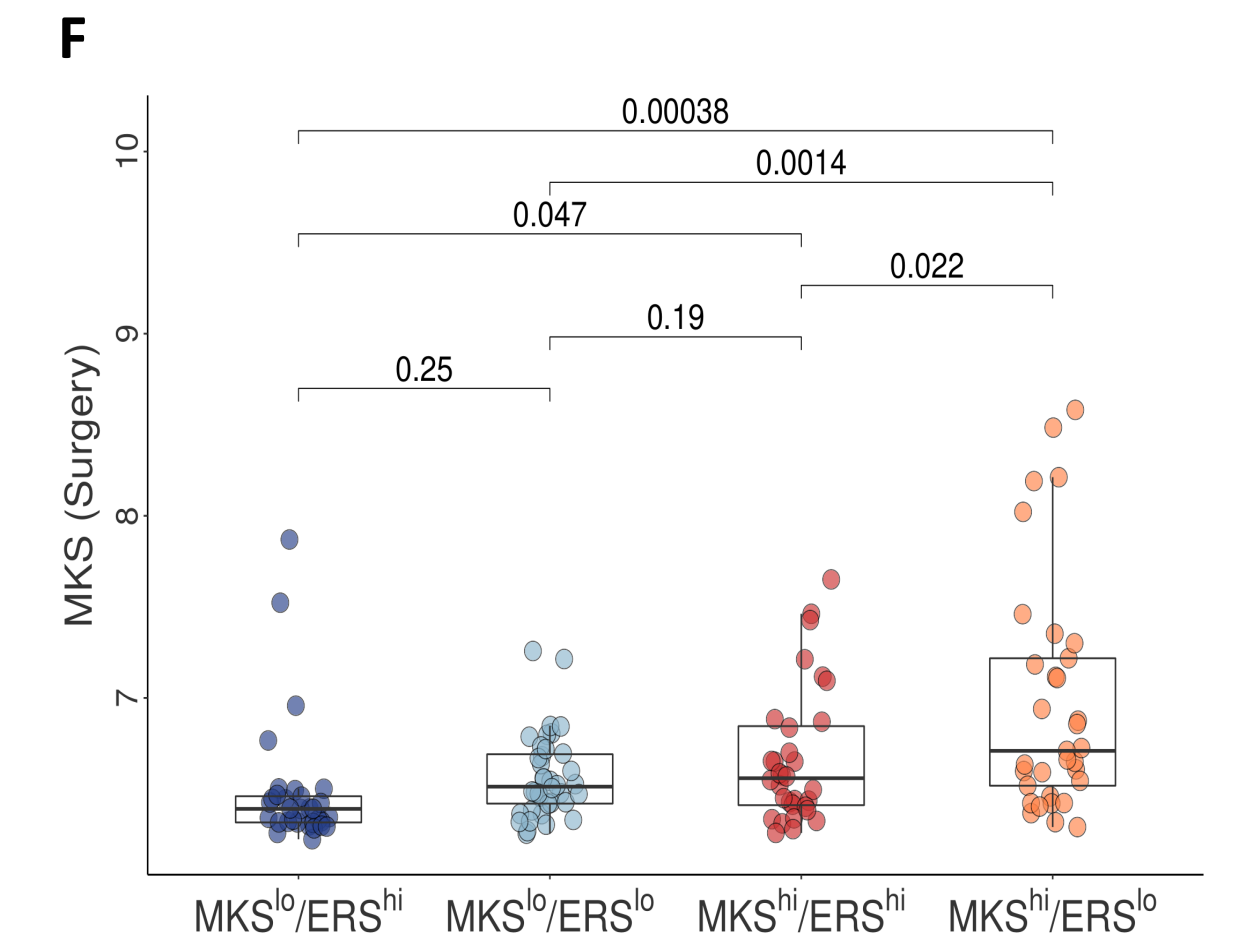
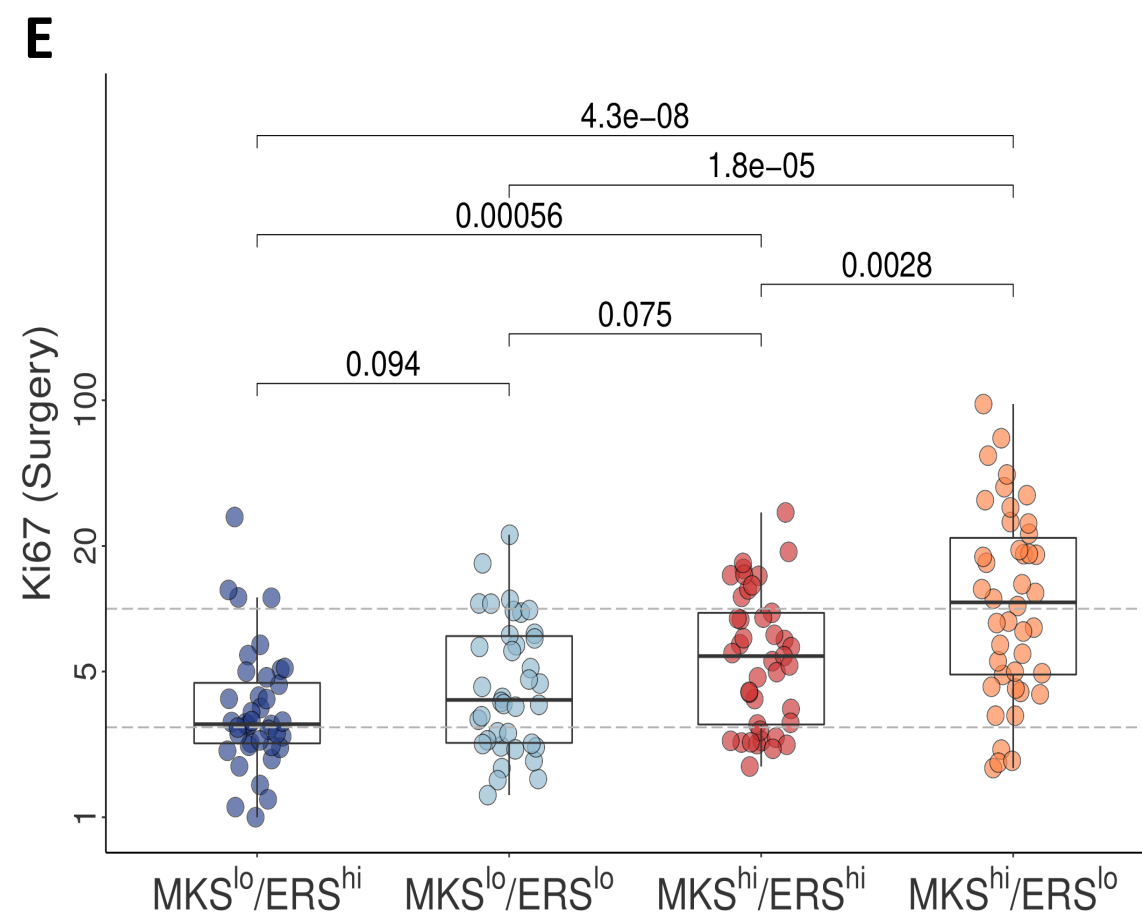
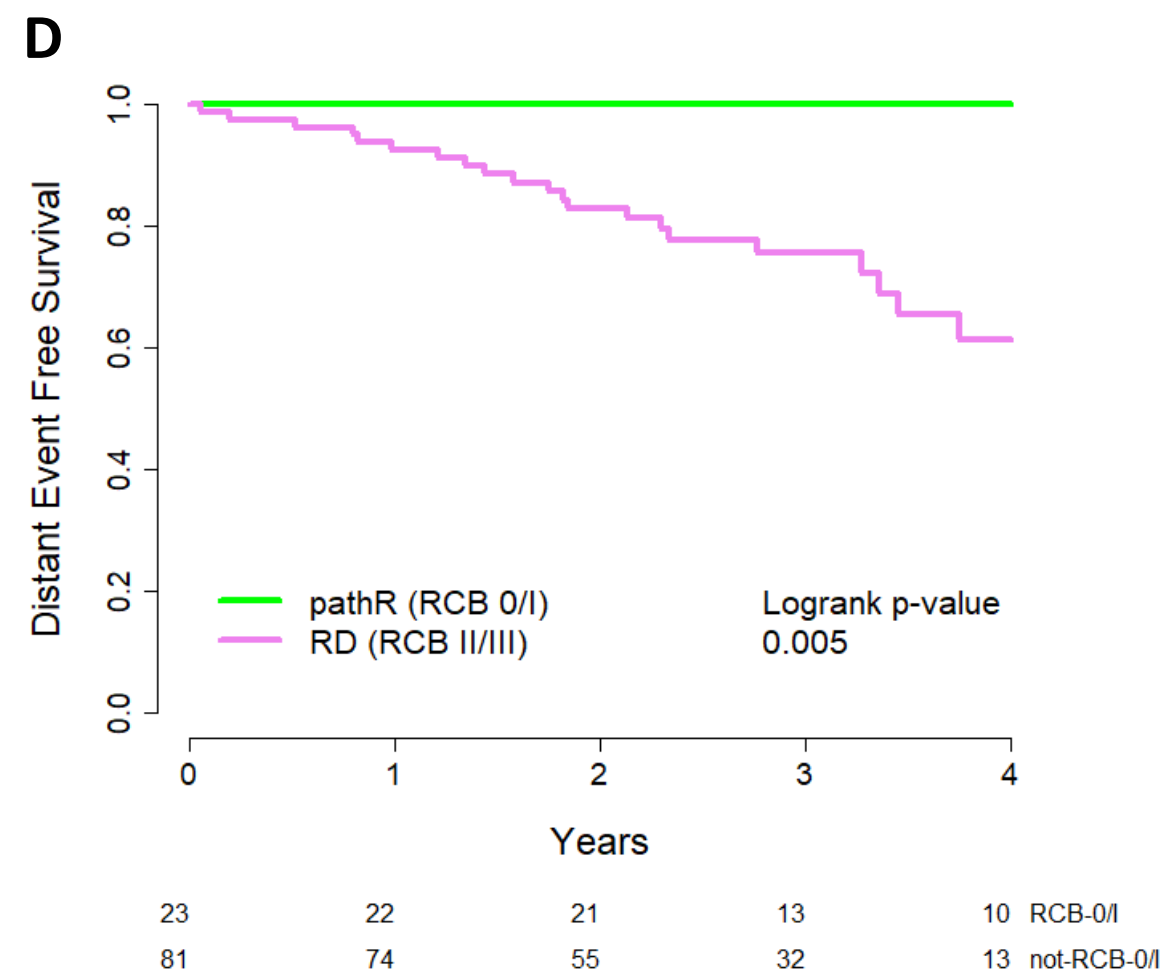
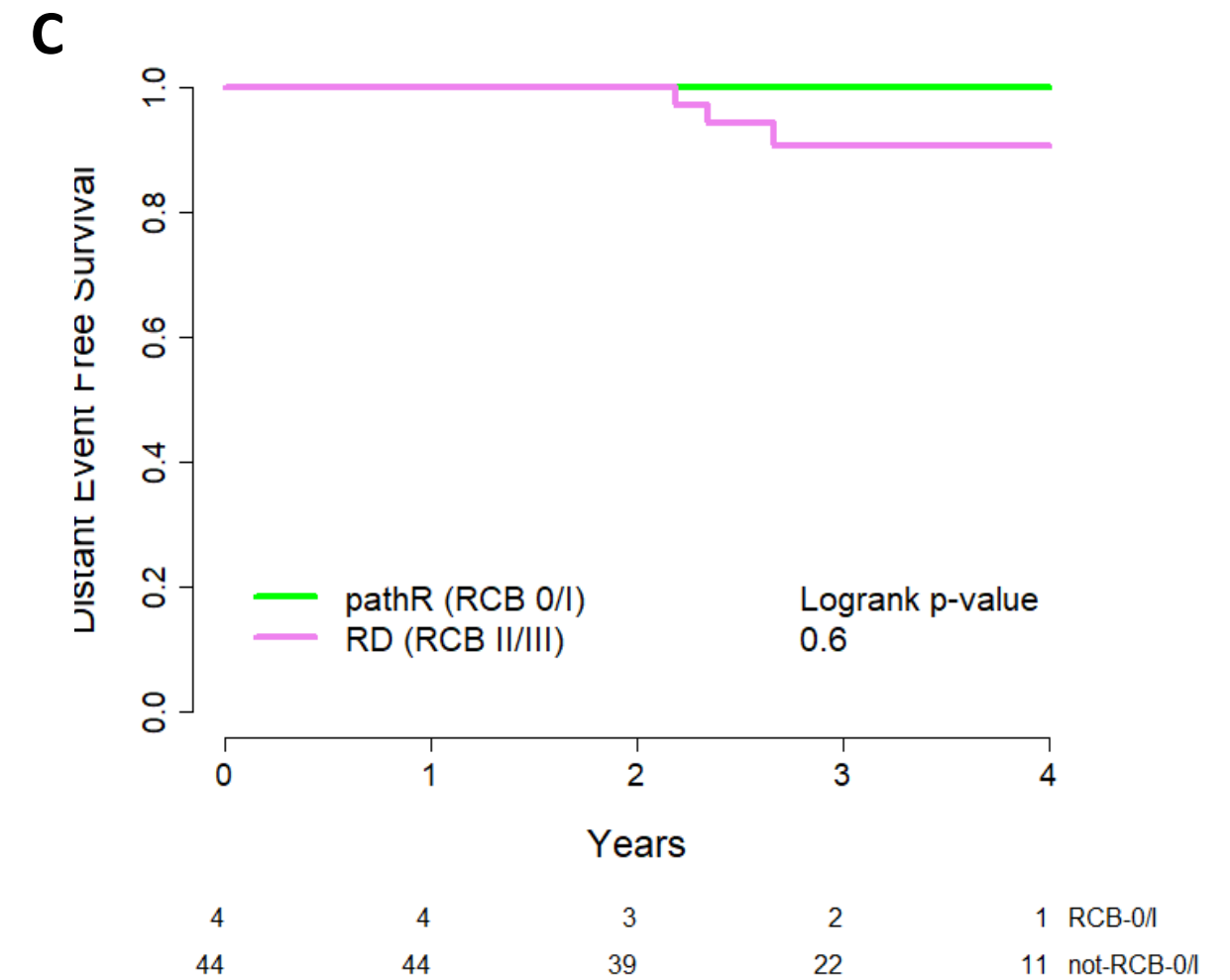
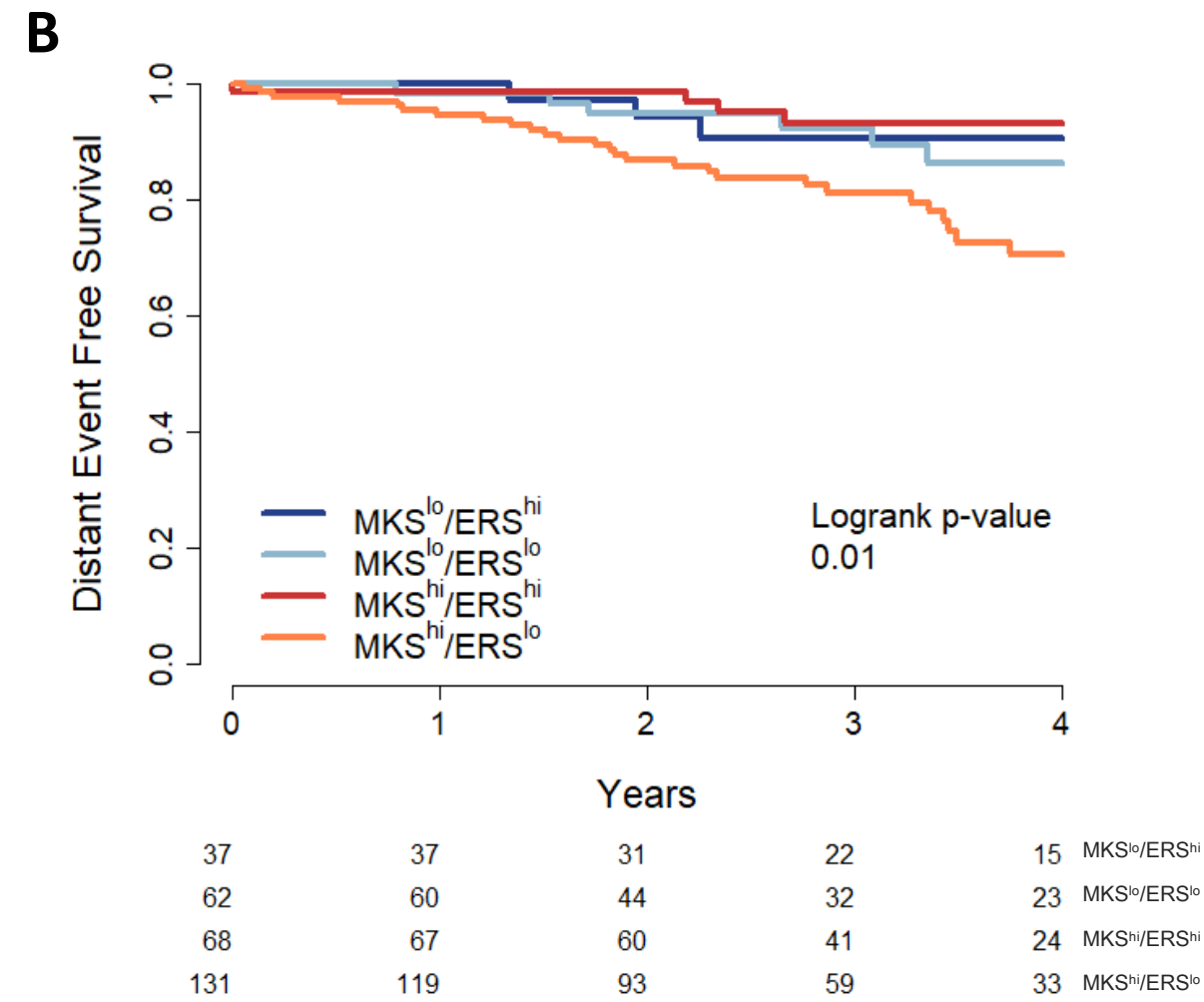
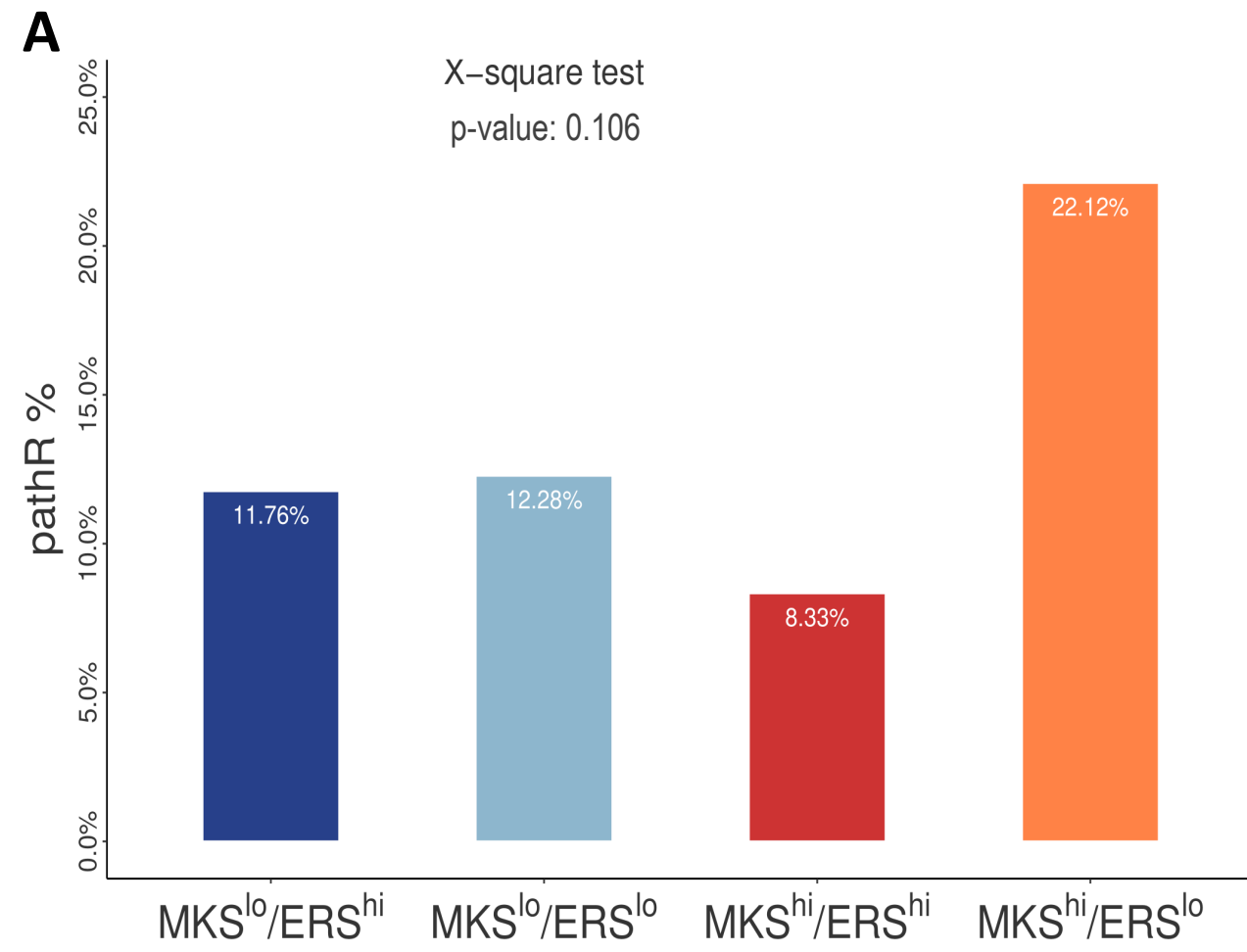
