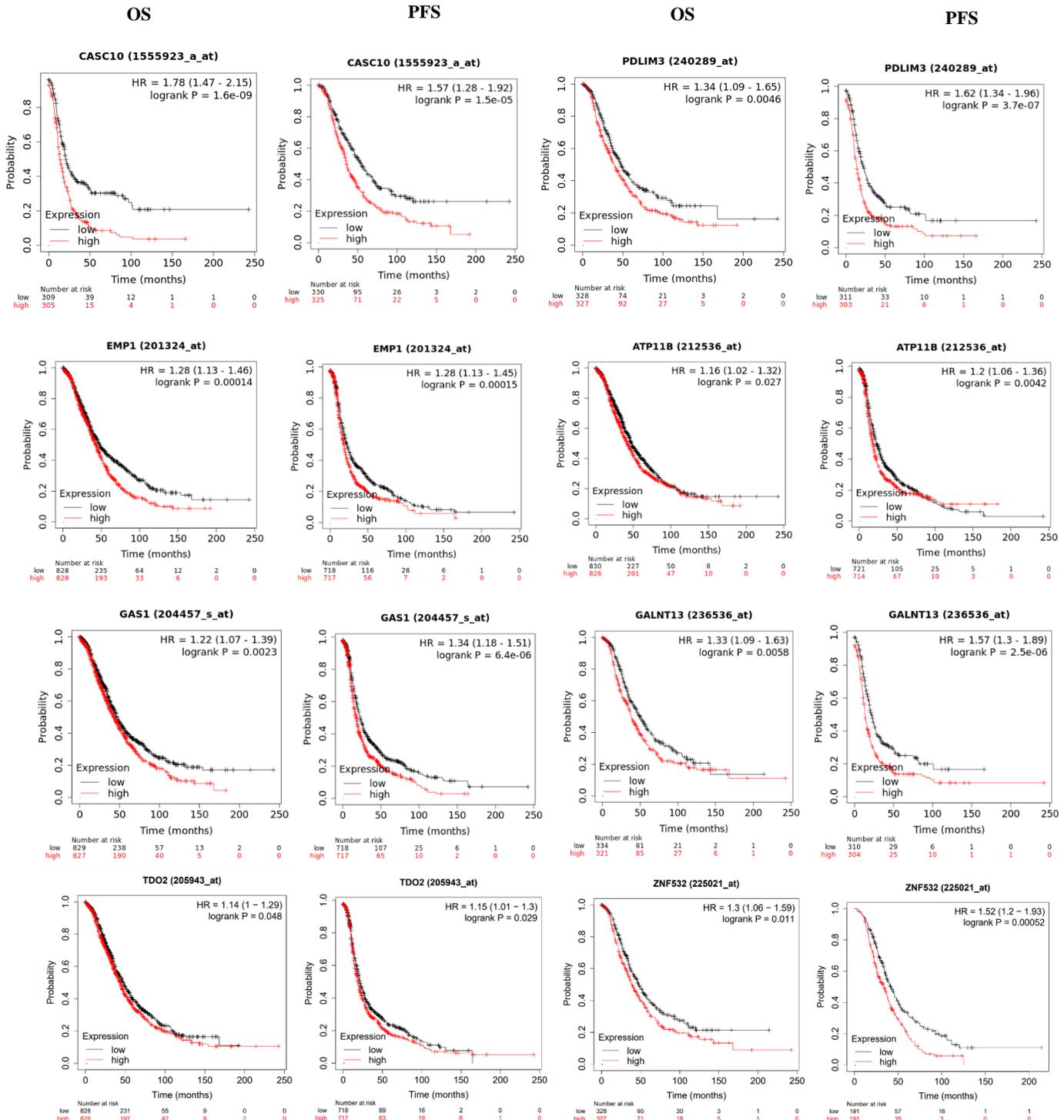
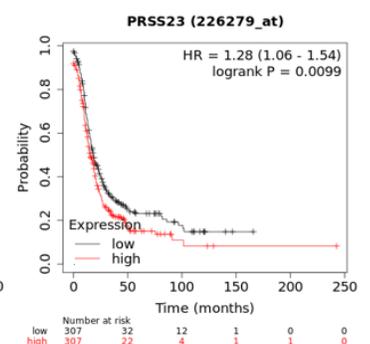
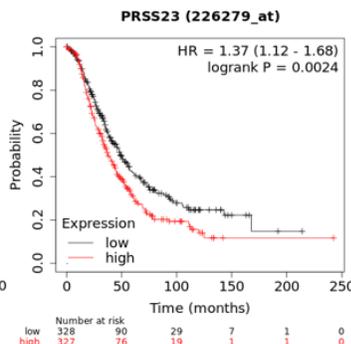
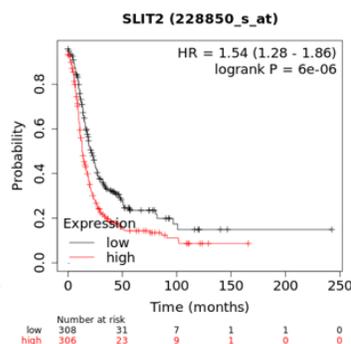
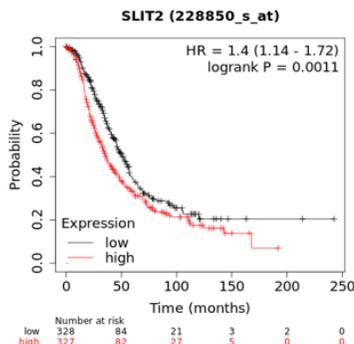
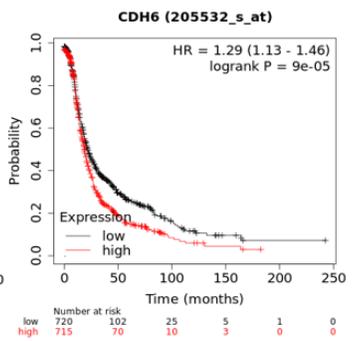
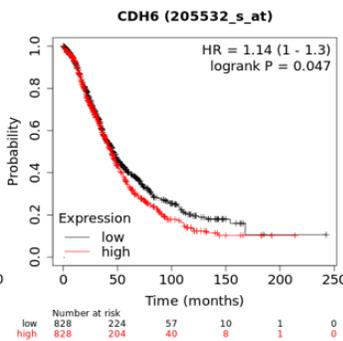
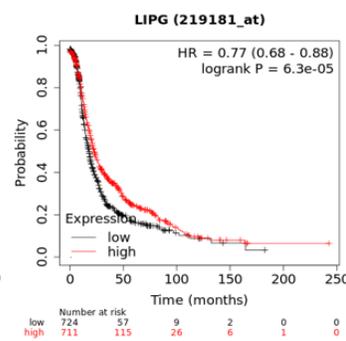
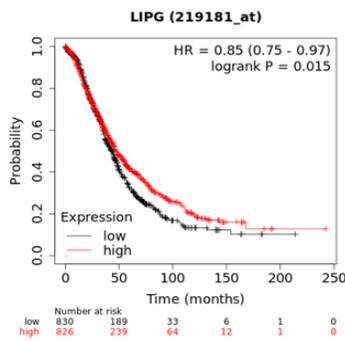
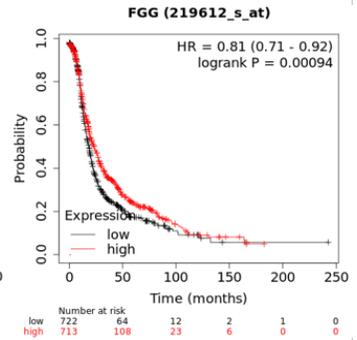
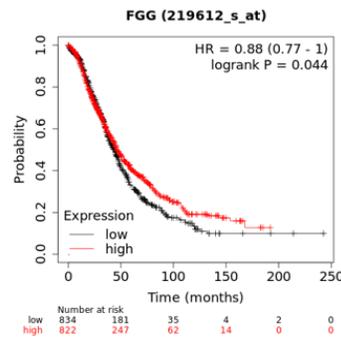
