

## Supplementary Materials

### **High expression of interferon pathway genes CXCL10 and STAT2 is correlated with activation of T-cell signature and better outcome of oral cancer patients**

Yun-Cian Huang <sup>1</sup>, Jau-Ling Huang <sup>2</sup>, Lu-Chia Tseng <sup>2</sup>, Ping-Hung Yu <sup>3</sup>, Si-Yun Chen <sup>1</sup> and Chang-Shen Lin <sup>1,4,5,6,\*</sup>

<sup>1</sup> Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung 807, Taiwan; yuncian1103@gmail.com (Y.C.H.); qoxoruby@gmail.com (S.Y.C.); csl@kmu.edu.tw (C.S.L.)

<sup>2</sup> Department of Bioscience Technology, College of Health Science, Chang Jung Christian University, Tainan 711, Taiwan; jaulingh@mail.cjcu.edu.tw (J.L.H.); luke20000820@gmail.com (L.C.T.)

<sup>3</sup> Department of Nursing, National Taichung University of Science and Technology, Taichung 404, Taiwan; pt1013@nutc.edu.tw; oxfordocean@gmail.com (P.H.Y.)

<sup>4</sup> Center for Cancer Research, Kaohsiung Medical University, Kaohsiung, Taiwan

<sup>5</sup> Department of Medical Research, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

<sup>6</sup> Department of Biological Sciences, National Sun Yat-sen University, Kaohsiung, Taiwan

\* Correspondence: csl@kmu.edu.tw; changshenlin@gmail.com

**Table S1.** Significant enriched Hallmark pathways in each of the 5 oral cancer data sets. (Corresponding to Figure 2).

<b>TCGA</b>	<b>ES</b>	<b>NES</b>	<b>NOM-p</b>	<b>FDR-q</b>
HALLMARK_E2F_TARGETS	0.68	2.89	0.00	0.00
HALLMARK_G2M_CHECKPOINT	0.66	2.77	0.00	0.00
HALLMARK_INTERFERON_ALPHA_RESPONSE	0.66	2.53	0.00	0.00
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION	0.58	2.46	0.00	0.00
HALLMARK_INTERFERON_GAMMA_RESPONSE	0.54	2.31	0.00	0.00
HALLMARK_MITOTIC_SPINDLE	0.51	2.14	0.00	0.00
HALLMARK_ANGIOGENESIS	0.55	1.83	0.00	0.00
HALLMARK_MYC_TARGETS_V1	0.41	1.73	0.00	0.00
HALLMARK_INFLAMMATORY_RESPONSE	0.40	1.71	0.00	0.00
HALLMARK_ALLOGRAFT_REJECTION	0.40	1.69	0.00	0.00
HALLMARK_DNA_REPAIR	0.38	1.57	0.00	0.01
HALLMARK_MYC_TARGETS_V2	0.44	1.54	0.01	0.01
HALLMARK_TNFA_SIGNALING_VIA_NFKB	0.36	1.52	0.00	0.02
HALLMARK_MTORC1_SIGNALING	0.35	1.45	0.00	0.03
HALLMARK_IL6_JAK_STAT3_SIGNALING	0.37	1.38	0.02	0.05
HALLMARK_GLYCOLYSIS	0.33	1.37	0.00	0.05
HALLMARK_APICAL_JUNCTION	0.31	1.34	0.01	0.06
HALLMARK_COAGULATION	0.32	1.30	0.03	0.08
<b>GSE23558</b>	<b>ES</b>	<b>NES</b>	<b>NOM-p</b>	<b>FDR-q</b>
HALLMARK_E2F_TARGETS	0.71	3.45	0.00	0.00
HALLMARK_INTERFERON_ALPHA_RESPONSE	0.73	3.18	0.00	0.00
HALLMARK_INTERFERON_GAMMA_RESPONSE	0.62	2.99	0.00	0.00
HALLMARK_G2M_CHECKPOINT	0.61	2.93	0.00	0.00
HALLMARK_MYC_TARGETS_V2	0.70	2.80	0.00	0.00
HALLMARK_MYC_TARGETS_V1	0.57	2.73	0.00	0.00
HALLMARK_TNFA_SIGNALING_VIA_NFKB	0.52	2.54	0.00	0.00
HALLMARK_MTORC1_SIGNALING	0.48	2.31	0.00	0.00
HALLMARK_DNA_REPAIR	0.49	2.26	0.00	0.00
HALLMARK_MITOTIC_SPINDLE	0.45	2.14	0.00	0.00
HALLMARK_IL6_JAK_STAT3_SIGNALING	0.47	2.04	0.00	0.00
HALLMARK_UNFOLDED_PROTEIN_RESPONSE	0.42	1.86	0.00	0.00
HALLMARK_GLYCOLYSIS	0.37	1.78	0.00	0.00
HALLMARK_INFLAMMATORY_RESPONSE	0.36	1.78	0.00	0.00
HALLMARK_APICAL_JUNCTION	0.34	1.66	0.00	0.01
HALLMARK_UV_RESPONSE_UP	0.33	1.55	0.00	0.01
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION	0.31	1.52	0.00	0.01
HALLMARK_P53_PATHWAY	0.31	1.49	0.00	0.02
HALLMARK_APOPTOSIS	0.31	1.45	0.00	0.02
HALLMARK_COMPLEMENT	0.30	1.44	0.00	0.02
HALLMARK_ALLOGRAFT_REJECTION	0.30	1.44	0.00	0.02
HALLMARK_ANGIOGENESIS	0.40	1.41	0.05	0.03
HALLMARK_KRAS_SIGNALING_UP	0.29	1.39	0.01	0.03
HALLMARK_IL2_STAT5_SIGNALING	0.28	1.37	0.01	0.04
HALLMARK_OXIDATIVE_PHOSPHORYLATION	0.27	1.27	0.03	0.08

