

Supplemental Data

Integrating imaging and RNA-seq improves outcome prediction in cervical cancer

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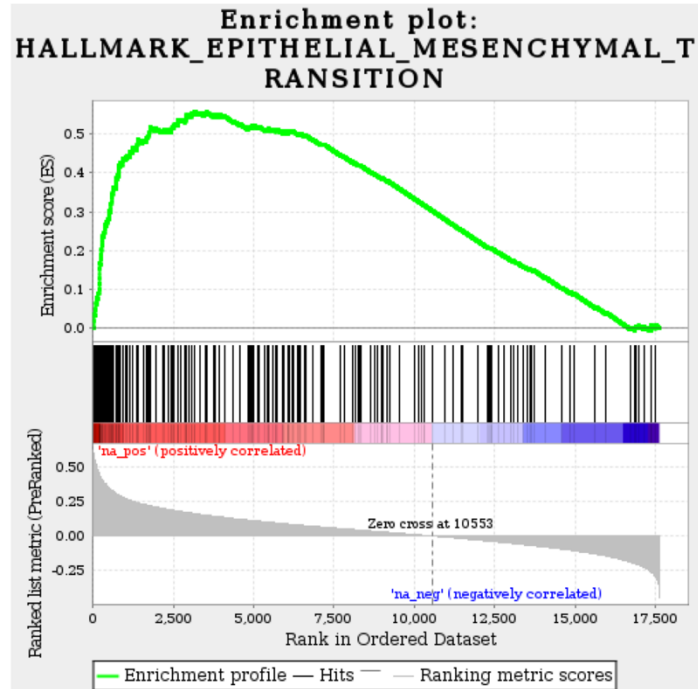


Figure S1. Enrichment of hallmark-epithelial-to-mesenchymal-transition genes positively correlate to SUV_{max} . SUV_{max} and gene expression are from institutional PET imaging and RNA-seq data ($n=67$). GSEA was used in the analysis.

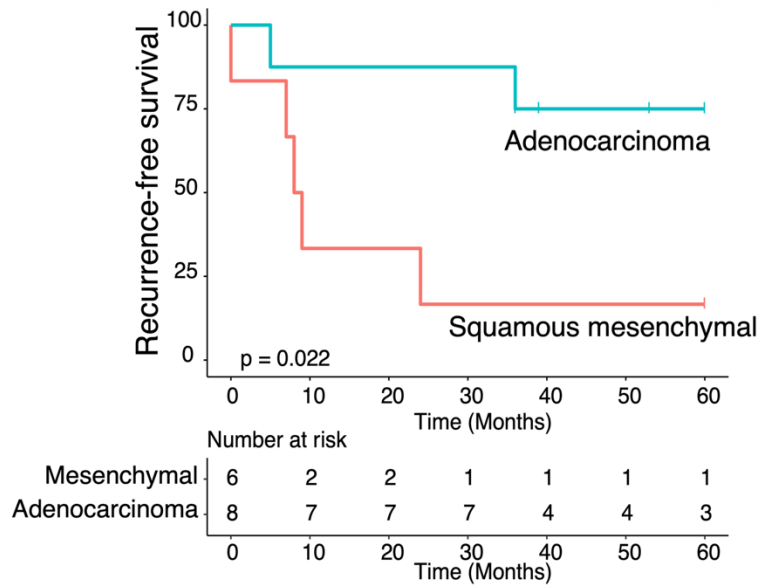


Figure S2. Squamous mesenchymal patients show inferior recurrence-free survival compared to adenocarcinoma patients. RNA-seq data are from an institutional cervical cancer cohort ($n=67$). The mesenchymal group was identified as in Figure 1B. Logrank test was used in the analysis with $p=0.022$.

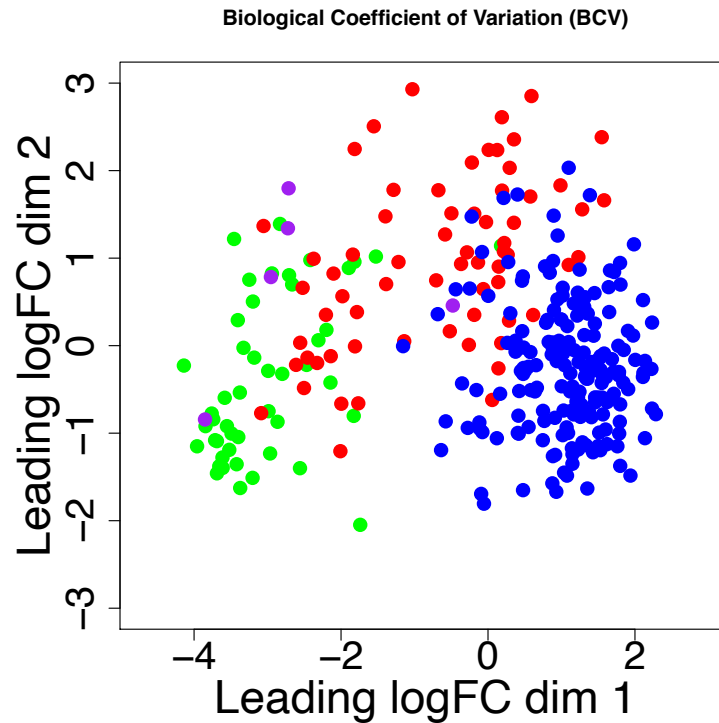


Figure S3. Biological coefficient of variation (BCV) analysis using all expressed genes from TCGA data. Using 12,463 genes expressed in TCGA-CESC cohort ($n=304$), BCV analysis continues to show significant separation of the three major sub-histology EMT groups (blue: squamous epithelial, red: squamous mesenchymal, green: adenocarcinoma), indicating that the grouping based on EMT and histology represents a major biological process in cervical cancer progression. Adenosquamous samples ($n=5$) are shown in purple.

