Expanded View Figures

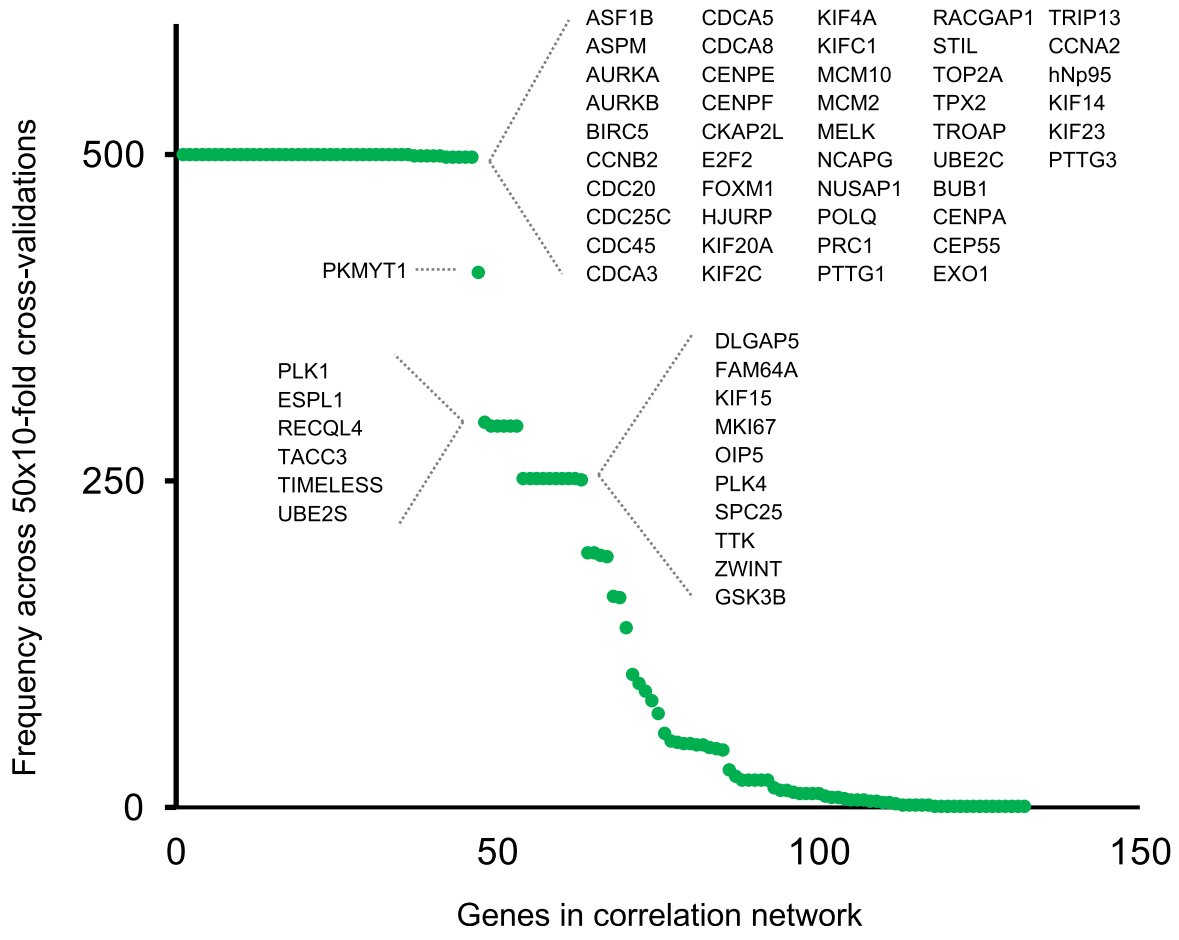
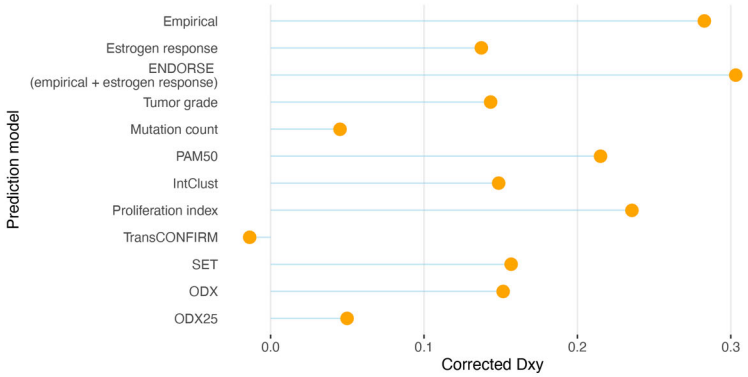


Figure EV1. Frequency of genes appearing in the 500 correlation networks generated across 50 × 10-fold cross-validations of the LASSO-regularized Cox proportional hazards model in the METABRIC cohort.

