Figure S1. NMF consensus clustering was performed to identify the different groups of FRGs. (A) Relationship between cophenetic, dispersion, evar, residuals, rss, sparseness, and silhouette coefficients concerning the number of clusters. (B) Consensus matrix of NMF clustering when *k*=3, 4, 5, 6 and 7 in the GSE20685 cohort. NMF, non-negative matrix factorization; FRG, ferroptosis-related gene.

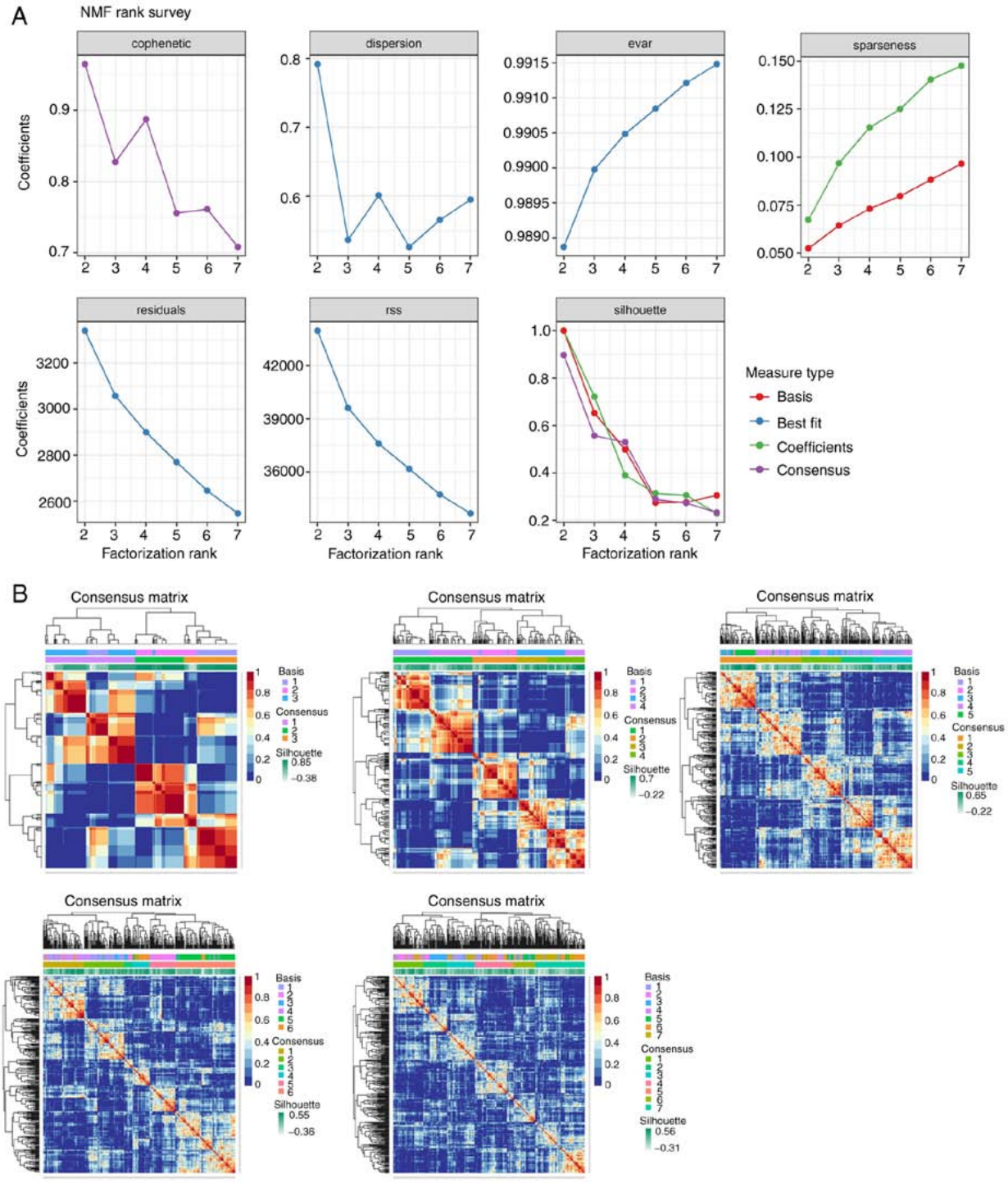

Figure S2. mRNA expression levels of ferroptosis-related genes in normal breast tissues and breast cancer tissues in the METABRIC database. METABRIC, Molecular Taxonomy of Breast Cancer International Consortium.