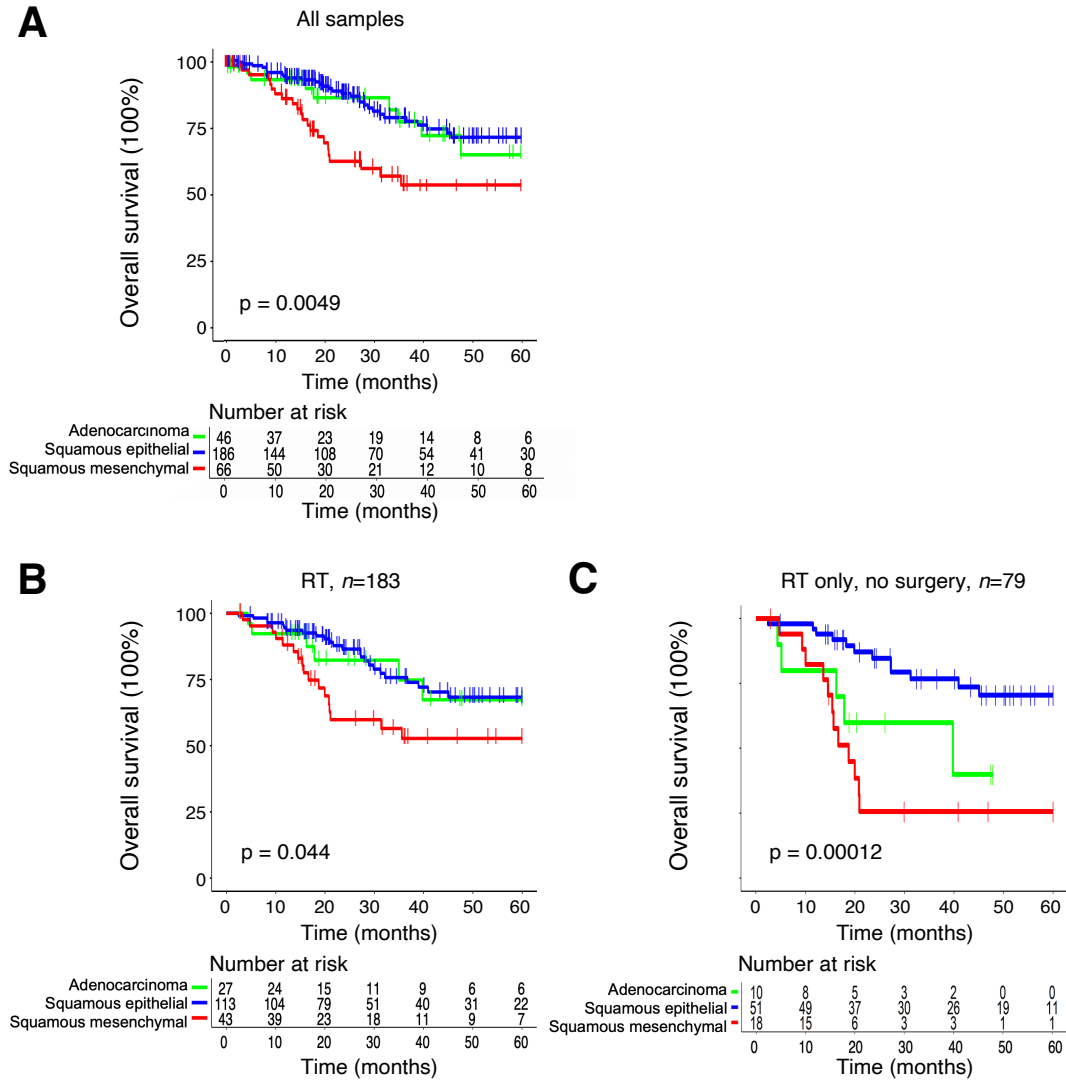


Figure S4. Overall survival for all TCGA-CESC patients and sub-cohort of patients treated with radiation therapy. (A) Squamous mesenchymal patients show inferior overall survival (Logrank test, $p=0.0049$) comparing to other molecular subgroups ($n=298$). **(B)** Kaplan-Meier survival analysis for patients with RT or CRT ($n=183$). Even with the smaller sized sub-histology EMT groups treated with RT, squamous mesenchymal patients still show inferior overall survival compared with the squamous epithelial and adenocarcinoma groups (Logrank test, $p=0.044$). **(C)** Kaplan-Meier survival analysis for patients with RT or CRT but not surgery ($n=79$). Squamous mesenchymal patients still show inferior overall survival compared with the squamous epithelial and adenocarcinoma groups (Logrank test, $p=0.00012$).

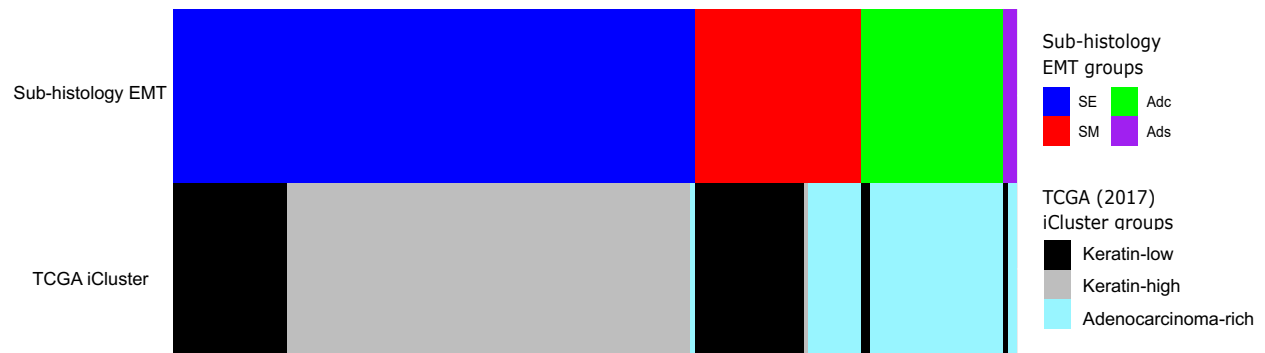


Figure S5. Comparison of our sub-histology EMT groups in this study and iCluster-derived molecular groups in TCGA consortium study ($n=178$). TCGA consortium previously identified 3 molecular sub-groups (i.e., keratin-low, keratin-high, and adenocarcinoma-rich) using a cervical cancer subcohort of 178 patients by integrating copy number, methylation, mRNA and microRNA data using iCluster (Nature, 2017). Comparison with the sub-histology EMT groups we have identified in TCGA-CESC data (squamous epithelial (SE), squamous mesenchymal (SM), adenocarcinoma (Adc), adenosquamous (Ads)) for the same 178 cases shows that the two groupings are independent (Chi-squared test $p < 1e-15$).

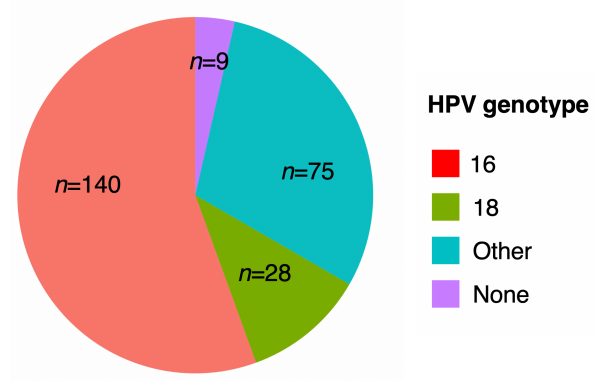
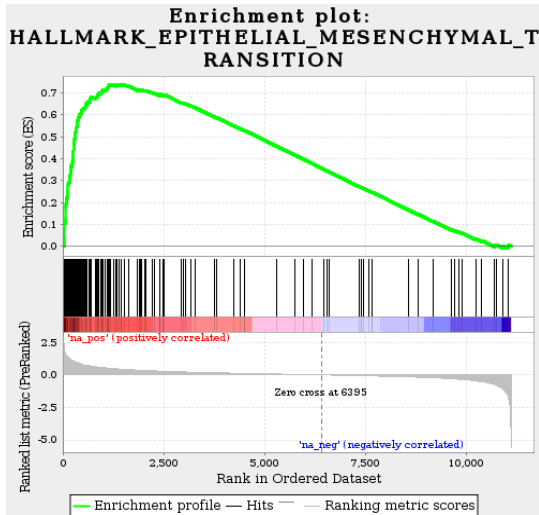


Figure S6. Distribution of HPV genotypes among SCC samples in TCGA data.

A

NOM p-val, FDR and FWER 0.000

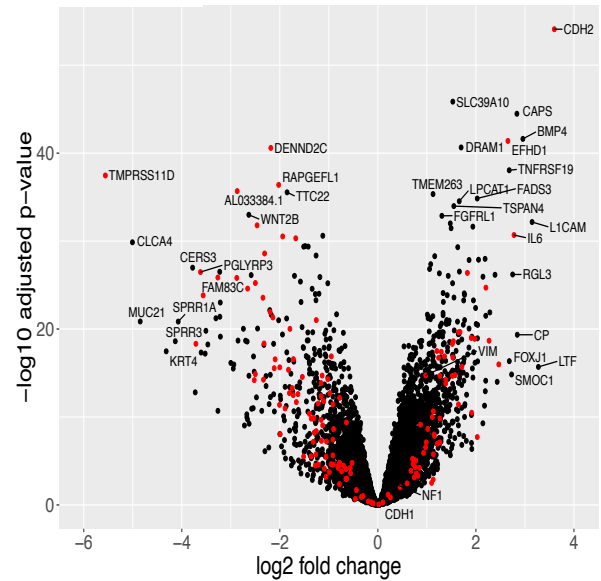
B

Figure S7. Discovery of DE genes between squamous mesenchymal and squamous epithelial groups. (A) GSEA ranked “Hallmark Epithelial Mesenchymal Transition” as the most enriched pathway in the squamous mesenchymal subgroup using TCGA data. **(B)** 264 DE genes ($|\log_2 \text{fold-change}| > 1.58$ and $\text{FDR} < 0.01$) were identified between squamous mesenchymal ($n=66$) and squamous epithelial ($n=186$) groups. *CDH2* (N-Cadherin) is the most up-regulated gene in the squamous mesenchymal subgroup. Red color represents genes from Figure 2A, which are correlated with *CDH1*, *CDH2*, *VIM*, or *NF1* expression.

