

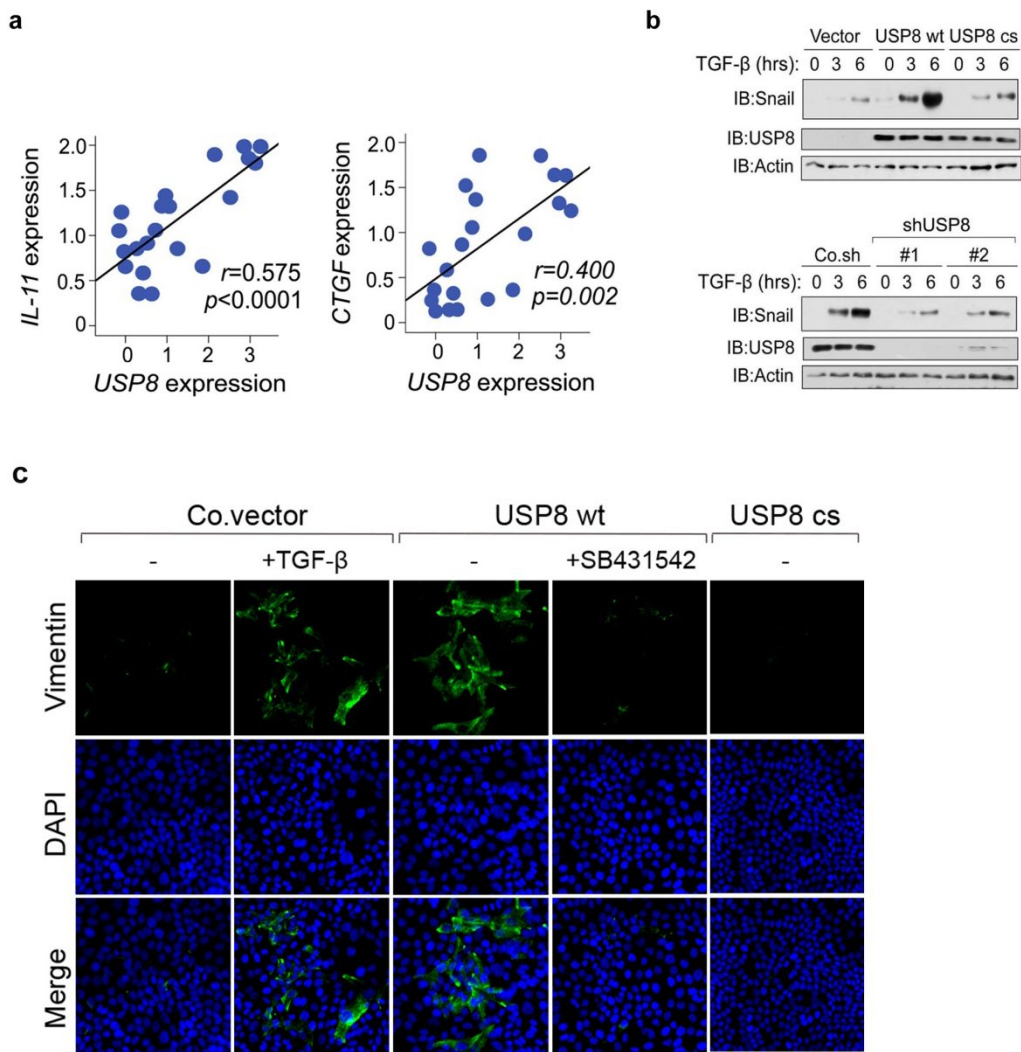
## Appendix

### USP8 promotes cancer progression and extracellular vesicle-mediated CD8+ T cell exhaustion by deubiquitinating the TGF- $\beta$ receptor T $\beta$ RII

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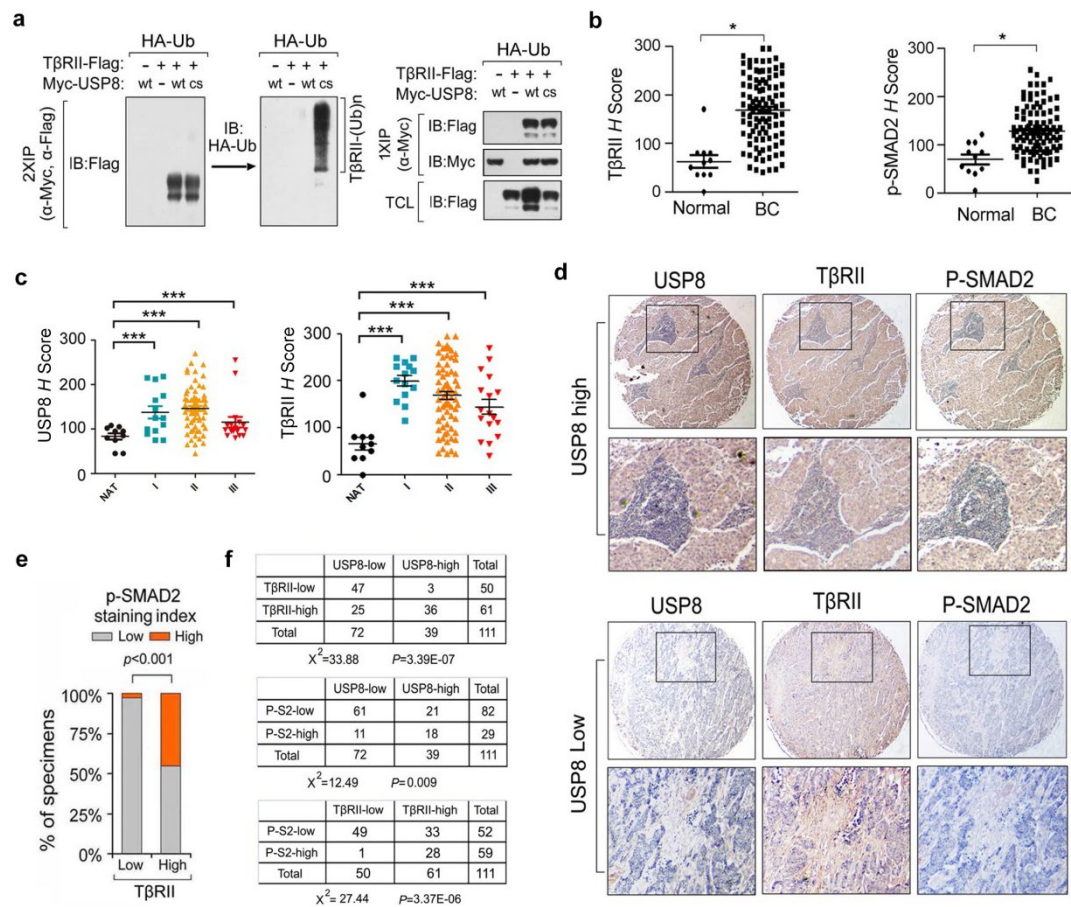


**Appendix Figure S1. USP8 promotes TGF- $\beta$  downstream signals and EMT.**

**a**, *Ex vivo* qRT-PCR analysis of correlation between *USP8* and *IL-11* or *CTGF* expression in the cells isolated from the metastatic nodules. This is related to results shown in Figure 2c. p values from Pearson correlation test were indicated.

**b**, IB of cell lysate from control and parental MDA-MB-231 cells ectopic expressed USP8-wt/cs (upper panel) or depleted of USP8 with two independent shRNA (lower panel) and treated with TGF- $\beta$  (5 ng/ml) as indicated time points.

**c**, Immunofluorescence and 4, 6-diamidino-2-phenylindole (DAPI) staining of HaCaT cells infected with control or USP8 wt/cs and treated with TGF- $\beta$  (2.5 ng/ml) and SB431542 (10  $\mu$ M) for 72 hrs. Scale bar, 20  $\mu$ m.



## Appendix Figure S2. USP8 correlates with TβRII in human specimens.

**a**, IB of total cell lysate (TCL) and immunoprecipitates (two times immunoprecipitation: first with anti-Myc antibody and the precipitant was denatured in 2% SDS and diluted 20 times then followed with anti-Flag antibody) derived from HA-Ub stably expressed HEK293T cells transfected with indicated plasmids.

**b**, Expression of TβRII and p-SMAD2 of normal tissues (n = 11) and breast cancer patients (n = 110). H score of every tissue samples of TβRII and p-SMAD2 was calculated. p values from Student's t tests were indicated.

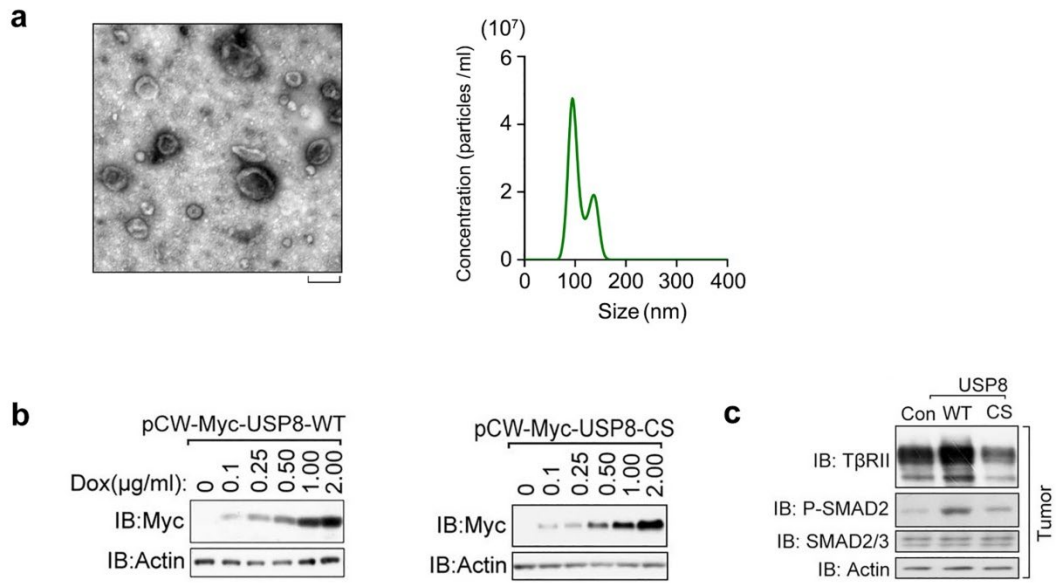
**c**, Expression of USP8 and TβRII of normal tissues (n = 11) and breast cancer patients (n = 110) at different malignant stage (I-III). H score of every tissue samples of USP8 and TβRII were calculated. p values from Student's t tests were indicated.

**d**, Immunohistochemistry analysis of USP8, TβRII and p-SMAD2 in breast cancer tissue microarrays.

**e**, Percentage of specimens displaying low or high TβRII level compared to the expression levels of p-SMAD2. p values from Student's t tests were indicated.

**f**, Case number of specimens showing low or high TβRII, p-SMAD2 (P-S2) expression in relation to the expression levels of USP8.

\* $p < 0.05$ , \*\*\*  $p < 0.001$ , Data are shown as means  $\pm$  SD (**b**, **c**).

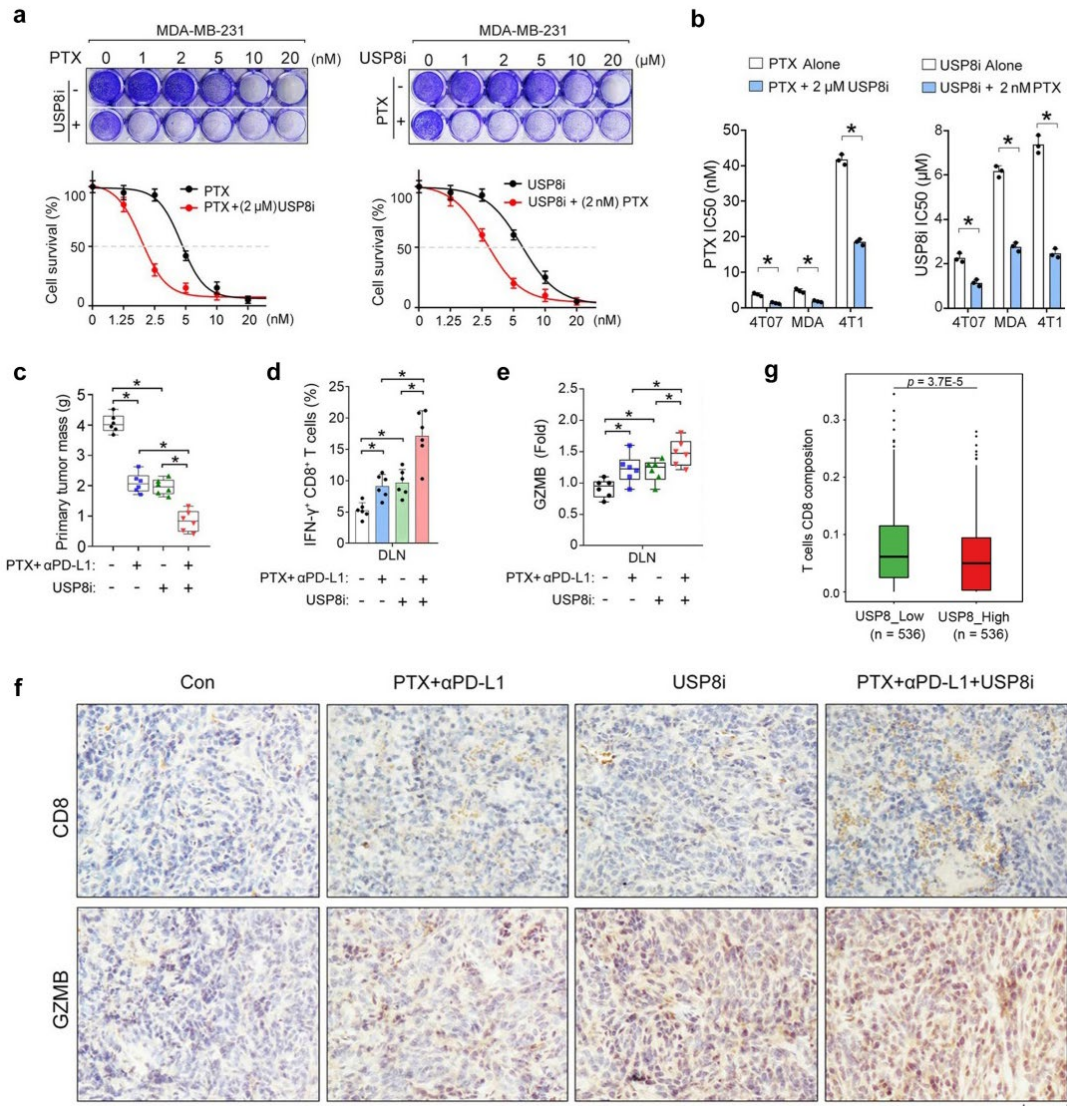


**Appendix Figure S3. T $\beta$ RII levels are specifically enhanced by the inducible USP8-wt in the metastatic tumor cells.**

**a**, A representative TEM image of purified EVs from the plasma of breast cancer patients (left), and nanoparticle tracking of purified EVs (right). Scale bar (left panel), 100 nm.

