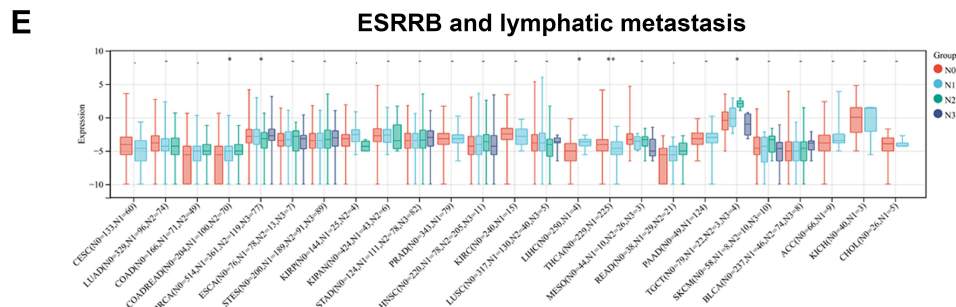
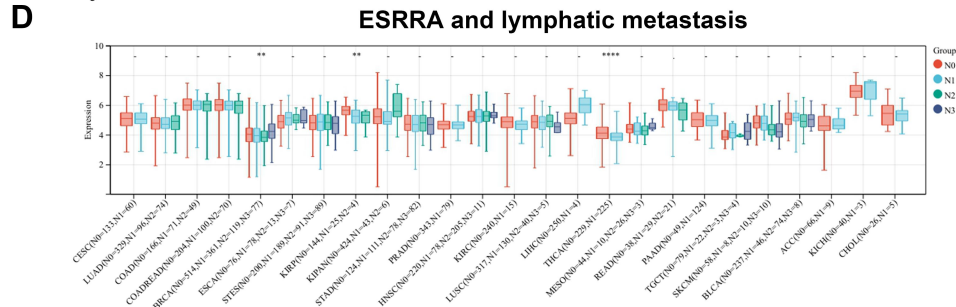
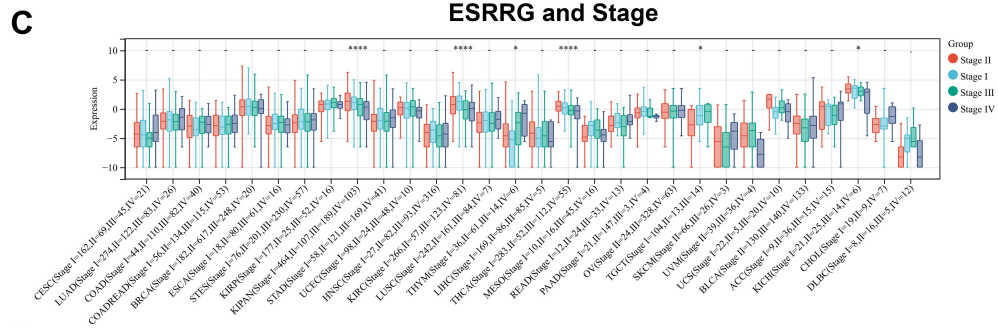
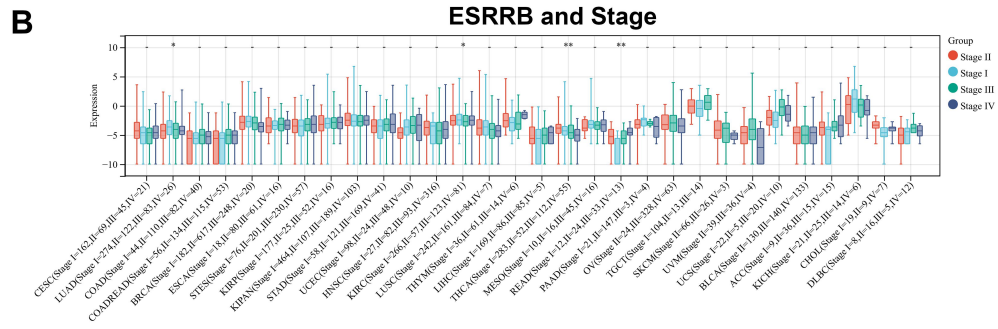
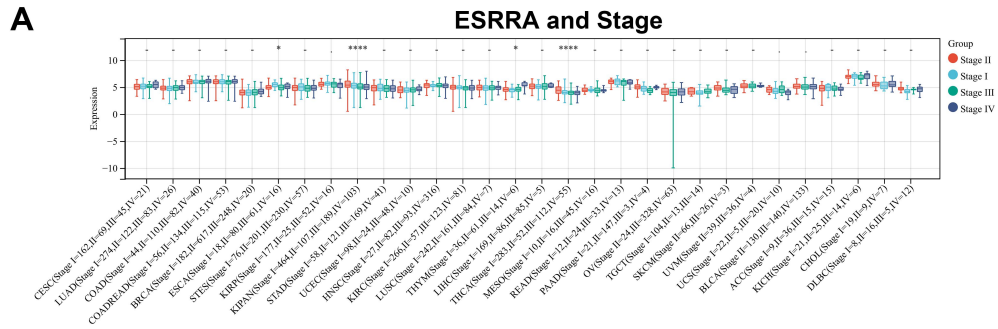