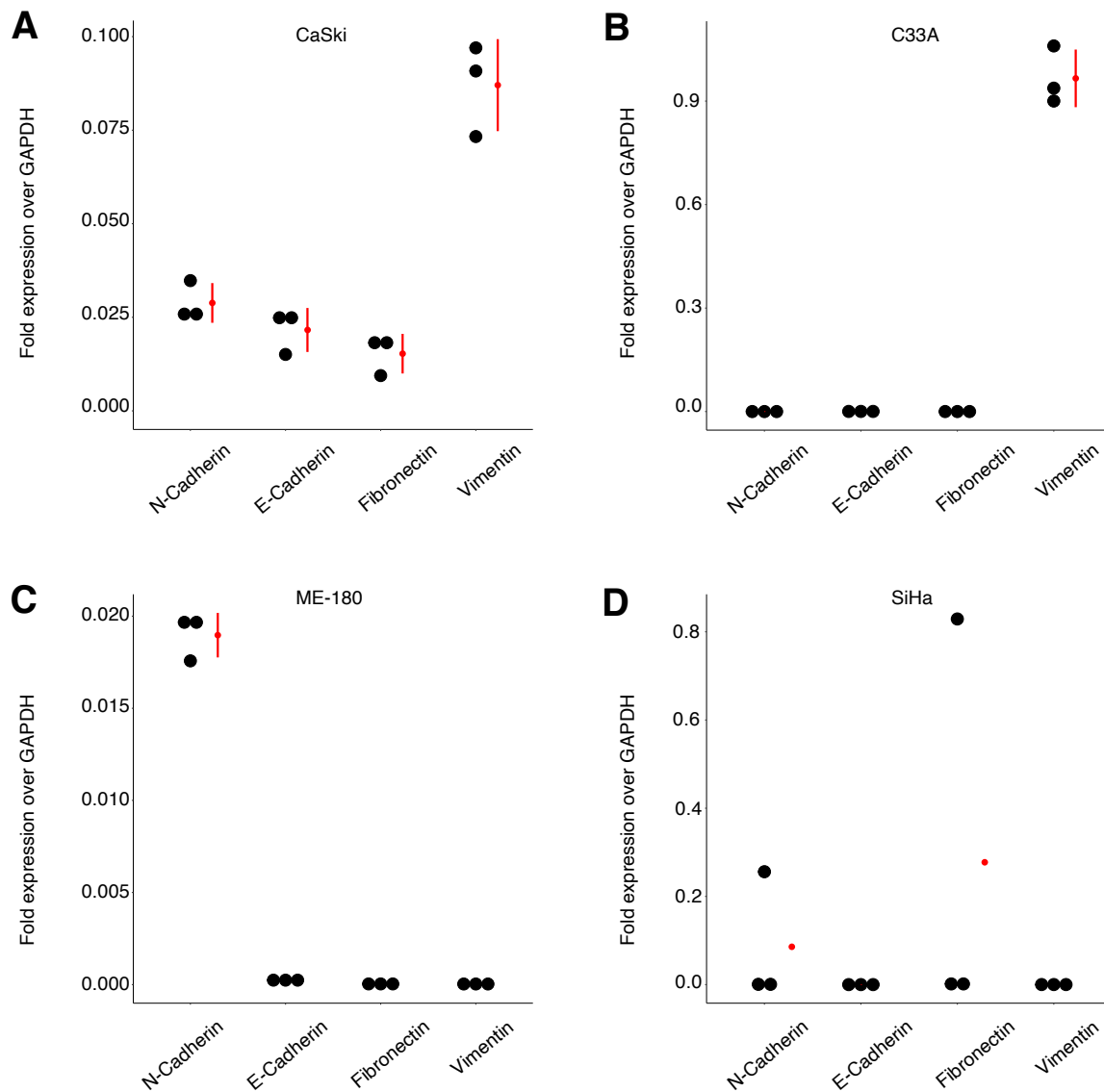


Figure S8. mRNA expression of mesenchymal and epithelial marker genes in four cell lines using qRT-PCR. (A) CaSki has expression for all three mesenchymal marker genes, *CDH2* (N-Cadherin), *FN1* (Fibronectin), and *VIM* (Vimentin). **(B)** C33A only has expression in *VIM*. **(C)** ME-180 only has expression of *CDH1* (E-Cadherin), the epithelial marker gene. **(D)** SiHa has very low expression of *CDH1*, *FN1*, and *VIM*.

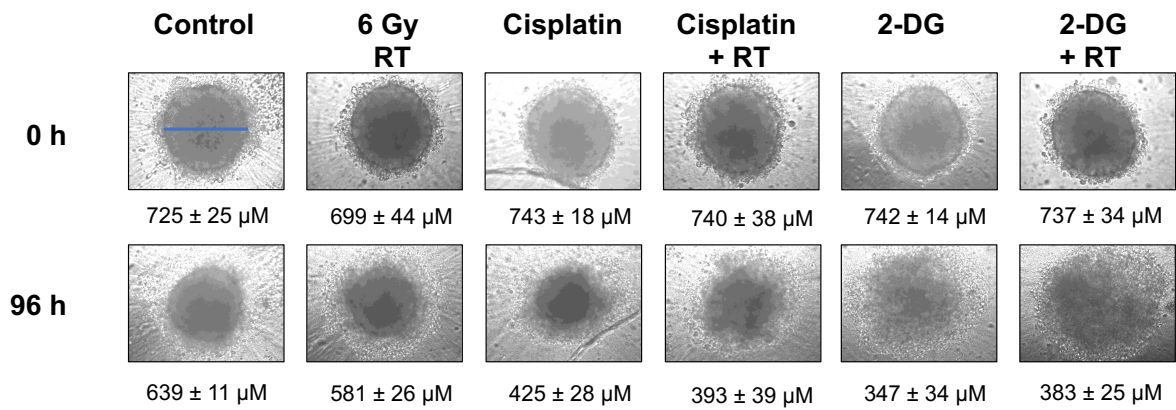


Figure S9. Measurement of diameters of CaSki spheroids treated with sham, 6Gy of radiation (RT), Cisplatin (with/without RT), and 2-DG (with/without RT). The blue line shows the measurement of the diameter of a 3D spheroid. Experiments were repeated 6 times.

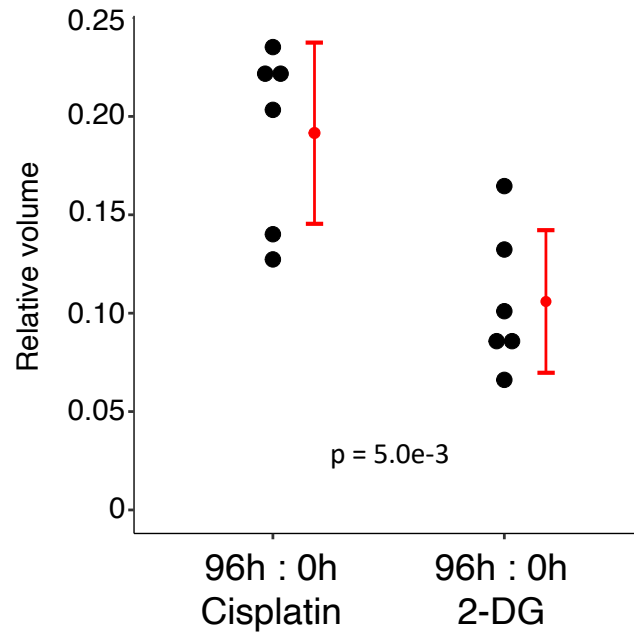


Figure S10. Relative volumes for CaSki 3D spheroids. As shown in Figure 4D, the relative diameters of CaSki 3D spheroids treated with Cisplatin and 2-DG are significantly different. Estimating the volume of the spheroids based on the measurements of diameters, the difference is more obvious. Experiments were repeated 6 times.

Table S1. Patient characteristics for institutional data and TCGA-CESC data.