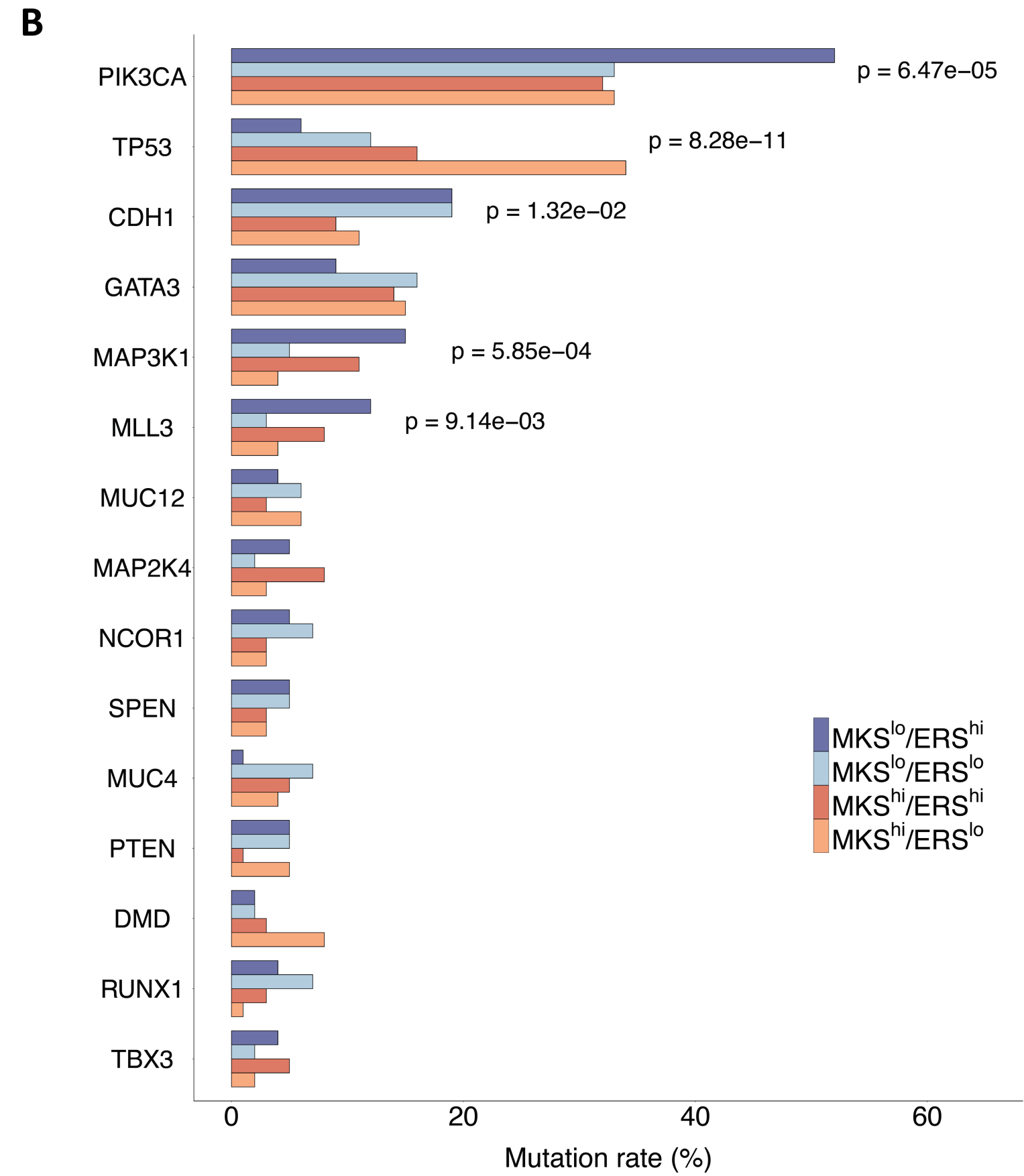
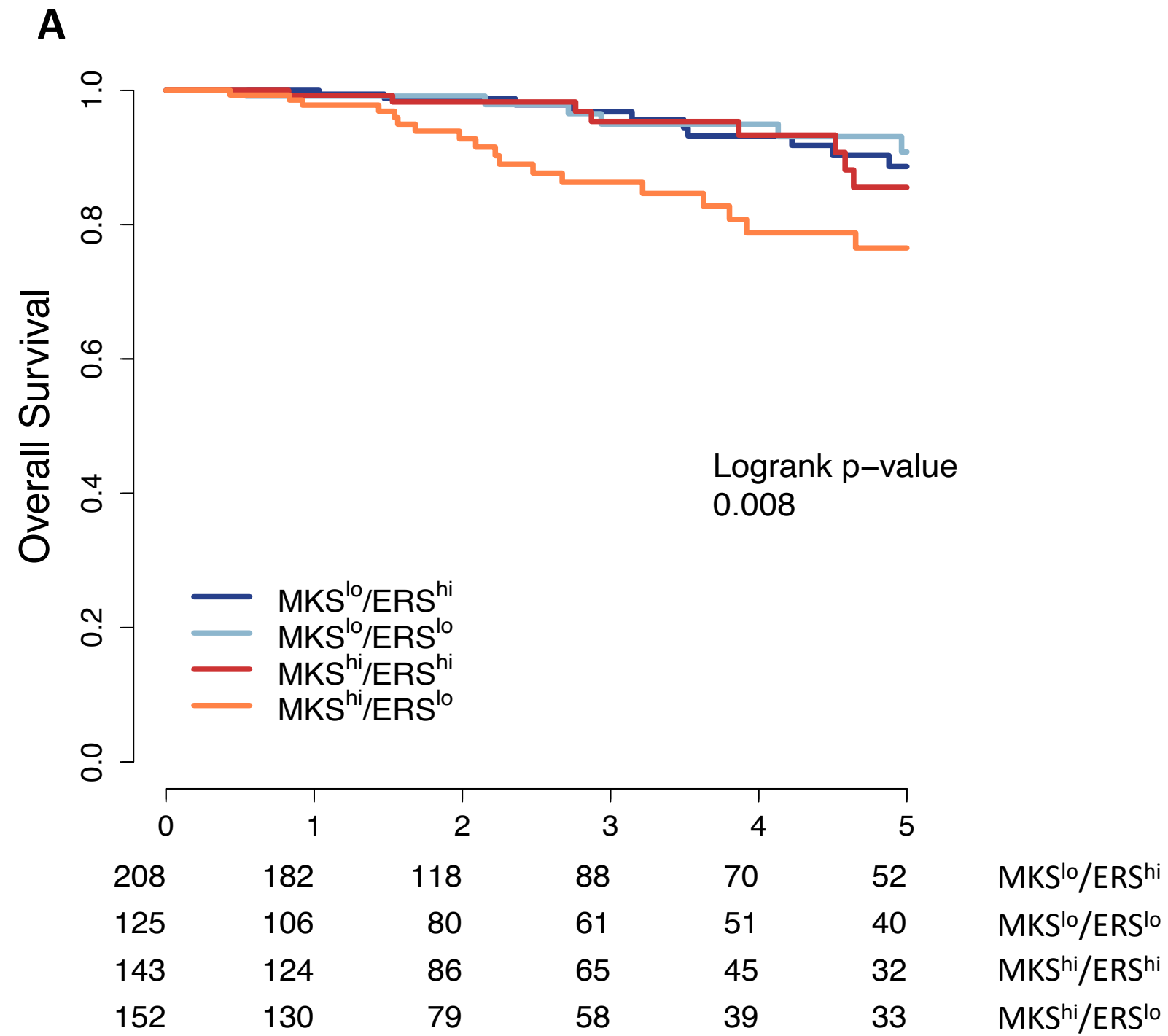


Supplementary Figure 1. Clinical and pathological outcomes of patients treated with neoadjuvant systemic therapy stratified according to MKS and ERS status
A, B) PathR rates **(A)** and 4-year distant event-free survival rates **(B)** in patients receiving taxane-anthracycline-based neoadjuvant chemotherapy at MD Anderson Cancer Center. **C, D)** 4-year distant event-free survival rates in patients with MKS^{hi}/ERS^{hi} **(C)** and MKS^{hi}/ERS^{lo} **(D)** tumors according to pathological response. **E, F)** Ki67 levels **(E)** and MKS expression **(F)** at surgery in patients receiving neoadjuvant AI in the POETIC study.