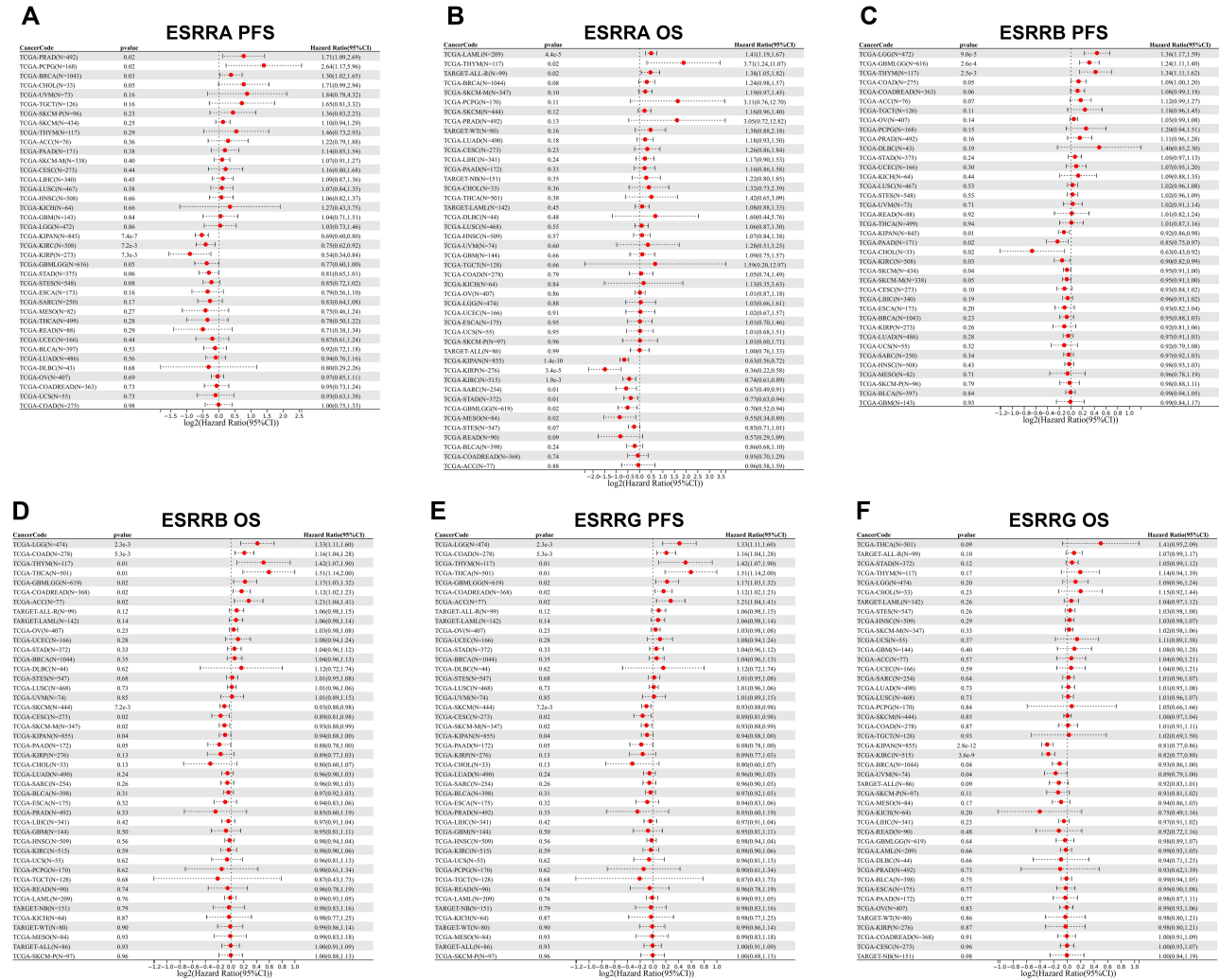
Supplementary Material

1 Supplementary Figures and Tables

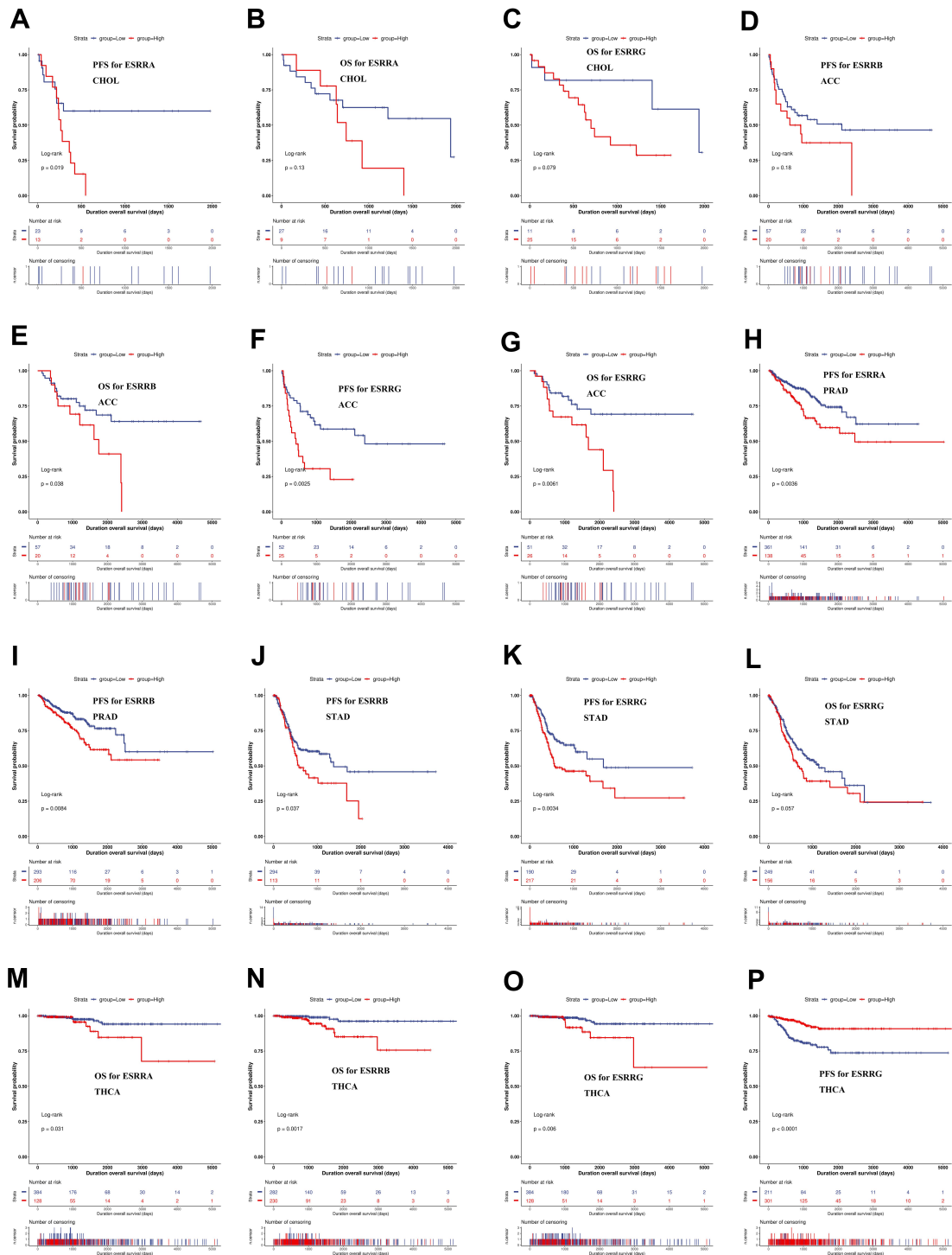
1.1 Supplementary Figures



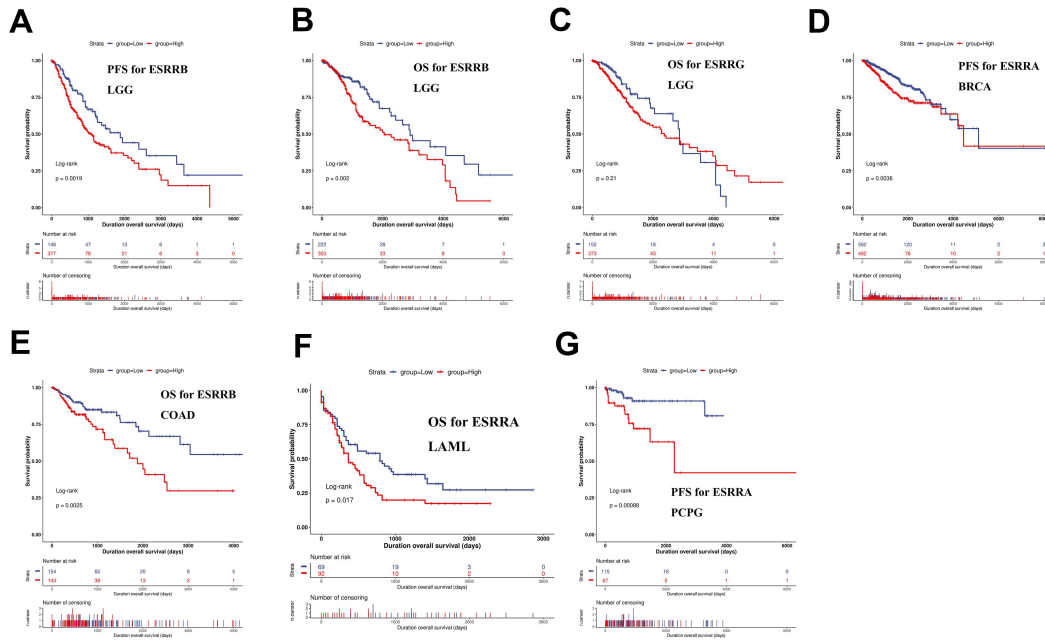
Supplementary Fig. S1. The correlation of ERRs with tumor stages and ymph node metastasis. (A-C) Expression of ESRRA (A), ESRRB (B), and ESRRG (C) at different pathological stages. (D-E) The association of ESRRA (A) and ESRRB (B) with lymph node metastasis in pan-cancer.