	Institutional Cohort	TCGA cohort	p-value
Number of patients	67	304	
Age (mean, range)	54.3 years, 25-81 years	48.6 years, 20-88 years	0.00088
Race			
Caucasian	48 (71.6%)	196 (64.5%)	0.060
Black	14 (20.9%)	28 (9.2%)	
Asian	3 (4.5%)	20 (6.6%)	
Hispanic	2 (3.0%)	24 (7.9%)	
Other		3 (1.0%)	
Not Reported		33 (10.9%)	
FIGO 2009 Stage			
I	20 (29.9%)	162 (53.3%)	0.00011
II	24 (35.8%)	69 (22.7%)	
III	21 (31.3%)	45 (14.8%)	
IV	2 (3.0%)	28 (6.9%)	
NA	0 (0.0%)	7 (2.3%)	
Node Positive*		Not determined by PET	
Pelvic LN only	35 (52.2%)		
Pelvic and PA LN	23 (34.3%)		
	12 (17.9%)		
Histology			
Squamous cell carcinoma	54 (80.6%)	252 (82.9%)	0.053
Adenocarcinoma	9 (13.4%)	47 (15.5%)	
Adenosquamous	2 (3.0%)	5 (1.6%)	
Small Cell	2 (3.0%)	0 (0.0%)	
Definitive Therapy			
RT	2 (3.0%)	35 (11.5%)	1.1e-13
CRT	65 (97.0%)	152 (50.0%)	
Other	0 (0.0%)	66 (21.7%)	
Unknown	0 (0.0%)	51 (16.8%)	
Status			
NED	35 (52.2%)	216 (71.1%)	1.1e-6
AWD	1 (1.5%)	28 (9.2%)	
DOD	23 (34.3%)	28 (9.2%)	
DICD	6 (9.0%)	32 (10.5%)	
DToxicity	1 (1.5%)	0 (0.0%)	

* as determined by FDG-PET. FDG-PET = fluorodeoxyglucose-positron emission tomography. FIGO = International Federation of Gynecology and Obstetrics. RT = radiation therapy. CRT = chemoradiation therapy. NED = no evidence of disease. AWD = alive with disease. DOD = died of disease. DICD = died of intercurrent disease. LN = lymph node. PA LN = para-aortic. Wilcoxon–Mann–Whitney test is used to compare the two cohorts.

Table S2. Clinical characteristics for squamous mesenchymal patients (n=6) in the institutional cohort.

Sample	Recurrence	Histology	EMTstatus	Age	Stage	Volume	LNinvolved	HPVtype	hasDistantMets	Cervix.SUV
700514_706432	Yes	Squamous	Mesenchymal	49	IIb	147.67	Yes	HPV18	FALSE	11.46
700514_704397	No	Squamous	Mesenchymal	53	IVa	65.42	No	HPV16	FALSE	13.3
700514_713956	Yes	Squamous	Mesenchymal	61	IIIb	144.03	Yes	HPV59	FALSE	18.48
700514_703822	Yes	Squamous	Mesenchymal	61	IIIb	198.33	No	HPV16	FALSE	7.53
700514_710725	Yes	Squamous	Mesenchymal	46	Ib2	58.98	No	HPV59	FALSE	11.79
700514_707630	Yes	Squamous	Mesenchymal	48	IIb	29.49	Yes	HPV18	FALSE	9.27

Table S4. Multivariate analysis (MVA) for outcome in TCGA-CESC and institutional data.

MVA were performed analyzing sub-histology EMT groups (Adenocarcinoma, SE = squamous epithelial, SM = squamous mesenchymal) and other prognostic factors for survival and compared with univariate analyses.

TCGA-CESC cohort (n=299, events=62), overall survival*						
Covariate	Univariate analysis			Multivariate analysis		
	HR	95% CI	p-value	HR	95% CI	p-value
Sub-histology EMT group						
SM vs SE	2.36	(1.37-4.09)	0.002	2.81	(1.60-4.94)	<0.001
Adenocarcinoma vs SE	1.18	(0.56-2.48)	0.659	1.60	(0.74-3.47)	0.247
Age at diagnosis	1.01	(0.99-1.03)	0.178	1.00	(0.98-1.02)	0.714
FIGO stage						
II vs I	0.82	(0.40-1.68)	0.593	0.53	(0.25-1.13)	0.106
III vs I	1.34	(0.64-2.83)	0.437	0.71	(0.32-1.60)	0.417
IV vs I	4.91	(2.56-9.44)	<0.001	1.94	(0.94-4.04)	0.107
LN involvement	3.28	(1.61-6.67)	0.001	2.63	(1.41-4.92)	0.009
Had surgery	0.35	(0.21-0.60)	<0.001	0.41	(0.22-0.74)	0.005
Institutional cohort (n=63, events=26), recurrence-free survival**						
Covariate	Univariate analysis			Multivariate analysis		
	HR	95% CI	p-value	HR	95% CI	p-value
Sub-histology EMT group						
SM vs SE	2.82	(1.04-7.65)	0.042			
with FIGO stage				3.06	(1.13-8.32)	0.028
with LN involvement				3.38	(1.10-10.40)	0.033
with tumor volume				1.97	(0.66-5.89)	0.227
Adenocarcinoma vs SE	0.76	(0.22-2.57)	0.655			
with FIGO stage				1.57	(0.39-6.29)	0.528
with LN involvement				0.87	(0.25-3.02)	0.830
with tumor volume				0.65	(0.19-2.24)	0.495
FIGO stage						
II vs I	2.06	(0.62-6.83)	0.239	1.83	(0.54-6.17)	0.333
III vs I	4.63	(1.50-14.27)	0.008	4.53	(1.47-13.99)	0.009
IV vs I	4.00	(0.45-35.79)	0.216	1.30	(0.12-14.41)	0.832
LN involvement	2.93	(1.27-6.76)	0.012	3.31	(1.28-8.58)	0.014
Tumor volume	1.01	(1.00-1.02)	0.020	1.01	(1.00-1.02)	0.063

*For TCGA data, missing values (7 patients had missing values for FIGO stage, 46 for surgical status, and 100 for lymph node (LN) involvement) were replaced using Gibbs sampling and pooled results were from 10 simulations. Tumor volume is not available for TCGA data. **Due to the small number of events in the institutional dataset, the factors of LN, FIGO, and volume were analyzed in separate Cox MVA analyses, comparing with sub-histology EMT groups.

Table S5. Enriched Hallmark and KEGG pathways in the squamous mesenchymal group.

Top enriched gene pathways (FDR<0.05) in GSEA comparing squamous mesenchymal and squamous epithelial groups identified in TCGA data.

