#565 (538850) : Association of patient-reported stress and depression symptoms with ER-specific tumor transcriptional signatures in breast cancer (BC)

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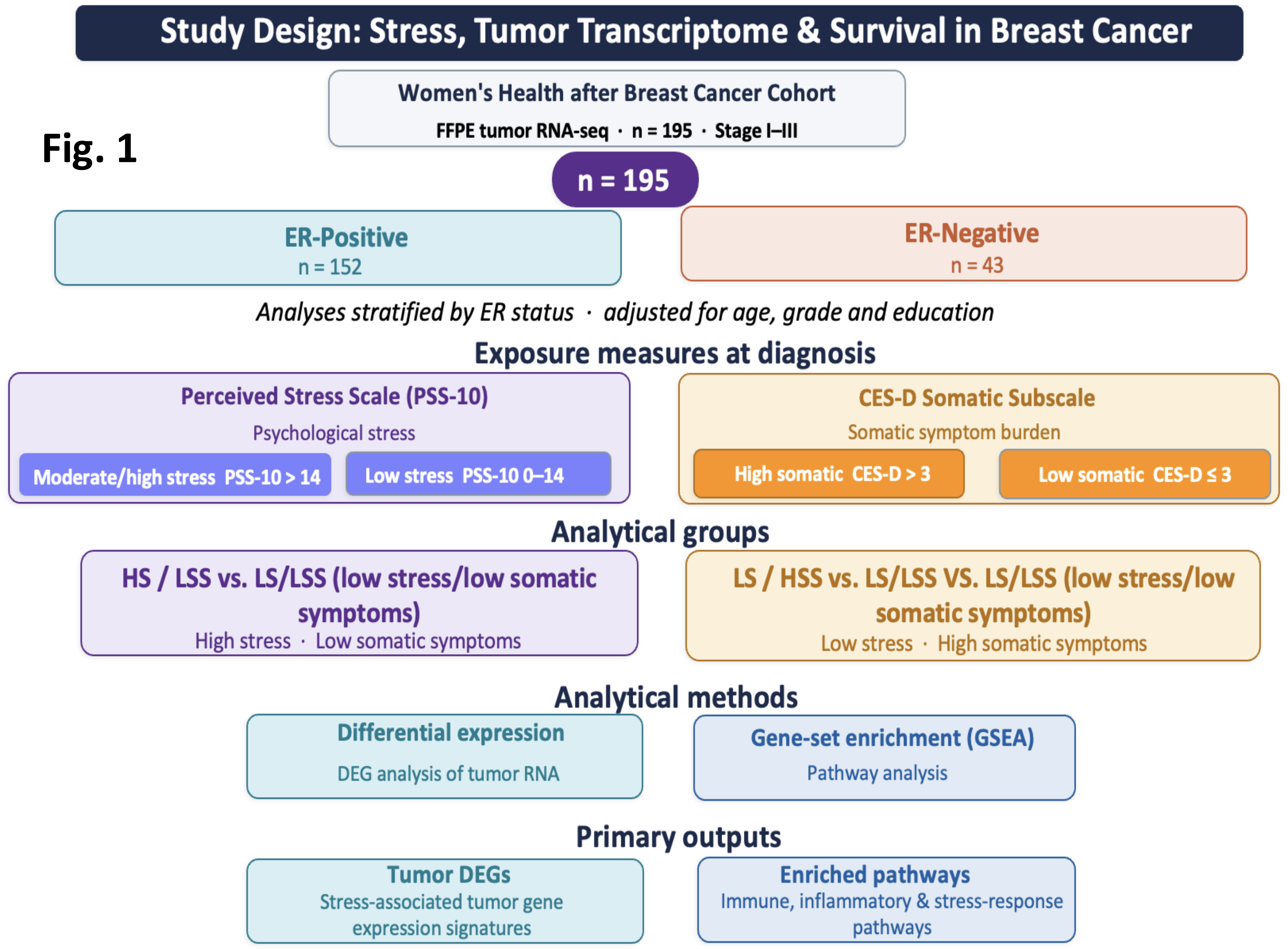
Background

- Chronic psychosocial distress may accelerate breast cancer progression by altering immune, inflammatory, and proliferative pathways, yet its genome-wide transcriptional effects in breast tumors remain unclear.
- This study uses RNA sequencing (RNA-seq) to characterize how distress influences transcriptional programs within the breast tumor microenvironment.