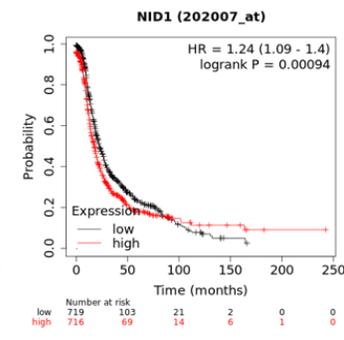
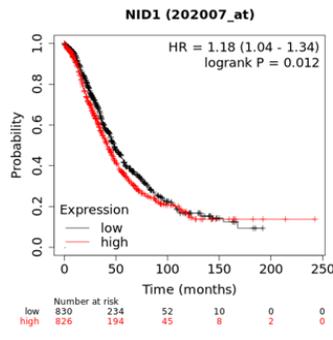
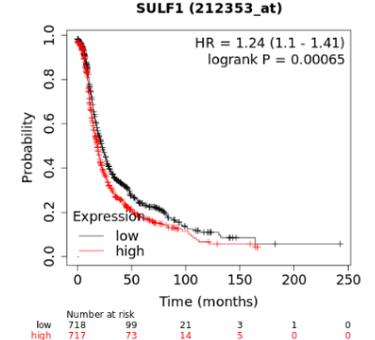
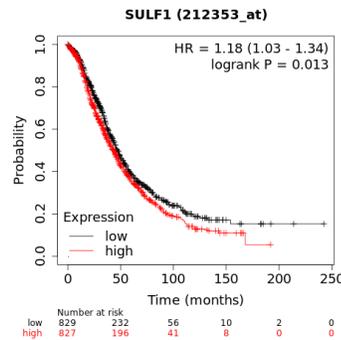
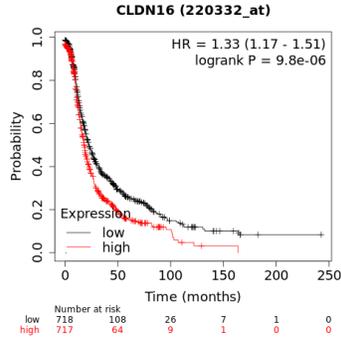
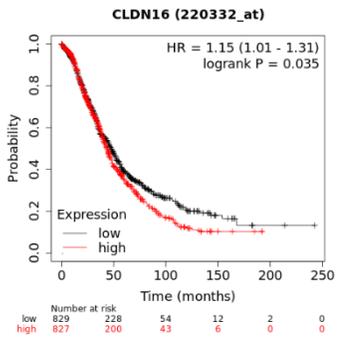
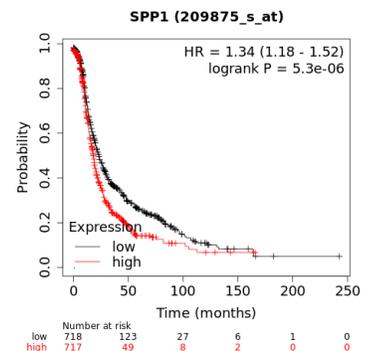
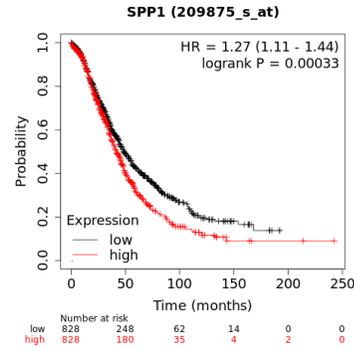
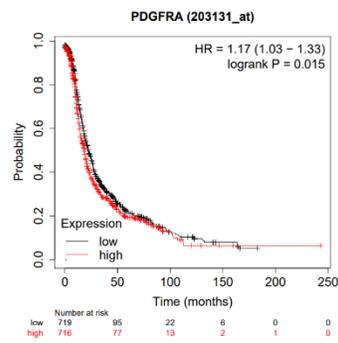
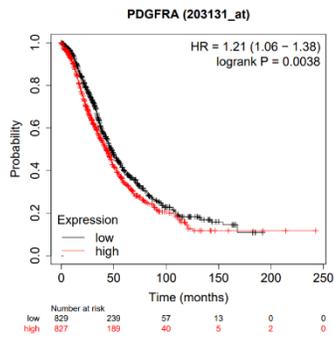
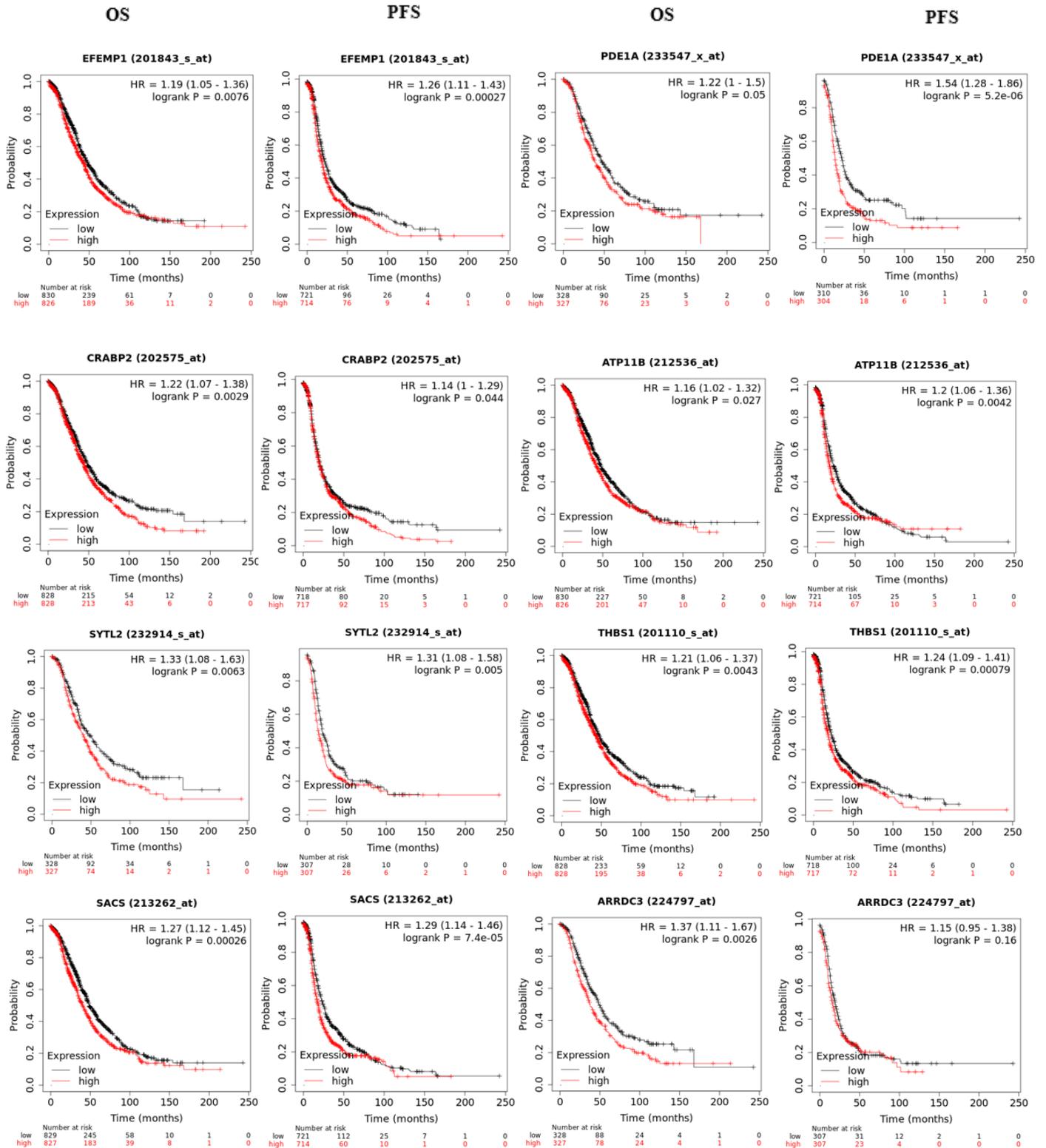