Y-axis represents frequency, and X-axis indicates index of unique genes. Genes on the top left appeared in all 500 cross-validations, whereas genes at the bottom right appeared only once. Genes appearing in at least 250 networks are marked on the plot.

METABRIC cohort (ER+/HER2-, n = 833)

A Prediction model validation (bootstrap resampling, B=150)



B Model comparisons

Model 1	*Model 2*	***Variance test*** *H1: Model 1 and Model 2 are distinguishable*	***Likelihood ratio test (nested)*** *H1A: Full model fits better than reduced model*	***Partial likelihood ratio test (non-nested)*** *H1A: Model 1 fits better than Model 2*
ENDORSE	Empirical	1.47×10^{-3}	1.09×10^{-3}	
	Estrogen response	3.83×10^{-6}	3.93×10^{-14}	
	METABRIC tumor characteristics and signatures			
	Tumor grade	$< 2 \times 10^{-16}$		2.08 x 10-3
	Mutation count	$< 2 \times 10^{-16}$		9.76 x 10-6
	PAM50	2.22 x 10-8		0.033
	IntClust	$< 2 \times 10^{-16}$		0.02
	Proliferation index	3.73×10^{-5}		4.42×10^{-5}
	External signatures			
	TransCONFIRM	1.67×10^{-7}		9.73×10^{-6}
	SET	$< 2 \times 10^{-16}$		3.53×10^{-5}
	ODX	2.18×10^{-7}		6.15×10^{-5}
	ODX25	1.49×10^{-6}		1.32×10^{-5}

Figure EV2. Model evaluation and comparison with other predictors in METABRIC.

A Lollipop plots displaying corrected Somer's D_{xy} indices of ENDORSE and various other univariate Cox proportional hazards models. The indices were calculated using 150-fold bootstrap resampling of the training dataset.

B Table comparing the ENDORSE model with various other univariate Cox models using partial likelihood ratio tests. The comparison between the nested ENDORSE model and its two components was performed using a likelihood ratio test, while other non-nested univariate models were compared using a partial likelihood ratio test.

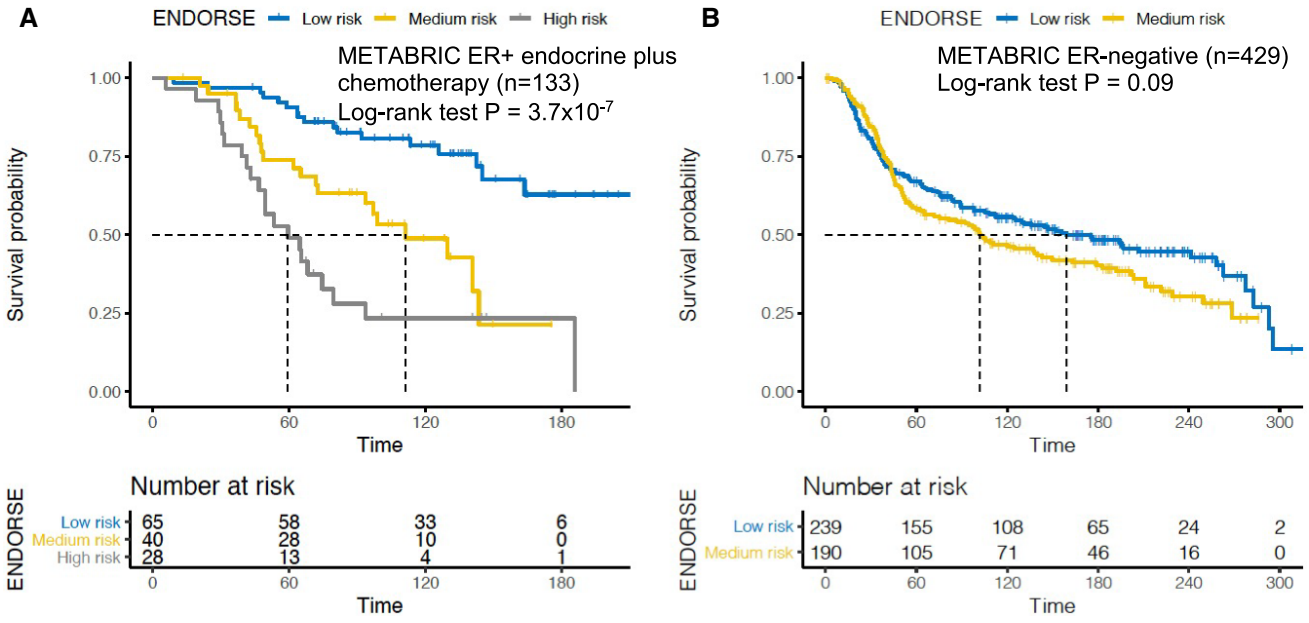


Figure EV3. ENDORSE evaluation in ER$^+$ tumors receiving chemotherapy and ER- tumors.

