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ORIGINAL ARTICLE

Identification of Endoplasmic Reticulum Stress-Related Gene Signature Reveals KRT8 as a Target in Ovarian Cancer

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SUMMARY

Background: **Ovarian cancer (OC) is an invasive gynecological cancer with an overall 5-year survival rate of less than 45%. Endoplasmic reticulum (ER) stress plays a crucial role in regulating oncogenic events and immune-modulatory pathways, influencing malignant progression, antitumor immunity, and treatment response. However, the full scope of ER stress in ovarian cancer remains poorly understood and warrants further investigation.**
Methods: **RNA sequencing and clinical data were sourced from the Cancer Genome Atlas (TCGA) and Gene Expression Omnibus database (GEO). ER stress-related genes associated with ovarian tumor prognosis were identified, and an ER stress risk score model was developed using LASSO regression. We utilized this ER stress risk score to explore differences in immune cell infiltration. Furthermore, the biological role and expression of the risk gene KRT8 were validated through molecular biology experiments.**
Results: **We identified 573 genes related to ER stress that were differentially expressed genes (DEGs) between normal and tumor tissues. The ER stress-related risk signature (ERRS) constructed using the TCGA dataset was regarded as an independent and significant prognostic model for predicting cancer progression and instructing clinical decisions. Additionally, KRT8 was found to be overexpressed in ovarian cancer cells and tissues. Downregulation of KRT8 inhibited ovarian cancer cell proliferation and migration (in both SKOV3 and OVCAR8 cells) *in vitro*.**
Conclusions: **The ER stress-related gene model we developed can be utilized to assess the prognostic risk for OC patients. Importantly, KRT8 was identified as a key risk gene in ovarian cancer, promoting tumor progression, and holds potential as a novel therapeutic target.**
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Supplementary Data