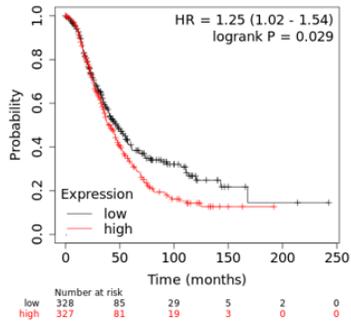
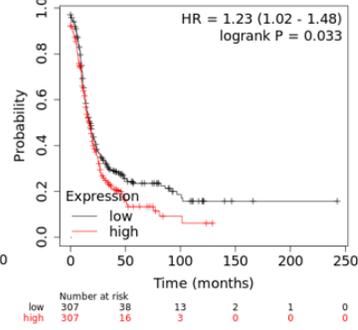
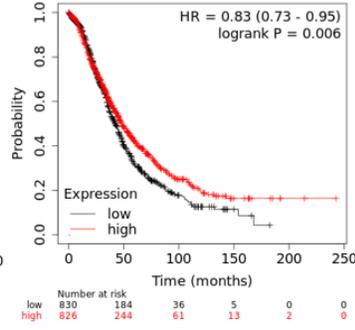
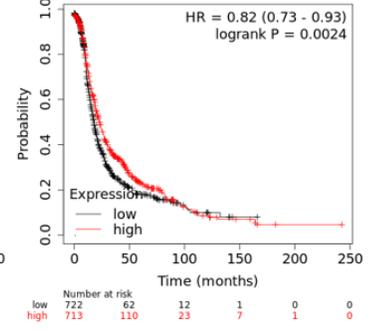
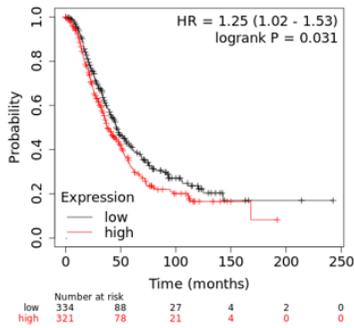
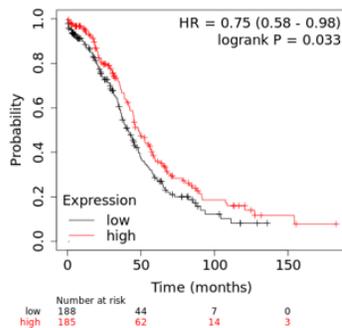
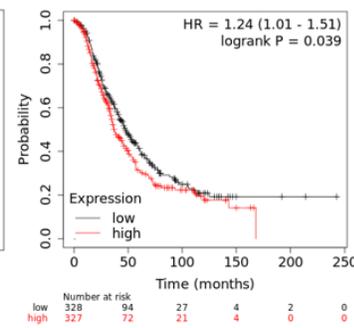
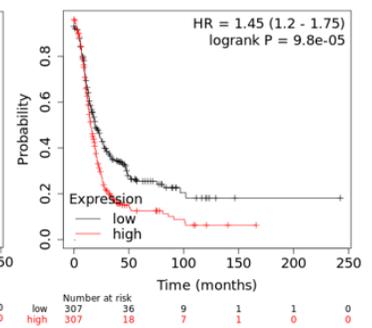
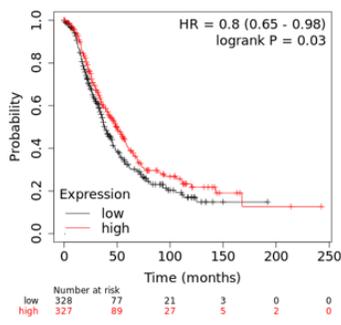
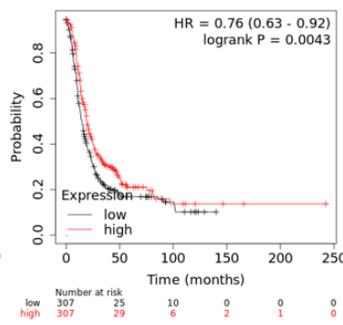
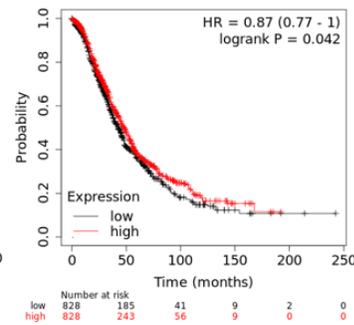
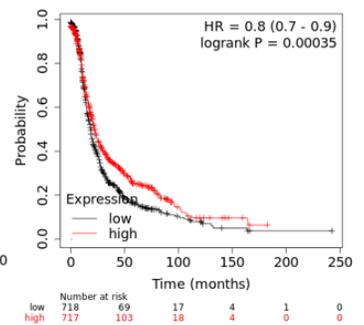
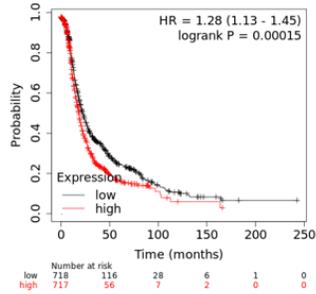
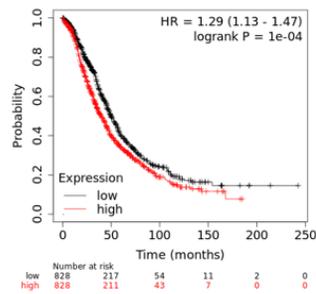
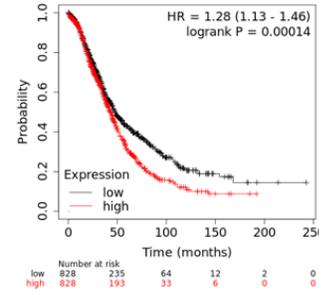
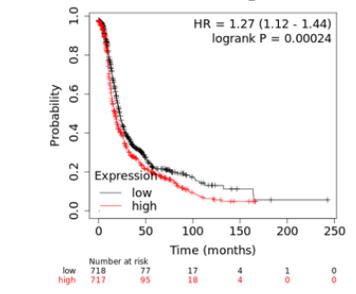
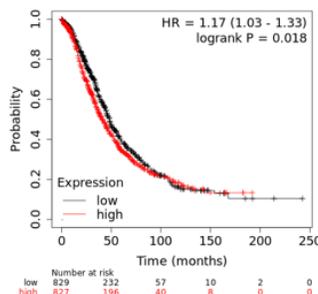
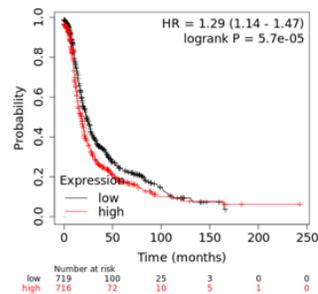
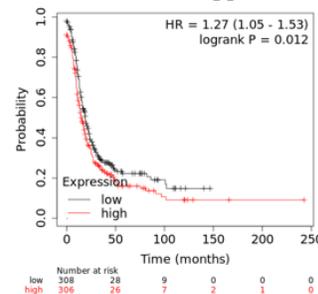
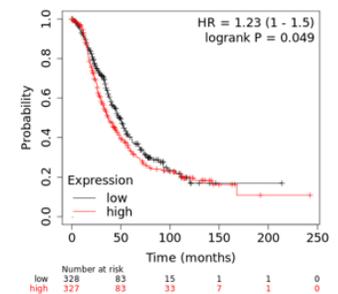
Upregulation of the Long Noncoding RNA CASC10 Promotes Cisplatin Resistance in High-Grade Serous Ovarian Cancer