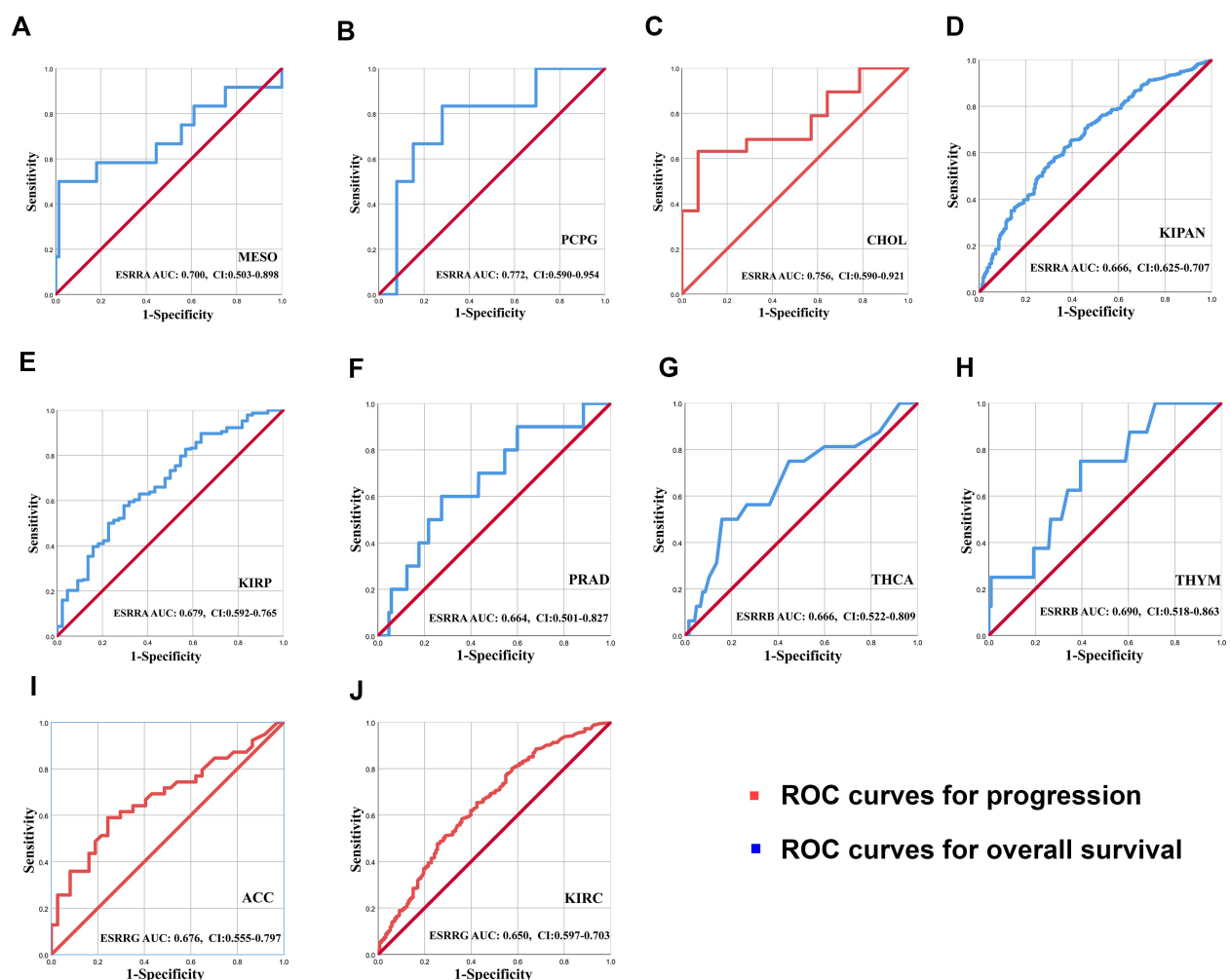
Supplementary Fig. S2: Associations between ERRs and PFS or OS were explored through COX regression analysis. (A-B) The association between ESRRA and tumor PFS (A) and OS (B). (C-D) The relationship between ESRRB and PFS (C) and OS (D). (E-F) The correlation between ESRRG and PFS (E) and OS (F).



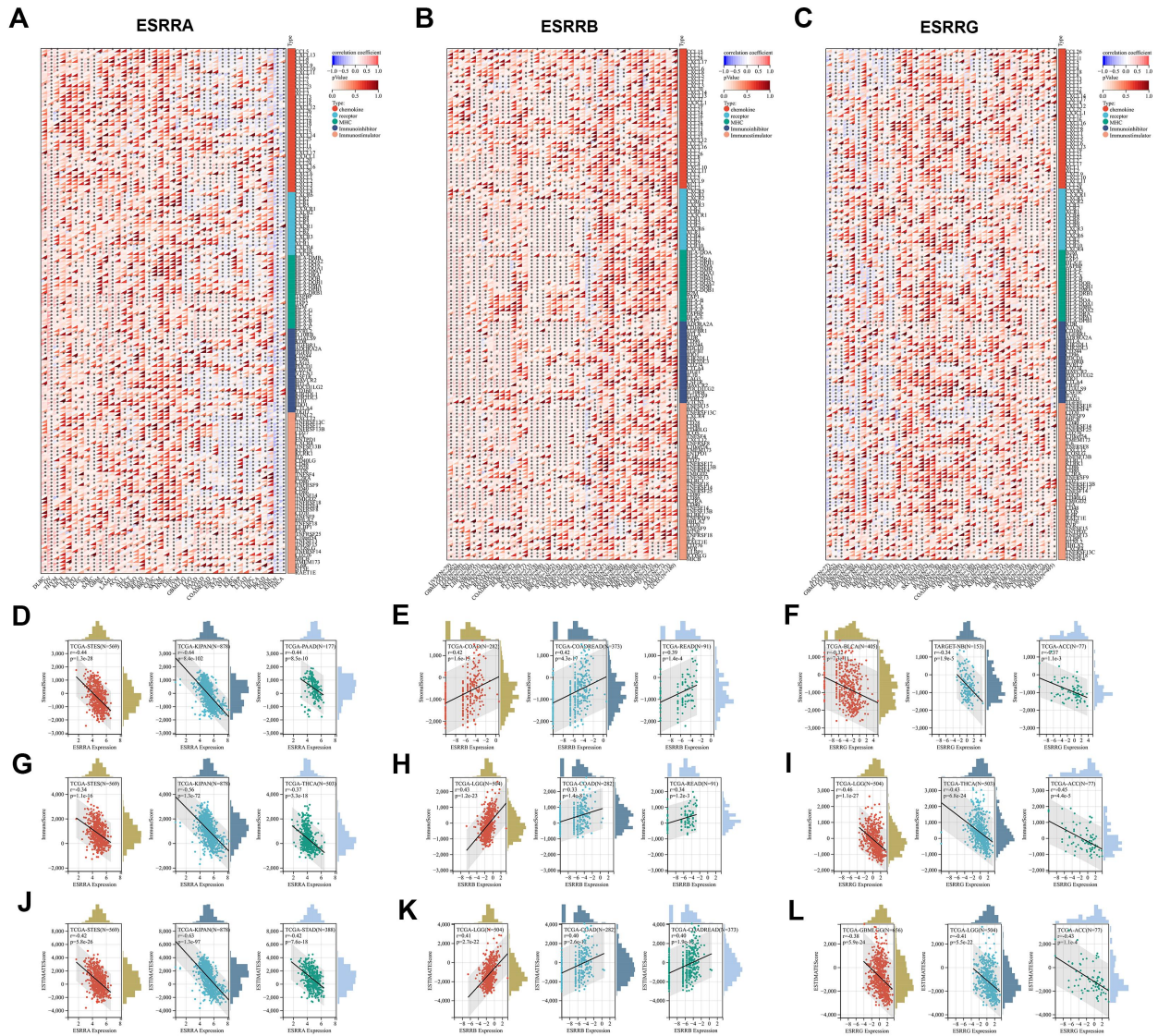
Supplementary Fig. S3: Kaplan-Meier survival analysis of ERRs with PFS and OS among cancers including CHOL (A-C), ACC (D-G), PRAD (H-I), STAD (J-L), and THCA (M-P).