<b>GSE30784</b>	<b>ES</b>	<b>NES</b>	<b>NOM-p</b>	<b>FDR-q</b>
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION	0.79	2.49	0.00	0.00
HALLMARK_INTERFERON_ALPHA_RESPONSE	0.80	2.33	0.00	0.00
HALLMARK_INTERFERON_GAMMA_RESPONSE	0.72	2.28	0.00	0.00
HALLMARK_TNFA_SIGNALING_VIA_NFKB	0.72	2.27	0.00	0.00
HALLMARK_INFLAMMATORY_RESPONSE	0.71	2.24	0.00	0.00
HALLMARK_ALLOGRAFT_REJECTION	0.66	2.09	0.00	0.00
HALLMARK_IL6_JAK_STAT3_SIGNALING	0.72	2.07	0.00	0.00
HALLMARK_E2F_TARGETS	0.65	2.06	0.00	0.00
HALLMARK_ANGIOGENESIS	0.82	2.05	0.00	0.00
HALLMARK_TGF_BETA_SIGNALING	0.72	1.90	0.00	0.00
HALLMARK_G2M_CHECKPOINT	0.60	1.87	0.00	0.00
HALLMARK_HEDGEHOG_SIGNALING	0.74	1.85	0.00	0.00
HALLMARK_APOPTOSIS	0.57	1.76	0.00	0.00
HALLMARK_COMPLEMENT	0.55	1.73	0.00	0.00
HALLMARK_UV_RESPONSE_UP	0.54	1.67	0.00	0.00
HALLMARK_COAGULATION	0.54	1.65	0.00	0.00
HALLMARK_KRAS_SIGNALING_UP	0.52	1.63	0.00	0.00
HALLMARK_HYPOXIA	0.52	1.63	0.00	0.00
HALLMARK_UV_RESPONSE_DN	0.53	1.62	0.00	0.00
HALLMARK_MITOTIC_SPINDLE	0.50	1.55	0.00	0.00
HALLMARK_APICAL_JUNCTION	0.48	1.53	0.00	0.01
HALLMARK_UNFOLDED_PROTEIN_RESPONSE	0.52	1.52	0.00	0.01
HALLMARK_MTORC1_SIGNALING	0.47	1.47	0.00	0.01
HALLMARK_IL2_STAT5_SIGNALING	0.49	1.53	0.00	0.01
HALLMARK_MYC_TARGETS_V2	0.63	1.67	0.00	0.01
HALLMARK_GLYCOLYSIS	0.44	1.40	0.00	0.02
HALLMARK_MYC_TARGETS_V1	0.42	1.34	0.02	0.04
HALLMARK_DNA_REPAIR	0.43	1.31	0.03	0.05
<b>GSE138206</b>	<b>ES</b>	<b>NES</b>	<b>NOM-p</b>	<b>FDR-q</b>
HALLMARK_INTERFERON_ALPHA_RESPONSE	0.66	3.07	0.00	0.00
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION	0.56	3.02	0.00	0.00
HALLMARK_INTERFERON_GAMMA_RESPONSE	0.56	3.01	0.00	0.00
HALLMARK_ALLOGRAFT_REJECTION	0.52	2.67	0.00	0.00
HALLMARK_E2F_TARGETS	0.51	2.55	0.00	0.00
HALLMARK_IL6_JAK_STAT3_SIGNALING	0.53	2.38	0.00	0.00
HALLMARK_INFLAMMATORY_RESPONSE	0.45	2.37	0.00	0.00
HALLMARK_ANGIOGENESIS	0.57	2.12	0.00	0.00
HALLMARK_COMPLEMENT	0.39	1.97	0.00	0.00
HALLMARK_TGF_BETA_SIGNALING	0.49	1.90	0.00	0.00
HALLMARK_TNFA_SIGNALING_VIA_NFKB	0.35	1.84	0.00	0.00
HALLMARK_G2M_CHECKPOINT	0.37	1.83	0.00	0.00
HALLMARK_DNA_REPAIR	0.43	1.78	0.00	0.00
HALLMARK_APICAL_JUNCTION	0.33	1.63	0.00	0.01
HALLMARK_COAGULATION	0.34	1.58	0.01	0.02
HALLMARK_UNFOLDED_PROTEIN_RESPONSE	0.40	1.55	0.03	0.02
HALLMARK_KRAS_SIGNALING_UP	0.28	1.46	0.00	0.04
HALLMARK_MITOTIC_SPINDLE	0.29	1.43	0.02	0.06
HALLMARK_APOPTOSIS	0.28	1.40	0.02	0.06