Ricardo Noriega-Rivera ^{1,2}, Mariela Rivera-Serrano ^{2,4}, Robert Rabelo-Fernandez ^{2,4}, Josu   P  rez-Santiago ^{2,3}, Fatima Valiyeva ², and Pablo E. Vivas-Mej  a ^{1,2*}



OS**PFS****OS****PFS**



OS**PFS****OS****PFS****SESN3 (225123_at)****SESN3 (225123_at)****SPRY4 (221489_s_at)****SPRY4 (221489_s_at)****CMBL (230995_at)****CMBL****ANKRD10 (223251_s_at)****ANKRD10 (223251_s_at)****SLC40A1 (223044_at)****SLC40A1 (223044_at)****DDAH1 (209094_at)****DDAH1 (209094_at)****EMP1 (201324_at)****BCHE (205433_at)****EMP1 (201324_at)****BCHE (205433_at)****HEG1 (213069_at)****HEG1 (213069_at)****CFL2 (224352_s_at)****CFL2 (224352_s_at)**

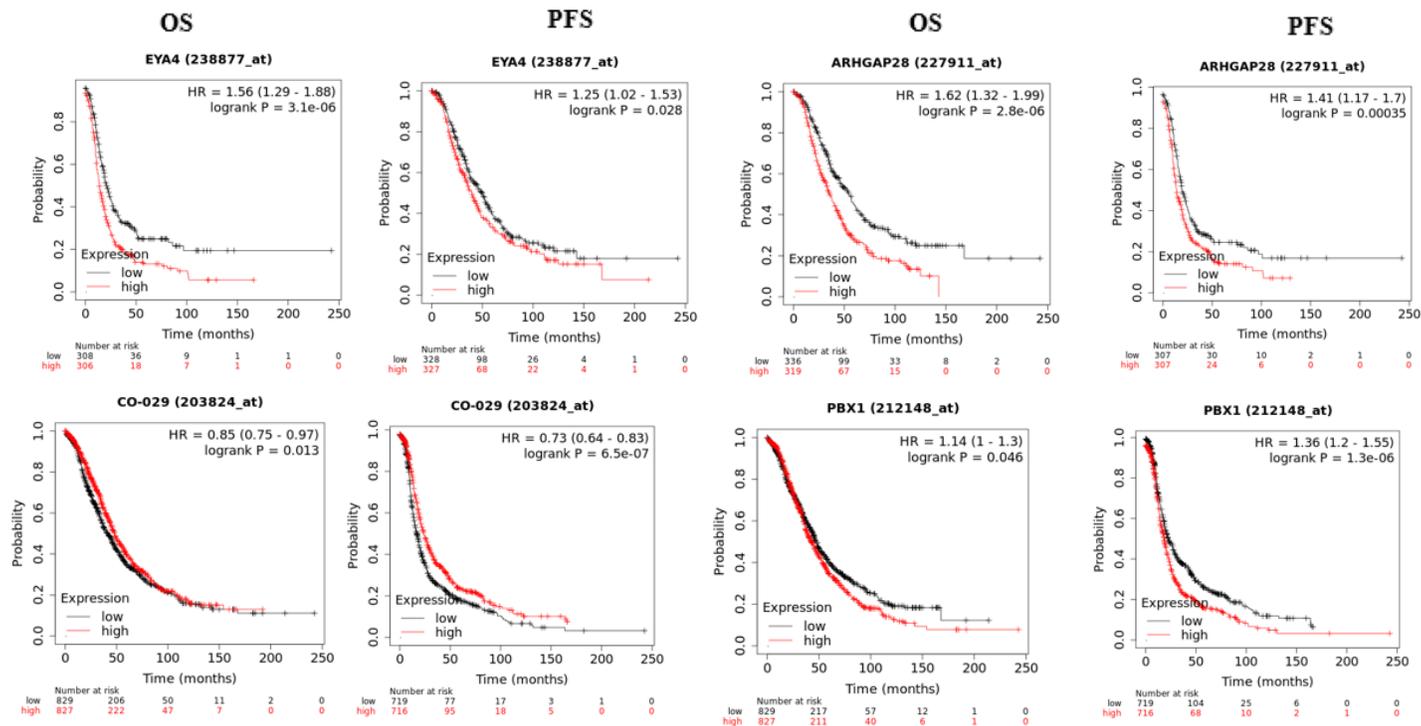


Figure S1. Kaplan–Meier (KM) plots for gene expression-based overall survival (OS) and progression-free survival (PFS) analysis. KM plots of ovarian cancer patients were generated using the KM plotter searchable database. The OS and PFS of patients with ovarian cancer are stratified by expression levels of the additional 57 clinically relevant genes in ovarian cancer. P-values < 0.05 were considered to be statistically significant.