Methods

- FFPE tumor RNA sequencing was conducted in 195 women with stage I-III BC (152 ER+, 43 ER–) from the Women's Health after Breast Cancer cohort (**Figure 1**).
- Caris Life Sciences CODEai evaluated overall survival (OS), from tissue collection to last contact.

Fig. 1



Study Design: Stress, Tumor Transcriptome & Survival in Breast Cancer

Women's Health after Breast Cancer Cohort
FFPE tumor RNA-seq · n = 195 · Stage I–III

n = 195

ER-Positive
n = 152

ER-Negative
n = 43

Analyses stratified by ER status · adjusted for age, grade and education

Exposure measures at diagnosis

Perceived Stress Scale (PSS-10)
Psychological stress
Moderate/high stress PSS-10 > 14
Low stress PSS-10 0–14

CES-D Somatic Subscale
Somatic symptom burden
High somatic CES-D > 3
Low somatic CES-D ≤ 3

Analytical groups

HS / LSS vs. LS/LSS (low stress/low somatic symptoms)
High stress · Low somatic symptoms

LS / HSS vs. LS/LSS VS. LS/LSS (low stress/low somatic symptoms)
Low stress · High somatic symptoms

Analytical methods

Differential expression
DEG analysis of tumor RNA

Gene-set enrichment (GSEA)
Pathway analysis

Primary outputs

Tumor DEGs
Stress-associated tumor gene expression signatures

Enriched pathways
Immune, inflammatory & stress-response pathways

- *Patient-reported stress and depressive somatic symptoms map to distinct, ER-specific tumor transcriptional signatures involving immune regulation, proliferation, and differentiation.*
- *Concordant survival associations support potential clinical relevance and warrant validation to identify actionable targets.*