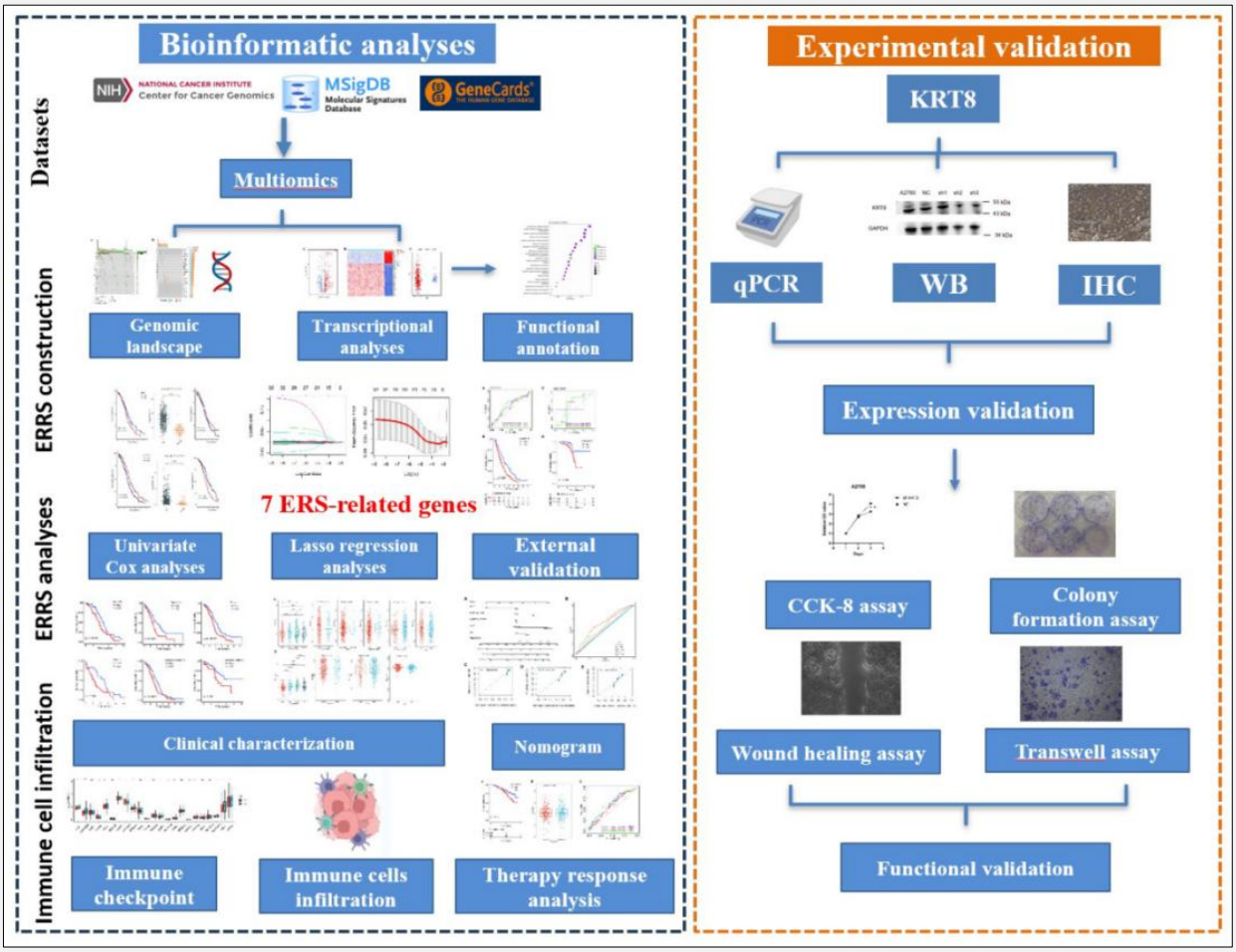


Figure S1. The flow chart of this study.

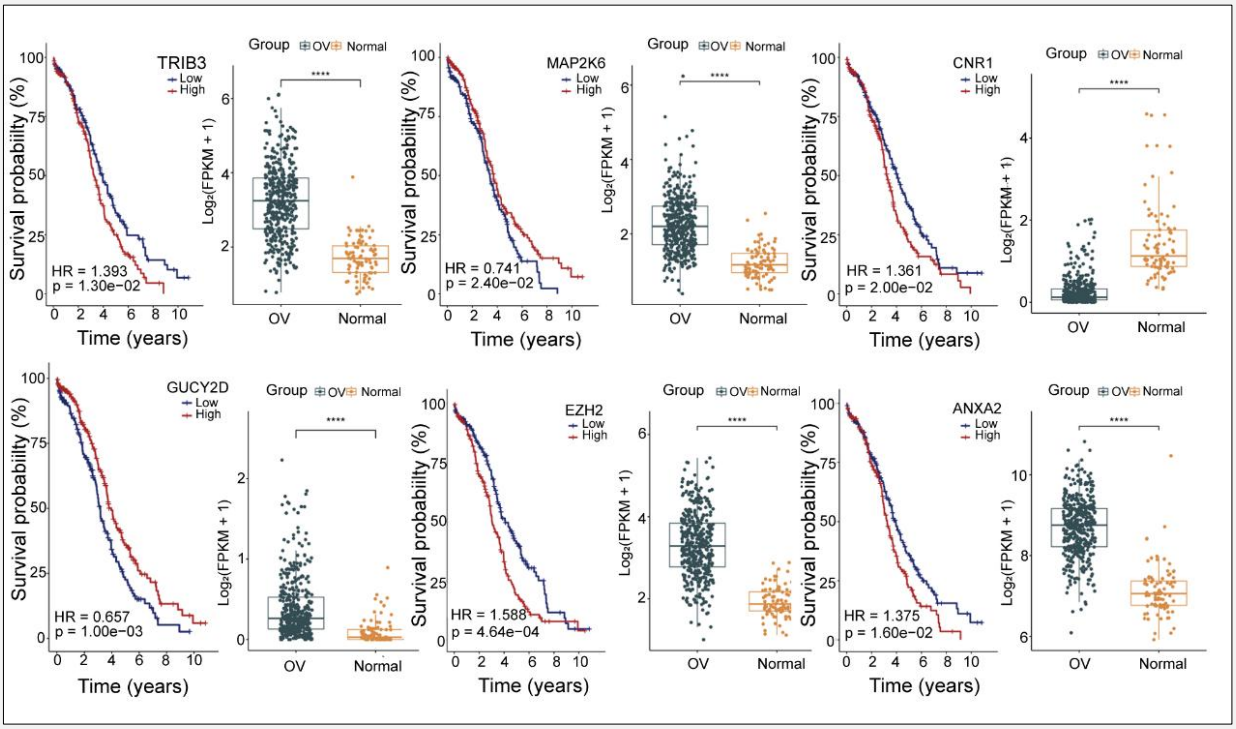


Figure S2. Prognostic value and differential expression of endoplasmic reticulum stress-related genes in ovarian cancer. * - p < 0.001, **** - p < 0.0001 (significant difference detected between the OV and normal groups).**