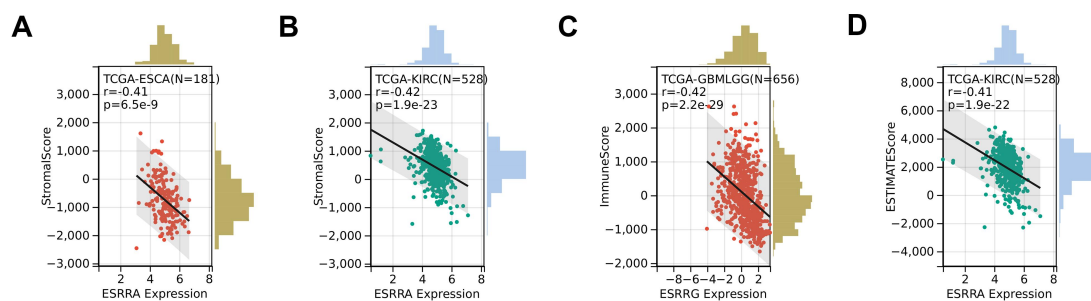
Supplementary Fig. S4. Kaplan-Meier survival analysis of ERRs with PFS and OS among cancers including LGG (A-C), BRCA (D), COAD (E), LAML (F), and PCPG (G).



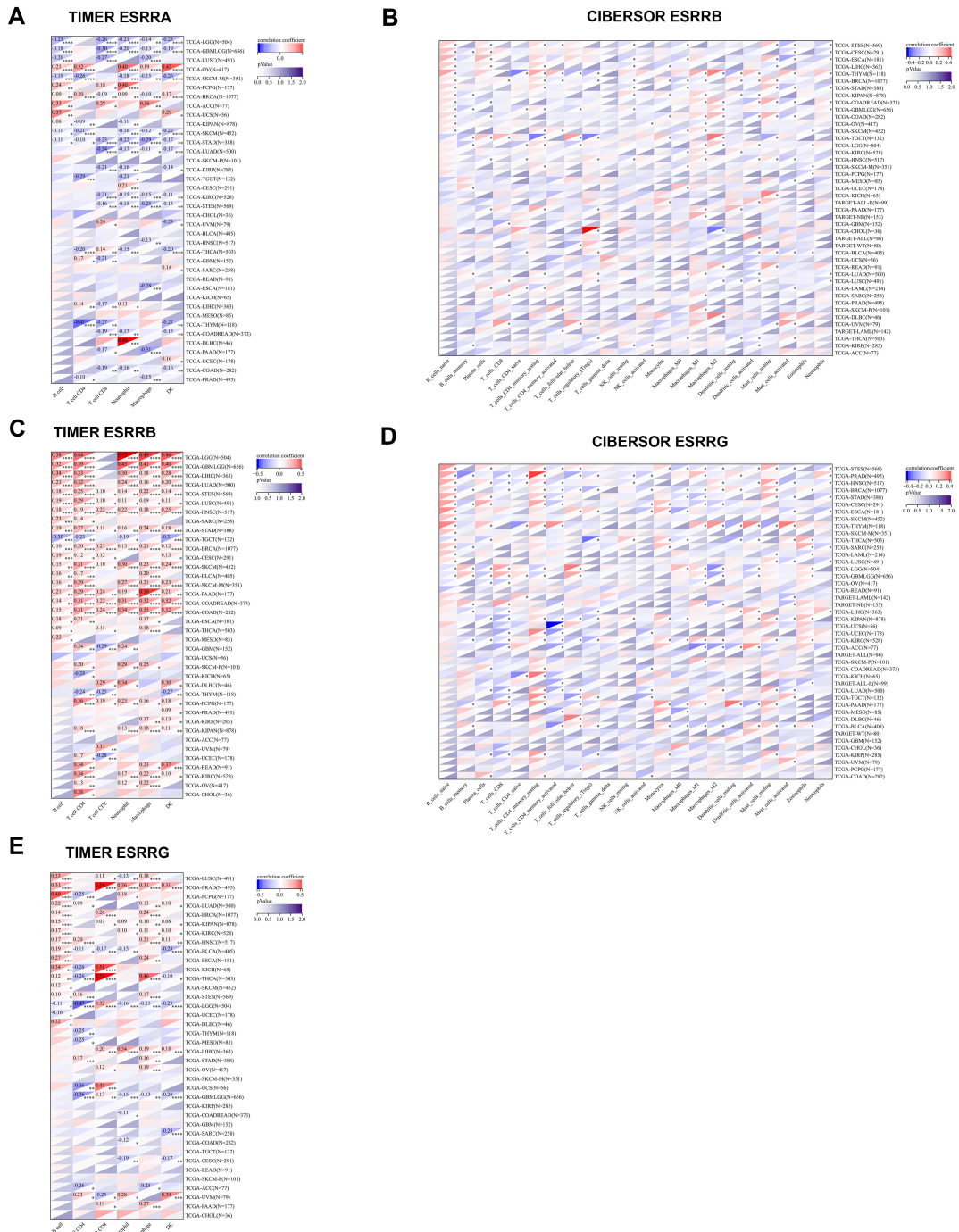
Supplementary Fig. S5.: ROC curves for ERRs. (A-B, D-F) Models with accuracy for survival predication were ESRR for MESO (A), PCPG (B), KIPAN (D), KIRP (E) and PRAD (F). **(C)** Models with accuracy for the progression predication were ESRR for CHOL. **(G-H)** Models with accuracy for survival predication were ESRRB for THCA (G) and THYM (H). **(I-J)** Models with accuracy for progression predication were ESRRG for ACC (I) and KIRC (J).