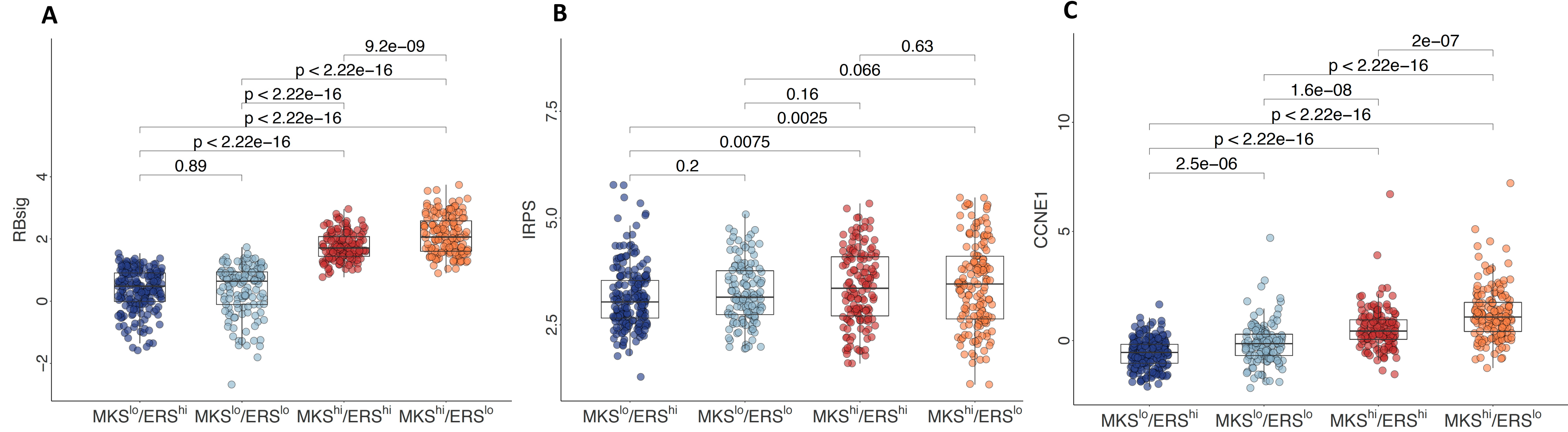


Supplementary Figure 2. Clinical outcomes and genomic alterations of ER+/HER2- tumors stratified according to MKS and ERS status in TCGA

A) 5-year Overall Survival. B) Most frequently mutated genes

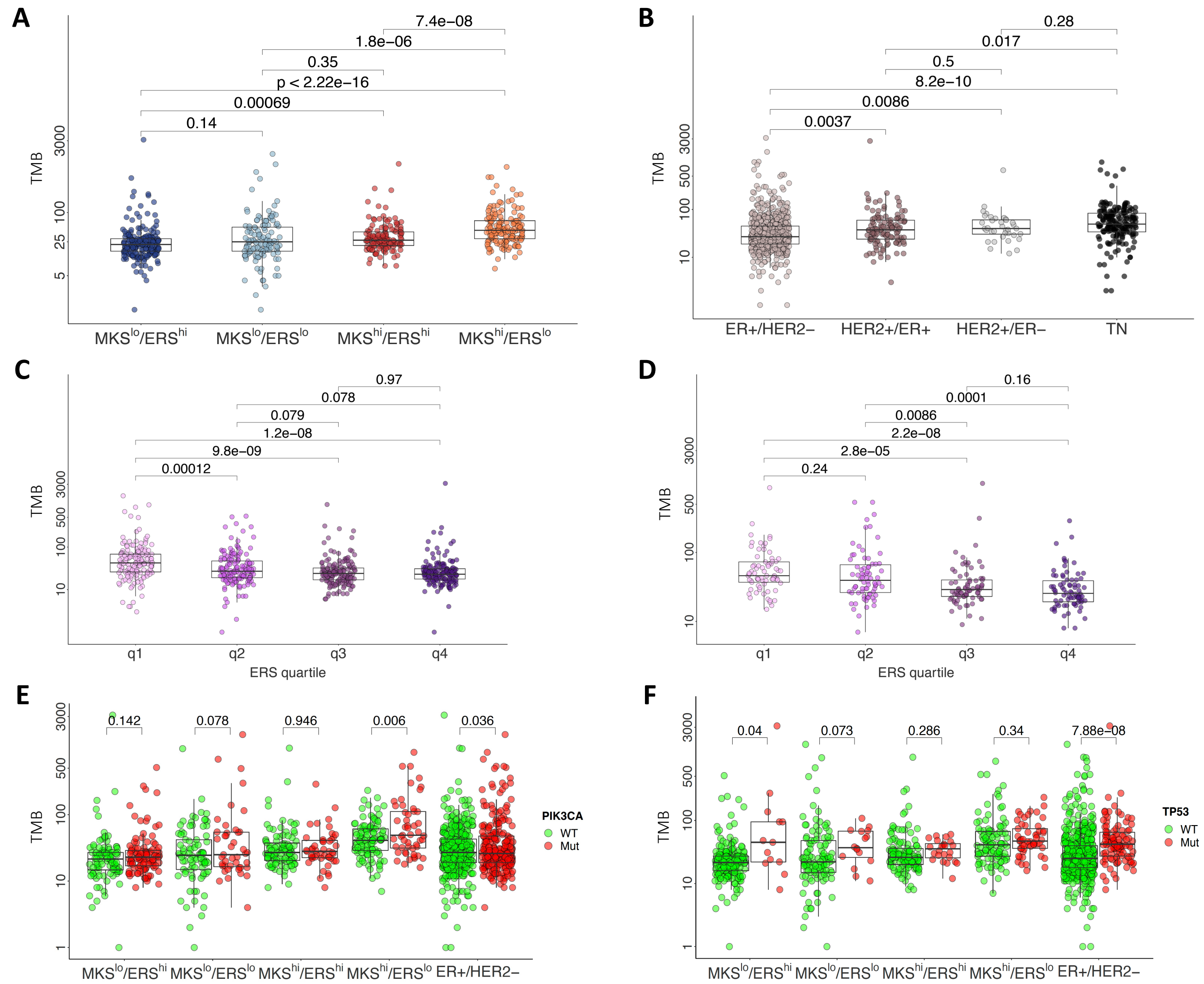


Supplementary Figure 3. Expression of potential predictive biomarkers for CDK4/6 inhibitors in ER+/HER2- tumors stratified according to MKS and ERS status in the TCGA dataset. A) RB signature expression