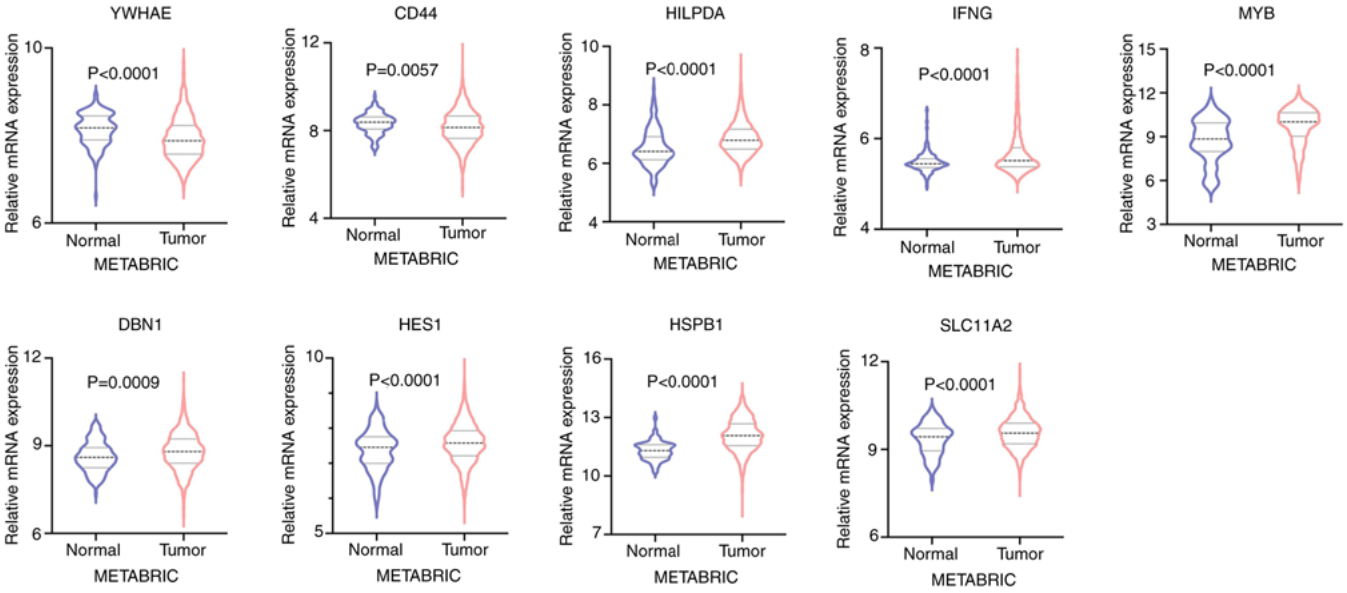

Figure S3. Immune infiltration of patients with breast cancer with different risk scores based on the CIBERSORT and ssGSEA algorithms. (A) Immune infiltration of 22 immune cell types in individual patients with breast cancer in the GSE20685 cohort. (B) Correlation between risk score and immune infiltration patterns in patients with breast cancer in the GSE20685 cohort. (C) Violin plots were used to visualize the fractions of different immune cells in the high-risk and low-risk groups in the METABRIC cohort. (D) Correlation between risk score and immune infiltration patterns in patients with breast cancer in the METABRIC cohort. (E) Heatmap indicating the abundance of immune cell populations in individual patients with breast cancer in the GSE20685 cohort. ssGSEA, single-sample gene set enrichment analysis; METABRIC, Molecular Taxonomy of Breast Cancer International Consortium.