Results

Fig. 2A. ER+

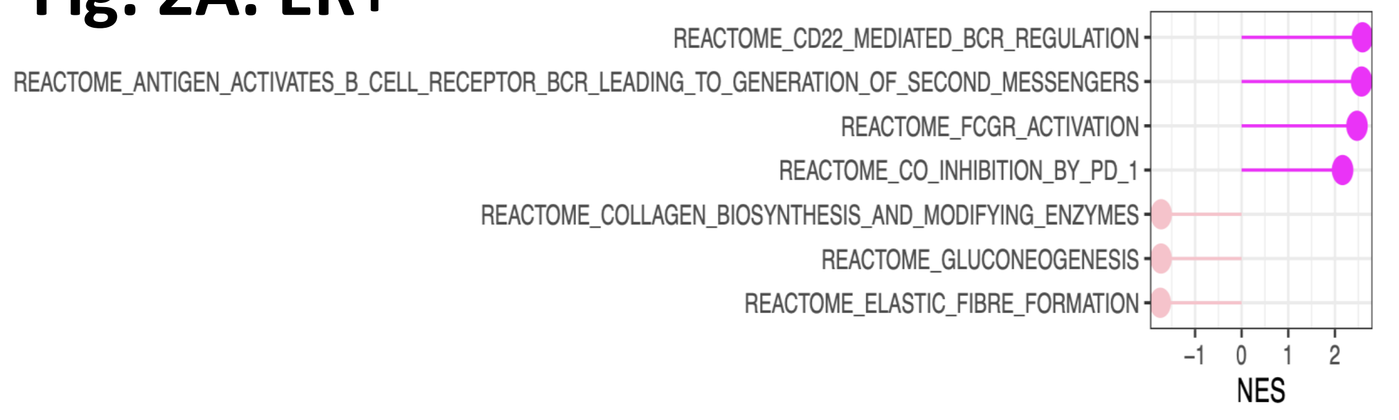


Fig. 2C. ER+

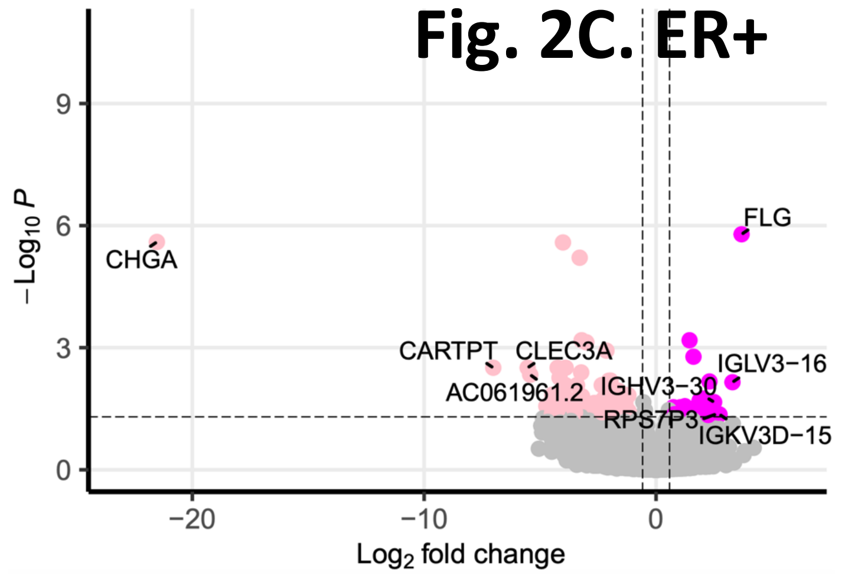


Fig. 2B. ER-

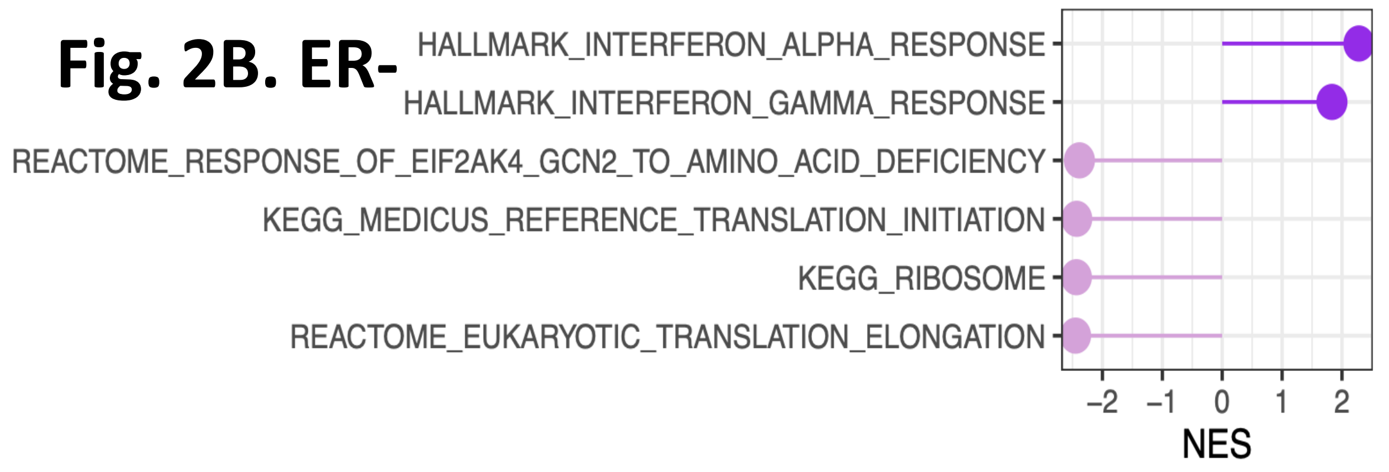


Fig. 2D. ER-

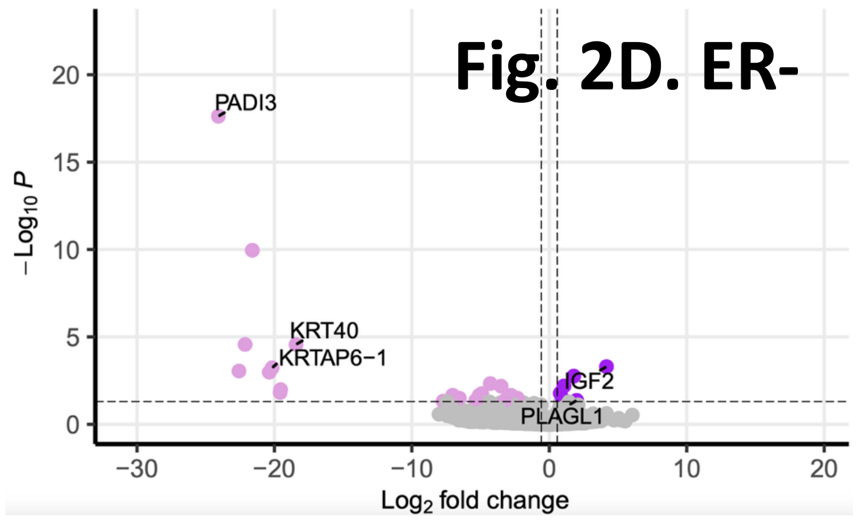