levels. B) Interferon-Related Palbociclib-Resistance Signature expression levels. C) Cyclin E expression levels

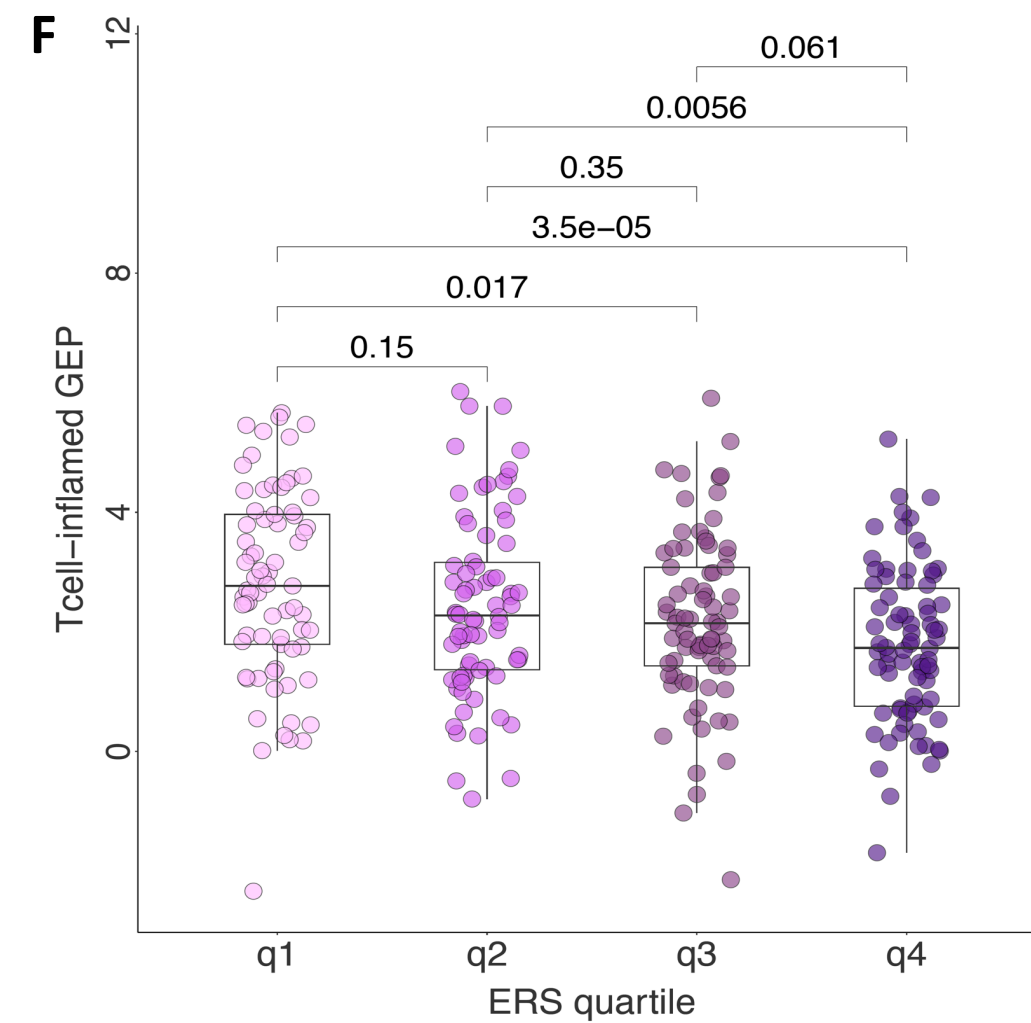
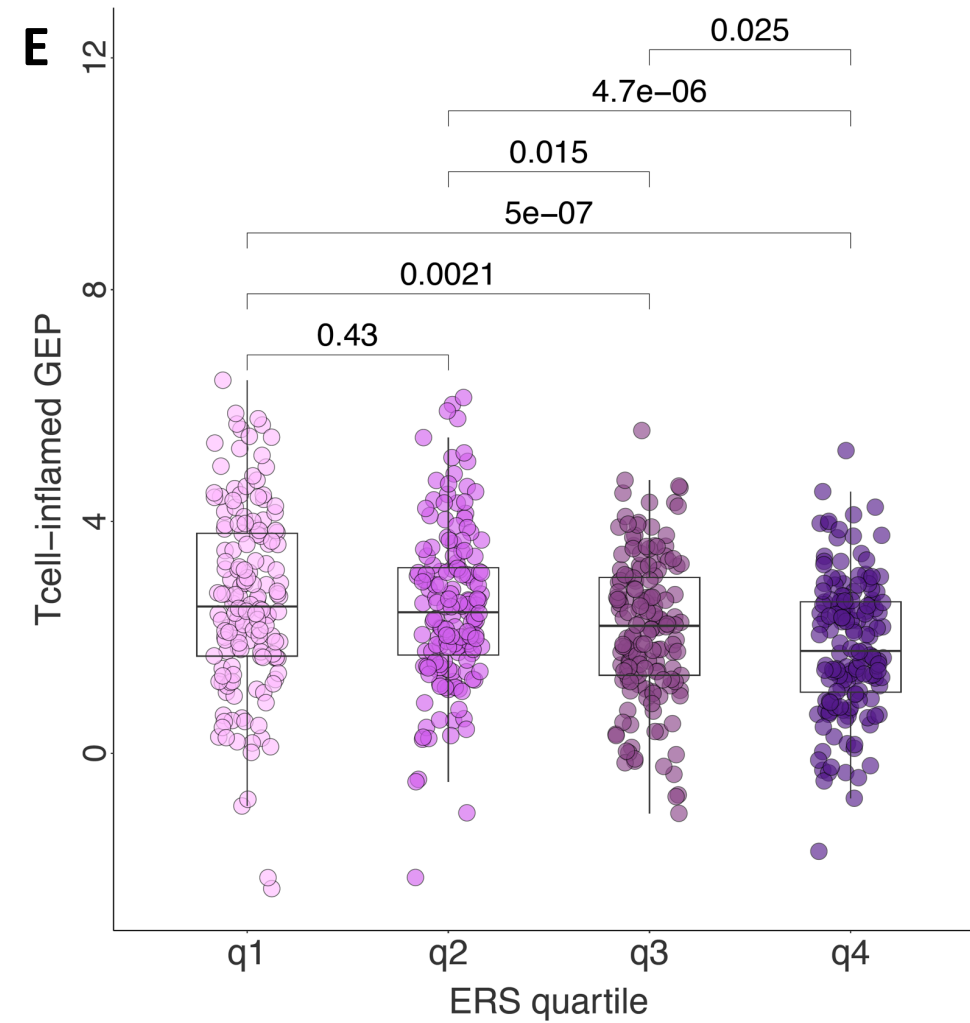
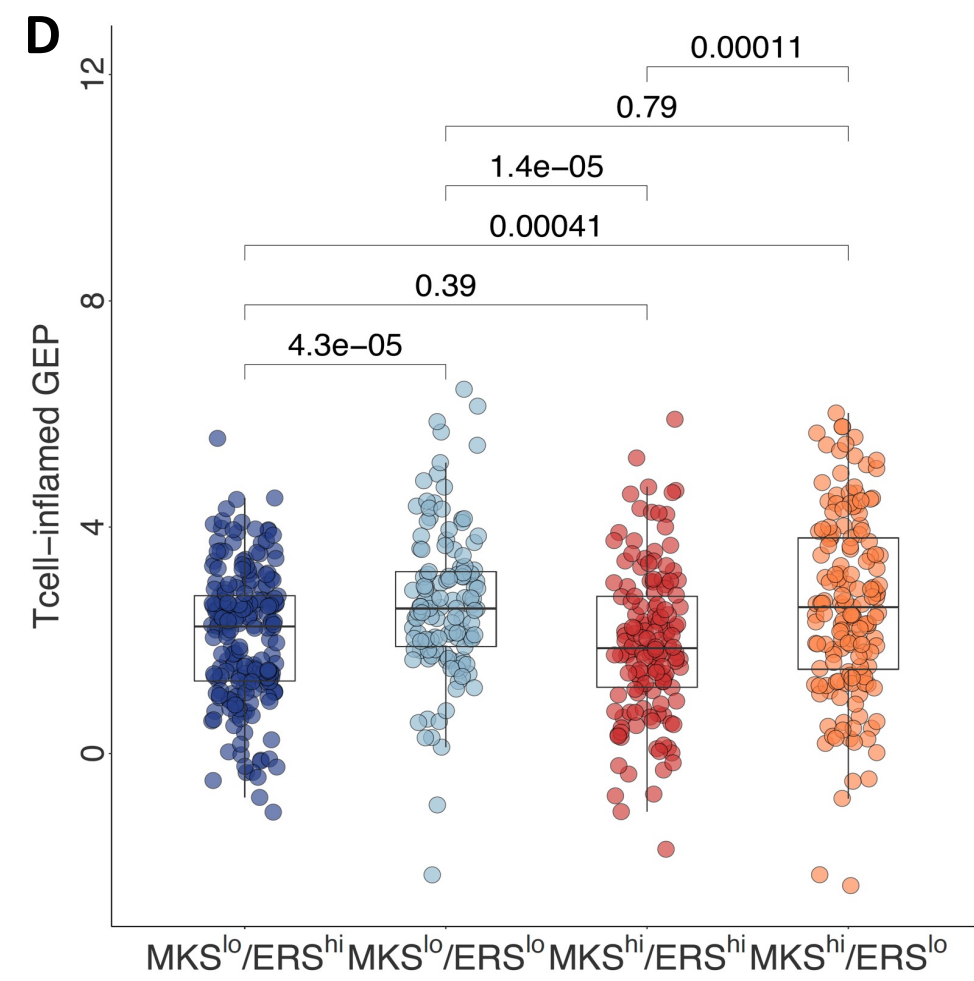
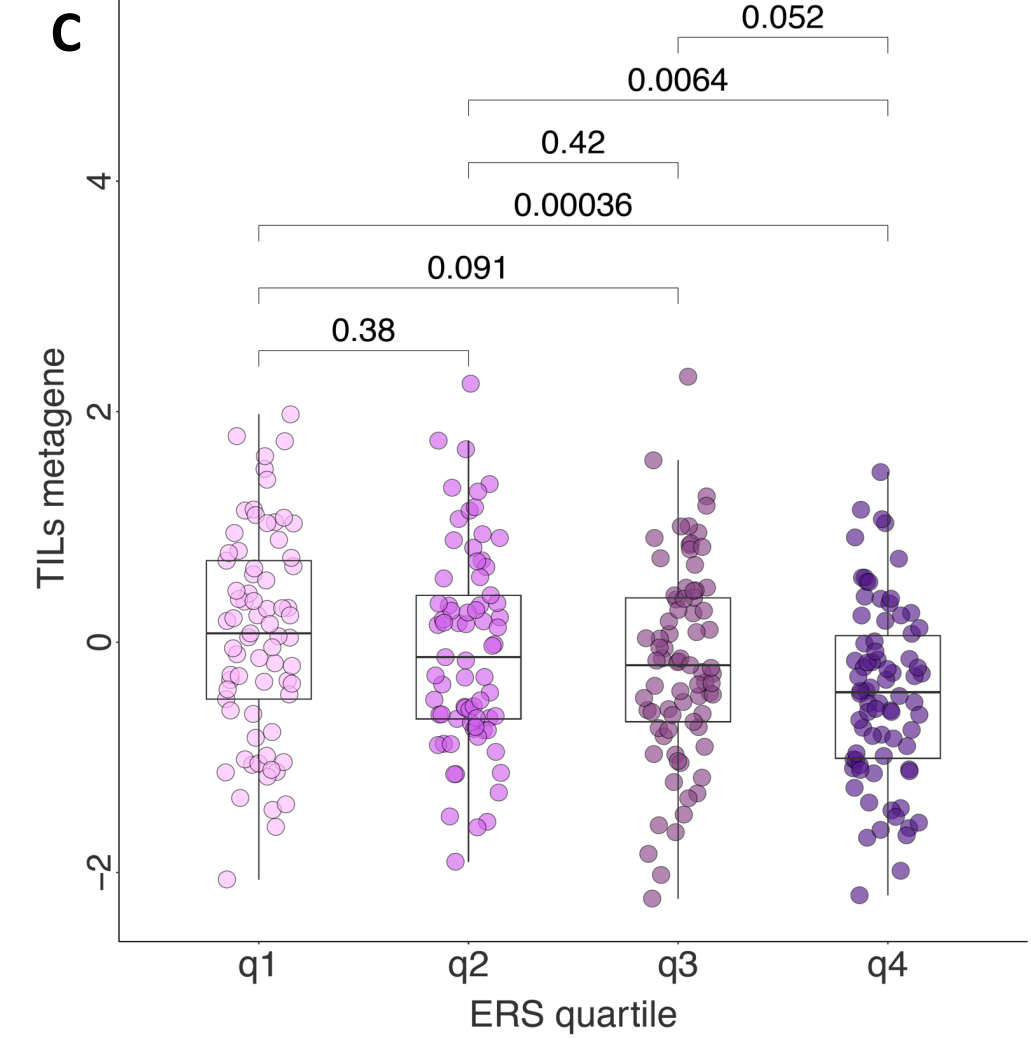
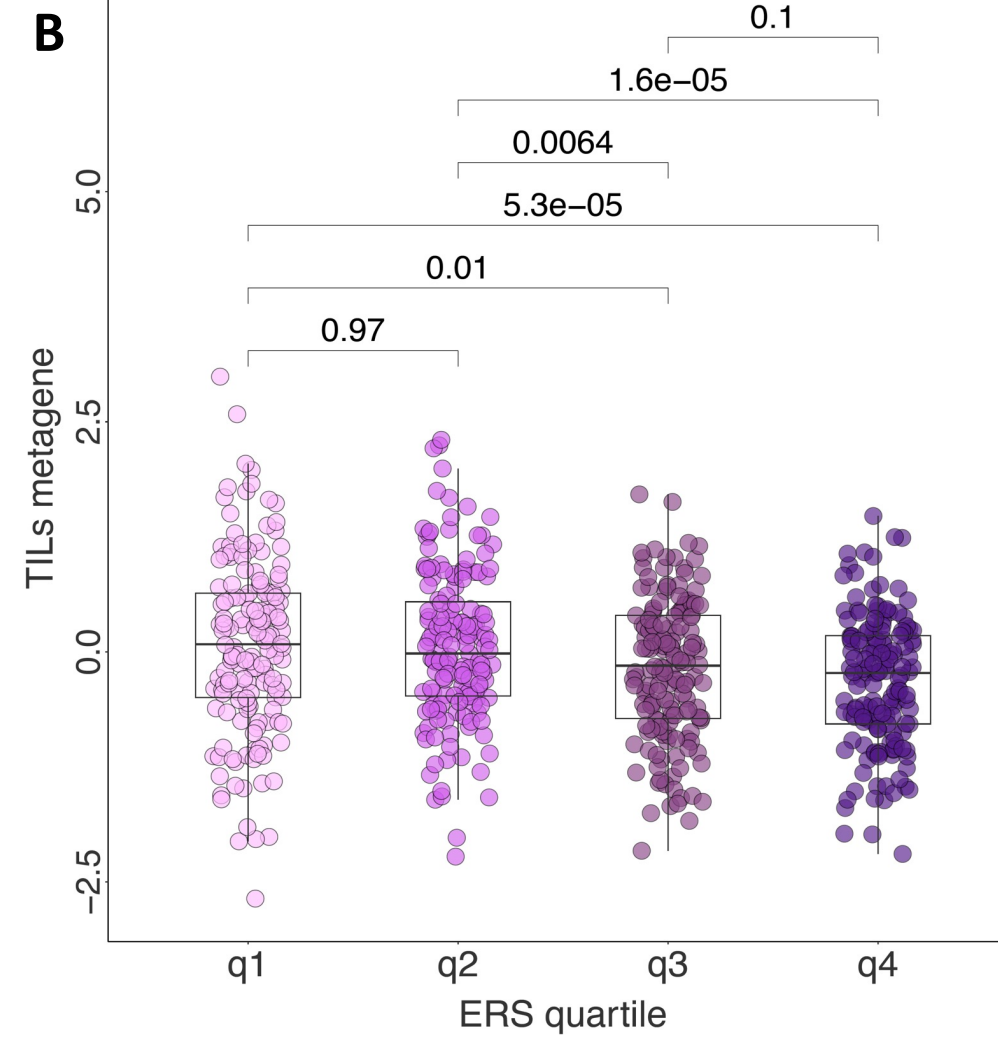
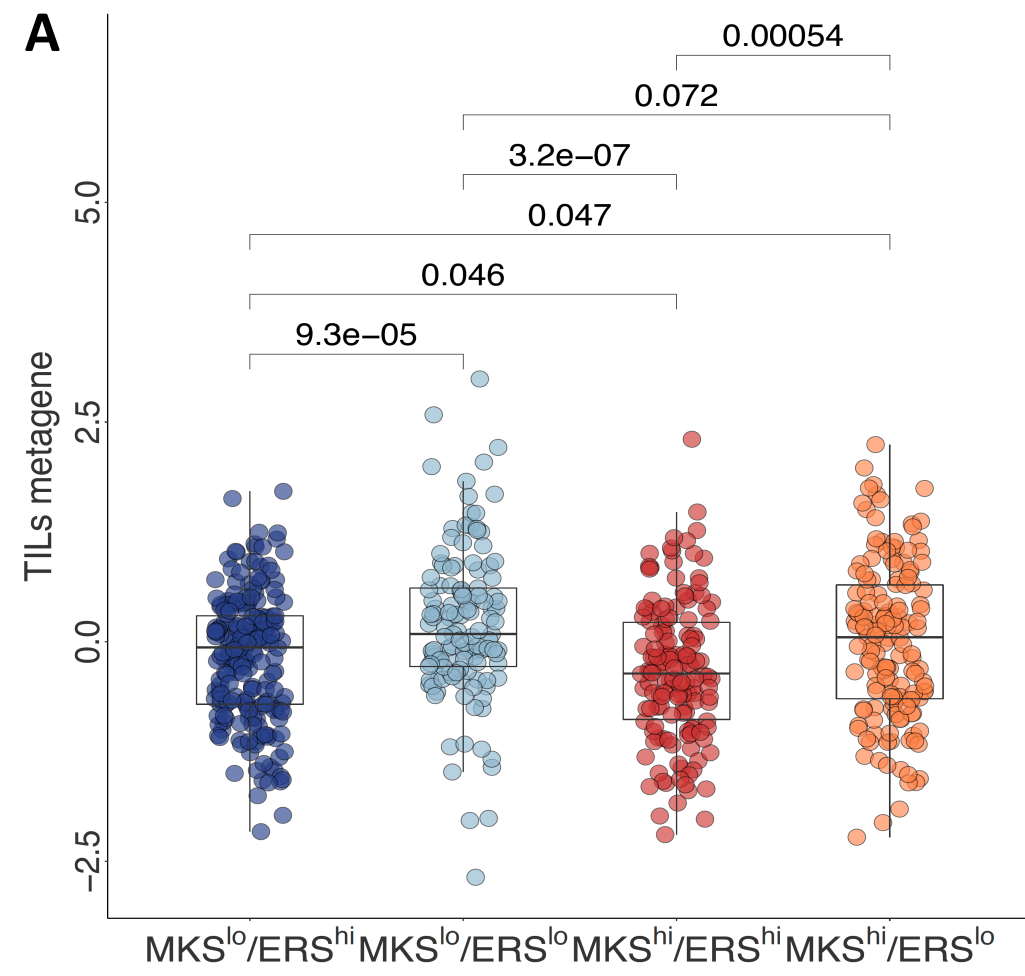


Supplementary Figure 4. Tumor mutational burden (TMB) in breast cancer subgroups in TCGA.

A) TMB in ER+/HER2- tumors stratified according to MKS and ERS status. **B)** TMB in the whole breast cancer cohort stratified according to ER and HER2 status. **C)** TMB in ER+/HER2- tumors stratified according to ERS quartiles. **D)** TMB in MKS^{hi} tumors stratified according to ERS quartiles. **E, F)** TMB in ER+/HER2- tumors (whole cohort and molecular subgroups) stratified according to PIK3CA (**E**) and TP53 (**F**) mutation status



Supplementary Figure 5. Expression of potential predictive biomarkers for immune checkpoint inhibitors in ER+/HER2- tumors in TCGA dataset. TILs metagene (A, B, C) and T cell-inflamed GEP (D, E, F) expression levels in ER+/HER2- tumors stratified according to MKS and ERS status (A and C), in ER+/HER2- tumors stratified according to ERS quartiles (B and D), in MKS^{hi} tumors stratified according to ERS quartiles (C and F)



Supplementary Figure 6. Distribution of ER (A) and PgR (B) expression levels by IHC within MKS^{hi}/ERS^{hi} (red bars) and MKS^{hi}/ERS^{lo} (orange bars) tumors in TCGA