A, B Kaplan–Meir recurrence-free survival curves and risk tables of METARBIC cohort ER$^+$ patients that received endocrine therapy in (A) combination with chemotherapy (n = 133) and (B) METABRIC ER$^-$ patients (n = 429). In each analysis, the patients were stratified according to ENDORSE predicted risk scores. P-values were obtained using log-rank tests.

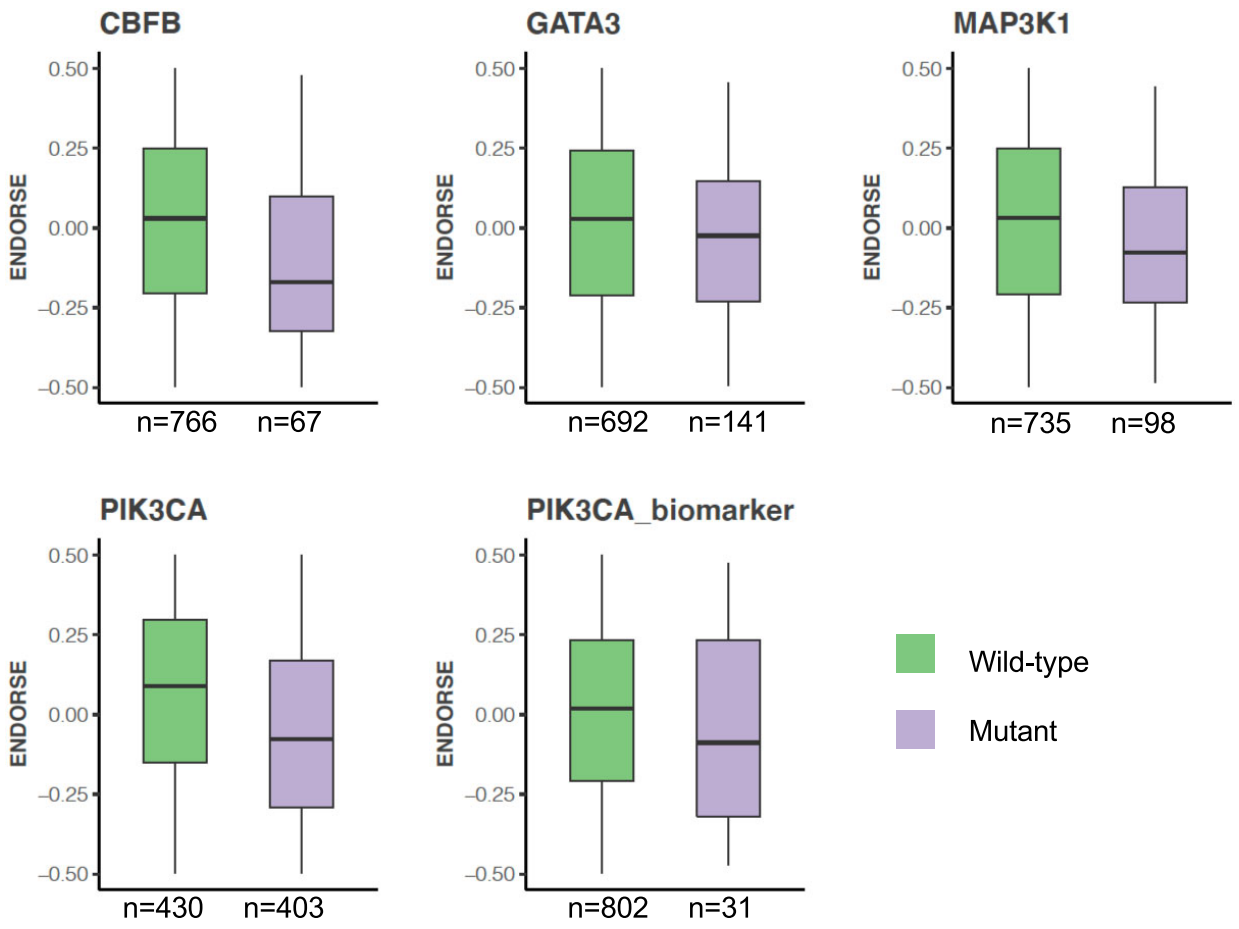


Figure EV4. Somatic variants associated with ENDORSE scores.