**b**, Immunoblot analysis showing Dox inducible expression of Myc-USP8 WT/CS in 4T07-Luc cells.

**c**, Immunoblot analysis of metastatic tumor cells, related to Figure 4i.



### Appendix Figure S4. Pharmacological inhibition of USP8 improves breast cancer immunotherapy.

**a**, MTT assay to measure the drug resistance of combined use of PTX and USP8 inhibitor with increasing amount of concentration as indicated. Cytotoxic crystal violet staining (upper panel) and quantification of the cell survival (bottom panel) are shown.

**b**, IC<sub>50</sub> of PTX with combined use of USP8 inhibitor (2 μM) (left) and the IC<sub>50</sub> of USP8 inhibitor with combined use of PTX (2 nM) (right) in 4T07, MDA-MB-231 (MDA) cells and 4T1 cells by MTT assay. p values from Student's t tests were indicated.

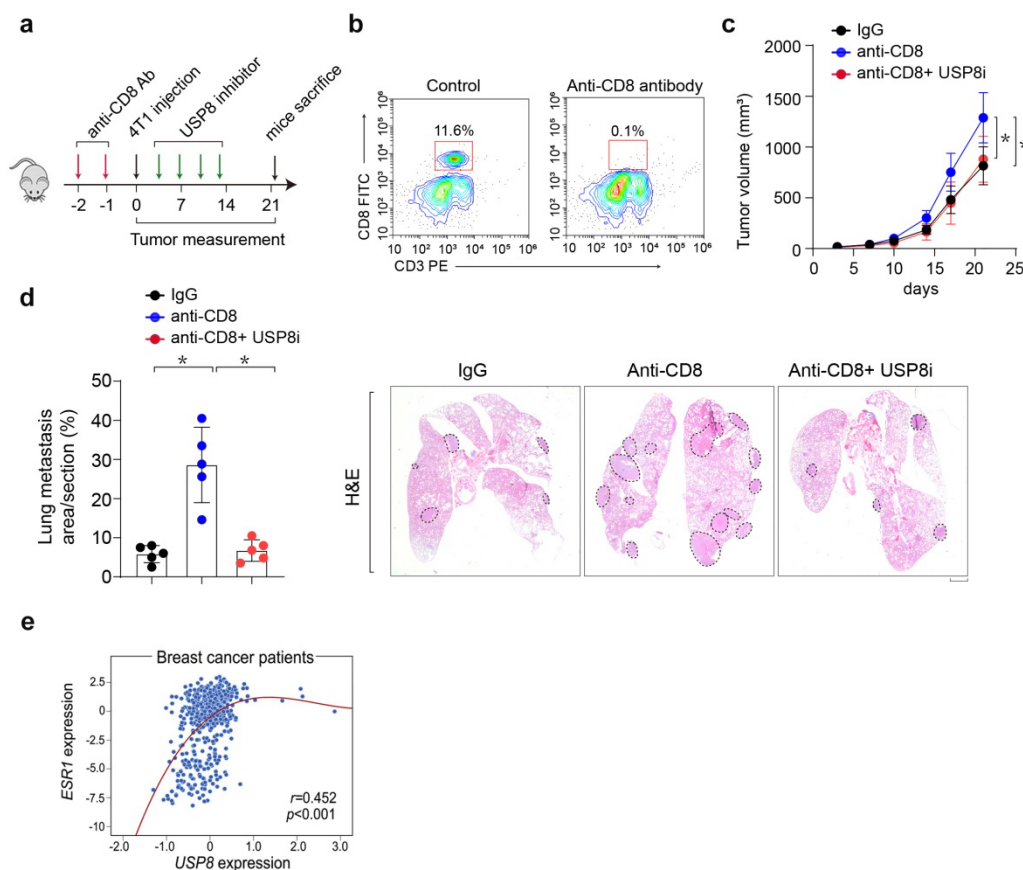
**c-e**, Quantification of the mass of primary tumor in each group ( $n = 6$ ) (**c**). Quantification of the percentage of IFN $\gamma^+$  cells among the CD8 $^+$  T cells populations from DLN (**d**). Fold change relative to the control of CD8 $^+$  T cell GZMB mean fluorescence intensity by flow cytometry (**e**). p values from Student's t tests were indicated. Box-and-whisker plots, boxes show 25-75th percentile, lines show median, and whiskers show range of data point.

**f**, Representative images of CD8 (upper panel) and GZMB (lower panel) by immunohistochemistry at day 35 in the primary tumor. Scale bars, 50 μm.



g. Infiltration of breast cancer tumors by immune cell population (CD8<sup>+</sup> T cells) was further analyzed by CIBERSORT, a method for characterizing the cell composition of complex tissues on the basis of their gene expression profiles (n = 1072). Gene expression data (RPKM) were obtained from TCGA. p values from Student's t tests were indicated. The box-and-whisker plots represent the medians (middle line), first quartiles (lower bound line), third quartiles (upper bound line), and the  $\pm 1.5\times$  interquartile ranges (whisker lines).

\* $p < 0.05$ . Data are shown as mean + SD (b, d) or as means  $\pm$  SD (a, c, e).



### Appendix Figure S5. USP8 inhibitor impairs tumor growth in immunocompromised mice.

**a-d**, Experimental analysis *in vivo*: BALB/c mice were intraperitoneally injected with anti-CD8 antibody (100  $\mu$ g per mouse) for two days before 4T1-luc cells nipple inoculation ( $2 \times 10^5$  cells per mouse), followed by intraperitoneal-injection of USP8 inhibitor (1 mg/kg) (n = 5 per group) (**a**). FACS analysis of the percentage of CD8<sup>+</sup> T cells in plasma samples from mice at week 3 (**b**). Tumor volume measurement of mice from each group at the indicated times (**c**). Tumor metastases area per HE stained lung section and representative HE stained lung sections from each group at week 3. Scale bar, 1 mm (**d**).

**e**. Correlation between USP8 and ESR1 expression in breast cancer patients (n = 522).

\* $p < 0.05$  (two-tailed Student's t test (**d**) or two-way ANOVA (**c**)). Data are shown as mean  $\pm$  SD (**c**, **d**).

**Appendix Table S1. Gene signatures microarray correlated with USP8 expression**

**in a comparison of breast cancer patients with USP8-high (n = 38) versus with USP8-low (n = 39)**

Gene	USP8 low patients (n=39)											
	Sample. 123	Sample .125	Sample .126	Sample .133	Sample. 146	Sample. 147	Sample .148	Sample. 157	Sample. 167	Sample .169	Sample .176	Sample. 178
ABCC3	0.028	0.059	-0.008	-0.014	-0.198	-0.001	-0.065	-0.071	0.017	0.169	-0.126	-0.002
ACAT1	0.022	0.128	-0.076	0.269	0.312	0.055	0.043	-0.009	0.195	0.26	-0.051	0.059
ACYP1	0.229	0.227	0.202	0.108	0.495	0.227	0.368	0.169	0.194	0.16	0.142	0.212
ASPH	0.005	-0.201	-0.005	-0.116	-0.19	0.047	0.054	-0.223	-0.004	-0.111	-0.081	0.053
BLCAP	0.061	-0.067	-0.023	0.017	0.082	-0.063	0.079	-0.044	0.024	-0.157	-0.006	0.044
CCT6A	0.136	0.134	0.172	0.116	0.238	0.258	0.209	0.095	0.165	0.184	0.366	0.205
CCT8	0.126	0.022	-0.022	0.05	0.211	0.1	0.038	0.011	0.096	0.081	-0.042	0.21
CEBPG	0.111	-0.022	0.141	0.017	0.241	0.329	0.092	0.026	0.118	0.056	0.171	0.06
CLCN3	-0.108	-0.216	-0.112	-0.193	0.028	-0.206	0.224	-0.189	-0.036	-0.09	-0.096	0.017
CLNS1A	-0.073	-0.103	-0.089	-0.116	0.003	0	-0.052	-0.214	-0.039	-0.091	-0.161	0.217
COL4A5	0.209	0.075	0.238	0.106	0.458	0.055	-0.005	0.102	0.348	-0.107	-0.094	0.354
CPNE2	0.274	-0.037	0.069	0.137	0.252	0.369	0.301	0.069	0.153	-0.193	0.054	0.228
CSRP1	-0.059	-0.207	-0.041	0.005	-0.089	-0.024	0.033	-0.216	0.066	0.173	-0.05	0.162
CTNND1	0.133	0.117	0.158	0.107	0.205	0.175	0.11	-0.047	0.205	-0.008	0.101	0.181
CTNND1	0.101	0.075	0.044	0.082	0.088	0.06	0.112	-0.09	0.181	0.001	0.077	0.216
CTNND1	0.133	0.117	0.158	0.107	0.205	0.175	0.11	-0.047	0.205	-0.008	0.101	0.181
CTNND1	0.101	0.075	0.044	0.082	0.088	0.06	0.112	-0.09	0.181	0.001	0.077	0.216
DAG1	0.175	0.113	0.213	0.163	0.298	0.251	0.25	0.132	0.221	0.144	0.046	0.237
DUSP6	0.263	0.117	0.093	0.155	-0.024	0.318	0.137	0.039	0.277	0.427	0.204	0.385
EIF5	0.256	0.242	0.232	0.185	0.251	0.41	0.27	0.164	0.243	0.166	0.077	0.226
ENSA	0.051	-0.016	0.048	-0.031	0.059	0.039	-0.163	-0.096	0.137	0.213	-0.068	0.051
FBXO3	-0.023	-0.041	-0.049	-0.047	0.101	0.101	0.152	-0.073	0.066	0.029	0.01	0.079
FEZ2	-0.028	-0.064	-0.1	0.002	0.004	0.029	0	-0.114	0.083	0.034	0.007	0.062
FLRT2	0.099	0.004	-0.089	0.085	-0.034	-0.024	-0.084	-0.113	0.185	-0.304	0.202	0.122
G6PD	-0.112	-0.14	-0.033	-0.075	-0.091	-0.035	-0.084	-0.137	-0.1	-0.152	-0.135	-0.098
GADD45A	0.056	0.046	-0.067	0.123	0.161	0.21	0.056	0.263	0.237	0.099	0.19	0.276
GCSH	0.173	0.149	0.252	0.17	0.335	0.283	0.391	0.163	0.243	0.063	0.283	0.144
GLRX	0.061	0.154	0.04	0.221	0.18	0.107	-0.043	0.147	0.051	0.18	-0.165	-0.12
HSD17B7	0.097	0.096	0.11	0.127	0.148	-0.092	0.093	0.166	0.101	0.166	0.04	0.083
IKBKAP	0.321	0.264	0.307	0.253	0.362	0.421	0.339	0.278	0.304	0.196	0.188	0.268
IP6K2	0.16	0.246	0.239	0.222	0.419	0.169	0.369	0.295	0.312	0.057	0.138	0.221
KCNS3	0.226	0.118	-0.012	0.375	0.604	0.389	0.143	0.107	0.36	0.037	-0.068	0.194
LSM5	0.145	0.08	0.078	0.031	0.124	0.067	-0.018	0.005	0.044	0.202	0.058	0.027
MAD2L1	-0.202	-0.207	0	-0.195	0.025	0.095	-0.007	-0.155	-0.035	-0.144	-0.085	-0.193
MADD	0.069	-0.022	0.036	0.001	0.03	0.013	0.153	-0.119	-0.031	-0.054	-0.056	-0.023
MAN2C1	-0.011	-0.007	-0.085	-0.054	0.147	0.066	0.151	-0.105	0.021	-0.016	0.014	0.05
MAPKAPK5	0.036	-0.065	0.028	0.022	0.121	0.11	-0.024	-0.107	0.072	0.02	-0.021	-0.003
MFAP1	0.055	0.066	0.112	-0.021	0.175	0.069	0.172	-0.002	0.037	-0.012	-0.021	0.025
MNT	0.147	0.014	0.044	0.094	0.131	0.111	0.128	0.042	0.2	0.099	0.083	0.198
MTX2	0.128	0.081	0.144	0.133	0.276	0.154	0.215	0.135	0.183	0.263	0.214	0.097
NFKB1	0.09	0.049	-0.007	0.051	0.08	0.084	0.051	-0.068	0.124	0.054	-0.037	0.059
OGG1	0.003	0.057	0.073	0.099	0.139	0.176	0.135	0.079	0.104	0.044	-0.05	0.07
OXR1	0.072	0.059	-0.019	-0.001	0.038	0.027	-0.003	-0.079	0.025	-0.022	0.028	0.035
PAN2	0.049	0.04	0.031	0.065	0.194	0.143	0.087	0.005	0.091	0.03	0.019	0.046
PCM1	-0.051	0.065	-0.039	-0.195	-0.113	-0.1	-0.156	0.002	0.091	0.053	-0.127	-0.088
PDHB	0.227	0.312	0.192	0.272	0.365	0.366	0.304	0.321	0.239	0.112	-0.11	0.211
PIGB	0.109	0.118	0.06	0.049	0.309	0.162	0.08	0.068	0.22	0.231	0.124	0.106