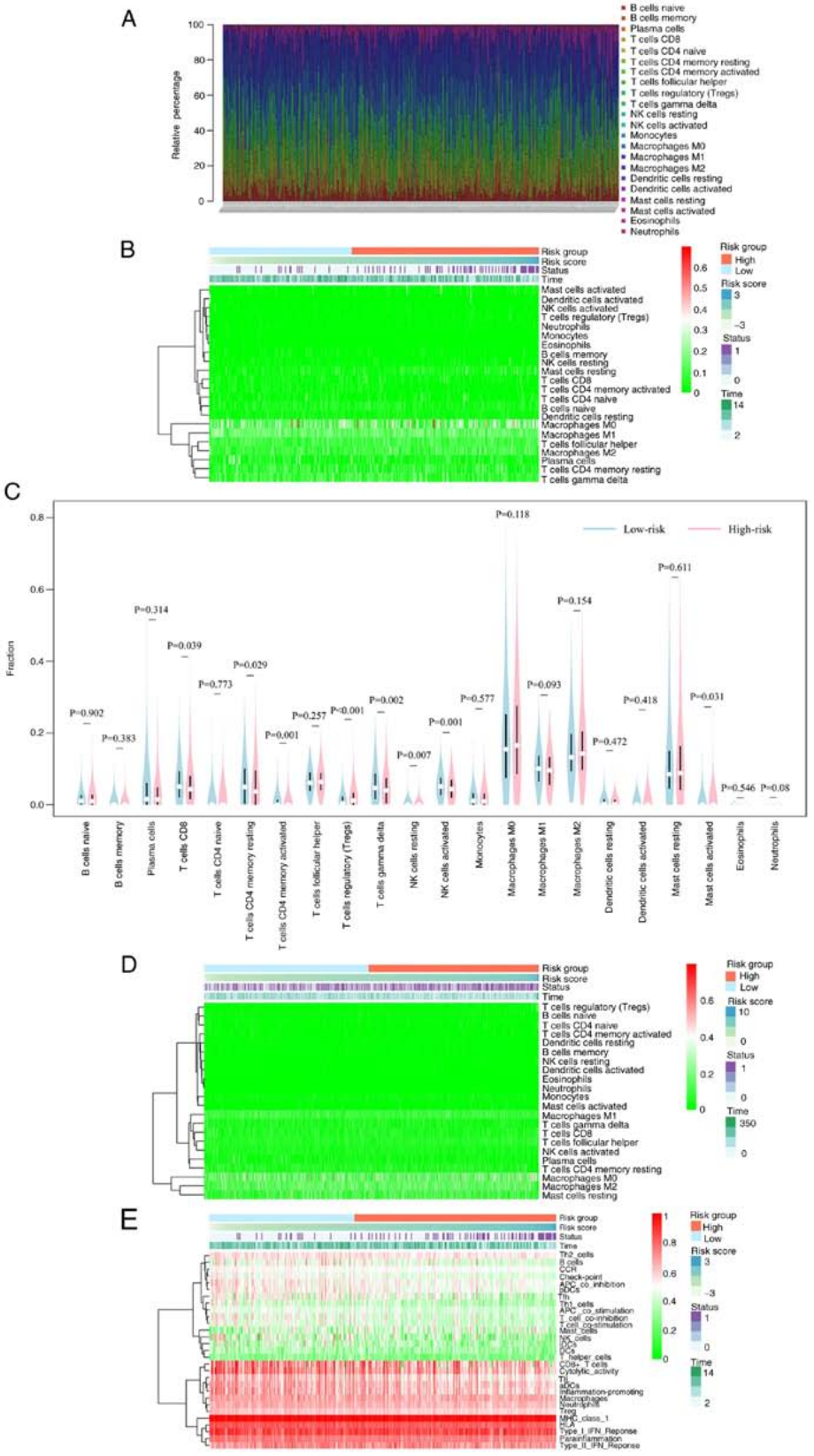

Figure S4. Immune infiltration of patients with breast cancer with different risk scores. (A) Violin plots were used to visualize the fractions of 16 immune cells in the high-risk and low-risk groups in the METABRIC cohort. (B) Radar maps were used to visualize the scores of 13 immune-related functions in the high-risk and low-risk groups in the METABRIC cohort. (C) Heatmap describing the abundance of immune cell populations in individual breast cancer patients in the METABRIC cohort. *P<0.05, **P<0.01, ***P<0.001, high risk group vs. low risk group. METABRIC, Molecular Taxonomy of Breast Cancer International Consortium.