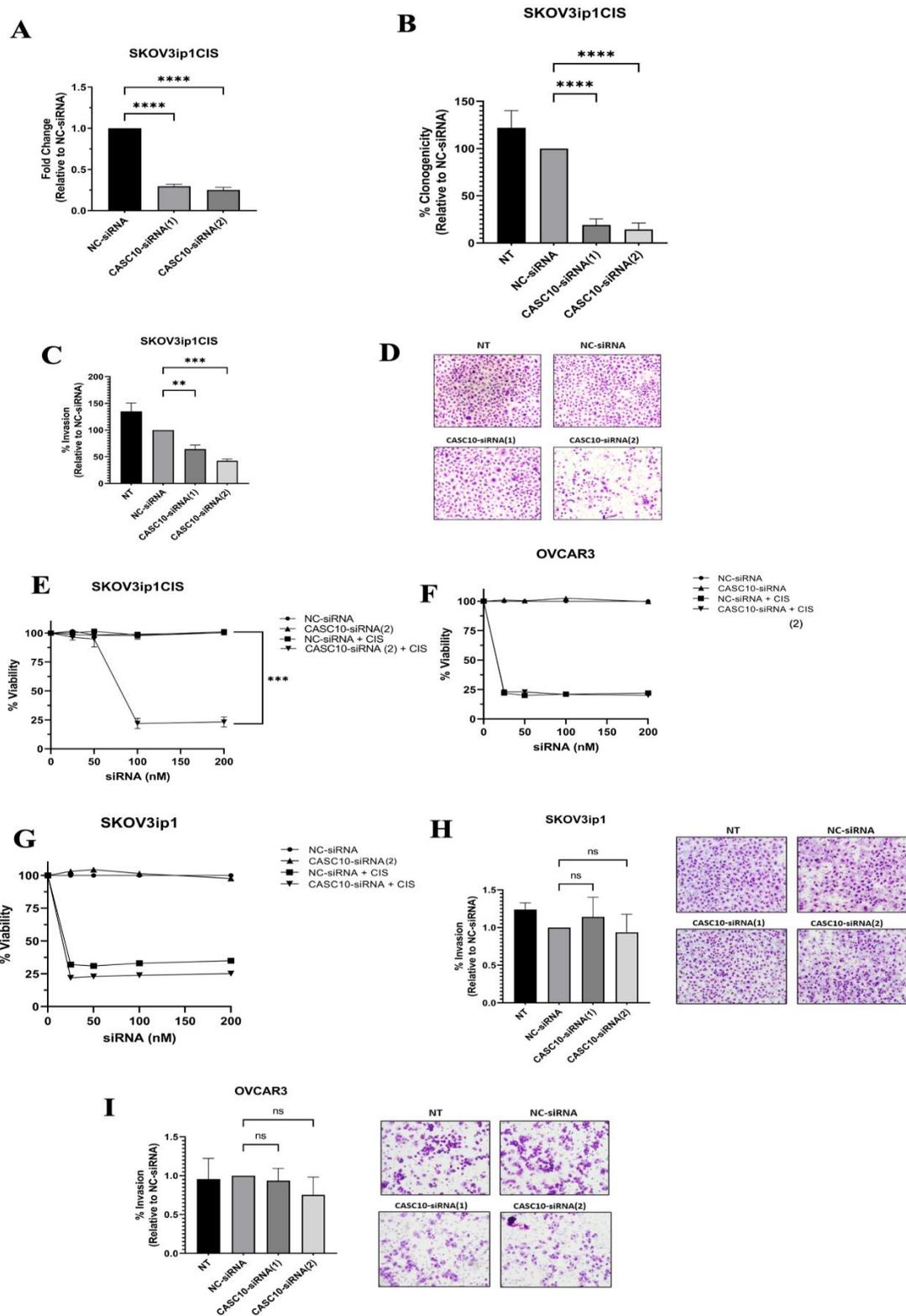


Figure S2. siRNA-mediated CASC10 knockdown reduced cell growth, invasion, and viability in SKOV3ip1CIS. (A) RT-qPCR following transfection of siRNA in SKOV3ip1CIS cells. (B) colony formation assay, and (C-D) invasion ability following siRNA transfections in SKOV3ip1CIS cells. (E) Cell viability following siRNA transfections in SKOV3ip1 cells. Cell viability was performed with and without CIS (2.5 μ M). (F-I) Cell viability and invasion following siRNA transfections in OVCAR3 and SKOV3ip1 cells. Mean \pm SEM is shown relative to NC-siRNA (* p < 0.05, ** p < 0.01, *** p < 0.001, and **** p < 0.0001).

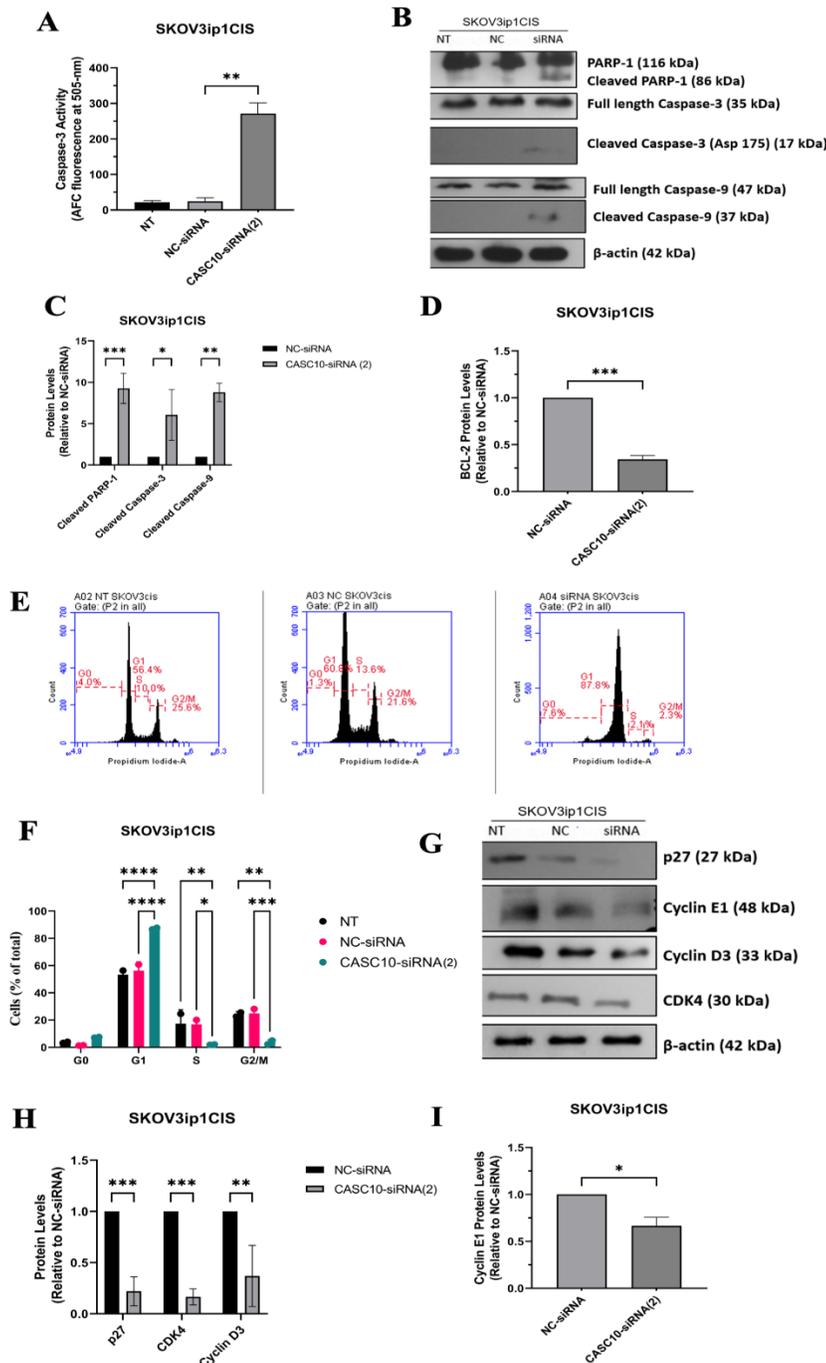


Figure S3. CASC10 siRNA-mediated knockdown induced apoptosis and cell cycle arrest in SKOV3ip1CIS. SKOV3ip1CIS cells were transfected with 100 nM NC-siRNA or 100 nM CASC10-siRNA(2). **(A)** Caspase-3 fluorometric activity assay in SKOV3ip1CIS cells 72 hr after siRNA transfection. **(B)** Western blot analysis of apoptotic-related proteins. **(C-D)** Densitometric analysis of the band intensities shown in B. **(E)** Histogram showing cell cycle arrest at G0/G1 to S phase transition after CASC10-siRNA(2) transfection in SKOV3ip1CIS cells. **(F)** Quantification of the flow cytometry data shown in E. Values were expressed relative to NC-siRNA. **(G)** Western blot analysis of cell cycle-related proteins 48 hr after siRNA transfection. **(H-I)** Densitometric analysis of the band intensities shown in G. Mean \pm SEM is shown relative to NC-siRNA (* p < 0.05, ** p < 0.01, *** p < 0.001, and **** p < 0.0001).