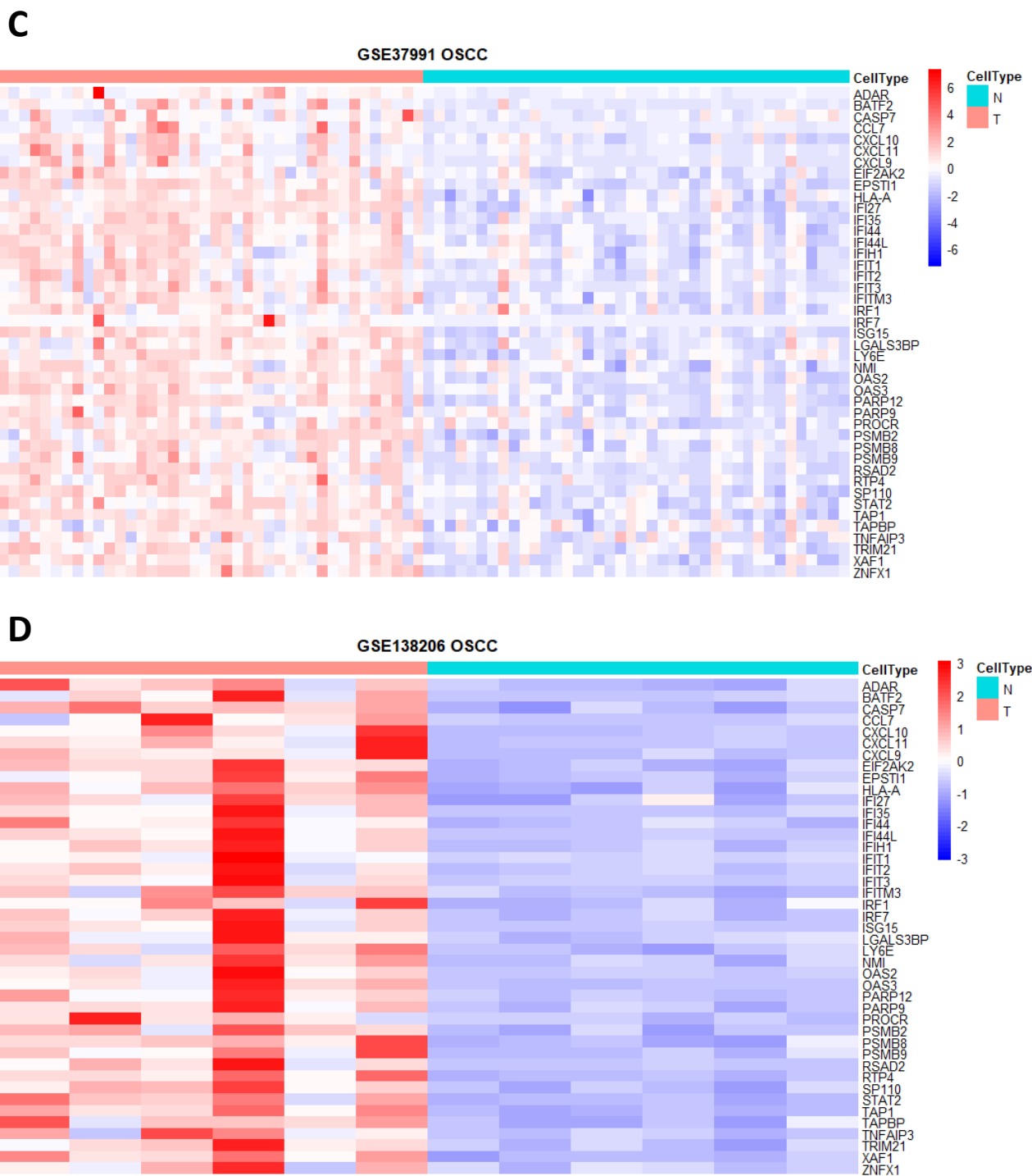
<b>GSE37991</b>	<b>ES</b>	<b>NES</b>	<b>NOM-p</b>	<b>FDR-q</b>
HALLMARK_INTERFERON_ALPHA_RESPONSE	0.69	2.74	0.00	0.00
HALLMARK_E2F_TARGETS	0.57	2.54	0.00	0.00
HALLMARK_INTERFERON_GAMMA_RESPONSE	0.55	2.51	0.00	0.00
HALLMARK_G2M_CHECKPOINT	0.53	2.33	0.00	0.00
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION	0.51	2.30	0.00	0.00
HALLMARK_MITOTIC_SPINDLE	0.43	1.95	0.00	0.00
HALLMARK_MYC_TARGETS_V2	0.54	1.90	0.00	0.00
HALLMARK_DNA_REPAIR	0.43	1.84	0.00	0.00
HALLMARK_UNFOLDED_PROTEIN_RESPONSE	0.45	1.82	0.00	0.00
HALLMARK_INFLAMMATORY_RESPONSE	0.40	1.82	0.00	0.00
HALLMARK_ALLOGRAFT_REJECTION	0.40	1.80	0.00	0.00
HALLMARK_COMPLEMENT	0.40	1.80	0.00	0.00
HALLMARK_MYC_TARGETS_V1	0.40	1.78	0.00	0.00
HALLMARK_APICAL_JUNCTION	0.39	1.77	0.00	0.00
HALLMARK_MTORC1_SIGNALING	0.38	1.72	0.00	0.00
HALLMARK_APOPTOSIS	0.38	1.70	0.00	0.00
HALLMARK_TNFA_SIGNALING_VIA_NFKB	0.37	1.69	0.00	0.00
HALLMARK_TGF_BETA_SIGNALING	0.46	1.67	0.00	0.00
HALLMARK_IL6_JAK_STAT3_SIGNALING	0.39	1.58	0.00	0.01
HALLMARK_ANGIOGENESIS	0.46	1.54	0.02	0.01
HALLMARK_GLYCOLYSIS	0.33	1.52	0.00	0.01
HALLMARK_IL2_STAT5_SIGNALING	0.31	1.38	0.01	0.04
HALLMARK_COAGULATION	0.31	1.36	0.02	0.05
HALLMARK_KRAS_SIGNALING_UP	0.30	1.35	0.02	0.05
HALLMARK_P53_PATHWAY	0.28	1.29	0.02	0.08