NAME	SIZE	ES	NES	NOM p-val	FDR q-val	FWER p-val	RANK AT MAX
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION	148	0.7387197	2.7555652	0	0	0	1429
KEGG_RIBOSOME	84	0.7240871	2.534822	0	0	0	2660
KEGG_FOCAL_ADHESION	139	0.58683795	2.1924849	0	0	0	2012
KEGG_ECM_RECEPTOR_INTERACTION	48	0.6845429	2.1397283	0	0	0	1297
HALLMARK_ANGIOGENESIS	25	0.7327462	2.054984	0	4.19E-04	0.002	1353
HALLMARK_UV_RESPONSE_DN	116	0.56087184	2.0381591	0	3.49E-04	0.002	933
KEGG_SYSTEMIC_LUPUS_ERYTHEMATOSUS	47	0.64029354	2.0304546	0	2.99E-04	0.002	2558
HALLMARK_KRAS_SIGNALING_UP	127	0.53092754	1.9733493	0	7.90E-04	0.006	1218
KEGG_TYPE_I_DIABETES_MELLITUS	25	0.713553	1.9477265	0	0.001072719	0.009	2346
KEGG_VIRAL_MYOCARDITIS	48	0.60954934	1.9271525	0	0.00121201	0.011	2346
KEGG_GRAFT_VERSUS_HOST_DISEASE	22	0.7091895	1.9150723	0	0.001712302	0.017	1895
HALLMARK_COAGULATION	83	0.55226487	1.9129237	0	0.00156961	0.017	1162
HALLMARK_ALLOGRAFT_REJECTION	131	0.5117178	1.9099478	0	0.001701114	0.02	2358
KEGG_INTESTINAL_IMMUNE_NETWORK_FOR_IGA_PRODUCTION	21	0.72416407	1.8961034	0	0.001815521	0.023	1983
KEGG_AUTOIMMUNE_THYROID_DISEASE	22	0.6922641	1.8722271	0	0.002289047	0.03	1895
KEGG_HEMATOPOIETIC_CELL_LINEAGE	33	0.63441986	1.8481969	0	0.003159498	0.042	1930
KEGG_CYTOKINE_CYTOKINE_RECEPTOR_INTERACTION	96	0.51735765	1.8262594	0	0.003644497	0.052	2156
HALLMARK_TNFA_SIGNALING_VIA_NFKB	175	0.47585994	1.8259066	0	0.003442025	0.052	1531
KEGG_ALLOGRAFT_REJECTION	22	0.69226396	1.8197997	0.001715266	0.003620078	0.058	1895
KEGG_LEISHMANIA_INFECTION	51	0.56407607	1.7856356	0.001694915	0.005243548	0.089	1479
KEGG_HYPERTROPHIC_CARDIOMYOPATHY_HCM	31	0.60915816	1.7823031	0.001689189	0.005201953	0.093	1306
KEGG_CELL_ADHESION_MOLECULES_CAMS	63	0.53199667	1.767732	0	0.005964329	0.112	1919
HALLMARK_COMPLEMENT	136	0.45748794	1.6974982	0	0.015316949	0.284	1531
KEGG_NOD_LIKE_RECEPTOR_SIGNALING_PATHWAY	44	0.5489092	1.6802555	0.001666667	0.018059503	0.338	891
HALLMARK_MYC_TARGETS_V1	196	0.427079	1.6653016	0	0.021184266	0.393	4550
KEGG_SMALL_CELL_LUNG_CANCER	71	0.49792463	1.6627614	0.001652893	0.020997938	0.402	1776
KEGG_COMPLEMENT_AND_COAGULATION_CASCADES	32	0.5660506	1.6351794	0.010238908	0.02686484	0.491	1324
HALLMARK_ANDROGEN_RESPONSE	87	0.4577213	1.6095481	0	0.033702526	0.577	1899
KEGG_O_GLYCAN_BIOSYNTHESIS	16	0.6357356	1.5988777	0.024734983	0.03713439	0.62	1817
KEGG_N_GLYCAN_BIOSYNTHESIS	38	0.52723724	1.5915729	0.009836066	0.038585898	0.65	4309
HALLMARK_APICAL_JUNCTION	133	0.4218373	1.5830379	0	0.04045783	0.681	1940
HALLMARK_IL2_STAT5_SIGNALING	150	0.41138822	1.5765133	0	0.042208515	0.703	1222
KEGG_GLYCOSAMINOGLYCAN_BIOSYNTHESIS_CHONDROITIN_SULFATE	17	0.6307832	1.5727694	0.021702837	0.042702664	0.716	2027
HALLMARK_INFLAMMATORY_RESPONSE	122	0.42102888	1.5505711	0.002989537	0.052318115	0.798	2430

Table S6. Differentially expressed genes between squamous mesenchymal and squamous epithelial groups. TCGA-CESC data was used in this analysis.

geneName	logFC	logCPM	PValue	FDR	fpkm_mean_SM	fpkm_mean_SE
CDH2	-3.599976693	3.117601511	8.10E-55	9.62E-51	5.285019221	0.448080062
SLC39A10	-1.529060513	4.761923583	1.39E-46	8.23E-43	7.532804488	2.685914711
CAPS	-2.836434016	5.495708201	3.32E-45	1.31E-41	25.57079314	3.929261257
BMP4	-2.958495993	3.302339382	2.38E-42	7.05E-39	9.371636794	1.169018343
EFHD1	-2.653214712	3.678477061	4.07E-42	9.66E-39	11.70236073	1.830317593
DRAM1	-1.698494124	5.377405916	2.24E-41	4.29E-38	20.00870525	6.389398428
DENND2C	2.183589308	4.932031825	2.53E-41	4.29E-38	1.155859012	5.243575399
TNFRSF19	-2.680060797	3.492654197	8.82E-39	1.31E-35	6.190813704	0.933221314
TMPRSS11D	5.559254764	7.160404857	3.44E-38	4.54E-35	1.180296586	57.55751405
TMPRSS11A	6.434816478	6.080015797	2.79E-37	3.32E-34	0.258223411	23.19302876
RAPGEFL1	2.02387224	7.346095772	4.05E-37	4.37E-34	8.896355094	36.2378934
AL033384.1	2.869674919	2.570729892	2.06E-36	2.04E-33	0.327996105	2.394413569
TTC22	1.852462819	5.777936304	2.84E-36	2.60E-33	3.103815512	11.18744804
FADS3	-2.027312459	4.933996994	1.42E-35	1.13E-32	10.69193124	2.643451632
LPCAT1	-1.660180436	6.507941732	2.94E-35	2.18E-32	28.24542558	8.956631841
TSPAN4	-1.549378382	4.912672423	1.05E-34	7.31E-32	9.63761288	3.438974085
WNT2B	2.632675038	4.340873536	1.02E-33	6.74E-31	0.340702877	2.112856571
L1CAM	-3.146594782	4.378661483	6.79E-33	4.03E-30	7.925022833	0.915742331
GRHL3	2.464004379	5.929215715	1.62E-32	8.73E-30	3.708443379	19.8804061
KRT18	-1.938116993	9.37162878	2.28E-32	1.18E-29	415.5578795	114.1541889
IL6	-2.777370039	2.918723321	2.05E-31	9.74E-29	9.556247115	1.453802864
DUOXA1	1.940917021	5.762928756	2.95E-31	1.30E-28	4.719230631	18.07614091
TMEM79	1.675511698	6.216066379	4.77E-31	2.02E-28	9.22372658	29.42016603
CLCA4	5.006840854	6.381031747	1.36E-30	5.57E-28	0.99643842	33.19148504
EVPL	1.513169697	7.881919472	4.25E-30	1.58E-27	13.29290983	37.84648099
FSTL1	-1.629390602	7.676577434	4.90E-30	1.76E-27	47.25688259	15.46968951
ZNF750	2.310329978	6.454462349	2.55E-29	8.89E-27	6.155435799	30.24223052
AKAP12	-2.188096957	4.096184729	1.05E-28	3.36E-26	4.793107792	1.053770137
PADI2	-2.053691907	3.923548918	1.32E-28	4.11E-26	6.129264516	1.413738961
QPCT	-1.861350815	3.041388252	1.42E-28	4.31E-26	7.002343936	1.886896047
CERS3	3.779316945	5.368345014	1.06E-27	3.07E-25	0.768821043	10.54026915
FERMT2	-1.663537211	4.209763393	2.93E-27	8.08E-25	4.49143645	1.435198656
SLC39A2	3.226455636	3.233390446	3.08E-27	8.32E-25	0.839712724	7.748305926
PGLYRP3	3.619099062	3.658499195	3.32E-27	8.76E-25	1.141886496	14.27153831
LOXL2	-1.826583053	5.649138539	4.13E-27	1.07E-24	18.48844758	5.30176337
RGL3	-2.749448526	2.64808897	6.25E-27	1.54E-24	4.054512907	0.595082186
BIRC3	-2.39023931	6.925337502	6.75E-27	1.64E-24	37.62080879	7.727678657
SH3PXD2A-AS1	2.584255612	2.55815601	7.32E-27	1.74E-24	0.555829226	3.413171507
CSTB	1.701192536	9.800050722	8.95E-27	2.06E-24	132.5223689	425.5684781
DUSP4	-2.144096738	5.211340666	1.13E-26	2.53E-24	11.92801757	2.742671968
CAPNS2	3.264538818	4.544351991	1.39E-26	2.99E-24	3.115945725	30.39018421
DSG3	2.87839757	9.432178093	1.53E-26	3.25E-24	21.70034278	161.552946
LTB4R	1.579907498	6.063283085	4.03E-26	8.39E-24	6.166732111	18.0590295
CSTA	2.498964421	8.60264086	5.83E-26	1.19E-23	62.3241246	353.818154
SPRY4	-1.524168188	4.047180221	6.16E-26	1.23E-23	5.61694402	1.898948641
TGFB2	-2.203990499	3.581688902	1.95E-25	3.80E-23	5.459021963	1.226071411
BNIP1	2.65697521	4.888760638	2.52E-25	4.82E-23	2.184324407	13.22278614
CYGB	-1.762423282	3.466000795	8.82E-25	1.61E-22	7.755626156	2.308399077
ARHGAP29	-1.768532841	4.392010113	1.29E-24	2.25E-22	2.908144462	0.848472272
FAM83C	3.564002806	5.199913959	1.48E-24	2.51E-22	1.399710004	15.60889739
TPM1	-1.552678207	7.221991043	2.62E-24	4.38E-22	23.24557789	8.151870098
P2RY1	2.343982312	5.538153156	2.74E-24	4.52E-22	1.795259497	8.88698272
PXDN	-1.949905914	6.561457628	5.51E-24	8.82E-22	18.88688508	4.928993193
MYADM	-1.750759815	6.303898969	5.57E-24	8.82E-22	44.63305433	13.32718774
DUOX1	1.567198439	6.726095507	8.42E-24	1.30E-21	5.074009608	14.73265725
GBP6	3.215079386	6.265442406	9.69E-24	1.48E-21	3.654039883	33.74814882
TGM2	-1.993795895	7.864763239	4.01E-23	6.02E-21	65.18594381	16.40795
BCL2L10	2.205333634	3.068418026	7.16E-23	1.06E-20	1.718986688	8.034718095
PKP1	2.19777008	9.879625685	1.13E-22	1.66E-20	40.71106466	190.4931127
TMPRSS3	-2.285000056	4.130661862	1.29E-22	1.87E-20	7.193121496	1.575818596
SMIM5	2.175007051	2.759535042	2.40E-22	3.31E-20	0.377956449	1.665368034
EFEMP1	-2.201143061	7.107690602	3.10E-22	4.18E-20	80.5916253	18.12922561
APOBEC3A	3.223134128	5.056671666	3.98E-22	5.25E-20	1.948061983	17.62047319
TINCR	2.141150183	5.210413533	4.76E-22	6.15E-20	2.839007218	11.97246479
KRT78	3.304475555	4.058097356	5.95E-22	7.51E-20	0.660739677	6.505993979
DSC2	1.86161199	8.406702522	6.30E-22	7.87E-20	9.447171805	33.18461394