Fig. 2. Key up- and down-regulated signatures (GSEA and DEG) in **high stress/low somatic symptom group** (HS/LSS) vs. low stress/low somatic symptom (LS/LSS) group. GSEA in ER+ **(A)** and ER negative **(B)**. Volcano plots in **(C)** ER+ and **(D)** ER negative. ER positive: increased humoral-immune activity and checkpoint signatures, with reduced neuroendocrine activation. ER negative: growth-factor-driven proliferation with reduced epithelial differentiation and greater immune activation.

Fig. 3A. ER+

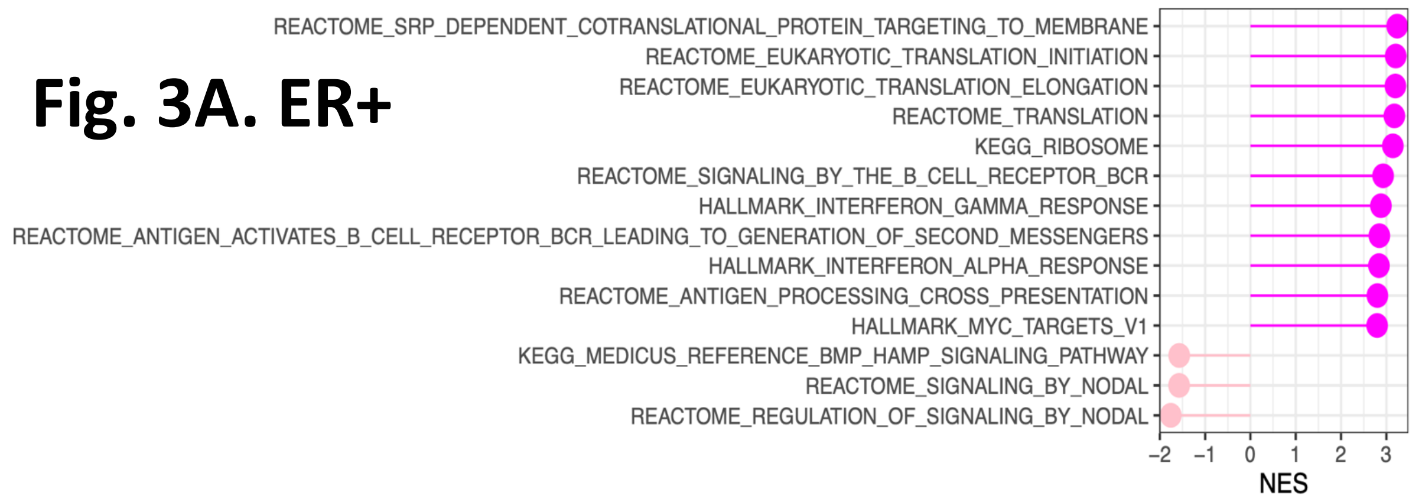
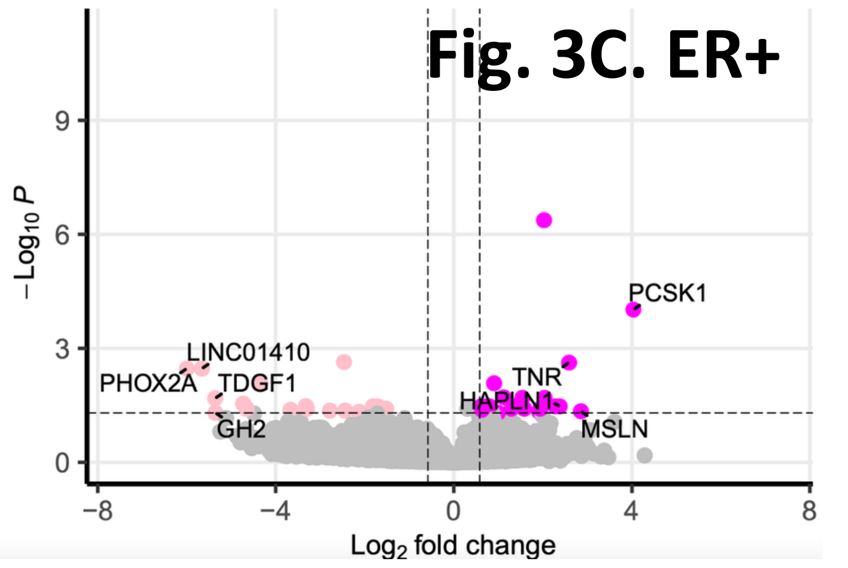