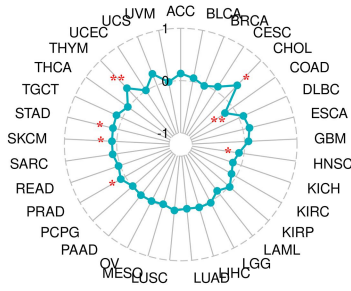
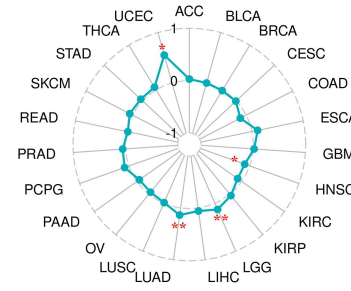
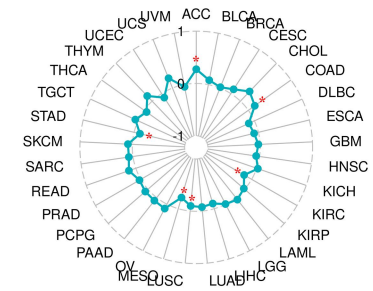
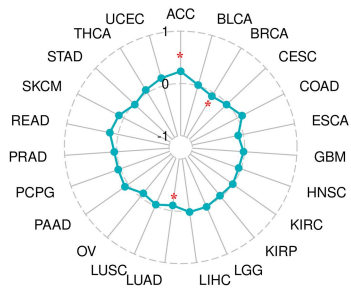
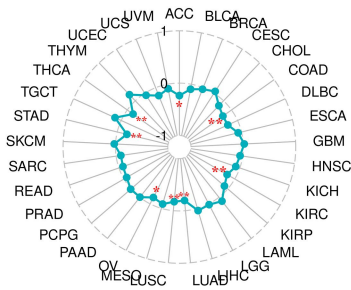
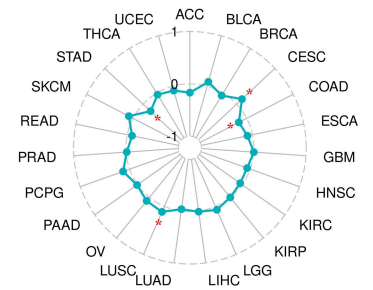
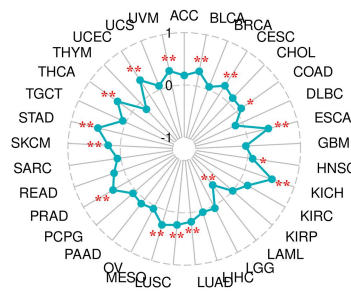
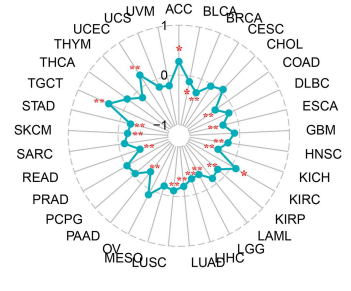
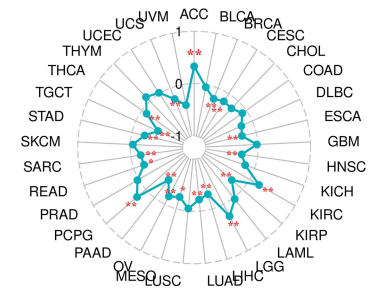
Supplementary Fig. S6: Relationship of ERRs with immune checkpoints and immune infiltration. (A-C) Correlation of ESRR A (A), ESRR B (B) and ESRR G (C) with immune checkpoint-related genes and immune infiltrating genes in pan-cancer. **(D-F)** The association of ESRR A (D), ESRR B (E) and ESRR G (F) expression with StromaScore. **(G-I)** The association of ESRR A (G), ESRR B (H) and ESRR G (I) expression with ImmuneScore. **(J-L)** The association of ESRR A (J), ESRR B (K) and ESRR G (L) expression with EstimateScore.



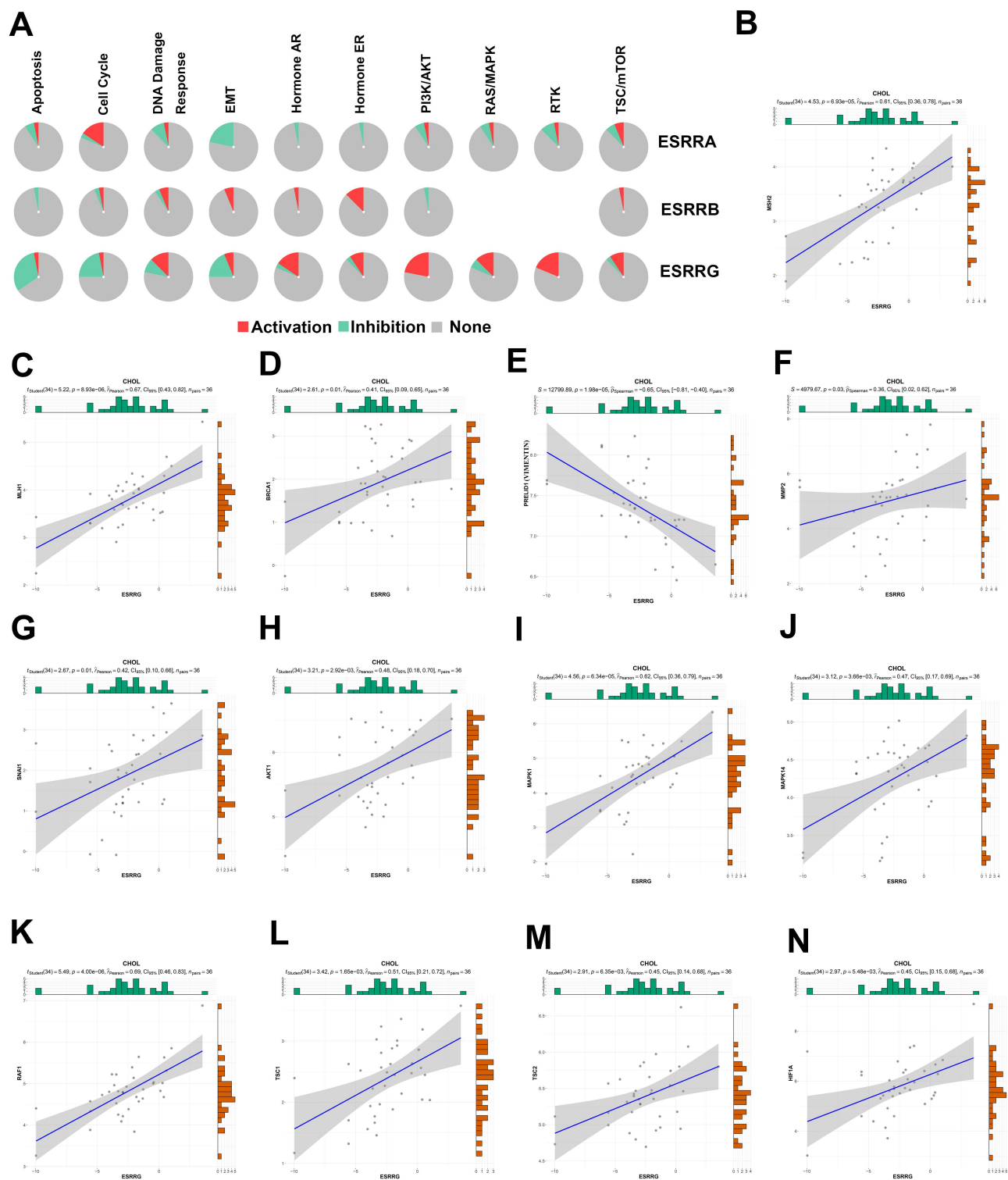
Supplementary Fig. S7: Relationship of ESRRR with immune infiltration. (A-B) The association of expression with Stromal Score in ESCA (A) and KIRC (B). (C) The association of ESRRR expression with Immune Score in GBMLGG. (D) The association of ESRRR expression with Estimate Score in KIRC.