**Table S2.** Multivariate Cox model analysis of overall survival.

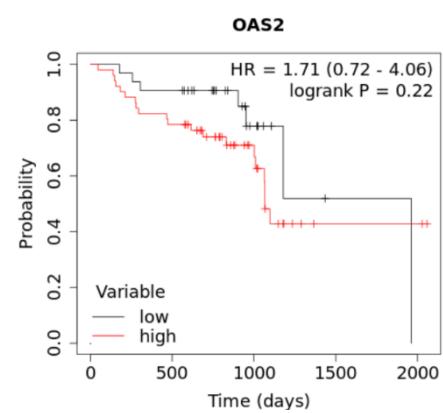
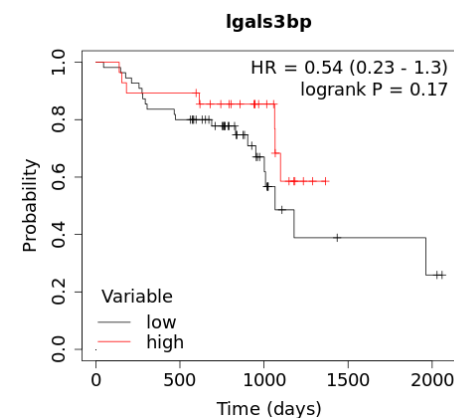
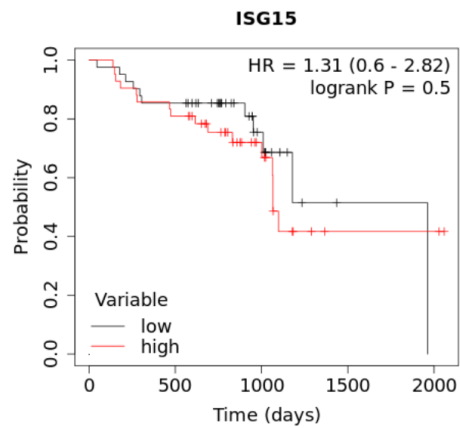
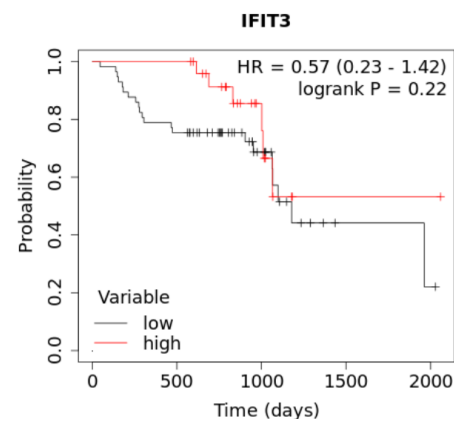
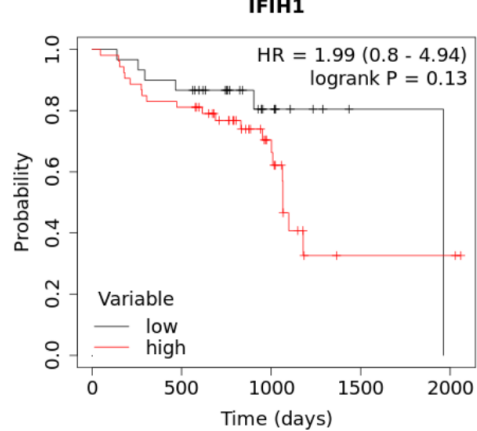
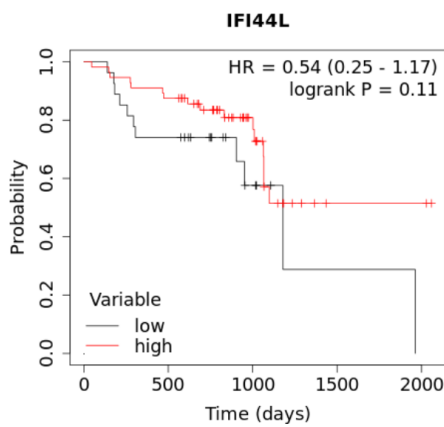
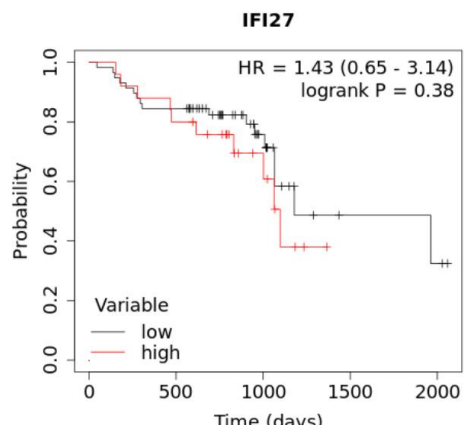
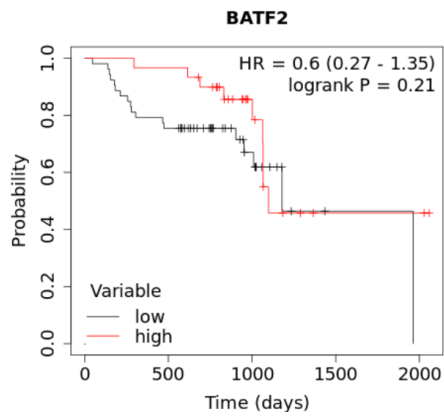
<b>TCGA</b>	<b>Case No.</b>	<b>HR</b>	<b>95% CI</b>	<b><i>p</i></b>
HH vs LL <sup>a</sup>	91 vs 128	0.751	0.491-1.149	0.187
T <sub>3-4</sub> vs T <sub>1-2</sub>	137 vs 82	2.384	1.465-3.878	<0.001
N <sub>1-3</sub> vs N <sub>0</sub>	125 vs 94	1.463	0.966-2.215	0.072
<b>GSE65858</b>	<b>Case No.</b>	<b>HR</b>	<b>95% CI</b>	<b><i>p</i></b>
HH vs LL <sup>a</sup>	34 vs 22	0.146	0.041-0.522	0.003
T <sub>3-4</sub> vs T <sub>1-2</sub>	29 vs 27	6.912	1.872-25.520	0.004

<sup>a</sup> CXCL10 and STAT2 expression, both high (HH), both low (LL).