Fig. 3C. ER+



Results

Fig. 3B. ER-

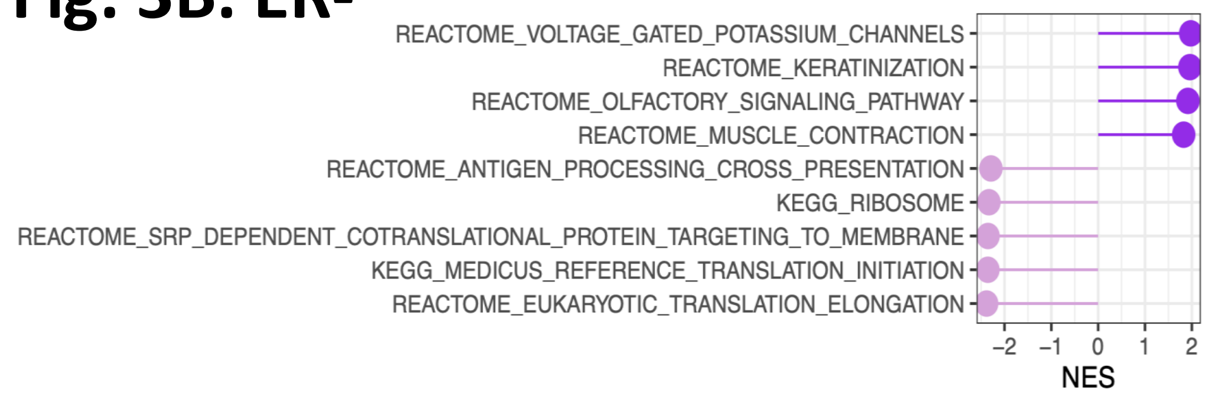


Fig. 3D. ER-

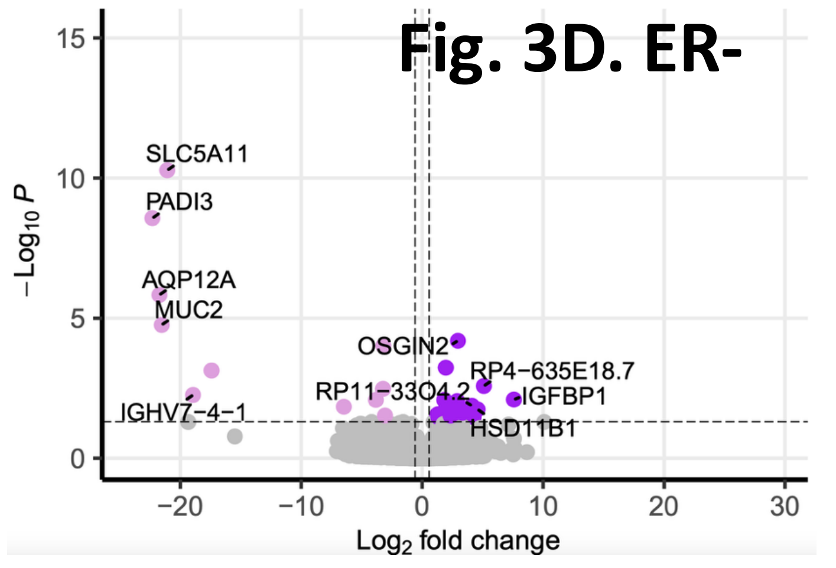
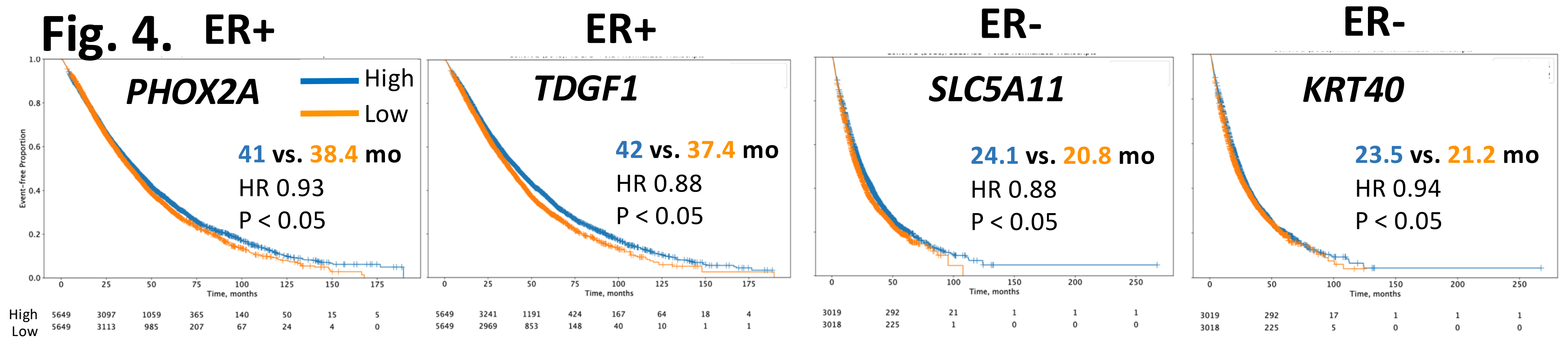


Fig. 3. Key up- and down-regulated signatures (GSEA and DEG) in **low stress/high somatic symptom group** (LS/HSS) vs. low stress/low somatic symptom (LS/LSS) group. GSEA in ER+ **(A)** and ER negative **(B)**. Volcano plots in **(C)** ER+ and **(D)** ER negative. ER positive: enriched for ribosome biogenesis, immune and cell-cycle pathways, with loss of epithelial regulatory programs. ER negative: Loss of epithelial/immune programs and increased keratinization, consistent with impaired antigen presentation and altered differentiation.

- Using Caris Life Sciences CODEai, overall survival associated with select genes was calculated from tissue collection to last contact in ER+ (n=11,309) and ER negative (n=6,402) tumors (**Fig. 4**).

Fig. 4.



Acknowledgements

- Funding: R03TR004607, K08CA279766
- For any questions, please contact Shipra Gandhi (Shipra.Gandhi@emory.edu) or Chi-Chen Hong (chi-chen.hong@roswellpark.org