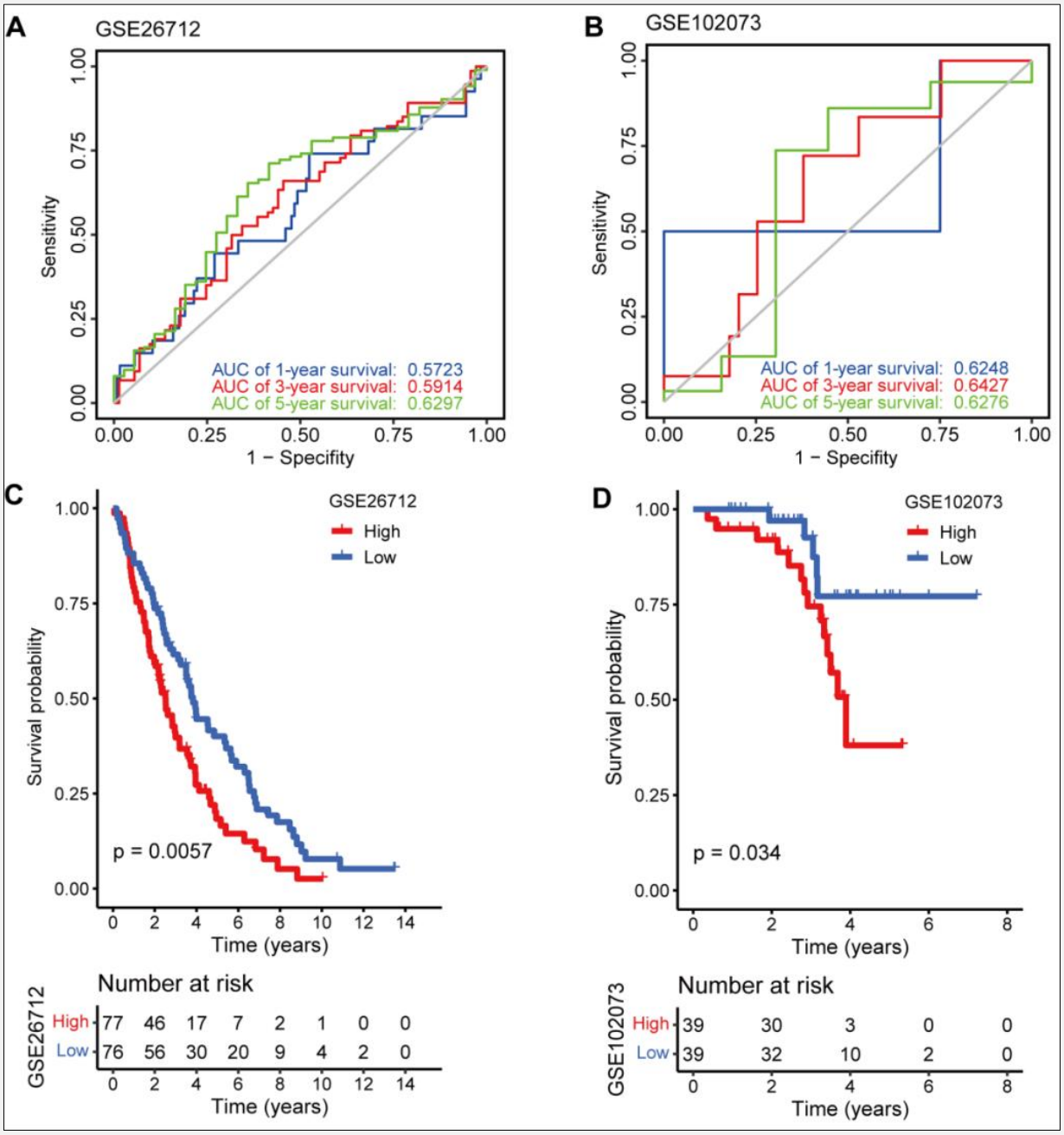


Figure S3. Validation of ERRS in an independent external dataset.