PLAT	0.614	0.072	0.753	0.495	0.463	0.399	0.781	0.241	0.531	-0.076	0.096	1.055
POLD4	0.045	0.099	0.112	0.075	0.081	0.088	0.006	0.032	-0.013	0.102	-0.045	-0.038
POLI	-0.194	-0.004	-0.017	-0.081	0.149	-0.067	0.069	-0.027	-0.114	-0.089	-0.071	-0.119
POLR2G	0.11	0.052	0.151	0.079	0.138	0.296	0.118	0.129	0.091	0.106	0.077	0.052
PPL	0.059	0.111	0.033	0.079	0.027	0.241	0.033	0.095	0.186	0.131	-0.115	0.253
PPP2CB	-0.012	-0.007	-0.033	-0.055	0.051	0.102	0.013	-0.1	0.022	-0.035	-0.066	-0.01
PRKAR1A	0.25	0.059	0.288	0.079	0.278	0.206	0.388	0.102	0.287	0.201	0.237	0.333
PRPS2	0.268	0.2	0.142	0.353	0.467	0.279	0.214	0.045	0.339	0.41	0.155	0.305
PSMD9	0.207	0.168	0.215	0.126	0.312	0.241	0.166	0.093	0.21	0.242	0.167	0.258
PSME3	0.041	-0.025	0.053	0.031	0.309	0.13	0.07	0.034	0.123	-0.05	-0.066	0.029
QDPR	0.392	0.379	0.305	0.414	0.963	0.357	0.323	0.419	0.646	0.649	0.207	0.33
RABGGTA	0.035	-0.058	0.088	-0.012	0.155	0.108	0.118	-0.024	0.021	-0.081	-0.045	0.016
RALGDS	-0.074	-0.086	-0.016	-0.042	0.04	0.043	0.235	-0.264	-0.061	-0.304	-0.24	-0.033
RBM6	-0.061	0.04	0.04	-0.08	-0.056	-0.105	-0.007	-0.048	0.018	-0.233	-0.256	-0.09
RGS5	0.126	-0.102	-0.139	-0.008	0.014	-0.058	0.2	-0.024	0.167	-0.014	0.017	0.218
RNASE4	-0.071	-0.108	-0.225	-0.08	0.073	-0.129	-0.174	-0.181	0.011	-0.15	-0.133	-0.122
RNF2	0.219	0.213	0.067	0.093	0.143	0.019	0.161	0.167	0.256	0.093	0.206	0.242
RNF4	0.156	0.102	0.192	0.137	0.292	0.254	0.213	0.15	0.177	0.081	0.098	0.147
RNF6	-0.005	-0.018	0.018	-0.129	0.018	0.026	-0.018	-0.119	-0.007	-0.075	-0.105	-0.077
RPL30	-0.067	-0.018	-0.066	-0.097	0.178	0.072	-0.015	-0.073	0.021	0.045	-0.123	-0.103
RPL6	-0.042	-0.036	0.021	-0.124	0.049	0.007	0.124	-0.039	0.069	0.022	-0.076	0.009
SLC2A1	-0.061	0.092	0.257	-0.065	0.191	0.202	0.485	-0.028	-0.038	-0.211	-0.205	-0.134
SON	0.065	0.017	-0.003	-0.061	0.006	0.035	0.116	-0.042	0.02	-0.123	-0.284	0.002
STAT3	0.057	-0.061	-0.127	0.133	0.047	-0.03	-0.135	0.03	0.086	-0.122	-0.139	0.038
TANK	0.071	-0.002	0.052	0.02	0.085	0.118	0.066	-0.045	0.092	0.18	0.124	0.137
TARS	-0.026	-0.017	0.056	-0.031	0.095	0.175	0.106	0.048	0.044	-0.093	0.054	0.03
TIMM9	-0.045	-0.085	-0.12	-0.092	0.033	-0.132	-0.088	-0.097	0.07	-0.039	-0.189	-0.032
TNFAIP1	0.093	-0.057	-0.061	0.097	0.099	0.343	0.238	0.016	0.004	-0.077	-0.097	0.001
TSG101	-0.055	-0.05	-0.007	-0.011	0.123	0.049	0.127	-0.056	-0.024	0.01	-0.034	0.032
TUFT1	0.141	-0.155	0.181	0.215	0.218	-0.002	-0.046	0.159	0.174	0.075	0.087	0.193
USP8	-0.047	-0.033	-0.005	-0.081	0.016	-0.047	0.136	-0.081	-0.004	-0.087	-0.049	-0.021
WRB	0.076	-0.043	-0.007	-0.03	0.022	-0.007	0.131	0.085	0.142	0.198	0.116	0.084
ZNF140	0.114	0.157	0.118	0.175	0.023	0.143	0.149	0.049	0.102	0.017	0.126	0.112
ZNF263	0.147	0.264	0.21	0.194	0.328	0.109	0.308	0.257	0.284	0.262	0.182	0.169
ZNF282	0.145	-0.002	0.131	0.09	0.137	0.186	0.2	0.233	0.171	-0.005	0.188	0.18
ZNF32	0.139	0.219	0.172	0.175	0.284	0.256	0.084	0.188	0.197	0.238	0.115	0.168



USP8 low patients (n=39)												
Sample. 256	Sample. 261	Sample. 267	Sample. 274	Sample. .280	Sample. 283	Sample. 290	Sample. 293	Sample .319	Sample. 323	Sample. 329	Sample. 334	Sample. 342
-0.19	0.109	-0.178	-0.125	-0.098	-0.153	0.191	0.134	-0.247	0.085	-0.07	-0.147	-0.079
0.04	0.038	-0.022	0.171	0.133	0.174	0.267	0.181	0.123	-0.016	0.019	0.245	-0.008
0.46	0.234	0.152	0.117	0.253	0.631	0.242	0.5	0.327	0.268	0.319	0.383	0.6
-0.069	-0.007	-0.115	-0.074	0.056	0.002	-0.099	-0.378	-0.081	-0.215	-0.221	-0.174	0.08
-0.094	-0.063	-0.008	-0.007	0.088	-0.014	-0.078	-0.136	-0.03	0.023	-0.061	-0.029	0.085
-0.127	0.11	0.175	0.082	0.167	0.246	0.16	0.132	0.287	0.123	0.23	0.228	0.222
-0.074	0.051	0.059	-0.084	0.049	-0.052	0.158	0.05	0.146	0.105	0.129	0.123	0.134
-0.108	0.028	0.147	0.078	0.068	0.13	0.128	0.124	0.197	-0.101	0.19	0.116	0.216
-0.266	-0.116	-0.255	-0.182	-0.142	-0.273	-0.097	-0.105	-0.261	-0.169	-0.025	0.121	0.104
-0.235	-0.018	-0.15	-0.207	-0.095	-0.061	-0.1	-0.034	0.13	-0.069	0.12	-0.026	0.152
0.247	0.134	-0.071	0.287	0.235	0.525	0.103	-0.145	0.277	-0.118	0.215	-0.01	0.028
0.221	0.103	0.024	-0.095	0.068	-0.045	-0.02	-0.22	0.253	0.262	0.095	0.126	0.28
-0.249	-0.06	0.025	-0.22	0.019	-0.198	0.044	0.065	-0.01	-0.048	-0.084	0.023	-0.02
0.193	0.236	-0.101	0.088	0.04	0.112	0.053	-0.038	0.108	0.135	-0.187	0.07	0.147
0.143	0.078	-0.057	0.041	0.075	0.102	0.001	-0.1	0.166	0.128	0	0.049	0.069
0.193	0.236	-0.101	0.088	0.04	0.112	0.053	-0.038	0.108	0.135	-0.187	0.07	0.147
0.143	0.078	-0.057	0.041	0.075	0.102	0.001	-0.1	0.166	0.128	0	0.049	0.069
-0.044	0.238	0.178	0.064	0.096	0.024	0.157	-0.016	0.127	0.081	0.236	0.18	0.205
-0.102	0.354	0.182	0.108	0.117	0.187	0.378	0.1	-0.07	0.028	0.127	-0.101	0.111
-0.021	0.23	0.132	0.133	0.27	0.273	0.313	0.266	0.205	0.18	0.24	0.233	0.421
-0.3	0.046	0.064	-0.03	0.016	0.029	0.222	0.257	0.006	-0.095	0.138	-0.034	0.196
-0.325	-0.099	-0.13	-0.03	0.039	-0.011	0.031	0.101	0.011	0.026	-0.046	0.012	0.185
-0.127	-0.076	-0.088	-0.02	0.006	-0.036	0.012	0.007	-0.063	0.031	-0.056	0.018	0.029
0.094	0.069	-0.153	0.112	0.241	0.06	-0.067	-0.326	-0.033	0.106	-0.066	0.027	0.027
-0.06	-0.003	0.149	-0.151	-0.065	-0.158	-0.12	-0.224	-0.148	-0.202	-0.195	-0.087	-0.07
-0.15	0.01	0.02	-0.081	0.161	0.088	0.318	0.456	0.038	0.154	0.03	0.162	0.202
0.225	0.094	0.232	0.257	0.246	0.27	0.226	0.208	0.259	0.279	0.344	0.446	0.269
0.019	0.05	0.085	0.285	0.068	0.169	0.032	0.27	0.02	0.277	-0.008	0.103	0.001
0.197	0.002	-0.191	0.122	0.177	0.184	0.136	0.266	0.122	0.063	0.267	-0.046	0.166
0.258	0.24	0.175	0.37	0.348	0.409	0.254	0.277	0.199	0.178	0.26	0.36	0.327
0.326	0.266	0.167	0.03	0.169	0.386	0.116	0.15	0.351	0.377	0.322	0.405	0.434
0.171	0.354	0.261	0.13	0.187	0.17	0.403	0.601	0.175	0.335	0.391	0.367	0.194
-0.031	-0.098	0.092	0.137	0.09	0.225	0.204	0.235	0.371	0.225	0.265	0.101	0.159
-0.362	-0.275	-0.014	-0.129	-0.197	0.055	-0.024	0.116	0.157	-0.073	0.182	-0.419	0.099
0.067	0.025	-0.14	-0.048	-0.061	-0.038	-0.042	-0.117	0.065	0.017	-0.061	0.107	0.056
0.265	0.002	-0.053	-0.054	-0.012	0.016	-0.054	-0.103	0.073	-0.032	0.016	0.016	0.023
-0.204	-0.019	0.006	-0.008	-0.001	0.055	0.098	0.027	0.101	-0.075	0.033	0.083	0.014
0.071	0.06	-0.091	-0.144	0.083	-0.067	0.04	-0.06	0	0.065	0	0.074	0.177
-0.076	0.15	0.04	-0.05	0.104	-0.062	0.149	-0.108	-0.004	0.031	0.122	0.178	0.121
0.195	0.102	0.149	0.228	0.179	0.346	0.213	0.271	0.305	0.18	0.253	0.176	0.165
0.068	0.17	0.004	0.027	0.062	-0.055	0.114	-0.092	-0.026	0.146	0.068	0.048	0.07
-0.171	0.062	0.059	0.032	0.067	0.12	0.037	0.063	0.033	0.028	0.028	0.012	0.079
0.07	0.109	0.13	0.096	0.03	0.253	0.041	0.039	0.106	0.046	0.106	0.005	0.237
-0.028	0.03	0.044	0.088	0.095	0.106	0.171	0.142	0.067	0.005	0.101	0.11	0.167
-0.199	0.098	-0.23	-0.001	0.043	0.071	0.008	0.019	-0.218	-0.071	-0.393	-0.022	-0.071
-0.007	0.189	0.381	0.144	0.159	0.286	0.3	0.246	0.416	0.313	0.287	0.412	0.386
-0.004	0.29	-0.009	0.065	0.171	0.136	0.189	0.176	0.146	0.01	0.108	0.182	0.113