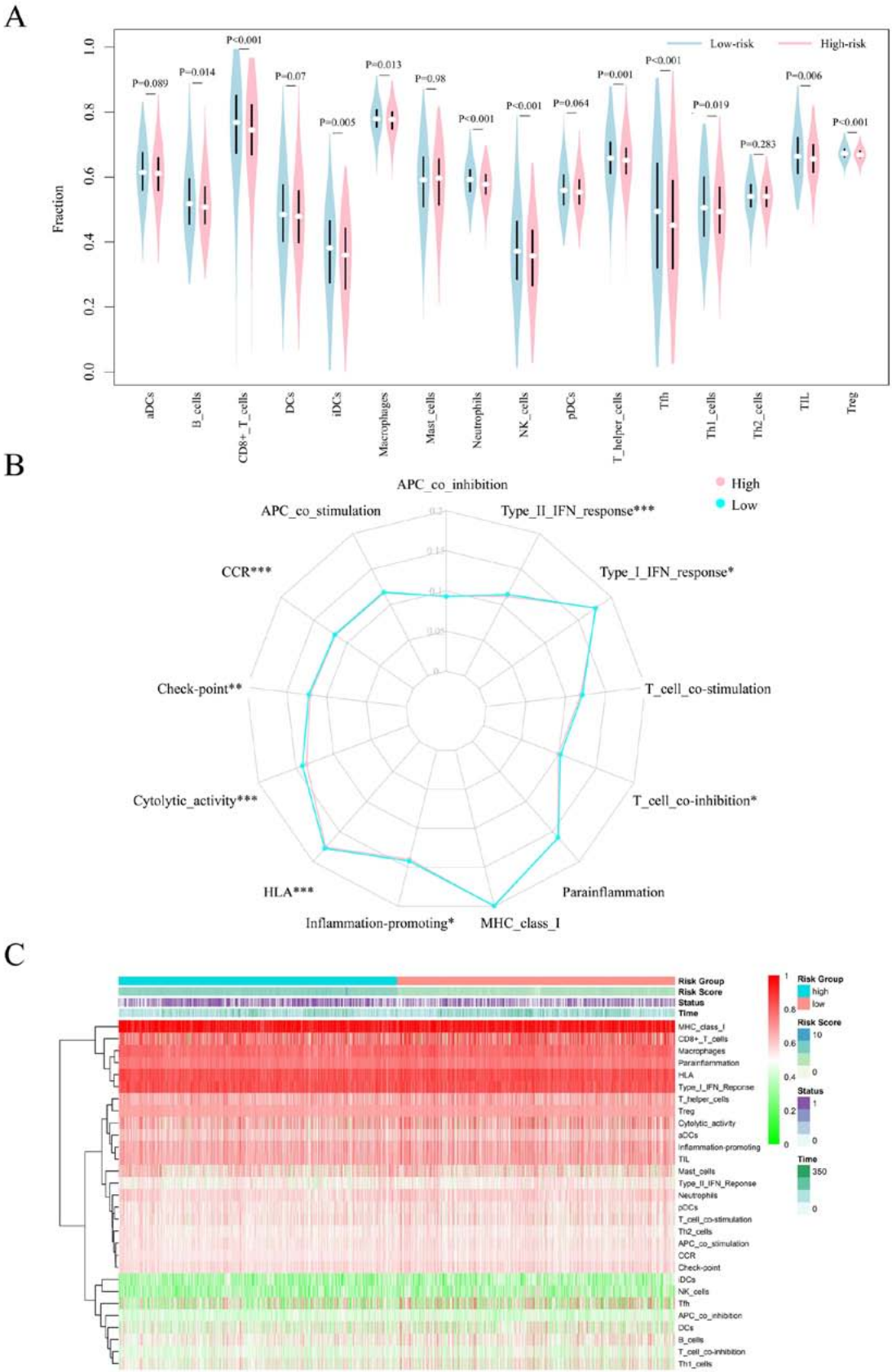

Figure S5. Expression of immune checkpoints in patients with breast cancer with different risk scores. Expression of several immune checkpoint genes in the high-risk and low-risk groups in the (A) GSE20685 and (B) METABRIC cohorts. METABRIC, Molecular Taxonomy of Breast Cancer International Consortium.