BIRC2	-1.770123899	6.894227177	9.63E-22	1.15E-19	55.86636739	16.28592293
AC007342.5	2.024511665	2.427049775	1.00E-21	1.19E-19	0.770154438	3.143385525
MUC21	4.848736544	4.930741169	1.38E-21	1.60E-19	0.368461153	10.85328625
SPRR1A	4.073257275	7.136839748	1.42E-21	1.62E-19	40.99499709	665.7420451
KLHL29	-1.624510118	3.111270894	1.44E-21	1.63E-19	1.589865467	0.51549561
BAMBI	-2.005536357	4.055070177	2.68E-21	2.87E-19	16.88156543	4.014196582
LIF	-1.742480368	3.394345322	3.21E-21	3.38E-19	5.548738973	1.660827391
IL11	-2.035049358	3.005879432	3.38E-21	3.52E-19	6.505308913	1.624973834
OVOL1	1.545641812	5.12297433	6.03E-21	6.17E-19	3.762145391	10.91039448
TWIST1	-1.860551617	2.761858743	8.77E-21	8.84E-19	7.491850521	1.964997354
PRSS27	2.454145604	4.755918032	8.78E-21	8.84E-19	1.051526487	5.686051209
ASPG	2.743486748	3.801284202	9.31E-21	9.29E-19	0.43860525	2.935602459
AL512274.1	1.794151252	3.461843111	9.40E-21	9.30E-19	1.953323948	6.594755752
PDE4B	-1.55803066	3.57771146	1.43E-20	1.39E-18	2.783473171	0.937423656
SPINK5	3.508198136	7.336276157	1.58E-20	1.51E-18	4.364204998	46.83931067
FKBP10	-1.676174285	6.310174687	2.18E-20	2.05E-18	37.54881076	11.84387869
KRT1	6.24355588	7.881609534	2.26E-20	2.11E-18	1.7593936	122.9583322
BICC1	-1.648491778	2.685826152	2.30E-20	2.12E-18	1.938602557	0.632706876
SNAI1	-1.656009495	2.394009851	3.54E-20	3.05E-18	6.135752469	1.992242615
HES6	-1.640296674	4.219193541	3.86E-20	3.30E-18	20.4218679	6.259852506
LYPD3	1.946141182	8.907469334	4.16E-20	3.53E-18	60.44135587	234.9627738
CP	-2.844372275	5.694676526	4.47E-20	3.74E-18	21.1427174	2.925731501
PCP4L1	3.212768017	4.340052528	7.35E-20	5.98E-18	2.230767691	19.06926893
ASPHD1	-1.918590357	2.89579809	7.51E-20	6.06E-18	5.718125961	1.832026835
NNMT	-1.905491008	6.627427764	1.04E-19	8.31E-18	69.02402317	19.32147571
SEMA3B	-2.032125817	5.402732476	1.13E-19	8.97E-18	15.73544083	4.087171126
FN1	-1.975765765	9.496706242	1.30E-19	1.02E-17	92.79452468	24.05652893
LIFR	-1.71231318	4.042876693	1.54E-19	1.20E-17	2.968529554	0.900278994
SLC10A6	2.85311949	2.646426049	2.05E-19	1.56E-17	0.72426019	5.434944602
LRRC4	2.698939074	4.216296934	2.12E-19	1.59E-17	0.950238442	5.982272129
PNMA8A	-2.268804351	2.313712304	2.12E-19	1.59E-17	3.346688505	0.683991449
SPRR3	4.132731652	8.539307201	2.43E-19	1.78E-17	19.12270625	335.3746286
MPDZ	-1.541026048	3.24078394	2.44E-19	1.78E-17	1.705687063	0.577853922
AKR1B15	2.665796325	3.490110356	2.64E-19	1.91E-17	0.688352306	4.274670223
C1QTNF1	-1.641057977	4.850642028	3.09E-19	2.20E-17	12.45076254	3.78842914
EPHX3	2.321846195	6.1056779	4.37E-19	3.05E-17	8.072979407	42.9684605
C10orf99	3.712558847	5.74965856	4.75E-19	3.29E-17	6.022922917	78.58041982
AQP3	2.126904441	10.03612741	4.77E-19	3.29E-17	105.7936306	450.8277938
CTNNA1	-1.519612204	4.815631227	4.83E-19	3.31E-17	17.36797401	6.039393927
SPRR1B	3.468466153	8.505560348	5.69E-19	3.84E-17	68.5253508	740.0949518
ALOX12	2.325437814	2.877659616	6.31E-19	4.23E-17	0.708343847	3.524266084
PITX1	1.523944364	8.198152148	1.15E-18	7.43E-17	33.58165583	100.8497815
C3	-1.858307498	8.55562248	1.27E-18	8.09E-17	93.30472027	27.33856649
TRIM7	1.517418542	4.683729058	1.40E-18	8.79E-17	1.444503428	4.256749569
LIMCH1	-1.595917492	4.771605211	3.03E-18	1.84E-16	4.945779568	1.65367371
KRT4	4.318244806	8.483784426	3.39E-18	2.01E-16	7.91435941	146.7200185
INHBB	-1.956207869	3.067983855	4.34E-18	2.55E-16	6.081791344	1.498310992
IL1RN	1.85791323	7.753571258	4.46E-18	2.61E-16	21.61813052	80.86504773
KRT13	3.60557805	11.63765969	4.70E-18	2.72E-16	116.6489205	1417.536584
TMPRSS11E	3.52310321	5.786831272	6.21E-18	3.54E-16	3.025866312	33.99948638
TFPI	-1.832214089	4.503898394	7.73E-18	4.31E-16	4.115164631	1.177063738
SPOCK2	-1.530584974	5.420099145	8.52E-18	4.70E-16	11.75869496	4.4626191
FSTL3	-1.526487727	5.39372472	8.76E-18	4.82E-16	25.00039584	9.138063055
KRT10	2.537175567	8.012755876	1.30E-17	6.81E-16	26.99822676	151.6494012
ZNF853	-1.528703483	2.23209518	1.71E-17	8.81E-16	2.440045567	0.850179571
GMPR	-1.541662852	2.769577111	1.76E-17	8.98E-16	6.010195783	2.037516431
OSBP2	-1.754662753	5.225236862	2.08E-17	1.05E-15	11.02050464	3.500257556
KRT8	-1.758845131	10.14691664	2.43E-17	1.22E-15	438.4861269	136.8658907
FGFR3	1.722371633	7.614627249	2.67E-17	1.34E-15	16.04405896	50.13788349
DSC3	2.095748818	9.374409301	2.77E-17	1.38E-15	27.36726229	118.7924766
SRRM3	1.814995766	4.402072666	3.35E-17	1.64E-15	1.073212555	3.736048197
FOXJ1	-2.681393174	4.657102853	4.45E-17	2.14E-15	25.17004916	4.140249826
STC1	-2.035429684	5.145863152	4.72E-17	2.25E-15	19.56680486	4.902423794
RGMA	1.714527897	5.163928363	5.09E-17	2.42E-15	1.075199887	3.41211222
HID1	-1.625378702	4.369782834	5.48E-17	2.59E-15	6.886314462	2.218924427
ARNT2	-1.750940774	3.940187451	6.18E-17	2.86E-15	4.240840657	1.258677563
MOXD1	-1.981955308	4.279969783	6.76E-17	3.10E-15	8.864675429	2.149635773