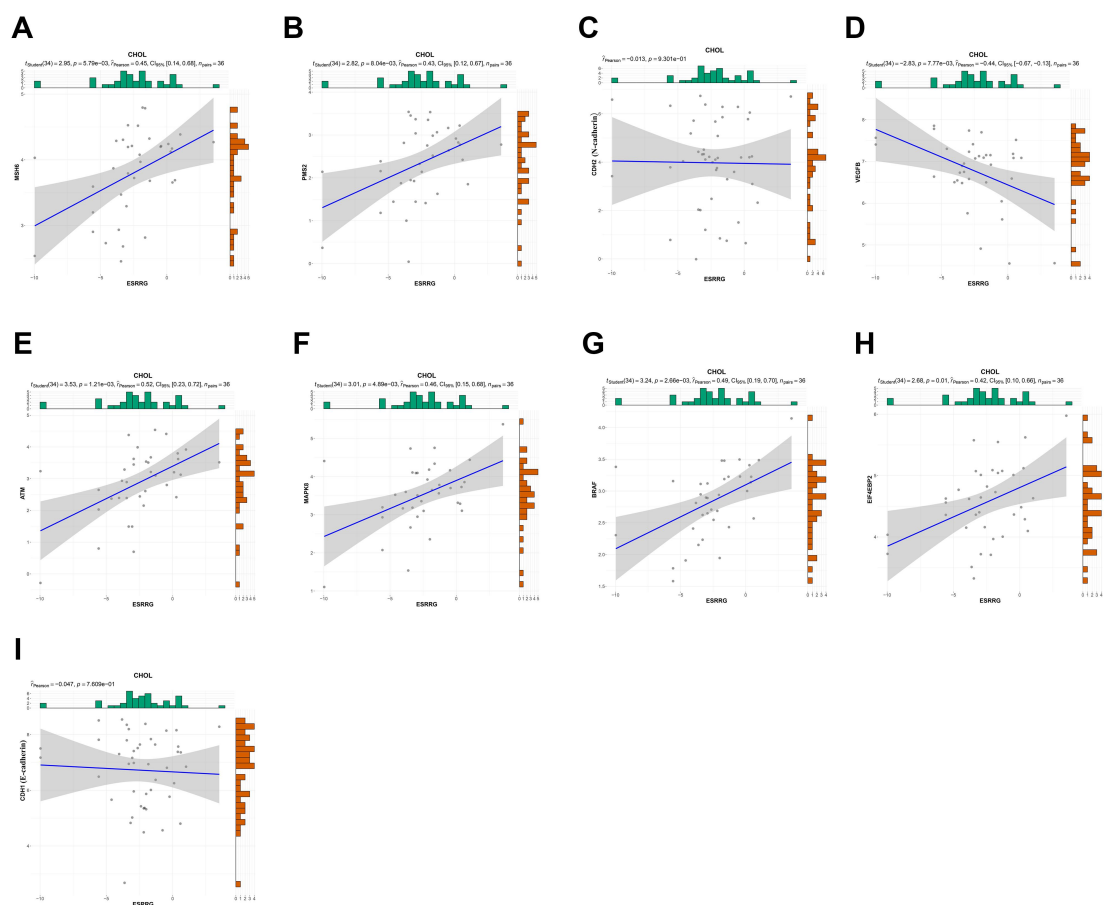
Supplementary Fig. S8. Correlation of ERRs with the level of immune infiltrating cells from pan-cancer. (A) Correlation of ESRR with the level of immune infiltrating cells using TIMER algorithms. (B-C) Correlation of ESRRB with the level of immune infiltrating cells using CIBERSORT (B) and TIMER (C) algorithms. (D-E) Correlation of ESRRG with the level of immune infiltrating cells using CIBERSORT (D) and TIMER (E) algorithms.

A**ESRRA mRNA TMB****B****ESRRA mRNA MSI****C****ESRRB mRNA TMB****D****ESRRB mRNA MSI****E****ESRRG mRNA TMB****F****ESRRG mRNA MSI****G****ESRRA mRNA stemness****H****ESRRB mRNA stemness****I****ESRRG mRNA stemness**

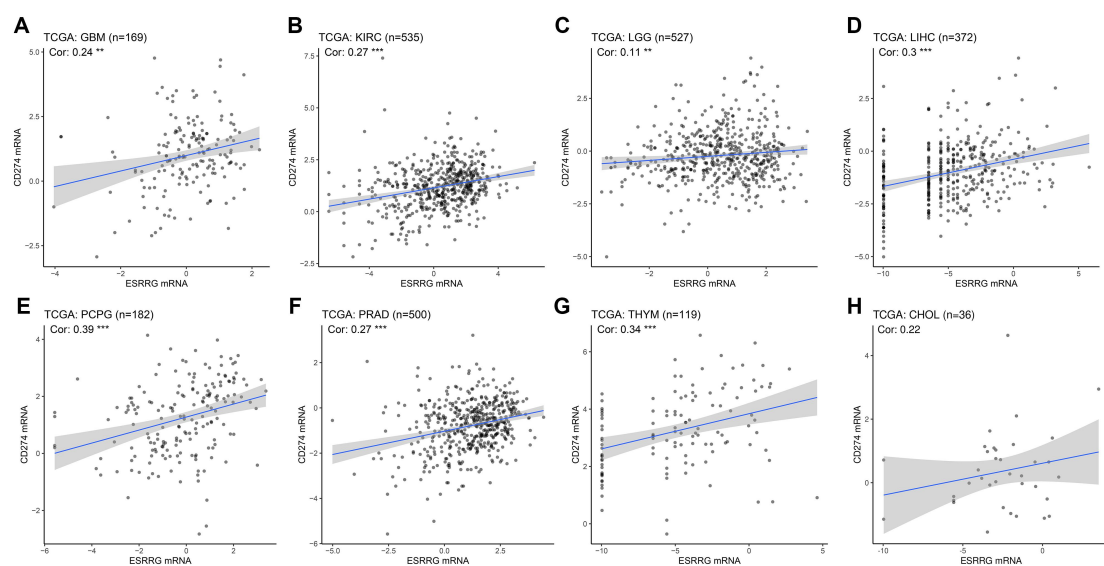
Supplementary Fig. S9: The correlation of ERRs mRNA expression with MSI, TMB, and stemness in pan-cancer. **(A-B)** The correlation of ERRA mRNA expression with TMB (A) and MSI (B). **(C-D)** The correlation of ERRB mRNA expression with TMB (C) and MSI (D). **(E-F)** The correlation of ERRG mRNA expression with TMB (E) and MSI (F). **(G-I)** The correlation between stemness scores and ESRRA (G), ESRRB (H) and ESRRG (I).



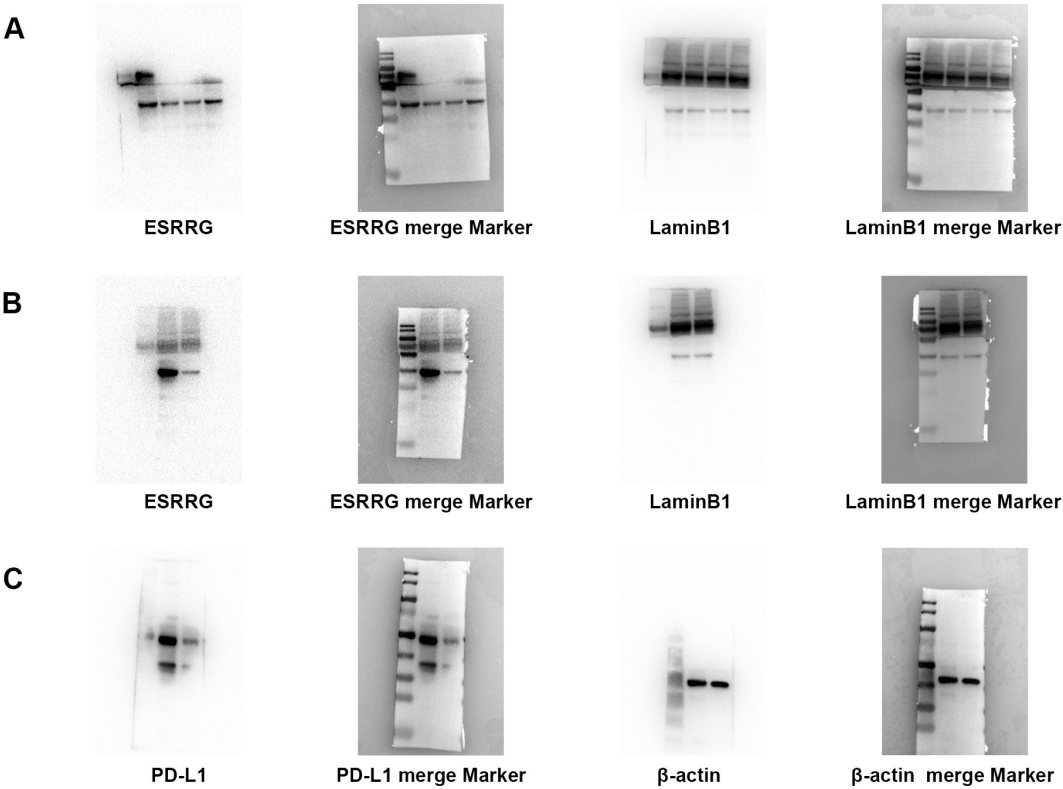
Supplementary Fig. S10: GeneMANIA analysis of ERRs-associated genes. (A) GSCAlite pathway activity module calculated the correlation between ERRs and signaling pathways. **(B-N)** Validation of the correlation between ESRRG expression and key regulators in the above signaling pathways in CHOL.