0.107	0.375	0.229	0.331	0.501	0.141	0.611	0.4	0.212	0.371	0.409	0.259	0.81
0.046	0.089	0.059	0.023	-0.008	-0.026	0.16	-0.001	-0.02	0.072	0.098	0.091	0.206
0.009	0.039	-0.196	0.003	0.039	0.149	0.054	-0.015	0.195	0.004	-0.027	0.091	-0.067
0.01	0.003	-0.096	0.046	0.169	0.15	0.191	0.15	0.216	0.096	0.307	0.163	0.268
-0.182	0.15	0.046	-0.045	0.116	-0.218	0.187	-0.277	-0.133	0.148	-0.012	0.129	0.106
-0.328	0.03	-0.147	-0.13	-0.007	-0.088	0.034	-0.011	-0.005	-0.013	-0.243	0.055	0.017
0.027	0.014	0.131	0.152	0.208	0.306	0.186	0.214	0.237	0.312	0.312	0.431	0.31
0.027	0.319	0.217	0.047	0.165	0.269	0.322	0.438	0.162	0.255	0.51	0.955	0.35
-0.012	0.244	0.087	0.122	0.156	0.147	0.259	0.197	0.205	0.142	0.176	0.168	0.284
-0.041	0.079	-0.084	-0.104	-0.054	-0.161	0.041	-0.145	-0.055	-0.026	-0.108	0.108	0.2
0.312	0.642	0.329	0.151	0.64	0.302	0.64	0.777	0.393	0.344	0.485	0.811	0.605
-0.016	0.015	0.051	-0.085	-0.051	-0.097	-0.01	-0.059	0.059	-0.06	0.087	0.186	0.158
0.145	0.035	-0.106	-0.168	-0.148	-0.014	-0.179	-0.057	0.254	0.259	0.059	0.081	0.117
0.159	-0.043	-0.153	-0.088	-0.139	0.103	-0.189	-0.165	-0.008	-0.05	-0.08	-0.029	-0.133
0.035	0.112	-0.19	-0.09	-0.015	0.006	0.471	-0.115	-0.073	0.031	-0.025	0.026	0.162
-0.139	0.057	-0.274	-0.065	-0.013	-0.293	0.232	0.042	0.045	-0.114	-0.028	-0.13	-0.098
0.064	0.131	0.071	0.222	0.151	0.108	0.097	0.134	0.209	0.259	0.331	0.063	0.107
-0.162	0.077	0.099	0.042	0.087	0.082	0.126	0.102	0.009	-0.004	0.121	0.178	0.183
-0.175	-0.075	-0.328	-0.081	-0.095	-0.025	-0.045	-0.082	-0.075	-0.128	-0.183	-0.072	0.053
-0.045	-0.135	-0.123	-0.005	-0.05	0.099	0.107	0.189	0.256	0.054	0.114	-0.017	0.131
-0.17	0.019	-0.159	0.001	-0.041	0.008	0.025	0.476	-0.264	-0.246	-0.169	0.04	0.152
-0.133	0.017	-0.17	-0.16	-0.161	-0.279	-0.001	-0.191	0.045	-0.133	0.141	0.1	0.024
-0.212	-0.009	-0.093	-0.032	0.075	-0.059	-0.051	-0.154	-0.014	-0.009	-0.139	0.047	0.034
-0.343	-0.026	0.017	0.029	0.024	-0.121	0.101	-0.139	-0.125	-0.121	-0.03	0.003	-0.017
-0.125	0.025	-0.047	0.118	0.103	0.126	0.272	0.14	-0.028	0.014	0.117	-0.024	0.151
-0.281	-0.153	-0.004	-0.012	0.051	0.097	0.03	-0.011	-0.023	-0.2	-0.038	0.08	0.054
-0.167	-0.002	-0.124	-0.095	-0.11	-0.051	-0.022	-0.142	0.011	-0.062	0.017	-0.014	0.104
-0.287	0.031	0.007	0.014	-0.034	-0.159	0.003	-0.143	-0.136	-0.049	-0.087	-0.095	0.018
-0.054	0.036	-0.039	-0.038	-0.013	-0.06	0.062	0.016	0.086	0.034	-0.015	0.125	0.104
-0.158	0.045	0.184	0.086	0.1	0.122	0.075	0.174	0.277	0.219	0.215	-0.027	0.101
-0.059	-0.062	-0.077	0.013	-0.024	-0.083	-0.033	-0.005	0.065	-0.067	0.03	-0.087	-0.014
-0.11	0.032	-0.046	0.002	0.02	-0.009	0.128	0.144	-0.063	-0.045	0.009	0.088	0.143
-0.27	-0.187	0.035	0.142	0.137	0.142	0.14	0.094	0.038	-0.032	-0.244	-0.017	0.087
0.181	0.261	0.196	0.289	0.235	0.244	0.314	0.165	0.336	0.232	0.182	0.151	0.319
0.116	0.158	0.048	-0.07	0.114	-0.013	0.07	-0.062	0.184	-0.005	0.167	0.118	0.24
0.247	0.247	0.183	0.317	0.312	0.347	0.358	0.324	0.369	0.244	0.32	0.266	0.211

USP8 low patients (n=39)												
Sample .343	Sample. 345	Sample .351	Sample. 352	Sample. 354	Sample. 355	Sample. 363	Sample. 379	Sample .387	Sample. 389	Sample. 391	Sample. 397	Sample. 398
-0.094	-0.019	0.025	-0.1	-0.052	-0.131	0.135	-0.221	-0.288	-0.226	-0.069	-0.149	-0.074
0.159	0.279	0.088	0.119	-0.146	-0.073	-0.02	0.116	0.074	0	0.059	0.17	-0.046
0.172	0.162	0.274	0.289	0.558	0.137	0.24	0.214	0.231	0.326	0.13	0.475	0.106
-0.182	0.092	0.068	-0.049	-0.063	-0.146	-0.182	0.052	0.06	-0.084	-0.089	0.026	0.035
-0.026	-0.096	0.122	-0.022	0.101	-0.007	-0.17	0.1	-0.142	-0.02	-0.097	0.035	0.045
0.176	0.351	0.368	0.218	0.204	0.107	0.082	0.306	0.291	0.352	0.235	0.189	0.067
0.058	0.085	0.16	0.281	0.018	0.007	0.05	0.224	-0.03	0.056	0.045	0.078	-0.033
0.157	0.207	0.195	0.141	0.177	0.152	0.204	0.177	0.172	0.234	0.039	0.16	0.156
-0.126	-0.109	0.049	0.089	-0.074	-0.239	-0.192	-0.027	-0.183	-0.214	-0.143	-0.162	-0.257
-0.046	0.089	-0.052	-0.021	-0.045	-0.044	-0.072	-0.21	-0.096	0.013	-0.111	-0.054	-0.21
0.303	0.373	0.059	0.089	0.318	-0.161	-0.13	0.026	0.251	0.352	0.216	0.477	-0.048
0.128	0.2	0.245	0.185	0.145	0.14	0.102	0.092	-0.015	0.012	-0.043	0.095	0.114
0.017	0.043	0.086	-0.003	-0.089	-0.151	-0.176	0.037	-0.105	-0.075	0.064	-0.118	-0.081
0.146	0.154	0.148	0.256	0.219	0.024	0.213	0.341	0.038	0.006	0.194	0.069	0.019
0.09	0.027	0.077	0.055	0.078	-0.11	0.119	0.116	-0.101	-0.062	0.073	0.137	0.033
0.146	0.154	0.148	0.256	0.219	0.024	0.213	0.341	0.038	0.006	0.194	0.069	0.019
0.09	0.027	0.077	0.055	0.078	-0.11	0.119	0.116	-0.101	-0.062	0.073	0.137	0.033
0.163	0.206	0.154	0.14	0.179	0.117	0.163	0.228	0.167	0.145	0.228	0.231	0.138
0.106	0.163	0.149	0.202	0.112	-0.057	-0.046	0.093	0.079	0.17	0.296	0.136	-0.119
0.198	0.354	0.334	0.238	0.237	0.077	0.251	0.169	0.245	0.372	0.166	0.289	0.195
0.011	0.144	0.076	-0.015	0.079	-0.06	-0.104	0.068	0.047	0.108	0.013	-0.023	0.03
-0.017	0.117	0.127	0.042	0.107	-0.143	-0.001	0.124	0.119	-0.007	0.033	0.034	-0.373
-0.018	0.066	0.009	-0.002	-0.076	-0.192	-0.203	-0.008	-0.04	-0.045	-0.022	0.067	-0.162
0.118	0.024	0.018	0.051	-0.02	0.194	-0.074	-0.044	0.089	-0.111	0.014	0.084	-0.059
-0.066	-0.16	-0.065	-0.057	-0.035	-0.053	-0.074	-0.149	-0.102	0.146	-0.05	-0.13	-0.017
0.121	0.037	0.072	0.043	0.178	-0.027	-0.175	0.178	0.083	-0.026	0.099	0.197	0.297
0.153	0.128	0.296	0.253	0.288	0.329	0.18	0.271	0.273	0.237	0.223	0.195	0.321
0.085	0.264	0.227	0.127	0.045	-0.055	0.01	-0.122	0.241	0.225	0.005	0.375	0.104
0.054	0.091	0.149	0.198	0.345	0.05	0.054	0.128	0.166	0.059	0.073	0.312	0.009
0.262	0.313	0.366	0.268	0.365	0.182	0.162	0.389	0.291	0.177	0.293	0.479	0.187
0.239	0.244	0.261	0.293	0.305	0.164	0.355	0.332	0.133	0.208	0.206	0.319	0.047
0.301	0.42	0.148	0.187	0.147	0.254	0.131	0.262	0.216	0.474	0.31	0.297	0.147
0.131	0.241	0.084	0.1	0.141	0.126	-0.021	0.157	0.222	0.247	0.033	0.208	0.074
-0.155	0.005	0.137	-0.069	0.014	-0.193	0.041	0.31	0.116	0.137	-0.199	-0.03	0.099
0.073	0.061	0.099	0.158	0.187	0.083	0.13	0.202	-0.001	-0.063	0.082	0.02	-0.105
0.001	-0.048	-0.056	0.073	-0.062	-0.042	-0.089	0.044	-0.118	-0.095	0.073	0.015	0.044
-0.04	0.011	0.053	0.017	-0.003	-0.117	-0.08	0.23	0.004	-0.021	-0.064	0.133	0.004
-0.028	0.112	0.105	0.136	-0.023	-0.058	0.023	0.159	0.027	0.026	0.02	0.027	-0.071
0.11	0.055	0.087	0.141	0.121	-0.006	0.038	0.178	-0.1	-0.117	0.155	0.073	-0.054
0.104	0.183	0.185	0.287	0.308	0.129	0.217	0.313	0.255	0.226	0.13	0.351	0.149
0.029	0.208	0.16	0.073	0.098	0.094	-0.034	0.021	0.124	-0.035	0.138	0.171	0.038
0.108	0.037	0.064	0.082	-0.022	0.005	-0.11	0.23	0.027	0.152	-0.001	0.142	0.088
-0.059	0.065	0.031	-0.003	0.009	-0.062	0.251	0.016	0.208	0.053	0.016	0.165	-0.116
0.007	0.052	0.038	0.089	0.136	-0.019	0.061	0.107	0.051	0.131	-0.002	0.053	0.062
-0.095	-0.01	-0.13	-0.118	-0.112	-0.175	-0.25	0.06	0.056	-0.183	-0.024	0.023	-0.373
0.283	0.416	0.215	0.243	0.197	0.224	0.264	0.473	0.313	0.319	0.248	0.286	0.202
0.051	0.151	0.066	0.198	0.01	-0.085	-0.047	0.147	0.095	0.119	0.048	0.094	-0.077