RHCG	2.999910796	8.908879729	7.11E-17	3.25E-15	28.71934159	236.5455535
FBN2	-2.467150035	4.73905528	1.04E-16	4.61E-15	5.213152597	0.926786184
VEGFC	-1.719289521	3.166582102	1.05E-16	4.61E-15	7.239612567	2.273358794
PADI1	2.937139347	4.862351577	1.08E-16	4.74E-15	1.033503444	7.737046929
TGFBI	-1.622186727	8.574926892	1.87E-16	7.98E-15	93.82522806	30.57827488
APLN	-1.714181018	3.192173092	2.02E-16	8.52E-15	5.732086232	1.774383617
LTF	-3.27485983	6.995336421	2.02E-16	8.52E-15	91.58019892	9.503951232
TPRXL	2.000747205	3.095548806	2.26E-16	9.41E-15	0.742895994	2.93329333
FABP5	2.115309403	9.435583163	2.83E-16	1.15E-14	93.46296139	403.8802893
OLR1	-1.92793697	4.509139729	3.01E-16	1.21E-14	15.89835549	4.287754637
IVL	2.95061197	6.877567752	3.11E-16	1.25E-14	9.107399045	68.47361275
CALML3-AS1	1.82339259	3.538992039	4.32E-16	1.70E-14	0.859003204	3.041472494
RAB17	-1.680324126	3.336612806	5.23E-16	2.02E-14	3.949464114	1.35364372
FNDC4	-1.523952761	2.358854342	5.24E-16	2.02E-14	4.859819777	1.702267997
CCL2	-1.585466126	4.920227556	5.48E-16	2.10E-14	30.61171895	9.953399301
MOCS1	-1.527422786	2.814517038	6.73E-16	2.55E-14	2.612028081	0.918458601
DUOX2	2.523484377	6.966957614	7.07E-16	2.67E-14	2.77380508	16.25160079
TDRP	-1.743645894	2.655106093	8.61E-16	3.22E-14	3.76289	1.086014432
BCAM	-1.589477614	7.99877422	9.60E-16	3.56E-14	99.08614982	33.33036486
AC007342.9	1.773604853	2.436945995	1.20E-15	4.37E-14	1.39915905	4.788538818
SERPINB13	2.498968389	8.014562212	1.33E-15	4.82E-14	12.72811047	73.05164144
IL1B	-1.681597767	4.324357876	1.38E-15	4.99E-14	12.66937574	4.057783155
SMOC1	-2.727989844	5.244097267	1.46E-15	5.22E-14	21.96413027	3.48464234
C12orf54	2.194333867	2.713311773	1.61E-15	5.72E-14	0.933839099	4.406895541
QPRT	-1.813845161	3.607580254	1.70E-15	6.00E-14	6.244402009	2.028083703
FHOD3	-1.577963722	3.841569495	1.73E-15	6.09E-14	3.585561963	1.21016385
A2ML1	2.63022451	7.446772167	2.05E-15	7.04E-14	4.97144159	30.4726798
DAPK1	-1.521682364	4.929400664	2.11E-15	7.21E-14	6.480665637	2.313542392
PGLYRP4	2.282140883	2.904331765	2.23E-15	7.60E-14	0.837169643	4.067669676
TMPRSS4	1.540984645	7.509809821	2.77E-15	9.27E-14	7.770683199	22.40284031
SFRP1	-1.940092664	6.125981536	3.28E-15	1.08E-13	32.5832218	8.718535792
CLMP	-1.668733775	4.092693396	3.73E-15	1.21E-13	6.638680466	2.131833569
LY6D	2.333731728	9.626247462	5.68E-15	1.79E-13	119.2241073	624.4818787
S100A8	2.521617003	11.54145941	6.44E-15	2.01E-13	631.4127747	3544.547363
CLIC6	-2.200007693	4.625679467	7.50E-15	2.31E-13	16.90892929	3.477478895
CRACR2B	-1.755557029	4.407915975	7.51E-15	2.31E-13	11.1518	3.498195546
CLDN3	-2.434577556	4.816276112	1.01E-14	3.05E-13	48.81933451	9.959270058
HOPX	1.591815557	5.006370334	1.15E-14	3.45E-13	1.651567479	4.905193158
BCAT1	-1.643430225	4.624718134	1.25E-14	3.72E-13	4.100732373	1.341663599
YAP1	-1.653741963	8.294853973	1.27E-14	3.77E-13	98.05863543	31.75794457
RG52	-1.524779525	5.394251646	1.75E-14	5.09E-13	37.33487242	13.38311369
CD8B	-1.710122551	3.055540038	2.28E-14	6.58E-13	9.563797797	2.846445386
KRT16	2.280752575	11.13691311	3.02E-14	8.67E-13	232.3374256	1084.946862
ATG9B	1.650188693	3.877518511	3.59E-14	1.02E-12	0.900963683	2.822375537
VSNL1	1.892427068	5.787921199	3.70E-14	1.04E-12	4.889061713	17.8687558
HSPA6	1.802729379	4.611516909	3.97E-14	1.11E-12	3.648183745	12.07711897
HES2	1.594393227	6.749520835	4.79E-14	1.32E-12	7.962634849	24.0864508
FBXO2	-1.545957829	5.135305219	5.00E-14	1.38E-12	28.04195824	9.855333076
FOXP1	1.747515909	4.931793084	5.16E-14	1.41E-12	3.242670785	10.41700004
SLC7A2	-2.192020443	5.142312229	1.17E-13	3.02E-12	10.44773386	2.395343711
ECM1	1.736001472	7.193126506	1.32E-13	3.39E-12	16.18973382	52.46448601
ADH7	3.725896686	6.09854304	1.58E-13	4.02E-12	2.394978977	29.84519521
ASRGL1	-1.570853792	3.753967	1.59E-13	4.05E-12	5.81494193	2.008953608
KCND3	1.804743546	3.469618752	1.91E-13	4.82E-12	0.517530185	1.748315176
ZBTB7C	1.630270821	5.858847268	2.48E-13	6.17E-12	3.097725587	9.383877399
BARX2	2.126078543	5.5929189	2.62E-13	6.47E-12	3.797414524	16.77495889
PRR15	-1.810256394	3.22830254	2.93E-13	7.18E-12	10.62399755	2.889897935
SUSD4	1.7259981	6.103485202	3.26E-13	7.89E-12	5.694669908	18.16618284
WFD2C1P	1.990248471	5.581114727	3.78E-13	9.01E-12	13.03143869	53.5402633
BASP1	-1.516160689	6.457802989	4.24E-13	1.00E-11	75.04386642	26.22435268
SCEL	2.191974208	5.474152584	5.42E-13	1.25E-11	2.886303075	13.07569775
GJB6	2.477372462	6.763374254	5.82E-13	1.32E-11	10.82891723	60.5584102
S100A3	-1.524220729	3.863365514	6.48E-13	1.46E-11	31.04570654	9.892816655
NT5E	-1.611573685	4.762969134	7.37E-13	1.64E-11	11.5433239	3.879172446
ADGRF1	1.983500641	4.90306216	9.56E-13	2.11E-11	0.774232959	3.009564209
IL20RB	1.663135881	7.346165826	2.02E-12	4.22E-11	24.78311795	79.86979588
KRT15	2.218359029	10.51461597	3.44E-12	6.96E-11	59.78024259	260.704662