A - B - Survival curve AUC and KM analysis of the GSE26712 dataset. C - D - Survival curve AUC and KM analysis of the GSE102073 dataset.

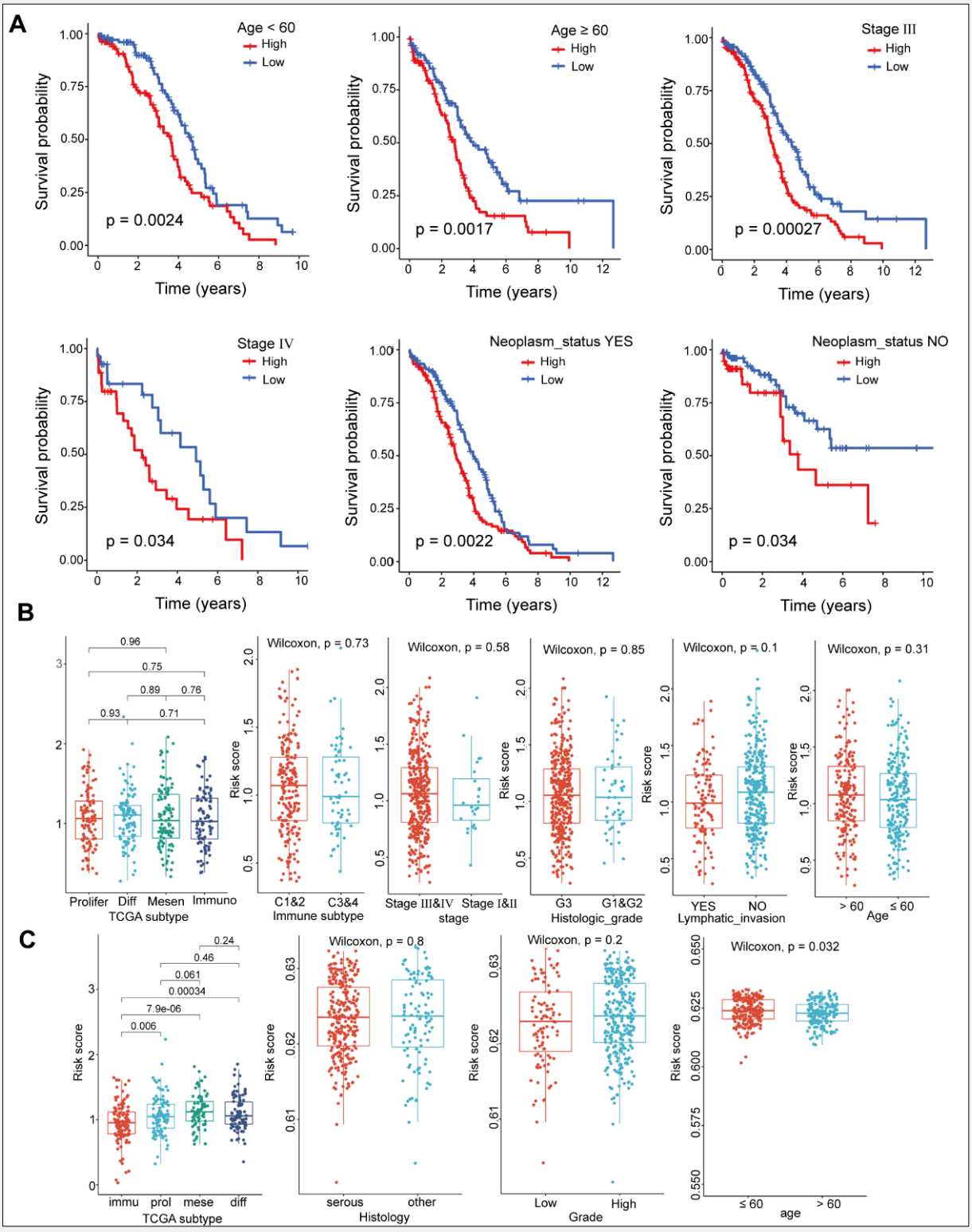


Figure S4. Correlation of the risk score with clinical characteristics.

A - The Kaplan-Meier survival curves of OC patients with age > 60 or age ≤ 60, stage III - IV, and neoplasm status. B - C - Boxplots of risk score based on age, cancer staging, TCGA subtypes, immune subtypes, and histological scores in the training and validation cohorts.