0.422	0.54	0.535	0.61	0.598	0.238	0.513	0.404	0.198	0.082	0.372	0.391	0.184
0.049	0.118	0.612	0.18	0.171	0.191	-0.017	0.149	0.122	0.052	0.064	0.16	-0.041
-0.033	0.031	-0.18	0	0.095	-0.158	-0.065	-0.062	0.001	-0.087	0.007	0.186	-0.058
0.153	0.193	0.085	0.189	0.231	0.165	0.142	0.311	0.25	0.306	0.078	0.24	0.155
0.138	0.061	0.013	0.148	0.068	-0.111	0.061	0.009	-0.12	-0.028	0.136	0.066	0.2
-0.039	0.174	0.108	-0.007	-0.142	-0.223	-0.064	0.19	-0.102	-0.11	-0.02	-0.061	-0.246
0.158	0.255	0.237	0.235	0.179	-0.066	0.364	0.249	0.207	0.291	0.139	0.027	-0.071
0.205	0.317	0.439	0.222	0.311	0.114	0.291	0.362	0.325	0.343	0.255	0.053	0.189
0.139	0.254	0.276	0.236	0.176	0.107	0.057	0.449	0.251	0.179	0.207	0.197	0.079
0.034	0.024	0.08	0.034	0.085	-0.012	0.054	0.078	-0.037	-0.016	0.004	0.003	0.19
0.495	0.474	0.214	0.46	0.6	0.378	0.377	0.381	0.529	0.194	0.598	0.355	0.282
0.024	-0.06	0.065	0.107	0.051	0.008	-0.068	0.083	-0.113	-0.047	0.006	0.022	0.053
0.027	0.107	0.028	0.192	0.163	-0.036	0.16	0.156	-0.06	-0.142	-0.094	-0.001	-0.152
-0.087	-0.066	-0.145	-0.087	-0.085	-0.058	-0.205	-0.056	-0.186	-0.232	-0.192	0.167	-0.017
-0.085	0.082	0.083	0.049	-0.004	-0.031	0.646	0.132	0.058	-0.135	0.02	-0.042	-0.214
-0.214	-0.099	-0.081	-0.136	-0.101	-0.247	-0.392	-0.094	-0.089	-0.217	-0.122	-0.107	-0.418
0.169	0.275	0.08	0.011	0.255	0.048	0.233	0.143	0.239	0.049	0.197	0.121	-0.079
0.079	0.097	0.081	0.123	0.191	0.009	0.094	0.194	0.048	-0.047	0.05	0.218	0.152
-0.089	0.007	0.036	0.026	-0.044	-0.171	-0.067	-0.067	0.021	-0.072	-0.009	0.006	-0.061
-0.051	0.127	0.086	0.111	-0.041	-0.223	0.001	0.016	0.257	0.103	-0.054	0.012	-0.064
-0.081	-0.021	0.063	0.055	0.049	-0.443	-0.075	0.086	-0.005	-0.015	-0.071	-0.067	-0.212
-0.086	-0.009	0.135	0.118	0.108	0.02	0.433	-0.048	-0.264	-0.204	-0.161	-0.044	0.557
-0.003	0.065	0.004	0.095	-0.088	-0.182	-0.037	0.078	-0.055	-0.091	-0.035	0.107	-0.132
-0.022	-0.027	-0.126	-0.037	-0.025	-0.022	-0.203	-0.004	-0.079	-0.143	-0.013	0.035	0.098
-0.004	0.084	0.052	0.117	0.08	0.014	-0.15	0.137	0.137	0.085	0.095	0.104	-0.035
-0.068	0.034	0.15	0.053	-0.049	-0.087	-0.185	0.13	0.014	0.053	-0.029	0.146	0.04
-0.126	-0.005	0.088	-0.015	0.05	0.015	-0.142	-0.075	-0.001	0.058	-0.046	-0.093	-0.2
0.053	-0.042	0.048	-0.017	0.064	0.034	-0.089	-0.026	-0.093	-0.163	-0.109	0.066	-0.012
0.019	0.075	0.057	0.058	0.022	-0.111	0.114	0.103	-0.008	-0.069	0.011	-0.025	-0.093
0.094	0.054	-0.002	0.024	0.159	-0.044	-0.226	0.306	0.225	-0.052	0.124	0.356	0.178
-0.027	0.034	-0.065	0.005	-0.027	-0.048	-0.054	-0.022	0.018	-0.033	-0.067	-0.087	-0.056
-0.054	0.044	-0.134	-0.044	0.005	-0.202	-0.005	0.134	0.052	0.082	-0.006	0.044	-0.282
0.135	0.168	0.203	0.159	0.157	0.062	-0.036	0.212	0.206	0.169	0.107	0.145	0.006
0.203	0.316	0.337	0.292	0.348	0.314	0.409	0.376	0.328	0.225	0.247	0.209	0.076
0.13	0.212	0.183	0.19	0.184	0.059	0.221	0.233	0.092	0.041	0.125	0.182	0.108
0.186	0.303	0.16	0.256	0.179	0.212	0.154	0.207	0.302	0.249	0.207	0.388	0.179

USP8 high patients (n=38)												
Sample. 170	Sample .172	Sample .174	Sample .175	Sample .181	Sample .183	Sample .189	Sample. 190	Sample .205	Sample .208	Sample. 209	Sample .218	Sample .222
-0.08	-0.103	-0.367	-0.278	0.025	-0.23	-0.17	-0.038	-0.056	-0.079	-0.376	-0.222	-0.224
0.256	0.098	-0.227	0.012	0.104	0.109	0.225	0.109	-0.08	0.101	-0.48	-0.121	0.014
0.279	0.297	-0.055	0.283	0.039	0.039	0.28	-0.005	-0.022	-0.02	-0.435	0.206	0.112
-0.318	-0.087	-0.656	0.029	-0.255	-0.313	-0.443	-0.314	-0.156	-0.065	-0.521	-0.016	-0.095
-0.085	0.161	-0.278	-0.086	0.08	-0.015	0.001	0.012	-0.151	-0.039	-0.236	-0.094	-0.091
-0.088	0.131	-0.181	0.289	0.079	-0.105	-0.145	-0.144	-0.185	0.173	-0.421	0	0.258
-0.233	0.133	-0.321	-0.052	0.009	-0.031	-0.145	-0.127	-0.157	-0.089	-0.363	0.027	0.028
-0.233	-0.132	-0.403	0.137	-0.186	-0.365	-0.378	-0.436	-0.124	-0.108	-0.497	0.133	0.295
-0.704	-0.554	-0.991	-0.446	-0.257	-0.721	-0.679	-0.733	-0.27	-0.349	-0.595	-0.193	-0.253
-0.537	-0.149	-0.709	-0.261	-0.29	-0.189	-0.583	-0.365	-0.369	-0.244	-0.532	0.444	-0.036
0.256	0.228	-0.211	-0.127	-0.282	0.396	0.115	0.465	0.277	0.228	-0.043	0.14	0.112
-0.606	-0.213	-0.878	-0.207	-0.148	-0.335	-0.717	-0.609	-0.308	-0.086	-0.565	0.209	0.24
-0.234	-0.15	-0.521	-0.21	0.022	-0.166	-0.292	-0.069	-0.227	0.071	-0.322	-0.143	-0.057
-0.362	-0.047	-0.689	-0.084	-0.064	0.049	-0.348	-0.274	-0.058	0.012	-0.455	0.125	0.105
0.069	0.114	-0.511	0.116	-0.028	0.092	-0.349	-0.172	-0.152	0.013	-0.481	-0.014	0.009
-0.362	-0.047	-0.689	-0.084	-0.064	0.049	-0.348	-0.274	-0.058	0.012	-0.455	0.125	0.105
0.069	0.114	-0.511	0.116	-0.028	0.092	-0.349	-0.172	-0.152	0.013	-0.481	-0.014	0.009
-0.298	0.01	-0.302	-0.148	-0.004	-0.11	-0.374	-0.12	-0.064	-0.006	-0.206	0.188	0.077
0.21	0.207	-0.276	-0.093	0.37	0.092	0.043	0.048	-0.198	0.004	-0.328	-0.085	-0.082
-0.375	0.069	-0.526	-0.005	0.068	-0.013	-0.312	-0.311	-0.126	0.188	-0.394	0.178	0.226
-0.048	-0.114	-0.172	-0.105	0.029	-0.128	-0.175	-0.162	-0.171	0.059	-0.21	0.047	0.017
-0.155	0.043	-0.588	-0.119	-0.165	-0.304	-0.344	-0.242	-0.384	-0.156	-0.518	-0.055	-0.066
-0.134	0.003	-0.526	-0.028	-0.041	-0.041	-0.265	-0.159	-0.236	-0.014	-0.365	-0.068	-0.146
0.143	0.042	-0.713	0.126	-0.119	0.187	0.092	0.16	0.049	-0.077	-0.286	-0.21	-0.069
0.084	-0.014	0.005	-0.003	0.037	-0.135	0.094	-0.068	-0.142	0.112	-0.05	0.06	-0.069
0.129	0.117	-0.265	0.312	0.041	0.05	0.429	0.033	0.01	-0.001	-0.589	0.059	0.381
-0.235	0.197	-0.005	0.116	-0.001	-0.395	0.104	-0.151	-0.162	-0.021	-0.294	0.1	0.154
0.355	0.211	-0.073	-0.092	0.246	0.148	0.074	-0.055	-0.226	0.093	-0.501	0.037	0.168
0.006	0.06	-0.533	-0.101	0.003	0.059	0.017	0.203	-0.07	0.119	-0.222	0.109	0.217
-0.356	0.043	-0.517	0.082	0.167	0.058	0.006	0.028	-0.095	0.101	-0.471	0.319	0.262
-0.083	0.115	-0.288	-0.101	-0.059	0.079	-0.152	-0.112	-0.087	0.003	-0.547	0.109	0.159
0.358	0.344	-0.091	0.146	-0.053	0.146	0.083	0.063	-0.069	0.232	-0.463	0.121	0.033
-0.219	-0.019	-0.418	0.012	-0.013	-0.098	-0.143	-0.143	-0.135	-0.074	-0.315	-0.183	0.053
-0.508	-0.179	-0.742	0.123	-0.453	-0.395	-0.554	-0.65	-0.14	-0.158	-0.48	0.009	0.18
-0.219	-0.101	-0.489	-0.218	-0.191	-0.138	-0.378	-0.25	-0.287	-0.155	-0.339	0.124	0.02
-0.267	-0.187	-0.445	-0.247	-0.048	-0.111	-0.279	-0.311	-0.233	-0.108	-0.313	-0.032	-0.182
0.13	0.141	-0.173	0.136	0.07	-0.037	-0.001	0.036	-0.185	0.028	-0.496	-0.041	0.017
-0.194	0.031	-0.501	-0.191	-0.041	-0.238	-0.326	-0.187	-0.164	-0.137	-0.587	0.026	0
0.007	0.077	-0.246	0.013	-0.028	0.097	-0.063	0.022	-0.086	0.092	-0.343	-0.002	0.132
0.28	0.302	0.006	0.049	0.185	0.047	0.371	0.195	-0.057	0.235	-0.336	0.103	0.036
-0.051	-0.076	-0.515	-0.059	-0.017	-0.052	-0.269	-0.118	-0.214	0.054	-0.412	0.053	0.365
0.089	0.051	-0.061	-0.03	-0.022	-0.109	-0.242	-0.081	-0.118	-0.067	-0.467	0.016	0.12
-0.068	0.055	-0.018	0.149	-0.073	-0.126	-0.081	-0.186	0.006	-0.103	-0.372	-0.192	-0.083
-0.219	-0.059	-0.334	-0.119	0.023	-0.161	-0.282	-0.232	-0.19	-0.057	-0.342	-0.12	0.007
-0.007	-0.014	-0.405	-0.12	-0.232	-0.118	-0.055	-0.291	-0.18	-0.303	-0.545	-0.41	-0.262
0.319	0.309	0.143	0.17	0.102	0.124	-0.075	-0.083	0.013	0.091	-0.621	0.259	0.097
0.105	0.105	-0.223	-0.031	0.061	0.129	0.056	0.222	-0.134	0.079	-0.582	0.041	-0.053