Supplementary Fig. S11: Validation of the correlation between ESRRG expression and key regulators of related signaling pathways from GSVA analysis in CHOL.



Supplementary Fig. S12: Positive correlations between the expression of PD-L1 and ESRRG in eight cancer types.



Supplementary Fig. S13: Representative original gels. (A) The original gels of Fig. 11B. The images in Fig. 11B were cropped from ESRRG and LaminB1. (B) The original gels of Fig. 11D. The images in Fig. 11D were cropped from ESRRG and LaminB1. (C) The original gels of Fig. 12B. The images in Fig. 12B were cropped from PD-L1 and β -actin.

1.2 Supplementary Tables

Supplementary Table 1. The raw data of R-value and P-value for ERRs' stromal score, immune score, and estimate score.

	ESRRA						ESRRB						ESRRG					
Immu	Stroma lScore	Stroma lScore	Immun eScore	Immun eScore	ESTIMA TEScore	ESTIMA TEScore	Stroma lScore	Stroma lScore	Immun eScore	Immun eScore	ESTIMA TEScore	ESTIMA TEScore	Stroma lScore	Stroma lScore	Immun eScore	Immun eScore	ESTIMA TEScore	ESTIMA TEScore
Method	spearman _R	spearman _P	spearman _R	spearman _P	spearman _R	spearman _P	spearman _R	spearman _P	spearman _R	spearman _P	spearman _R	spearman _P	spearman _R	spearman _P	spearman _R	spearman _P	spearman _R	spearman _P
TCGA-GBM(N=152)	-0.22	5.61E-03	-0.23	4.49E-03	-0.24	3.32E-03	0.00	9.60E-01	0.00	9.83E-01	-0.01	9.26E-01	-0.09	2.77E-01	-0.15	6.65E-02	-0.13	1.04E-01
TCGA-GBMLGG(N=656)	-0.26	8.38E-12	-0.21	7.36E-08	-0.23	1.92E-09	0.27	2.28E-12	0.31	1.42E-16	0.30	1.74E-15	-0.29	4.80E-14	-0.42	2.20E-29	-0.38	5.94E-24
TCGA-LGG(N=504)	-0.22	4.68E-07	-0.14	1.77E-03	-0.17	1.05E-04	0.37	8.61E-18	0.43	1.25E-23	0.41	2.69E-22	-0.29	1.62E-11	-0.46	1.05E-27	-0.41	5.54E-22
TCGA-UCEC(N=178)	-0.31	2.51E-05	-0.09	2.34E-01	-0.18	1.52E-02	-0.19	9.55E-03	-0.11	1.36E-01	-0.15	4.87E-02	-0.12	1.26E-01	-0.29	1.02E-04	-0.23	1.66E-03
TARGET-LAML(N=142)	0.08	3.30E-01	0.32	1.11E-04	0.23	5.76E-03	-0.27	1.06E-03	-0.13	1.35E-01	-0.19	2.23E-02	-0.22	8.76E-03	-0.09	2.64E-01	-0.16	6.55E-02
TCGA-BRCA(N=1077)	-0.10	7.85E-04	0.09	4.11E-03	0.00	9.35E-01	0.19	1.88E-10	0.05	1.12E-01	0.13	3.75E-05	0.04	2.04E-01	-0.16	9.40E-08	-0.09	3.93E-03
TCGA-CESC(N=291)	-0.21	2.39E-04	-0.04	5.25E-01	-0.13	2.61E-02	0.14	1.73E-02	0.04	4.99E-01	0.10	8.89E-02	-0.06	3.38E-01	-0.33	6.56E-09	-0.23	6.14E-05
TCGA-LUAD(N=500)	-0.35	1.97E-15	-0.28	9.76E-11	-0.35	1.18E-15	0.13	2.51E-03	0.18	5.84E-05	0.17	1.07E-04	-0.01	7.81E-01	-0.05	2.64E-01	-0.04	4.19E-01
TCGA-ESCA(N=181)	-0.41	6.51E-09	-0.18	1.58E-02	-0.32	9.99E-06	0.18	1.82E-02	0.14	5.48E-02	0.18	1.31E-02	0.06	4.35E-01	0.09	2.20E-01	0.08	2.61E-01
TCGA-STES(N=569)	-0.44	1.29E-28	-0.34	1.12E-16	-0.42	5.84E-26	0.15	2.67E-04	0.10	1.75E-02	0.14	1.12E-03	0.07	1.20E-01	0.03	4.32E-01	0.05	2.03E-01
TCGA-SARC(N=258)	0.05	3.95E-01	0.16	8.44E-03	0.12	6.49E-02	0.03	6.11E-01	0.06	3.58E-01	0.06	3.65E-01	-0.13	3.95E-02	-0.28	7.15E-06	-0.24	7.02E-05
TCGA-KIRP(N=285)	-0.22	1.49E-04	-0.19	9.76E-04	-0.21	2.79E-04	0.03	6.45E-01	-0.07	2.60E-01	-0.03	6.24E-01	-0.14	1.91E-02	-0.33	1.43E-08	-0.27	3.84E-06
TCGA-KIPAN(N=878)	-0.64	8.40E-102	-0.56	1.29E-72	-0.63	1.31E-97	0.08	1.64E-02	-0.01	8.81E-01	0.05	1.73E-01	-0.24	1.71E-12	-0.32	5.90E-23	-0.30	1.49E-19
TCGA-COAD(N=282)	-0.34	2.70E-09	-0.32	4.88E-08	-0.35	8.91E-10	0.42	1.60E-13	0.33	1.36E-08	0.40	2.62E-12	-0.01	8.29E-01	-0.08	1.69E-01	-0.05	4.11E-01