CXCL2	-1.77659256	4.008699958	3.50E-12	7.06E-11	21.74025925	6.282045437
SORCS2	-1.644609996	3.170331063	3.68E-12	7.35E-11	2.864510985	0.918030922
ABO	2.006548003	5.18047472	4.19E-12	8.26E-11	1.858119141	7.277368253
PKDCC	-1.771887938	4.057616937	5.16E-12	9.98E-11	9.115633738	2.670016702
CCL19	-2.175985669	4.618228658	5.19E-12	1.00E-10	82.6461645	17.02850112
ANKRD35	1.869605754	4.183807322	5.67E-12	1.09E-10	1.937343292	6.574366632
HOXB9	-1.710947484	3.567569541	9.00E-12	1.68E-10	9.566748627	3.027559614
AKR1B10	2.543012399	7.14899643	9.97E-12	1.84E-10	17.74579042	100.684531
S100A9	1.892851081	11.90991296	1.07E-11	1.97E-10	2127.594985	8047.289402
IL36RN	2.57441796	3.416161586	1.15E-11	2.09E-10	0.673863775	4.037293225
RASD1	-1.602551578	4.014832134	1.41E-11	2.51E-10	18.42085794	6.132888001
GNPMB	1.621616372	8.965431262	1.61E-11	2.84E-10	34.98210417	104.3768959
KLK13	3.263111618	5.62044164	1.99E-11	3.43E-10	3.288340848	31.13985861
DUOXA2	2.368003033	4.222426498	2.01E-11	3.46E-10	1.741863512	9.262612215
CXCL3	-1.63537102	2.746359622	2.05E-11	3.52E-10	5.905970684	1.922564116
HAP1	1.713387733	3.936525408	2.23E-11	3.78E-10	0.925155526	3.045424456
FABP5P7	2.111679809	3.417312553	2.35E-11	3.96E-10	7.257283479	31.5123763
MFAP5	-1.913353783	4.356294097	3.26E-11	5.40E-10	10.65083363	3.090008349
GRIN2D	1.609534251	4.319359985	3.69E-11	6.04E-10	1.445183094	4.655064609
SPRR2D	2.673747999	6.762907283	5.03E-11	8.08E-10	19.98631239	126.9380759
DKK1	-1.909215078	5.137134047	5.96E-11	9.42E-10	35.93493734	9.486527789
CNFN	1.923539198	5.773962596	8.27E-11	1.29E-09	26.52126654	107.4239746
PRIMA1	1.64360406	4.296311238	8.35E-11	1.30E-09	2.012228096	6.182098192
SAA2	-1.768263271	3.675604163	9.92E-11	1.52E-09	11.53318591	3.374547795
KRT6C	2.672991563	8.323153264	1.08E-10	1.63E-09	21.29963608	129.7732464
POSTN	-1.620766917	6.333569101	1.77E-10	2.58E-09	29.20681851	9.766303733
MAL	2.659884191	5.278736731	1.87E-10	2.73E-09	5.213960728	34.03751921
CALML3	1.90701733	9.034255421	2.45E-10	3.49E-09	64.54804862	228.0806313
UBD	-1.519354669	3.894761352	3.33E-10	4.65E-09	26.4356554	9.368312491
GOS2	-1.536657526	5.024081146	3.42E-10	4.76E-09	68.54402309	24.23119891
CXCL8	-1.51593265	6.460997993	4.52E-10	6.16E-09	72.89244359	26.25341829
TFPI2	-2.142456968	4.414139083	5.19E-10	7.02E-09	17.82061974	4.040086171
SPRR2A	2.626199052	7.360615983	5.74E-10	7.69E-09	46.21135551	284.0325661
NDRG4	1.675558413	5.508146499	6.23E-10	8.28E-09	1.959755197	5.810834081
SAA1	-1.642704805	6.028659966	8.92E-10	1.15E-08	159.7157944	52.53415444
SBSN	2.722328127	7.5275062	9.25E-10	1.18E-08	17.62163117	116.1115756
CYP2S1	1.674059389	5.99320202	1.19E-09	1.50E-08	8.783755062	27.38818466
CRYAB	1.706275624	5.731836475	2.06E-09	2.49E-08	6.610020664	20.48348969
RAET1L	1.799810029	2.830571847	3.48E-09	4.01E-08	1.936458074	6.516486899
GJB2	1.677900957	8.602565422	3.85E-09	4.39E-08	59.7347127	191.0401885
RARRS1	-1.659476219	6.488888676	8.53E-09	9.10E-08	80.97928237	26.99950765
ZNF812P	2.0009242	3.5745183	8.73E-09	9.29E-08	1.654189254	6.345003411
FUT6	1.992198157	3.381704648	9.04E-09	9.59E-08	0.68786749	2.978035023
IGHM	-1.750698474	8.828438356	1.46E-08	1.48E-07	384.7698966	118.3472638
MMP10	-2.028192145	6.622792795	1.91E-08	1.89E-07	123.0410077	31.47763852
WFDC2	-1.56949987	7.596767617	2.48E-08	2.38E-07	263.9094529	96.12228976
TSPAN7	1.698308521	4.054228841	2.95E-08	2.78E-07	2.077305069	6.516211515
KLK11	1.904708066	5.784708029	4.19E-08	3.80E-07	6.119675297	21.89194724
PEG10	-1.804419989	4.805902907	5.17E-08	4.60E-07	9.485194317	2.601353627
AQP5	-1.910311338	4.698600833	9.07E-08	7.63E-07	29.54056199	8.104752537
KRT6B	1.70113433	9.187852088	1.12E-07	9.20E-07	89.79929538	297.8251481
SERPINB4	1.575919909	7.983691159	1.19E-07	9.77E-07	50.01332857	150.586562
CYP4F3	1.60090478	4.983925994	1.29E-07	1.05E-06	2.206424503	6.548253404
RRAD	-1.519291262	5.557594087	1.47E-07	1.19E-06	44.20435844	17.55396609
SPDEF	-1.712886923	3.957685695	1.48E-07	1.20E-06	16.5901627	5.287459001
PTPRZ1	1.661311213	5.428784503	1.50E-07	1.21E-06	1.777182724	5.449150692
IL36G	1.964720912	4.259177835	2.18E-07	1.71E-06	4.249625633	16.89141163
CEACAM7	2.224401717	4.840893688	2.94E-07	2.23E-06	2.573905508	13.61333945
CACNG4	-1.506088392	3.66742644	3.40E-07	2.54E-06	7.281992293	2.643761857
SLC34A2	-1.916613396	4.720687287	4.33E-07	3.16E-06	12.91195339	3.266315433
SPRR2E	2.30475841	6.480098227	7.80E-07	5.40E-06	29.81861804	145.9479898
HPGD	1.505219406	4.712991428	8.80E-07	6.05E-06	1.982309142	5.898416013
CALML5	1.916039769	7.611945772	1.03E-06	6.94E-06	81.1226525	274.0320412