0.323	0.595	-0.129	0.044	0.067	0.328	-0.482	0.243	-0.177	0.44	-0.458	0.272	0.296
0.051	0.119	-0.282	-0.226	0.067	-0.053	-0.157	-0.077	-0.235	0.016	-0.445	-0.066	-0.184
-0.096	-0.12	-0.319	-0.225	-0.382	-0.146	-0.261	-0.283	-0.265	-0.139	-0.311	-0.242	-0.222
-0.264	0.067	-0.469	0.061	0.061	-0.054	-0.267	-0.078	-0.068	-0.008	-0.337	0.129	0.181
-0.472	-0.264	-0.625	-0.32	-0.36	-0.163	-0.671	-0.608	-0.27	0.034	-0.468	0.104	0.061
-0.635	-0.194	-1.04	-0.286	-0.121	-0.325	-0.522	-0.446	-0.41	-0.16	-0.467	-0.065	0.013
0.149	0.194	-0.223	0.119	0.068	0.023	-0.148	-0.001	-0.007	-0.035	-0.135	0.198	0.202
0.036	0.134	-0.171	0.346	0.03	0.073	-0.134	0.005	-0.074	0.127	-0.267	0.21	0.441
-0.349	0.044	-0.623	0.006	0.084	0.017	-0.135	-0.091	0.081	-0.031	-0.427	0.211	0.122
-0.592	-0.232	-0.626	-0.227	-0.152	-0.159	-0.573	-0.346	-0.215	-0.05	-0.469	-0.027	-0.028
0.001	0.382	-0.041	-0.018	0.113	0.046	-0.355	-0.053	-0.117	0.074	-0.37	0.623	0.24
0.012	0.091	0.056	0.03	-0.013	-0.061	0.122	-0.002	-0.141	-0.008	-0.12	0.039	-0.026
-0.706	-0.508	-1.039	-0.447	-0.376	-0.428	-0.675	-0.696	-0.351	-0.102	-0.547	0.08	0.1
-0.372	-0.168	-0.664	-0.377	-0.289	-0.41	-0.504	-0.552	-0.216	-0.285	-0.51	-0.166	-0.191
0.388	0.133	-0.271	-0.21	-0.108	-0.057	-0.079	-0.072	-0.201	-0.294	-0.534	-0.261	-0.225
-0.191	-0.084	-0.726	-0.475	-0.387	-0.246	-0.364	-0.265	-0.339	-0.261	-0.488	-0.217	-0.318
0.073	0.063	-0.241	0.074	-0.013	-0.112	-0.099	0.149	-0.067	0.082	-0.34	-0.02	0.176
-0.396	-0.17	-0.661	-0.189	-0.057	-0.107	-0.435	-0.303	-0.18	0.019	-0.536	0.029	-0.088
-0.071	-0.15	-0.298	-0.162	-0.215	-0.287	-0.192	-0.293	-0.271	-0.113	-0.522	-0.089	-0.265
-0.462	-0.087	-0.548	-0.202	-0.082	-0.394	-0.4	-0.341	-0.342	-0.211	-0.599	-0.096	-0.24
-0.259	-0.186	-0.463	-0.099	-0.061	-0.032	-0.181	-0.287	-0.222	-0.069	-0.426	-0.1	-0.301
-0.813	-0.649	-0.906	-0.252	-0.598	-0.82	-0.809	-0.913	-0.287	-0.115	-0.435	0.127	0.018
0.03	0.095	-0.439	-0.081	-0.034	0.038	-0.143	-0.273	-0.179	-0.097	-0.242	0	0.041
-0.195	-0.004	-0.404	-0.105	-0.109	-0.1	-0.311	-0.251	-0.145	0.001	-0.158	-0.146	-0.017
0.007	0.06	-0.214	-0.106	0.04	-0.122	0.165	-0.015	-0.329	0.085	-0.512	-0.159	0.026
-0.574	-0.172	-0.744	-0.069	0.063	-0.207	-0.269	-0.294	-0.273	-0.14	-0.464	-0.017	0.117
-0.531	-0.268	-0.544	-0.295	-0.253	-0.368	-0.508	-0.327	-0.297	-0.337	-0.517	-0.15	-0.192
-0.475	-0.16	-0.484	-0.237	-0.048	-0.138	-0.329	-0.205	-0.117	-0.084	-0.16	-0.002	-0.134
-0.065	0.145	-0.319	-0.032	-0.053	-0.145	-0.227	-0.105	-0.299	0.259	-0.478	0.007	-0.125
0.126	0.182	-0.001	0.141	0.087	0.166	-0.123	-0.022	-0.065	0.073	-0.251	0.05	-0.032
-0.738	-0.428	-1.016	-0.555	-0.449	-0.581	-0.607	-0.619	-0.397	-0.386	-0.55	-0.395	-0.424
0.049	-0.049	-0.259	-0.056	0.053	0.051	0.144	0.061	-0.045	-0.089	-0.034	-0.118	-0.22
-0.209	-0.034	-0.491	0.057	0.046	0.062	-0.032	-0.202	-0.133	0.049	-0.441	0.115	0.103
-0.336	-0.05	-0.439	-0.234	0.046	0.081	-0.351	-0.24	0.013	0.005	-0.277	0.248	0.262
-0.184	0.062	-0.216	0.139	0.065	-0.025	-0.181	0.013	-0.193	-0.041	-0.473	0.149	0.145
0.038	0.13	-0.296	0.002	0.057	-0.083	0.054	0.053	-0.015	-0.009	-0.501	0.129	0.161



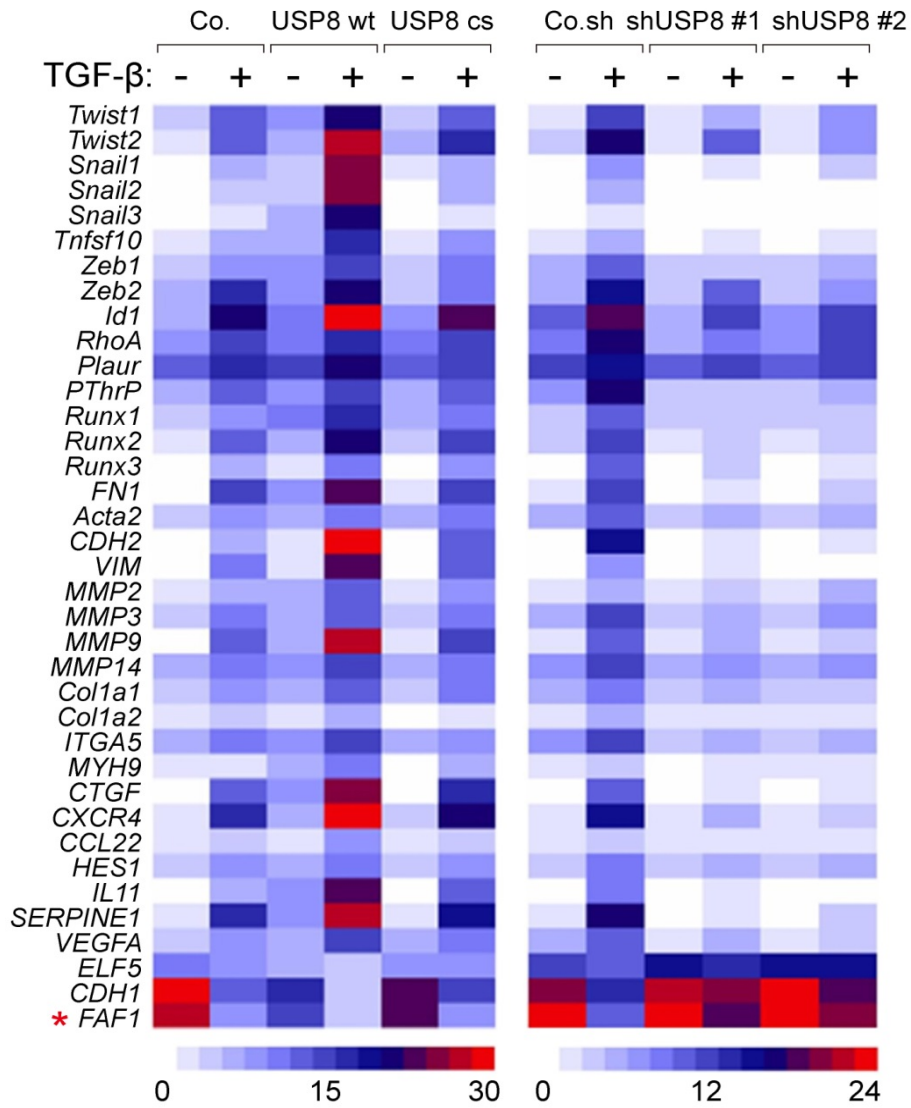
USP8 high patients (n=38)												
Sample .224	Sample. 243	Sample .245	Sample. 259	Sample. 265	Sample. 269	Sample .297	Sample. 310	Sample. 324	Sample .340	Sample .359	Sample .369	Sample. 401
-0.196	-0.242	0.106	-0.141	-0.235	-0.315	-0.249	-0.421	-0.47	-0.211	-0.123	0.348	-0.253
-0.19	0.034	0.143	-0.207	0.046	0.059	-0.161	-0.18	-0.197	0.008	0.043	-0.02	-0.03
0.052	0.168	0.142	-0.035	0.106	0.073	-0.032	0.257	0.174	0.434	0.228	0.122	0.009
-0.196	-0.204	-0.071	-0.304	-0.174	-0.387	-0.125	-0.046	-0.506	-0.254	0.019	-0.04	-0.157
-0.259	-0.178	-0.144	-0.347	-0.205	-0.061	-0.035	-0.249	-0.641	-0.008	-0.113	-0.182	-0.256
-0.109	-0.053	0.219	-0.048	0.107	0.105	-0.046	0.236	0.222	0.233	0.09	0.151	0.138
-0.107	-0.051	-0.034	-0.286	-0.069	-0.019	-0.05	0.132	-0.033	0.012	-0.014	0.156	-0.252
-0.155	-0.081	0.111	0.03	0.011	0.066	-0.203	0.14	0.166	0.089	-0.136	0.068	-0.08
-0.477	-0.506	-0.351	-0.493	-0.505	-0.391	-0.352	-0.082	-0.3	0.032	-0.362	-0.108	-0.491
-0.312	-0.083	-0.078	-0.2	-0.198	-0.138	-0.29	0.065	-0.394	-0.217	-0.102	-0.001	-0.284
-0.099	0.307	0.239	-0.049	-0.185	-0.137	-0.05	-0.005	-0.239	-0.104	-0.141	0.341	-0.044
-0.39	0.079	0.157	-0.003	-0.086	-0.287	-0.001	0.234	0.064	0.047	0.044	0.284	-0.31
-0.236	-0.105	-0.227	-0.329	-0.088	-0.113	-0.068	-0.283	-0.178	-0.06	-0.152	0.157	-0.305
-0.132	-0.098	0.037	-0.215	-0.126	-0.033	0.066	0.044	-0.411	-0.07	0.055	0.309	-0.274
-0.17	0.091	0.04	-0.183	-0.137	-0.007	-0.031	0.156	-0.231	-0.156	0.066	0.38	-0.178
-0.132	-0.098	0.037	-0.215	-0.126	-0.033	0.066	0.044	-0.411	-0.07	0.055	0.309	-0.274
-0.17	0.091	0.04	-0.183	-0.137	-0.007	-0.031	0.156	-0.231	-0.156	0.066	0.38	-0.178
0.031	0.154	0.045	-0.07	0.049	-0.033	0.101	0.034	0.015	0.137	0.113	0.038	0.109
-0.128	0.102	-0.043	-0.223	0.04	-0.034	0.013	-0.085	-0.28	-0.178	0.02	0.326	-0.203
-0.11	-0.038	0.245	0.007	0.162	0.065	0.006	0.196	-0.038	0.195	0.031	0.227	0.13
-0.257	-0.084	0.082	-0.137	-0.113	0.021	-0.018	0.076	-0.152	0.033	-0.113	-0.085	-0.07
-0.408	-0.216	-0.19	-0.312	-0.344	-0.278	-0.215	-0.063	-0.345	-0.144	-0.16	0.009	-0.347
-0.271	-0.126	-0.122	-0.27	-0.145	-0.205	-0.19	-0.059	-0.347	-0.051	-0.11	-0.137	-0.182
-0.136	-0.133	-0.214	-0.291	-0.164	-0.313	-0.116	-0.216	-0.879	-0.281	-0.127	-0.076	-0.293
-0.243	-0.129	-0.177	-0.065	-0.033	-0.115	-0.07	-0.167	-0.126	-0.107	-0.053	0.066	-0.001
-0.107	0.011	-0.143	-0.123	0.142	-0.203	-0.022	-0.216	-0.351	-0.05	-0.007	0	-0.076
0.047	0.025	0.029	0.054	-0.037	0.068	0.026	0.203	0.121	0.277	0.255	0.099	0.062
-0.218	-0.013	0.31	-0.151	0.084	0.016	-0.008	-0.154	-0.383	-0.13	0.025	-0.007	0.147
-0.031	-0.006	-0.02	-0.183	-0.16	-0.113	0.006	0.118	-0.173	0.126	-0.099	0.063	-0.118
-0.173	-0.007	0.148	-0.075	0.193	0.158	0.077	0.056	-0.213	0.319	0.036	0.215	-0.102
0.125	0.287	0.032	-0.072	-0.08	0.106	0.212	0.12	-0.067	0.347	0.122	0.013	0.072
-0.148	0.278	0.582	-0.176	-0.214	-0.226	-0.047	0.359	0.022	0.071	0.258	0.411	0.159
-0.15	-0.055	-0.124	-0.198	-0.187	-0.029	-0.256	0.057	0.005	0.151	0.007	-0.085	-0.179
-0.296	-0.209	-0.023	-0.186	-0.069	-0.151	-0.278	0.336	0.051	0.26	-0.218	0.005	-0.2
-0.151	0.039	-0.12	-0.154	-0.128	-0.161	-0.04	-0.172	-0.25	-0.105	-0.101	0.041	-0.044
-0.194	-0.004	0.051	-0.195	-0.122	0.061	0.046	-0.085	-0.007	0.017	-0.042	-1.002	0.027
-0.223	-0.176	0.017	-0.288	-0.034	-0.073	-0.031	-0.157	-0.292	0.13	-0.163	-0.158	-0.228
-0.19	-0.146	0.016	-0.305	-0.158	-0.097	-0.033	-0.055	-0.283	0.075	-0.116	-0.086	-0.157
-0.162	-0.027	-0.106	-0.208	0.064	0.108	0.133	0.093	-0.038	0.053	-0.073	0.054	-0.193
-0.199	-0.023	0.06	-0.2	0.184	0.18	0.052	0.282	0.085	0.268	0.187	0.139	-0.035
-0.231	-0.026	0.143	-0.227	-0.055	0.055	-0.043	-0.126	-0.095	-0.114	-0.06	0.115	-0.092
-0.143	0.031	-0.119	-0.21	-0.003	0.146	0.036	0.122	-0.176	0.088	-0.031	-0.26	0.02
-0.097	-0.23	-0.146	-0.244	-0.045	-0.165	-0.199	-0.043	-0.126	0.12	0.196	0.033	-0.296
-0.172	-0.199	-0.08	-0.216	-0.138	-0.249	-0.122	-0.079	-0.378	0.089	0.005	0.002	-0.292
-0.312	-0.378	-0.195	-0.442	-0.363	-0.286	-0.323	-0.325	-0.348	-0.215	-0.233	-0.304	-0.154
-0.166	0.214	0.136	-0.039	0.044	-0.003	0.116	0.221	0.13	0.207	0.096	0.289	0.167
-0.097	-0.08	0.062	-0.276	-0.086	0.083	0.157	-0.047	-0.234	0.131	-0.012	-0.072	-0.116