Table S1. List of the antibodies used for western blot analysis.

Primary Antibodies	Company	Species	Dilution
Caspase-9	Cell Signaling (9502)	Rabbit	1:500
Caspase-3	Cell Signaling (9665)	Rabbit	1:500
Cleaved Caspase-3	Cell Signaling (9664)	Rabbit	1:250
Cleaved Caspase-9	Cell Signaling (20750)	Rabbit	1:250
PARP-1	Cell Signaling (46D11)	Rabbit	1:1000
BCL-2	Abcam (7382)	Mouse	1:1000
CDK4	Cell Signaling (D9G3D)	Rabbit	1:500
Cyclin E1	Cell Signaling (HE12)	Mouse	1:1000
p27/Kip1	Cell Signaling (D69C12)	Rabbit	1:500
β -actin	Sigma	Mouse	1:10000

Table S2. Concentrations of cisplatin inhibiting 50% of cell viability. Incubation with cisplatin: 72-hr followed by Alamar Blue assay.

Cell line	IC ₅₀ cisplatin (μM)
A2780	0.5-0.8
A2780CP20	20-30
A2780CIS	4.3
OV90	3.5
OV90CIS	7.8
OVCAR3	2.8
OVCAR3CIS	7.5
SKOV3IP1	3.9
SKOV3IP1CIS	7.3

Table S3. List of the 414 differentially abundant RNA transcripts in cisplatin-sensitive vs. cisplatin-resistant HGSOC cells.

Gene Name	OV90log2FC (Resistant/Sensitive)	OVCAR3log2FC (Resistant/Sensitive)
BCAT1	2.849	4.562
SH3BP4	3.63	3.794
NABP1	-2.426	-5.027
FGF2	-5.443	-2.098
STARD4	-4.152	-3.39
RGS2	2.609	4.942
ID4	-6.583	-0.976
PCYT1B	-6.865	-0.760
THBS1	3.589	4.061
LMO7	5.368	2.285
TENM3	-2.439	-5.270
AKAP12	3.951	3.783
SYTL2	-3.189	-4.547
CYP1B1	3.069	4.801
F2RL1	3.652	4.226
ATP11B	-3.213	-4.713
OGFRL1	-3.043	-4.917
SLC39A8	-3.54	-4.474
TNFAIP2	6.296	1.946
CRABP2	-6.656	-1.622
PAX9	-5.501	-2.779
NLGN1	-3.428	-5.05
ANKRD1	-2.663	-5.829
PDE1A	0.964	7.528
QPRT	5.511	3.016
TMEM30B	-6.499	-2.105
GDF15	4.966	3.659
SP3P	-3.396	-5.275
ITM2B	4.733	3.947
CA2	6.825	1.868
PCDH17	-4.544	-4.152
BRINP3	-6.77	-1.955
AKAP6	-4.71	-4.035
ANTXR2	7.893	0.904
MMP16	-6.169	-2.687
NRP1	7.714	1.173
A2M	7.737	1.177

EFEMP1	8.179	0.765
ABCC2	7.886	1.073
ZDBF2	-4.461	-4.553
PRSS23	6.641	2.391
MUC15	-6.231	-2.856
ARL4A	-3.648	-5.454
SLIT2	-7.061	-2.093
MID1	-3.178	-6.01
FAM198B	4.885	4.342
CCL26	8.556	0.711
CDH6	8.573	0.742
FAS	-5.727	-3.592
PROM1	7.886	1.436
LIPG	3.67	5.678
NAALAD2	2.989	6.403
LIN28A	1.378	8.027
MMRN1	0.752	8.664
HIST1H2BH	0.755	8.683
RBM47	6.572	2.887
SLC7A7	7.533	1.93
FGG	8.522	1.004
ZFP42	0.876	8.785
GLDC	-6.067	-3.595
NRK	0.705	9.013
JAG1	8.212	1.523
ISL1	-4.549	-5.2
LAMC2	8.494	1.367
NID1	5.37	4.504
RP3-332B22.1	-6.373	-3.508
FRY	-5.233	-4.715
ZPLD1	1.86	8.16
LHX8	1.083	8.985
MSX1	1.8	8.323
CD24	8.619	1.508
ADGRL2	-4.868	-5.26
POU1F1	-6.368	-3.783
LAMA2	-4.911	-5.244
RP11-115D19.1	1.062	9.22
MBNL2	6.276	4.028
ADAM28	8.719	1.589

CRISPLD1	-6.566	-3.755
TM4SF1	8.555	1.792
C3orf58	-5.97	-4.393
AARD	-6.38	-3.992
C1S	6.658	3.802
RHOBTB1	3.937	6.563
SULF1	-6.791	-3.781
HIST1H3G	1.632	8.958
ACTA2	-7.269	-3.338
SEMA3D	-6.206	-4.422
CLDN16	-5.611	-5.292
SPP1	7.785	3.136
GRID2	-5.303	-5.68
ARID5B	3.283	7.713
ANK3	3.591	7.446
IQGAP2	6.336	4.8
GNAT3	-7.125	-4.09
HDAC9	3.747	7.556
TOX	-6.581	-4.901
MMP3	-6.707	-4.834
VGLL3	-6.179	-5.417
RGS1	2.701	8.926
GPRIN3	2.905	8.771
MLIP	-6.497	-5.213
SIM1	-6.263	-5.48
SDPR	-6.553	-5.299
NRG1	-6.513	-5.384
BICC1	4.73	7.199
SYNPO2	-6.801	-5.135
SEMA3E	-7.43	-4.543
SLC8A1	3.705	8.342
TENM2	-7.826	-4.225
HIST1H3C	8.647	3.475
TMEM2	5.24	7.101
AMIGO2	3.685	8.893
NTS	6.103	6.532
WDR72	8.587	4.104
NUPR1	6.008	6.844
CAV2	8.594	4.388
PDGFRA	8.246	4.799
TGFB2	5.758	7.377
HIST1H2BE	5.774	7.457

SATB1	4.759	8.473
CARD16	4.871	8.633
FUCA2	8.236	5.388
MEST	5.238	8.612
HSPA1A	7.348	6.879
HIST1H2BI	6.462	8.298
UNC13C	7.1	8.031
HIST1H2AL	7.753	7.459
ZNF532	7.147	8.119
TES	7.492	7.874
HIST1H3I	7.912	7.533
HIST1H4D	7.189	8.266
HIST1H1B	7.685	8.058
DKK1	7.451	8.426
FTH1	2.155	1.679
PNMAL1	-3.203	-0.632
SACS	-2.808	-1.027
MAP1A	2.177	1.674
ARRDC3	-1.682	-2.252
SESN3	-0.533	-3.407
ARL6IP5	-2.926	-1.04
KLF3	2.697	1.272
TMCO3	2.469	1.514
ABRACL	-2.029	-1.963
CASK	2.897	1.102
CRIM1	-2.361	-1.655
GJA1	-3.285	-0.789
SORT1	2.224	1.856
ADAM15	-3.681	-0.428
FAM234B	-2.457	-1.682
U1	-3.686	-0.496
HMGB1P6	-3.098	-1.088
OCLN	-0.438	-3.757
HSPA4L	-2.824	-1.39
SPRY4	2.373	1.907
EMP3	2.442	1.88
CMBL	3.615	0.71
ANKRD10	2.715	1.7
SLC40A1	3.524	0.932
DDAH1	-3.514	-0.965