TCGA-COADREAD(N=373)	-0.31	6.38E-10	-0.29	7.08E-09	-0.32	1.56E-10	0.42	4.30E-17	0.33	7.26E-11	0.40	1.89E-15	0.00	9.93E-01	-0.08	1.09E-01	-0.04	4.27E-01
TCGA-PRAD(N=495)	-0.25	1.03E-08	-0.21	2.86E-06	-0.25	2.44E-08	-0.02	6.55E-01	-0.06	1.53E-01	-0.05	2.64E-01	-0.08	9.20E-02	-0.11	1.09E-02	-0.11	1.44E-02
TCGA-STAD(N=388)	-0.42	8.64E-18	-0.34	1.18E-11	-0.42	7.58E-18	0.17	8.46E-04	0.11	3.00E-02	0.15	3.13E-03	0.03	6.21E-01	-0.05	3.57E-01	-0.01	7.89E-01
TCGA-HNSC(N=517)	-0.21	1.11E-06	-0.16	3.92E-04	-0.21	2.45E-06	0.19	9.65E-06	0.18	2.70E-05	0.21	1.46E-06	0.16	1.67E-04	0.00	9.75E-01	0.08	7.50E-02
TCGA-KIRC(N=528)	-0.42	1.85E-23	-0.32	2.80E-14	-0.41	1.93E-22	0.12	6.63E-03	0.05	2.40E-01	0.10	2.13E-02	-0.15	3.59E-04	-0.21	1.12E-06	-0.21	7.21E-07
TCGA-LUSC(N=491)	-0.32	1.74E-13	-0.22	6.72E-07	-0.29	5.43E-11	0.07	1.47E-01	0.10	2.42E-02	0.09	4.04E-02	-0.01	8.32E-01	-0.06	1.88E-01	-0.04	3.92E-01
TCGA-THYM(N=118)	-0.12	1.84E-01	-0.24	8.76E-03	-0.28	2.49E-03	0.17	7.16E-02	0.03	7.21E-01	0.08	4.01E-01	-0.07	4.33E-01	0.04	6.32E-01	-0.07	4.31E-01
TCGA-LIHC(N=363)	-0.08	1.06E-01	-0.23	1.18E-05	-0.18	4.13E-04	0.23	1.48E-05	0.09	7.17E-02	0.16	1.74E-03	0.12	1.88E-02	0.02	7.11E-01	0.07	1.86E-01
TARGET-WT(N=80)	-0.14	2.23E-01	-0.25	2.57E-02	-0.23	3.63E-02	0.10	3.97E-01	-0.07	5.16E-01	-0.01	9.55E-01	0.09	4.05E-01	-0.35	1.57E-03	-0.14	2.17E-01
TCGA-SKCM-P(N=101)	-0.26	9.16E-03	-0.21	3.39E-02	-0.24	1.53E-02	0.03	7.38E-01	0.13	2.04E-01	0.12	2.47E-01	-0.13	1.81E-01	-0.19	5.11E-02	-0.18	7.18E-02
TCGA-SKCM(N=452)	-0.31	1.56E-11	-0.29	2.38E-10	-0.32	2.95E-12	0.20	2.76E-05	0.17	3.05E-04	0.20	2.55E-05	-0.04	4.15E-01	-0.13	7.75E-03	-0.10	3.99E-02
TCGA-BLCA(N=405)	-0.33	9.38E-12	-0.18	3.71E-04	-0.28	1.48E-08	0.08	1.12E-01	0.06	2.37E-01	0.07	1.35E-01	-0.32	7.35E-11	-0.31	2.31E-10	-0.34	4.15E-12
TCGA-SKCM-M(N=351)	-0.32	6.36E-10	-0.31	1.62E-09	-0.34	4.39E-11	0.22	3.51E-05	0.16	3.13E-03	0.20	1.96E-04	-0.05	3.37E-01	-0.15	5.32E-03	-0.12	2.57E-02
TCGA-THCA(N=503)	-0.34	5.32E-15	-0.37	3.32E-18	-0.39	1.57E-19	0.02	5.88E-01	-0.05	2.99E-01	-0.02	6.80E-01	-0.20	5.70E-06	-0.43	6.82E-24	-0.35	4.55E-16
TARGET-NB(N=153)	0.10	2.16E-01	0.20	1.20E-02	0.17	3.48E-02	0.22	6.14E-03	0.31	1.04E-04	0.30	1.50E-04	-0.34	1.89E-05	-0.14	7.70E-02	-0.25	1.76E-03
TCGA-MESO(N=85)	-0.19	7.39E-02	0.02	8.59E-01	-0.09	4.23E-01	0.06	6.10E-01	-0.11	3.12E-01	-0.07	4.98E-01	-0.19	7.76E-02	-0.22	4.77E-02	-0.23	3.19E-02
TCGA-READ(N=91)	-0.18	9.00E-02	-0.22	3.59E-02	-0.22	3.67E-02	0.39	1.38E-04	0.34	1.16E-03	0.38	2.21E-04	0.03	7.43E-01	-0.10	3.41E-01	-0.02	8.20E-01
TCGA-OV(N=417)	0.06	2.29E-01	0.20	3.01E-05	0.14	3.67E-03	-0.10	3.50E-02	-0.19	8.71E-05	-0.16	1.42E-03	-0.11	2.70E-02	-0.20	2.99E-05	-0.17	5.81E-04
TCGA-UVM(N=79)	-0.25	2.64E-02	-0.14	2.34E-01	-0.19	1.01E-01	0.22	5.09E-02	0.25	2.92E-02	0.25	2.65E-02	-0.02	8.31E-01	-0.13	2.72E-01	-0.10	3.70E-01

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TCGA-PAAD(N=177)	-0.44	8.52E-10	-0.30	4.37E-05	-0.40	3.87E-08	0.24	1.42E-03	0.17	2.56E-02	0.21	5.66E-03	0.13	7.71E-02	0.10	1.90E-01	0.11	1.44E-01
TCGA-TGCT(N=132)	-0.01	9.46E-01	-0.24	5.31E-03	-0.17	5.00E-02	-0.01	8.82E-01	-0.26	2.69E-03	-0.20	2.01E-02	0.08	3.37E-01	-0.11	2.15E-01	-0.05	5.82E-01
TCGA-UCS(N=56)	0.18	1.73E-01	0.12	3.82E-01	0.19	1.69E-01	0.03	8.22E-01	-0.26	4.99E-02	-0.14	2.90E-01	0.06	6.53E-01	-0.29	2.86E-02	-0.17	2.17E-01
TCGA-LAML(N=214)	0.49	1.95E-14	0.27	5.88E-05	0.38	7.24E-09	0.00	9.45E-01	0.08	2.49E-01	0.05	4.45E-01	-0.02	7.26E-01	0.07	2.98E-01	0.04	5.43E-01
TARGET-ALL(N=86)	-0.10	3.83E-01	-0.10	3.73E-01	-0.13	2.25E-01	-0.13	2.41E-01	-0.35	8.04E-04	-0.30	5.69E-03	0.22	4.57E-02	0.05	6.48E-01	0.17	1.19E-01
TCGA-PCPG(N=177)	-0.03	6.64E-01	0.00	9.73E-01	-0.03	7.41E-01	0.19	1.31E-02	0.08	2.77E-01	0.14	7.23E-02	-0.11	1.59E-01	0.04	6.28E-01	-0.04	6.43E-01
TCGA-ACC(N=77)	-0.13	2.77E-01	-0.03	7.78E-01	-0.06	6.02E-01	-0.21	6.22E-02	-0.13	2.46E-01	-0.17	1.37E-01	-0.37	1.06E-03	-0.45	4.44E-05	-0.43	1.06E-04
TARGET-ALL-R(N=99)	0.33	9.14E-04	0.27	7.88E-03	0.30	2.45E-03	0.10	3.24E-01	0.16	1.08E-01	0.14	1.57E-01	-0.26	1.01E-02	-0.22	3.11E-02	-0.24	1.92E-02
TCGA-DLBC(N=46)	0.15	3.26E-01	0.18	2.22E-01	0.19	2.06E-01	0.22	1.50E-01	0.34	2.09E-02	0.39	7.29E-03	0.01	9.54E-01	0.15	3.26E-01	0.10	5.20E-01
TCGA-KICH(N=65)	-0.01	9.15E-01	0.12	3.33E-01	0.07	5.53E-01	-0.18	1.49E-01	-0.24	5.82E-02	-0.22	7.42E-02	-0.18	1.48E-01	-0.28	2.44E-02	-0.25	4.43E-02
TCGA-CHOL(N=36)	-0.25	1.41E-01	-0.23	1.70E-01	-0.26	1.32E-01	0.07	6.80E-01	0.04	8.33E-01	0.05	7.67E-01	0.03	8.59E-01	-0.16	3.51E-01	-0.08	6.42E-01