0.129	0.355	0.498	0.115	0.116	-0.164	0.372	0.026	0.023	0.374	0.178	0.262	0.118
-0.168	-0.117	-0.132	-0.324	-0.107	-0.144	0.06	-0.237	-0.349	0.218	-0.094	-0.038	0.035
-0.208	-0.306	-0.273	-0.35	-0.328	-0.321	-0.326	-0.194	-0.516	-0.107	-0.031	-0.188	-0.223
-0.089	-0.049	-0.112	-0.273	0.079	0.132	-0.029	0.092	-0.004	0.082	-0.042	-0.025	-0.243
-0.137	-0.037	0.189	-0.18	-0.108	0.267	0.032	0.26	0.035	-0.108	0.13	0.133	-0.192
-0.484	-0.103	-0.074	-0.293	-0.206	-0.134	-0.116	-0.153	-0.331	-0.073	-0.26	-0.067	-0.349
0.004	-0.069	0.046	-0.031	-0.077	-0.076	0.007	0.202	-0.044	0.494	-0.074	0.504	-0.141
0.045	0.025	0.265	-0.027	0.385	0.131	0.068	0.453	0.062	0.241	-0.089	0.377	-0.099
-0.112	0.052	0.051	-0.027	-0.014	-0.053	0.149	0.055	-0.099	0.272	0	0.016	-0.051
-0.152	-0.119	0.011	-0.192	-0.142	-0.189	0.107	0.055	-0.303	-0.03	-0.095	0	-0.034
0.203	0.343	0.357	0.068	0.194	0.115	0.128	0.205	-0.094	0.538	-0.04	0.408	0.128
-0.096	-0.07	-0.12	-0.182	0.024	0.009	0.069	-0.078	-0.067	0.112	-0.149	-0.711	0.01
-0.123	-0.001	-0.184	-0.198	-0.229	-0.479	-0.145	0.006	-0.396	0.03	-0.243	0.234	-0.338
-0.361	-0.113	-0.13	-0.333	-0.229	-0.238	-0.236	-0.266	-0.43	-0.071	-0.179	-0.257	-0.241
-0.117	-0.197	-0.066	-0.186	-0.111	-0.353	-0.193	0.087	-0.221	-0.011	-0.286	-1.256	-0.146
-0.42	-0.372	-0.383	-0.39	-0.434	-0.561	-0.294	-0.402	-0.517	-0.276	-0.203	-0.072	-0.353
0.007	0.067	-0.048	-0.149	0.088	-0.032	0.053	0.234	0.005	0.168	0.144	0.034	-0.172
-0.169	-0.091	-0.058	-0.109	-0.041	-0.03	0.055	-0.026	-0.213	0.189	-0.067	-0.093	-0.01
-0.36	-0.219	-0.157	-0.231	-0.236	-0.338	-0.289	-0.046	-0.604	-0.02	-0.021	-0.023	0.002
-0.229	-0.091	-0.141	-0.252	-0.241	-0.27	-0.247	0.157	-0.284	0.013	-0.089	-0.006	-0.161
-0.155	-0.246	-0.267	-0.194	-0.379	-0.347	-0.042	-0.238	-0.469	0.098	-0.096	-0.096	-0.16
0.041	-0.032	0.197	-0.095	-0.095	-0.415	-0.16	0.277	-0.43	-0.044	0.041	0.156	-0.07
-0.357	-0.206	-0.092	-0.362	-0.134	-0.095	-0.173	-0.047	-0.214	-0.081	-0.164	-0.106	-0.332
-0.229	-0.192	-0.183	-0.104	-0.157	-0.022	-0.122	-0.292	-0.144	-0.202	-0.112	-0.327	-0.151
-0.241	-0.257	-0.042	-0.2	-0.059	0.024	-0.207	0.186	-0.049	0.014	0.053	-0.12	-0.167
-0.333	-0.274	0.159	-0.358	0.019	0.075	-0.211	-0.068	-0.205	0.046	-0.111	-0.111	-0.233
-0.367	-0.269	-0.283	-0.382	-0.196	-0.234	-0.232	-0.185	-0.237	-0.926	-0.435	-0.173	-0.493
-0.244	-0.037	-0.004	-0.154	-0.151	-0.114	-0.094	-0.169	-0.393	-0.077	0.021	-0.178	-0.048
-0.177	-0.132	-0.004	-0.316	-0.088	-0.066	0.007	-0.016	-0.433	-0.027	-0.094	0.001	-0.253
-0.153	0.025	0.041	-0.163	-0.117	-0.076	0.165	0.162	-0.136	0.066	0.087	0.128	-0.023
-0.42	-0.391	-0.379	-0.41	-0.49	-0.396	-0.452	-0.389	-0.46	-0.383	-0.437	-0.497	-0.497
-0.303	-0.231	-0.068	-0.352	-0.015	-0.203	-0.11	0.057	-0.305	0.068	-0.172	-0.084	-0.282
-0.202	0.004	-0.056	-0.135	-0.085	0.06	-0.069	-0.127	-0.268	0.093	0.003	-0.028	0.058
0.111	0.063	0.171	0.084	-0.013	0.044	0.189	0.15	-0.092	0.322	0.227	0.213	-0.022
0.096	0.16	0.08	-0.031	0.088	0.176	0.236	0.303	0.153	0.196	-0.005	0.326	0.046
-0.318	0.143	0.096	-0.121	0.006	0.248	0.192	0.181	0.194	0.215	0.182	0.163	0.089

USP8 high patients (n=38)												
Sample. 402	Sample .111	Sample .7	Sample. 8	Sample. 9	Sample. 12	Sample. 13	Sample .14	Sample. 29	Sample. 45	Sample .51	Sample .57	Sample. 59
-0.271	-0.079	-0.327	-0.344	-0.183	-0.18	-0.318	-0.264	-0.335	-0.188	-0.185	-0.255	-0.208
0.103	-0.026	-0.028	-0.173	-0.083	-0.004	-0.066	0.046	0.111	0.023	-0.012	0.053	0.176
-0.013	-0.118	-0.347	-0.106	-0.236	-0.182	-0.143	-0.25	-0.312	-0.219	-0.107	0.03	-0.279
-0.239	-0.202	-0.139	-0.303	-0.67	-0.161	-0.379	-0.227	-0.264	-0.345	-0.183	-0.357	-0.059
0.138	-0.147	-0.092	-0.129	-0.216	-0.188	-0.111	-0.08	-0.149	-0.161	-0.188	-0.271	-0.077
0.031	0.149	0.009	0.101	0.015	0.222	0.124	0.15	0.001	0.009	0.136	0.178	0.239
-0.037	-0.255	-0.098	-0.139	-0.141	0.183	-0.096	0.013	-0.133	-0.13	-0.057	-0.036	0.033
-0.099	0.128	-0.154	-0.069	-0.163	-0.03	-0.077	-1.049	-0.108	-0.091	-0.062	0.122	0.072
0.116	-0.507	-0.467	-0.574	-0.567	-0.438	-0.59	-0.373	-0.56	-0.436	-0.426	-0.669	-0.352
0.011	-0.299	-0.186	-0.057	-0.234	-0.082	-0.267	0.004	-0.191	-0.227	0.044	-0.082	0.07
0.227	-0.321	-0.147	-0.23	-0.376	-0.201	-0.014	-0.124	0.05	-0.266	-0.341	-0.637	-0.34
-0.071	0.12	-0.04	-0.111	-0.095	0.309	-0.171	0.099	0.09	-0.028	0.038	-0.104	0.148
-0.22	0.019	-0.041	-0.185	-0.125	0.003	-0.059	0.099	-0.108	-0.124	-0.12	-0.243	0.132
-0.132	0.065	0.006	-0.187	-0.167	0.012	-0.116	0.114	-0.056	-0.116	-0.076	-0.201	0.018
-0.091	-0.275	-0.045	-0.107	-0.211	0.019	-0.144	0.078	-0.07	-0.159	-0.1	-0.086	-0.011
-0.132	0.065	0.006	-0.187	-0.167	0.012	-0.116	0.114	-0.056	-0.116	-0.076	-0.201	0.018
-0.091	-0.275	-0.045	-0.107	-0.211	0.019	-0.144	0.078	-0.07	-0.159	-0.1	-0.086	-0.011
-0.106	-0.269	0.031	-0.027	0.032	0.213	0.027	0.172	0.05	0.057	0.103	-0.161	0.295
-0.209	-0.047	-0.02	-0.139	-0.062	0.166	-0.011	-0.014	0.009	-0.062	0.012	-0.104	0.02
0.025	0.114	-0.018	0.062	-0.063	0.174	0.106	0.142	-0.022	0.185	0.16	0.324	0.146
-0.051	0.104	-0.112	-0.116	-0.199	-0.032	-0.145	0.22	-0.051	0.089	-0.052	0.095	0.128
-0.278	-0.272	-0.252	-0.413	-0.331	-0.196	-0.213	-0.044	-0.293	-0.247	-0.101	-0.251	-0.122
-0.08	-0.145	-0.144	-0.139	-0.243	-0.035	-0.175	-0.014	-0.221	-0.167	-0.125	-0.052	-0.012
-0.116	-0.334	0.073	-0.435	-0.062	0.016	-0.261	-0.003	-0.031	-0.294	0.039	-0.185	-0.225
0.111	0.18	0.003	0.146	0	0.098	0.107	0.001	0.06	-0.048	0.021	-0.097	0.104
0.086	-0.056	-0.159	-0.22	0.045	-0.024	0.019	-0.002	0.038	-0.088	0.203	-0.146	-0.047
0.092	0.059	0.004	-0.023	0.053	0.241	0.058	0.019	0.07	-0.02	0.173	0.225	0.066
0.025	-0.239	-0.204	0.162	-0.139	-0.14	-0.146	-0.017	-0.019	-0.016	0.063	0.026	-0.127
0.222	-0.113	-0.014	0.04	-0.13	0.167	-0.011	0.156	0.092	0.111	0.174	0.209	0.155
0.069	0.031	-0.066	-0.009	-0.136	0.045	0.042	0.071	-0.117	-0.023	0.089	0.116	0.158
-0.108	-0.03	0.01	-0.142	0.007	-0.02	0.015	0.115	-0.025	-0.011	0.017	-0.109	-0.048
-0.131	-0.039	-0.101	-0.18	-0.2	-1.594	-0.054	0.014	-0.073	-0.104	0.019	-0.27	-0.074
-0.216	-0.077	-0.145	0.053	0.001	0.01	-0.004	-0.018	0.003	-0.034	0.191	0.285	0.194
-0.248	0.103	-0.507	-0.277	-0.416	-0.301	-0.038	-0.5	-0.51	-0.275	-0.154	0.032	-0.189
-0.23	-0.115	-0.152	-0.14	-0.061	-0.087	-0.153	0.036	0.031	-0.125	-0.032	-0.284	0.083
-0.186	-0.049	0.024	-0.146	-0.069	0.027	-0.006	0.057	-0.061	0.019	0.016	-0.139	0.059
-0.031	0.007	-0.156	-0.09	-0.181	-0.105	-0.071	-0.062	-0.17	-0.088	-0.03	-0.091	0.083
-0.04	-0.063	-0.03	-0.043	-0.118	0.088	-0.048	0.09	-0.082	-0.032	-0.032	-0.146	-0.064
-0.129	-0.036	-0.039	-0.251	-0.22	0.043	-0.121	0.064	-0.211	-0.105	-0.077	-0.146	0.042
-0.009	-0.235	-0.122	-0.087	-0.131	-0.03	-0.02	-0.03	-0.113	-0.136	0.018	0.076	0.073
0.037	0.028	0.01	-0.022	-0.082	0.127	-0.039	0.119	0.061	-0.1	0.008	-0.077	0.001
-0.113	0.04	-0.099	-0.026	0.035	-0.317	0.069	-0.956	-0.003	0.081	0.084	0.082	0.064
-0.116	-0.108	-0.235	-0.093	-0.25	0.049	-0.071	-0.259	-0.21	-0.161	0.022	-0.05	-0.026
-0.047	-0.039	-0.178	-0.142	-0.156	-0.125	-0.105	-0.063	-0.128	-0.032	-0.066	-0.133	0.073
-0.245	-0.299	-0.361	-0.3	-0.424	-0.363	-0.479	-0.194	-0.176	-0.213	-0.188	-0.073	-0.226
-0.109	0.121	0.085	0.099	0.061	-0.917	0.09	0.19	0.141	0.113	0.262	0.261	0.315
-0.002	-0.213	-0.172	-0.219	-0.283	-0.202	-0.25	-0.011	-0.235	-0.045	-0.063	-0.216	-0.159