TNFRSF19	-2.188	-2.369
KLHL5	1.834	2.727
SLC9A7	-0.966	-3.632
CCDC138	-2.347	-2.258
SSX2IP	-1.997	-2.616
BCHE	-3.329	-1.31
HSPG2	3.957	0.747
PLAUR	3.63	1.076
MEIS2	2.529	2.209
PIK3CA	-2.523	-2.357
PSD3	-2.396	-2.506
TTC39A	-3.818	-1.105
ERRFI1	3.773	1.328
GCAT	-3.073	-2.125
EMP1	-4.032	-1.205
LIF	-3.039	-2.24
SLC12A6	-2.707	-2.612
MYO5A	-3.998	-1.396
IRS1	4.252	1.218
CFL2	-3.496	-1.976
USP53	-1.397	-4.087
MID1IP1	3.254	2.232
HEG1	4.39	1.12
NUP210	-3.884	-1.669
FTL	4.429	1.148
INSIG2	2.282	3.31
ATP11A	4.262	1.333
ARMCX6	-2.951	-2.659
KCNJ2	-0.944	-4.697
KITLG	4.409	1.269
TBC1D32	-3.796	-1.935
ACSL1	-4.365	-1.368
CITED2	-2.153	-3.59
LGR4	3.476	2.299
PCDH9	-2.982	-2.859
PCGF5	-0.707	-5.141
APOC1	4.111	1.749
KANK1	-0.771	-5.112
ADGRG6	-0.969	-4.949
ARHGAP28	-4.771	-1.238
PAX6	-1.634	-4.429
ABCA1	1.447	4.634

CPED1	0.989	5.124
PLAU	4.736	1.385
ABCA3	-5.623	-0.53
EYA4	-5.638	-0.581
CFH	-3.3	-2.926
TOM1L2	-3.066	-3.174
ARAP2	-1.707	-4.549
AMOT	4.067	2.21
IL1RAP	-1.151	-5.142
TSPAN8	5.502	0.827
CALCRL	-5.567	-0.867
PBX1	4.161	2.288
CASC10	-6.033	-0.497
HOXB9	-1.628	-4.934
MTUS1	2.154	4.438
FLRT3	-1.312	-5.297
SIX1	-5.996	-0.722
OXCT1	-5.918	-0.829
MPDZ	-5.772	-0.996
DNAJC22	5.946	0.843
GNAI1	-1.418	-5.373
HIC2	5.971	0.861
RGS5	6.339	0.575
PCDH7	-1.697	-5.227
ADAMTS3	-6.244	-0.715
NFKBIZ	4.895	2.12
SNRPN	-6.44	-0.589
ELOVL4	-4.846	-2.184
VCAN	1.392	5.639
MET	4.825	2.207
CDH12	6.2	0.865
SLC7A2	1.712	5.473
LRP1B	-2.117	-5.17
APOE	5.742	1.55
F2R	3.526	3.801
NEFH	-6.276	-1.054
RNLS	-2.753	-4.604
PLB1	5.712	1.654
XK	-2.238	-5.142
RUNX2	0.686	6.85
TP63	-4.481	-3.09
PAG1	4.002	3.577
ATP8B1	5.935	1.666

TOR4A	6.637	0.965
TDRP	-6.636	-1.074
RERG	3.067	4.657
HMCN1	5.949	1.803
SULF2	5.871	1.882
SCIN	-2.704	-5.048
C10orf10	5.244	2.526
SOSTDC1	3.635	4.183
MGAT3	4.748	3.083
C2orf72	5.504	2.334
TMCC3	5.595	2.255
S1PR1	0.768	7.114
PALD1	-7.191	-0.707
MCOLN2	-6.298	-1.61
PROCR	2.216	5.769
CCDC74A	-6.246	-1.759
CFP	6.971	1.163
PDGFC	-3.449	-4.711
RNF144B	-6.53	-1.645
VIL1	6.498	1.683
NYNRIN	4.242	3.95
TMEM178A	-4.283	-3.915
VTN	7.014	1.203
TGFBR3	3.754	4.464
ADGRB3	-6.687	-1.532
ZNF415	4.641	3.591
ZNF704	2.274	5.973
SULT1A1	4.823	3.435
CACNA1H	-3.147	-5.151
ESPN	-4.683	-3.694
NUDT11	-6.273	-2.126
LPAR1	-3.441	-5.001
CCDC74B	-6.883	-1.585
CDH10	-7.619	-0.872
COL17A1	6.168	2.348
NR3C1	7.019	1.502
FAM184A	-3.73	-4.797
RGL1	4.965	3.578
KIF1A	-7.199	-1.433
HPGD	7.569	1.277
SLITRK6	-6.079	-2.77
TMEM184A	-3.868	-4.986

MMP14	7.021	1.885
LRRC17	7.498	1.424
ABCB1	-4.17	-4.788
SH2D5	-6.523	-2.51
CFTR	7.291	1.814
NRXN1	-5.791	-3.448
PIK3C2G	7.315	2.103
PPP1R1C	4.773	4.724
FAT3	7.963	1.588
TRPM3	1.672	7.897
SLC5A5	7.696	1.898
RP1-261D10.2	-5.256	-4.339
IGFBP4	6.89	2.723
SYNE4	-5.479	-4.176
SLC16A14	-6.305	-3.386
TFEC	5.917	3.817
EPAS1	6.717	3.019
FBXL7	-7.228	-2.513
NLGN4X	0.932	8.871
LINC01351	-6.664	-3.153
PCLO	-6.521	-3.312
BST2	3.65	6.185
GRIK1	2.112	7.739
LSAMP	8.005	1.852
DISC1FP1	-5.6	-4.293
NPNT	7.795	2.108
HIST1H4L	8.824	1.158
PTGIS	7.141	2.896
OTOA	1.426	8.664
KCNT2	-5.007	-5.086
ARL10	3.691	6.456
PPARGC1A	8.514	1.695
DNAJC6	-4.159	-6.053
MXRA8	6.126	4.138
RUNX1	8.628	1.643
PDLIM3	-4.761	-5.558
ONECUT2	8.279	2.046
EPHA5	-7.009	-3.321
HIST1H2BB	5.909	4.44
IGFBP3	-7.315	-3.037

CCDC110	-5.467	-4.905
FZD8	4.698	5.787
SLITRK5	-7.027	-3.462
VWDE	-5.336	-5.231
TRPV2	6.268	4.389
TBX15	-6.049	-4.642
CFAP47	-5.781	-4.912
LRG1	7.975	2.723
EPDR1	-6.742	-3.985
TPH2	-2.766	-8.037
HIST1H3J	7.052	3.78
TRHDE	-3.021	-7.824
PTPRD	3.016	7.876
MYEOV	8.133	2.771
ZNF788	1.749	9.172
VEGFC	-6.108	-4.837
RASSF9	5.881	5.08
CAV1	5.354	5.612
USP44	7.722	3.286
CDCP1	8.535	2.478
TNS3	7.512	3.554
FAM110C	-7.228	-3.839
SNTG1	-6.821	-4.248
FMN1	-6.023	-5.088
FAM111B	6.931	4.201
GS1-600G8.3	-6.687	-4.473
PDE4B	-6.284	-5.017
SPAG6	-7.059	-4.258
SLC6A15	-5.882	-5.452
DCDC1	-6.34	-5.004
ELF3	7.918	3.49
GAS1	-6.48	-5.013
NID2	5.152	6.351
EOMES	3.634	7.871
INPP1	8.383	3.132
GSG1	-6.509	-5.125
PRRX1	-7.367	-4.314
SV2A	3.705	7.979
SATB2	-6.778	-4.926
TMEM207	-5.756	-5.968
ZNF521	2.909	8.816
LIN7A	-7.011	-4.716

