1:1000
HIF2A	abcam	ab207607	1:1000
β -actin	Sangon Biotech	D191047-0100	1:5000

Table S15 Sequences of primers used for RT-qPCR analysis

IL1a	Forward(5'-3')	TGTATGTGACTGCCCAAGATGAA
	Reverse(5'-3')	GGATGGGCAACTGATGTGAAATA
IL1b	Forward(5'-3')	CTACGAATCTCCGACCACCACTA
	Reverse(5'-3')	CTCGTTATCCCATGTGTCTGAAGA
IL6	Forward(5'-3')	TGAAAGCAGCAAAGAGGCACT
	Reverse(5'-3')	TTCACCAGGCAAGTCTCCTCA
IL8	Forward(5'-3')	TTCTAGGACAAGAGCCAGGAAGA
	Reverse(5'-3')	GGTCCACTCTCAATCACTCTCAG
MSH2	Forward(5'-3')	ACAGTGC GCCTTTTCGAC
	Reverse(5'-3')	TGGATGCCTTATTTCCAGCTC
CCL2	Forward(5'-3')	TCGCGAGCTATAGAAGAATCACC
	Reverse(5'-3')	GAATCCTGAACCCACTTCTGCTT
CDKN1A	Forward(5'-3')	CTGTCACTGTCTTGTACCCTTGT
	Reverse(5'-3')	CCCAGCAGAGGAACCACTACTA
CDKN2B	Forward(5'-3')	GCGTTCACCTCCAATGTCTGC
	Reverse(5'-3')	CTTACTGAAGCCCACCTCGG
P53	Forward(5'-3')	TCTGACTGTACCACCATCCACTA
	Reverse(5'-3')	TGTTCCGTCCCAGTAGATTACCA
CXCL3	Forward(5'-3')	CGAAGTCATAGCCCACTCAAGA
	Reverse(5'-3')	CTGCAGGAAGTGTCAATGATACG
ATM	Forward(5'-3')	TCCCTCCACCTGCATATGTATCT
	Reverse(5'-3')	AACATCTTGGTCACGACGATACA
COL5A1	Forward(5'-3')	CACCGGGCAGCTTATGATTACT
	Reverse(5'-3')	GCCGTCTCCTTCCGTGTAATATT
EGF	Forward(5'-3')	TGTGATTGCTTTCTGGGTATGA
	Reverse(5'-3')	CAGGGCTGTATGGGCAAAGTATA
FGF2	Forward(5'-3')	TCTCTGGCAGTTCCTTATGATAGA
	Reverse(5'-3')	ACAACCTCCCATCACCAGCAG
IGFBP3	Forward(5'-3')	CTTCTGCTGGTGTGTGGATAAGT
	Reverse(5'-3')	GGTCATGTCCTTGGCAGTCTTT
MMP1	Forward(5'-3')	TGATAGCACATGACTTTCCTGGA
	Reverse(5'-3')	TCCTGCAGTTGAACCAGCTATTA
uPA	Forward(5'-3')	AACGACATTGCCTTGCTGAAGAT
	Reverse(5'-3')	GTGACTTCAGAGCCGTAGTAGTG
β -Actin	Forward(5'-3')	ACCCGCCGCCAGCTCACC
	Reverse(5'-3')	GGGGGGCACGAAGGCTCATC

Table S16 The sequences of sgRNA for knockout of HIF1 α and HIF2 α

Target	Oligonucleotide sequence(5'-3')
HIF1A	GAACTCACATTATGTGGAAG
HIF2A	CTTGGAGGGTTTCATTGCCG