-0.276	0.529	0.181	-0.217	0.078	-2.128	0.178	0.731	0.449	0.663	0.494	-0.016	0.475
-0.07	0.033	0.098	0.082	0.107	0.03	0.222	0.188	0.11	0.358	0.211	0.044	0.169
-0.205	-0.294	-0.231	-0.344	-0.334	-0.35	-0.381	-0.296	-0.264	-0.285	-0.183	-0.355	-0.147
0.102	0.21	0.148	0.131	0.158	0.257	0.309	0.258	0.153	0.23	0.271	0.265	0.287
-0.093	-0.019	0.063	-0.058	-0.209	0.006	-0.138	0.079	0.027	-0.086	-0.169	-0.269	0.018
-0.228	-0.334	-0.253	-0.186	-0.391	-0.167	-0.009	0.029	-0.1	-0.132	-0.076	-0.098	-0.089
-0.151	0.065	-0.034	0.001	-0.097	0.202	-0.188	0.136	0.046	0.016	0.058	-0.092	0.243
0.299	0.223	-0.033	-0.057	-0.117	-0.068	-0.081	0.178	-0.093	-0.108	-0.116	0.106	0.179
0.094	0.196	0.118	0.128	0.159	0.106	0.125	0.179	0.128	0.23	0.118	0.143	0.216
-0.172	-0.005	-0.106	-0.088	-0.229	-0.073	-0.217	-0.08	-0.226	-0.038	-0.235	-0.356	-0.107
0.053	0.266	0.295	0.154	0.215	0.12	0.167	0.425	0.308	0.288	0.159	-0.092	0.18
-0.173	0.044	-0.181	-0.16	-0.204	-0.213	-0.098	-0.056	-0.117	-0.109	-0.051	-0.073	0.027
-0.37	-0.054	-0.283	-0.205	-0.323	-0.189	-0.338	-0.101	-0.15	-0.23	-0.106	-0.213	0.084
-0.231	-0.114	-0.159	-0.227	-0.194	-0.167	-0.196	-0.102	-0.139	-0.228	-0.09	-0.228	-0.092
-0.185	-0.633	-0.578	-0.645	-0.568	-0.59	-0.582	-0.384	-0.368	-0.494	-0.368	-0.694	-0.462
-0.399	-0.479	-0.311	-0.615	-0.398	-0.382	-0.362	-0.092	-0.312	-0.286	-0.232	-0.384	-0.436
0.328	0.045	0.019	0.151	-0.051	-0.082	-0.025	0.343	0.158	0.161	0.196	0.07	0.162
-0.063	-0.114	-0.179	-0.165	-0.195	-0.144	-0.081	-0.086	-0.21	-0.096	-0.144	-0.22	-0.019
-0.4	-0.52	-0.476	-0.326	-0.556	-0.401	-0.577	-0.382	-0.437	-0.541	-0.281	-0.376	-0.195
-0.183	-0.062	-0.251	-0.007	-0.21	-0.144	-0.082	-0.035	-0.123	-0.269	0.017	0.001	0.151
-0.085	-0.114	-0.241	-0.219	-0.364	-0.193	-0.276	-0.058	-0.282	-0.306	-0.158	-0.388	-0.102
-0.157	-0.019	-0.385	0.002	-0.241	0.251	-0.326	-0.23	-0.104	0.111	-0.144	-0.434	0.155
-0.328	0.019	-0.141	-0.223	-0.264	-1.267	-0.153	0.002	-0.066	-0.121	0.003	-0.084	0.034
-0.244	-0.027	-0.028	-0.084	-0.117	-0.254	-0.069	0.046	0.032	0.055	-0.02	0.006	-0.046
-0.179	-0.05	-0.155	-0.049	-0.114	0.101	-0.136	-0.2	-0.021	-0.106	0.099	0.151	-0.026
-0.073	-0.235	-0.09	0.018	-0.076	0.097	0.078	-0.069	-0.15	-0.04	0.016	0.123	0.034
-0.289	-0.039	-0.211	-0.198	-0.277	-0.089	-0.132	-0.013	-0.188	-0.171	-0.149	-0.244	-0.028
-0.146	0.307	-0.187	-0.233	-0.222	-0.143	-0.134	-0.056	-0.14	-0.182	-0.155	-0.364	-0.096
0.01	-0.124	-0.202	-0.182	-0.203	-0.11	-0.131	-0.033	-0.202	-0.05	-0.03	-0.193	0.122
0.03	0.083	-0.258	-0.156	0.09	-0.214	-0.007	0.095	0.022	-0.083	-0.027	0.043	0.077
-0.452	-0.466	-0.451	-0.498	-0.457	-0.371	-0.44	-1.526	-0.45	-0.411	-0.389	-0.506	-0.421
-0.062	-0.077	-0.283	-0.295	-0.377	-0.135	-0.222	-0.13	-0.352	-0.307	-0.183	-0.238	-0.137
-0.26	-0.066	-0.258	-0.176	-0.401	-0.244	-0.186	-0.078	-0.197	-0.348	-0.185	-0.261	-0.093
0.086	0.302	0.189	0.113	0.113	0.125	0.18	0.195	0.145	0.188	0.151	0.06	0.153
-0.002	-0.077	-0.206	-0.043	-0.281	0.001	-0.198	0.072	-0.066	-0.204	-0.074	-0.104	-0.149
0.106	0.034	0.049	0.119	0.024	0.131	0.186	0.163	0.138	0.141	0.16	0.25	0.152

**Appendix Table S2. Heatmap of TGF- $\beta$  target genes by qRT-PCR analysis**



### Appendix Table S3. Primers list

Gene	Forward	Reverse
TWIST1	5'-GCGCTGCGGAAGATCATC-3'	5'-AGGGTCTGAATCTTGCTCAGCTT-3'
TWIST2	5'-CACGCTGCCCTCTGACAAG-3'	5'-CTGCAGGACCTGGTAGAGGAA-3'
SNAIL1	5'-CCCCAATCGGAAGCCTAACT-3'	5'-GCTGGAAGGTAAACTCTGGATTAGA-3'
SNAIL2	5'-CAGCTACCCAATGGCCTCTCT-3'	5'-GGACTCACTCGCCCCAAA-3'
TNFSF10	5'-TCCTGGGAATCATCAAGGAG-3'	5'-CAAGTGCAAGTTGCTCAGGA-3'
ZEB1	5'-TGTGAATGGGCGACCAAGA-3'	5'-GTGGGACTGCCTGGTGATG-3'
ZEB2	5'-AAGATAGGTGGCGCGTGT-3'	5'-GACTGACGTGTTACGCCTCTTCTAA-3'
RHOA	5'-CGGTCCCTCCGTCGGTTCT-3'	5'-GAGACGAAGGCGGGTAGCT-3'
RUNX1	5'-CCCTAGGGGATGTTCCAGAT-3'	5'-TGAAGCTTTTCCCTCTTCCA-3'
RUNX2	5'-GCACAAGTAAATCATTGAACTACAGAAA-3'	5'-GAAGCCTGGCGATTTAGAGTTTT-3'
MMP3	5'-AGAGGCATCCACACCCTAGGT-3'	5'-TATCAGAAATGGCTGCATCGAT-3'
MMP9	5'-GGACGATGCCTGCAACGT-3'	5'-CAAATACAGCTGGTCCCAATCT-3'
VIM	5'-GGCTCGTCACCTTCGTGAAT-3'	5'-TCTCAATGTCAAGGGCCATCT-3'
MYH9	5'-GAAGAGCTAGAGGCGCTGAA-3'	5'-CTTTGCCTTCTCGAGTTTTG-3'
COL1A1	5'-CTGTTCTGTTCTTGTGTAAGTGTGTT-3'	5'-TGCCCCGGTGACACATC-3'
COL1A2	5'-CTGAAGTCTCTCAACAACCAGATTG-3'	5'-TGTGCGAGCTGGGTTCTTT-3'
NANOG	5'-AAAGCTTGCTTGTCTTTGAA-3'	5'-TTTCTTCAGGCCACAAATC-3'
SOX2	5'-TGCGAGCGCTGCACAT-3'	5'-TCATGAGCGTCTTGGTTTTCC-3'
OCT4	5'-CGACCATCTGCCGCTTTG-3'	5'-GCCGCAGCTTACACATGTTCT-3'
TAZ	5'-CGACAGCTCCCATGGAA-3'	5'-GGGTTGACAGCAGCCTGAAC-3'
USP8	5'-CTCCGGAGTCTGAAAGATGC-3'	5'-CATTGCGCAGGACAGTTTTA-3'
ANXA5	5'-TTTGATGAGCGGGCTGATG-3'	5'-ATCTGTGCCAAGCCTTCA-3'
CD81	5'-CCAGCACACTGACTGCTTTGA-3'	5'-GCCCGAGGGACACAAATTG-3'
CD9	5'-GAAACGCTGAAAGCCATCCA-3'	5'-ACGCCCCAGCCAAAC-3'
CHMP2A	5'-GCTGGGACTTAGCCTAACAGATG-3'	5'-AAGCGAGCCCCAGTTG-3'
HRS	5'-GCCACGAGCAGTTCCTGAAG-3'	5'-TCATGCGGTTACGAAGGT-3'
HSP60	5'-GCAATGTGTCCAGAGCAAGA-3'	5'-AAGCTCAACAGCTGGGAAAA-3'
HSP70	5'-TGACACGACATTGGGAGGTA-3'	5'-AATGCACGGATTTGGACTT-3'
HSP90	5'-CGACGTGCTCCTTTTGTCT-3'	5'-TTCAGGGATTAGCTCCTCACA-3'
HSPA5	5'-ACCAGGAATGAATTGAAAGC-3'	5'-CAGCTTTTCCATGGTTTCT-3'
HSPA8	5'-AAGGCAAGATTAACGATGAGGA-3'	5'-CAAATTCTTCTCAGCAGTC-3'
TSG101	5'-TGCCTATGGCTACTGGACAC-3'	5'-TTTGCATCAACATGCTTTCC-3'
VPS25	5'-TGGCCGTGGCAGTATCG-3'	5'-TGTCCACATTGGTTGTAACG-3'
SNAIL3	5'-CTTCCTGGTGAAAACGCACT-3'	5'-AGAGCAGGCACCATTGATTT-3'
ID1	5'-GGACGAGCAGCAGGTAAACG-3'	5'-TGGGCACCAGCTCCTTGA-3'
PLAUR	5'-CTGGAGCTGGTGGAGAAAAG-3'	5'-CTTCAAGCCAGTCCGATAGC-3'
PTHRP	5'-CCGCCTCAAAGAGCTGTGT-3'	5'-GGATGGACTTCCCCTTGTCA-3'
RUNX3	5'-TCGGAAGTGAACCCATTCTC-3'	5'-ATAATGCATCCTGGGGTCTG-3'
FN1	5'-ACCAACCTACGGATGACTCG-3'	5'-AACGGCATAATGGGAAACTG-3'
ACTA2	5'-ACCCACAATGTCCCATCTA-3'	5'-GAAGGAATAGCCACGCTCAG-3'
CDH2	5'-TAGCCCGTTTTTCATTTGAGG-3'	5'-CAATGTCAATGGGGTTCTCC-3'
MMP2	5'-TGAGCTATGGACCTGGGAGAA-3'	5'-CCATCGGCGTTCCCATAC-3'
MMP14	5'-GGCTCGAGCATTCCAGTGA-3'	5'-GCACAAAATTCTCCGTGCCAT-3'



ITGA5	5'-GCACCAACAAGAGAGCCAAAG-3'	5'-CTCCCGCTGCAAGAAAGTCT-3'
CTGF	5'-AGCCGCCTGTGCATGGT-3'	5'-TTTTGCCCTTCTTAATGTTCTCTTC-3'
CXCR4	5'-GAACCCTGTTTCCGTGAAGA-3'	5'-GTAGATGGTGGGCAGGAAGA-3'
CCL22	5'-CGCGTGGTCAAACACTTCTA-3'	5'-CGGCACAGATCTCCTTATCC-3'
HES1	5'-GGGAAAGATTGCAAGGTGAA-3'	5'-GGTGGAACTCCTTCAGGACA-3'
IL11	5'-GACAAATCCAGCTGACG-3'	5'-AGGGAATCCAGGTTGTGGTC-3'
SERPINE1	5'-GAGCTTTTGTGTGCCTGGTAGA-3'	5'-GGCAGGCAGTACAAGAGTGATG-3'
VEGFA	5'-ACGAGGGCCTGGAGTGTGT-3'	5'-TGAGGTTTGATCCGCATAATCTG-3'
ELF5	5'-CAAGGCCACCATCAAAGACT-3'	5'-TGCCACTTGTTTTCAAGCAG-3'
CDH1	5'-ACAGCCCCGCCTTATGATT-3'	5'-TCGGAACCGCTTCCTTCA-3'
ALIX	5'-CAACAAAGCATTGCCAGAGA-3'	5'-TGAGGACTGATACGCAGGTG-3'
CD63	5'-GCTGTGGGGCTGCTAACTAC-3'	5'-TCGACATGGAAGGGATTTTC-3'
HRS	5'-TGTGGGCAGATATTCTGTGG-3'	5'-GGGATGGTGGAGTACTTGGA-3'
RAB11A	5'-TTGCAACAAGAAGCATCCAG-3'	5'-CCCTGCTGTGTCCCATATCT-3'
RAB27A	5'-AAATGGTCATGCCTCTACGG-3'	5'-ACATGCCCTTTCTCCTTTT-3'
RAB27B	5'-ACTTTCGGGAAAAACGTGTG-3'	5'-TTCCCTGAAGATCCATTCG-3'
CDH11	5'-CCTATTTTTCGGTGGAAGCA-3'	5'-GGGTAGGGCTGTTCTGATGA-3'
TGFBR2	5'-TGTCTGTGGATGACCTGGCTAA-3'	5'-TTCTGGAGCCATGTATCTTGCA-3'