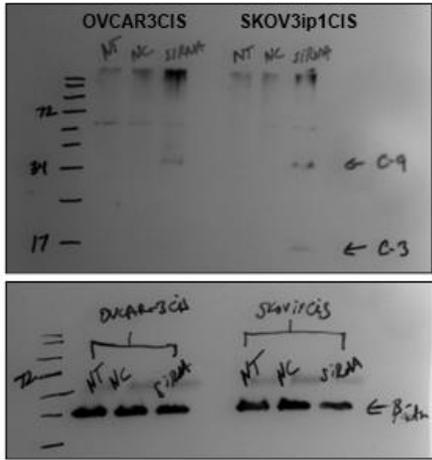
MAGI2-AS3	-7.043	-4.79
KIFC3	7.583	4.277
AF121898.3	-6.78	-5.114
ADAMTS9	8.532	3.404
GALNT13	-7.169	-4.782
ACSS3	-6.822	-5.131
MUSK	-6.5	-5.476
SLC9A9	-6.374	-5.631
CASP4	5.813	6.255
CPA4	7.797	4.435
RP11-865I6.2	-7.152	-5.089
TMEFF2	-8.146	-4.125
PRKG1	5.656	6.652
RP11-255H23.2	3.494	8.884
NRG3	9.075	3.33
ZNF595	4.361	8.078
SLC44A5	7.692	4.886
AGMO	5.557	7.102
PDGFD	5.224	7.436
SOX9	8.431	4.234
ELFN1	4.608	8.097
MGST2	8.215	4.519
TGFB2-AS1	5.167	7.593
RP11-2E11.6	4.689	8.176
PTPRQ	-6.108	-6.981
OLFML3	4.882	8.284
PLBD1	5.84	7.566
AVPR1A	8.135	5.296
ZNF841	7.715	5.867
ESRRG	5.439	8.144
ZNF681	5.459	8.4
FLNC	5.98	7.962
HSPB1	6.297	7.656
S100A11	7.449	6.726
TMEM156	8.629	5.626
GPX1	7.616	6.787

TGFB1I1	7.35	7.098
MDFIC	8.361	6.556
ALDH2	7.644	7.304
HIST1H4A	8.143	6.869
ZNF320	6.905	8.371
ZNF468	8.079	7.213
C14orf169	7.129	8.282
HIST1H3A	8.105	7.314
ZNF718	6.764	8.705

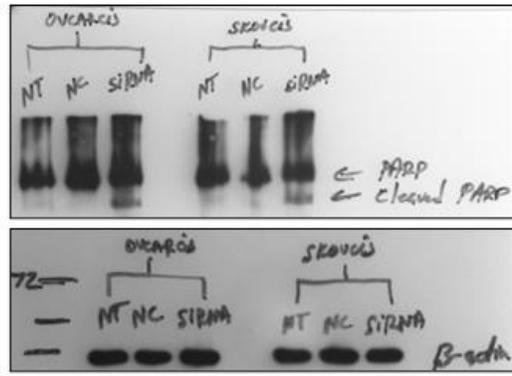
Table S4. CASC10 downstream signaling pathways generated by IPA.

Network	Diseases and Function	Molecules
1	<ul style="list-style-type: none">• Cell Death and Survival• Cellular Movement• Developmental Disorders	TPPP, PYM1, CD151, MAGOH, NRSN1, GLYR1, TMEM64, CELF1, PTBP1, MYC, SERINC3, Cyclin D, SNHG3, EPHA4, CDC42, MERTK, CDK4, PDLIM3, CDCA7L, TNF, CNN1, CDC42EP4, AQP3, TRIM5, FSH, ARHGAP1, IFRD2, WT1, SRY, SLC20A1, EFNA1, TNFRSF6B, TM6SF2, ETV5
2	<ul style="list-style-type: none">• Cell Cycle and Chromosomal Regulation• Cancer and Cell Survival	PCDH7, COL4A1, SMAD6, ANXA9, COL6A2, COL4A2, COL5A1, NFIB, HMGA1, ESTROGEN RECEPTOR, NORAD, EGLN2, ABCA1, TIMP2, KRT18, PDGFA, TGFBR2, FGFR3, CRNDE, LTB, SP1, RHOB, LIPA, NCOR2, GADD45B, , CR2, RB1, NOX4, SIN3A, CDC37, KDM5A, SIN3B, MORF4L1, MORF4L2, MRFAP1

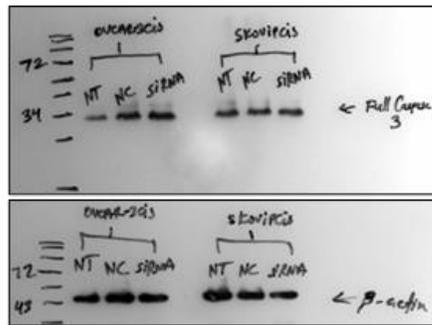
A



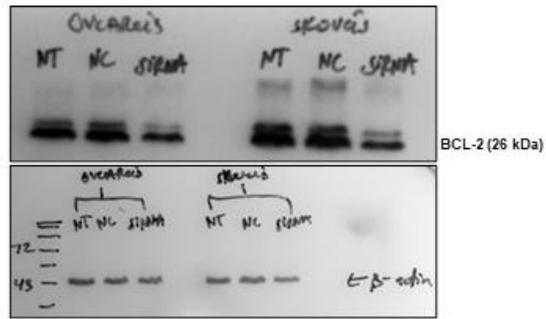
B



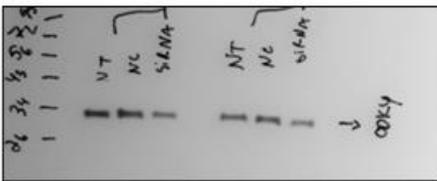
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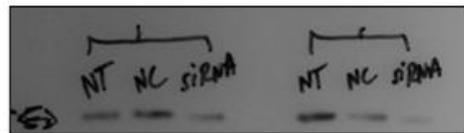
D



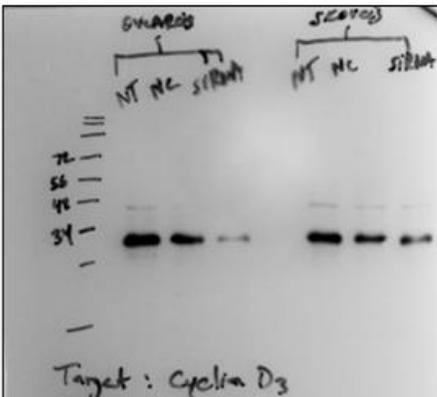
E



F



G



H

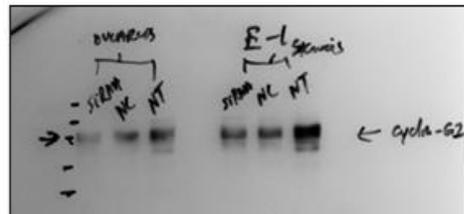


Figure S5. Western blot images. Protein bands and molecular markers are shown for (A) Cleaved Caspase-3 and Cleaved Caspase-9, (B) PARP and Cleaved-PARP, (C) Full Caspase-3, and (D) BCL-2. A-D corresponds to Figure 4B and Figure S4B. (E) CDK4, (F) p27, (G) Cyclin D3, (H) Cyclin E1. E-H corresponds to Figure 4G and Figure S4G.