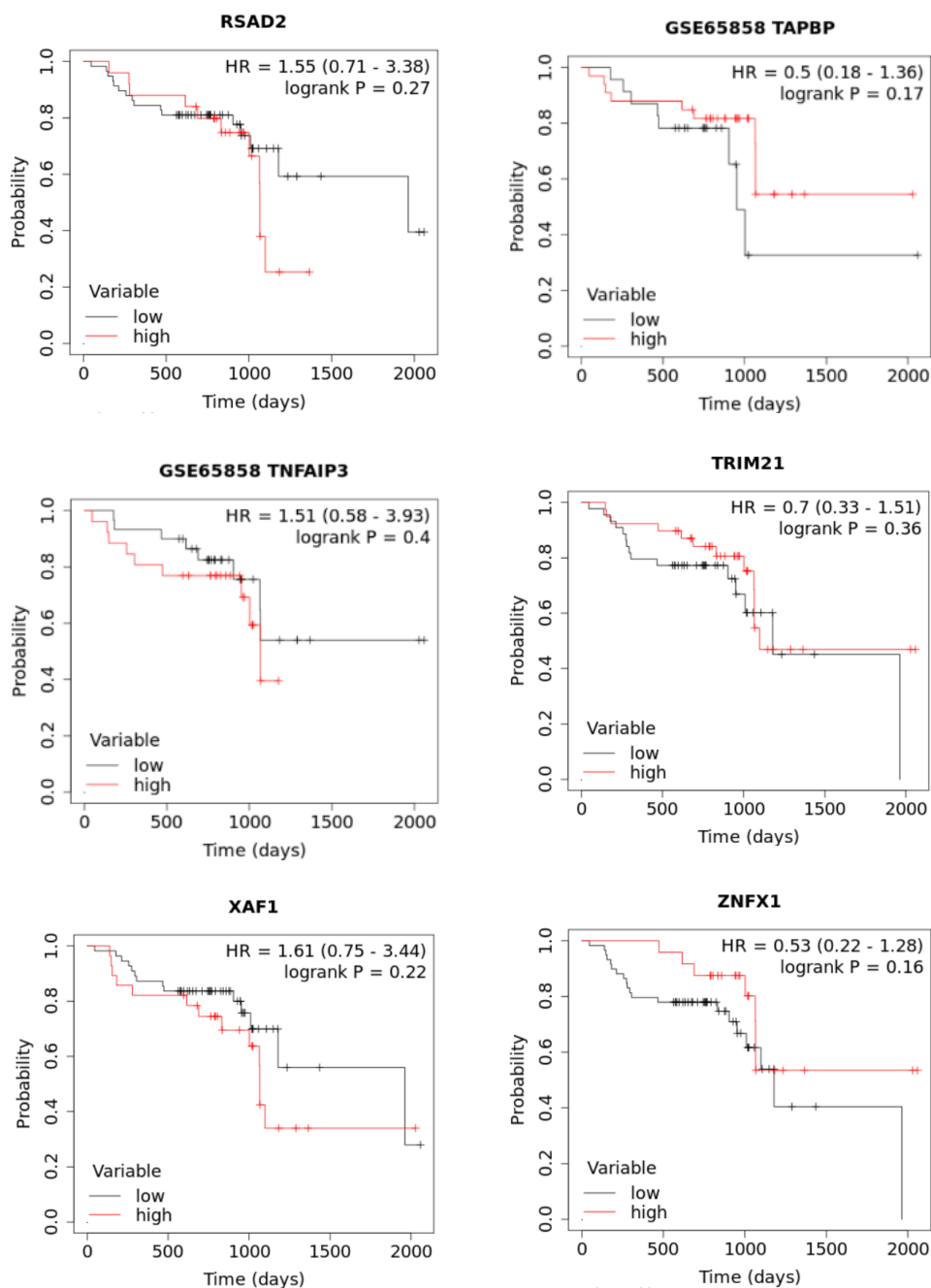




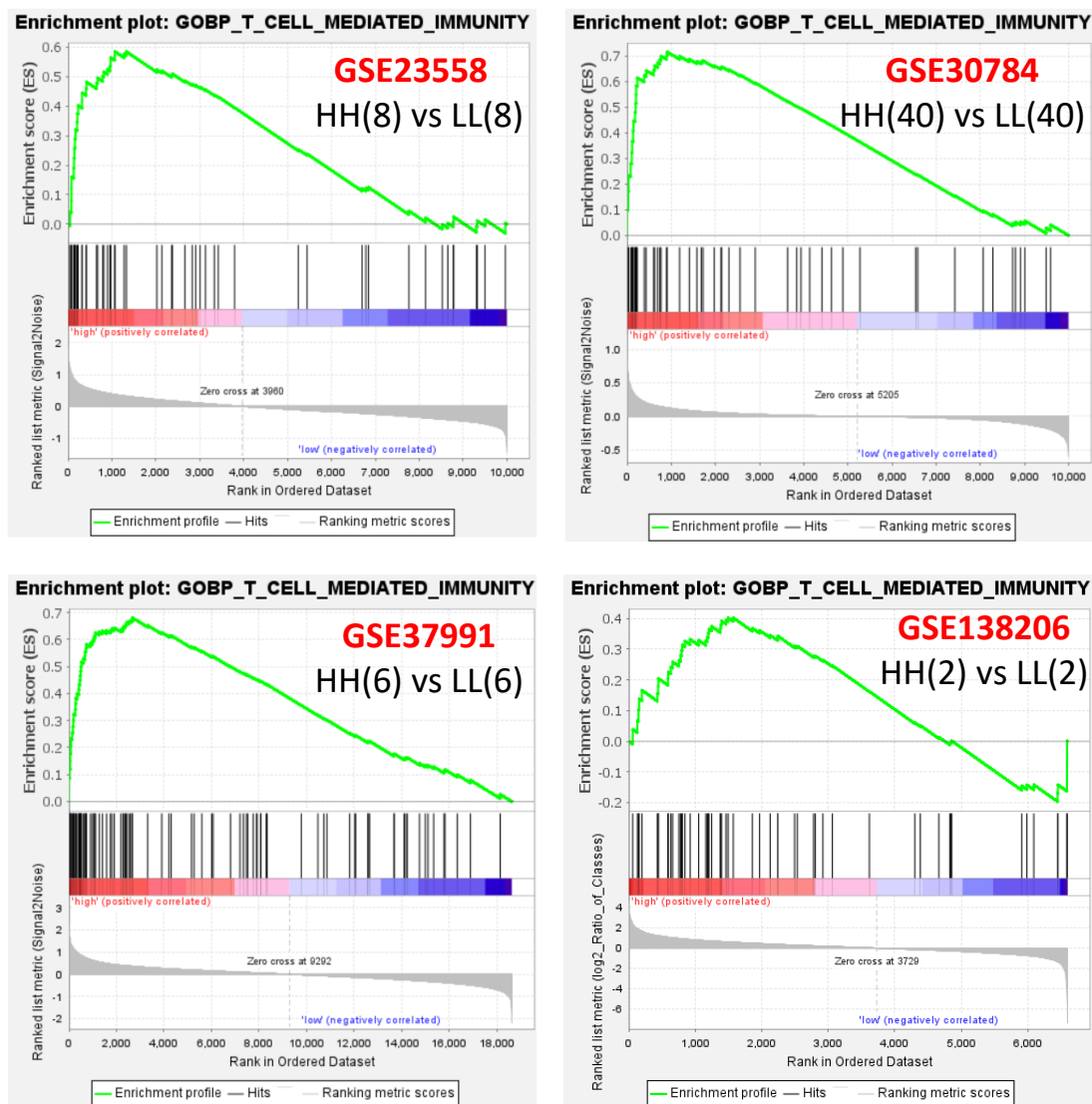
**Figure S1.** Heat map showing the differential expression of the 43 common interferon pathway genes in tumor (T) and normal (N) tissues of GSE23558 (A), GSE30784 (B), GSE37991 (C), and GSE138206 (D) data sets.(Corresponding to Figure 3).







**Figure S2.** Kaplan-Meier plots of overall survival based on the 14 interferon pathway genes in GSE65858 data set. (Corresponding to Figure 4B).



**Figure S3.** Enrichment plots of GOBP T-cell-mediated immunity pathway in GSE23558, GSE20784, GSE37991, and GSE138206 data sets based on the coordinated expression of CXCL10 and STAT2 (HH vs LL). The numbers in parentheses represent the numbers of patients with the most high (HH) and low (LL) expression levels of CXCL10 and STAT2, respectively, applied to gene set enrichment analysis. GOBP, Gene Ontology Biological Process. (Corresponding to Figure 6).