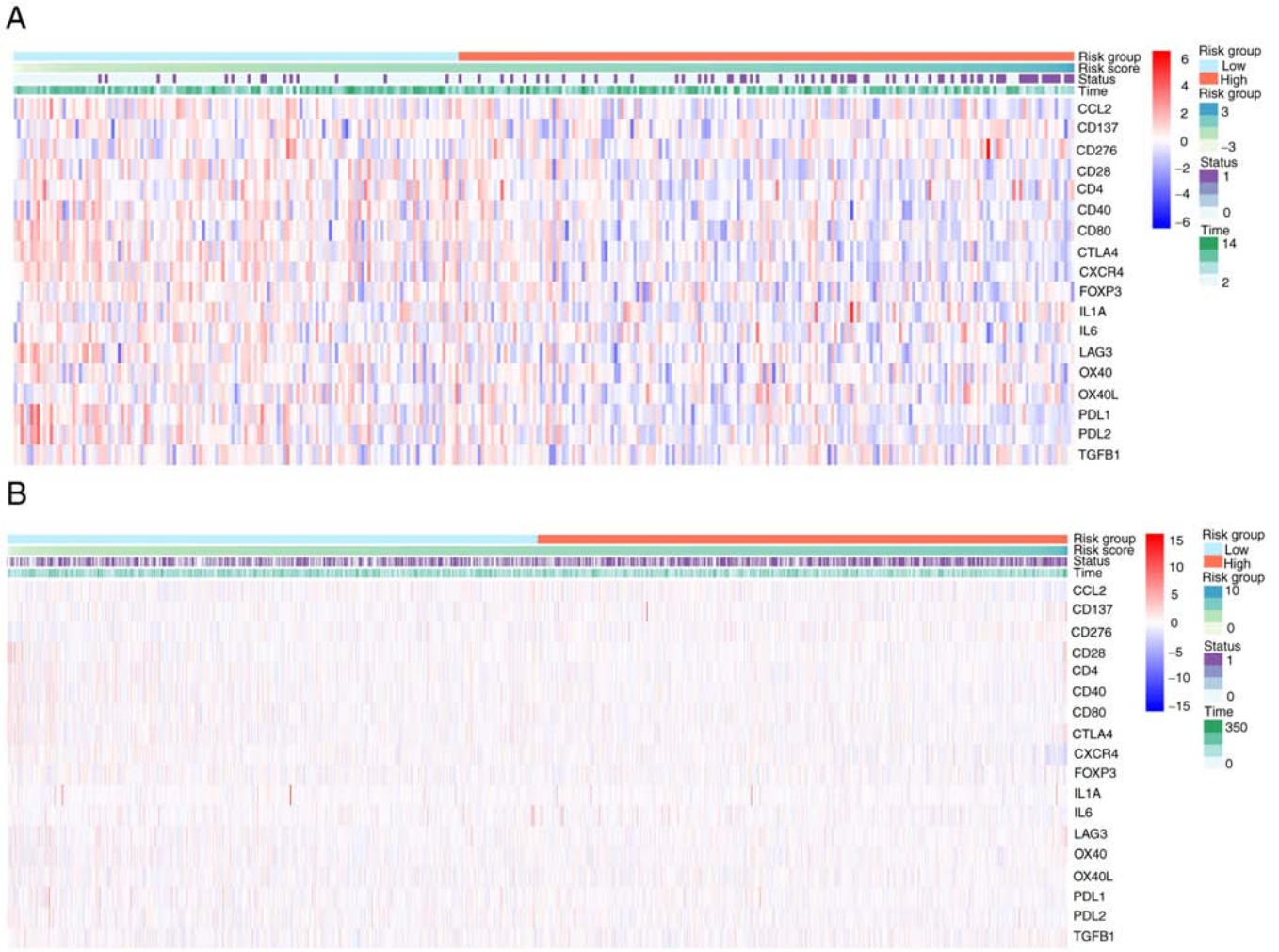

Figure S6. Erastin treatment suppresses proliferation, migration and drug resistance in breast cancer cells. Cells were treated with 10 or 20 μM erastin. Erastin treatment inhibited the (A) proliferation and (B) enhanced ROS accumulation of MCF-7 and T47D cells in a dose-dependent manner. Cells were treated with 10 μM erastin with or without 10 μM ferrostatin-1. Ferrostatin-1 (C) attenuated the suppression of cell proliferation and (D) reduced production of ROS induced by erastin. (E) Cells were treated with 10 μM erastin with or without 10 μM ferrostatin-1. Erastin treatment decreased the migratory ability of breast cancer cells relative to those of vehicle-treated cells, and ferrostatin-1 attenuated the suppression in cell migration induced by erastin. Scale bar, 200 μm. (F) Cells were treated with 10 μM erastin with or without 10 μM ferrostatin-1 or 5 μM TAM was used to treat cells at the meantime. Erastin treatment enhanced the TAM-induced cell death, while ferrostatin-1 attenuated the inhibitory effect of erastin on cell viability. **P<0.01, ***P<0.001. ROS, reactive oxygen species; TAM, tamoxifen.

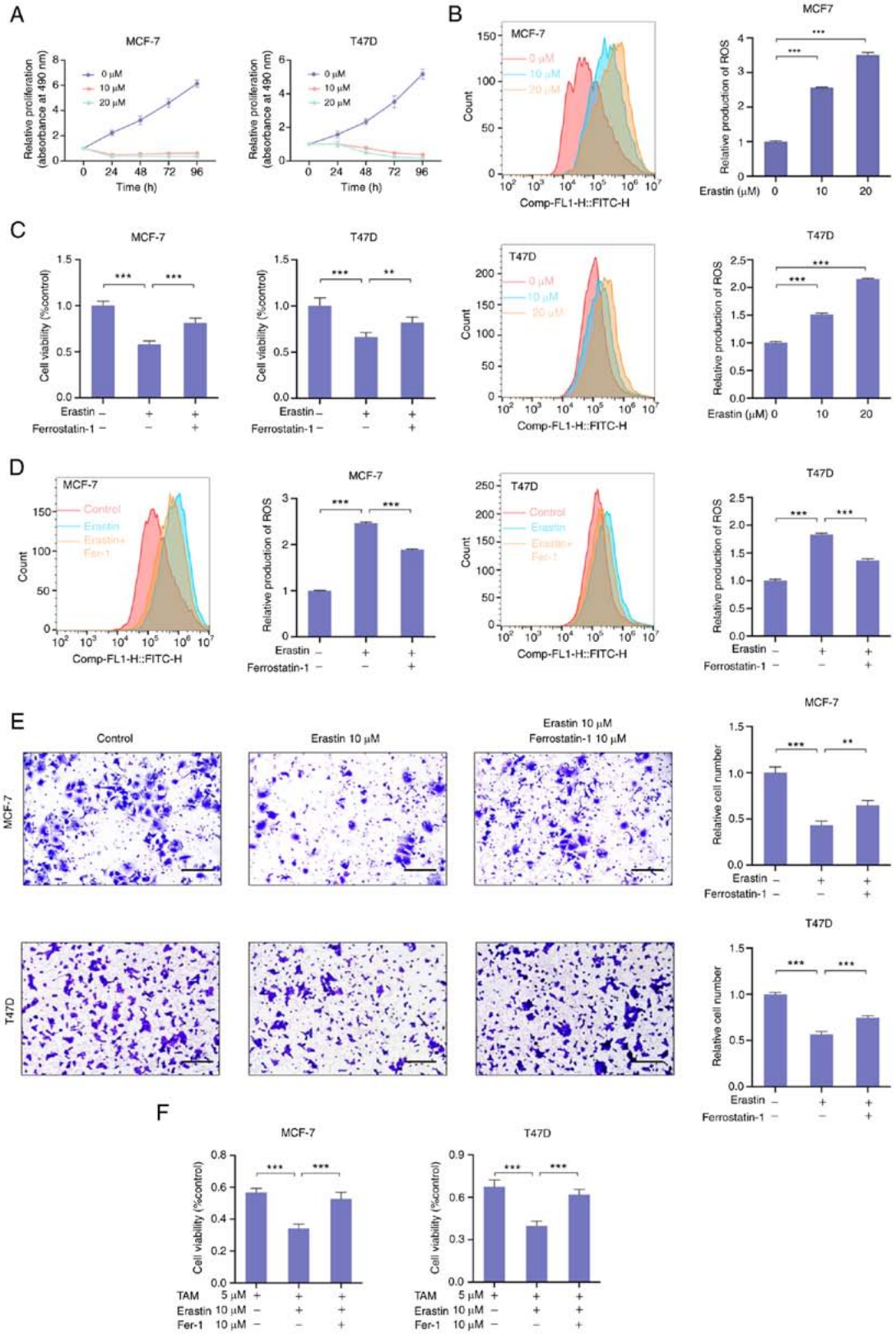

Figure S7. Correlation analysis between the expression of FRGs and drug sensitivity based on the CellMiner database. MYB expression was positively associated with the drug sensitivity of (A) chelerythrine, (B) nelarabine, (C) dexrazoxane and (D) palbociclib. (E) HSPB1 expression was negatively associated with the drug sensitivity of PX-316. MYB expression was positively associated with the drug sensitivity of (F) imexon, (G) ifosfamide, (H) PX-316, (I) XK-469, (J) fenretinide and (K) cyclophosphamide. DBN1 expression was negatively associated with the drug sensitivity of (L) selumetinib and (M) LDK-378. MYB expression was positively associated with the drug sensitivity of (N) carmustine, (O) oxaliplatin and (P) crizotinib. (Q) CD44 expression was negatively associated with the drug sensitivity of tamoxifen. (R) HILPDA expression was positively associated with the drug sensitivity of fenretinide. MYB expression was positively associated with the drug sensitivity of (S) dimethylaminoparthenolide and (T) lomustine. The x-axes represent the gene expression levels and the y-axes represents the average Z scores of drug sensitivity. Correlation coefficient R>0 was considered as a positive correlation, and P<0.05 was considered to indicate a statistically significant difference.