Boxplots showing ENDORSE predicted risk scores in METABRIC that were significantly different in mean values (false discovery rate-adjusted $P < 0.05$) in samples grouped by mutation status of cancer genes. The colored boxes display interquartile range with median, while the whiskers show 1.5 × interquartile range, with each sample representing a biological replicate. The numbers of wild type and mutated tumors serving as biological replicates are annotated below the boxplots for each gene.

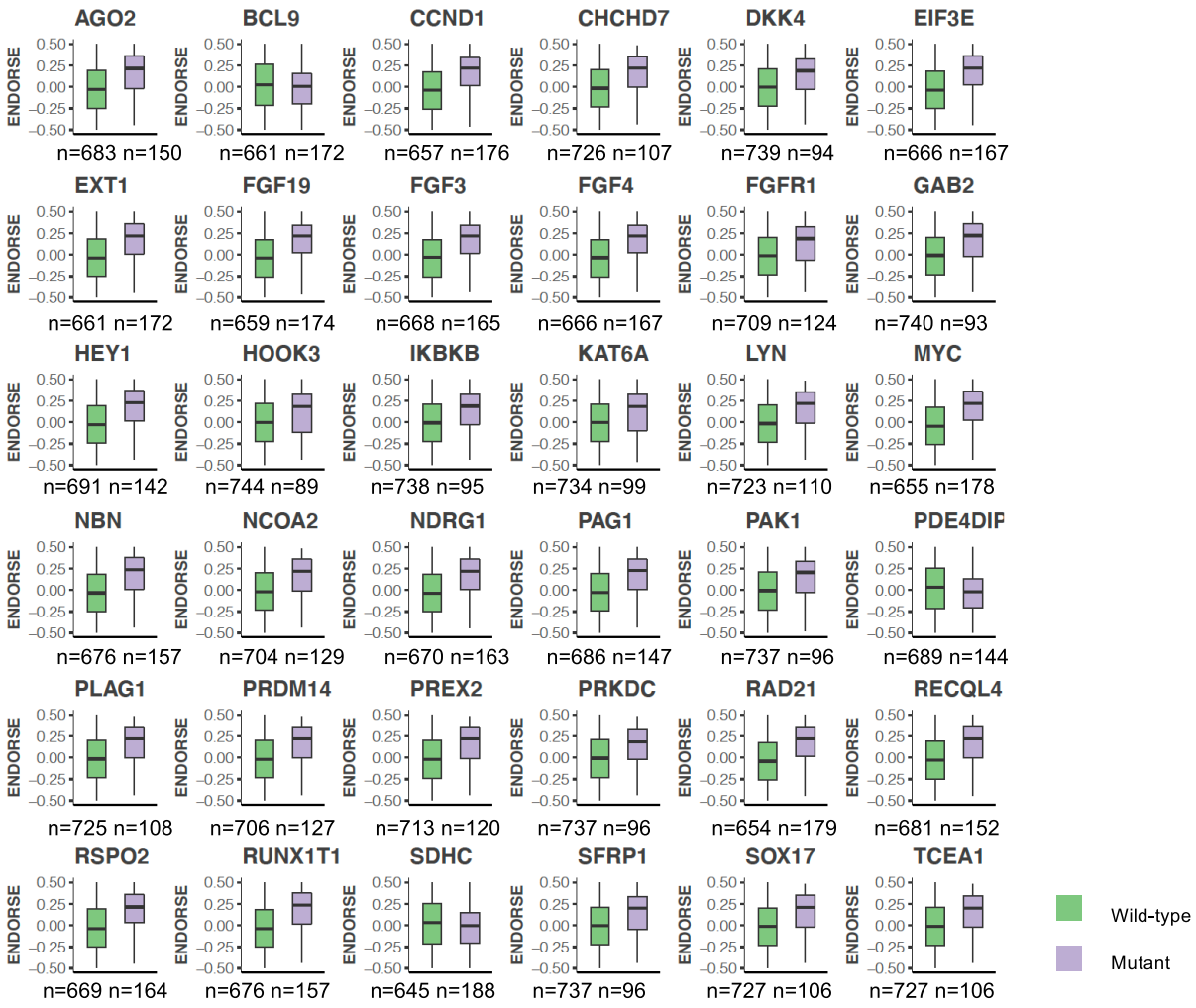


Figure EV5. Copy number amplifications associated with ENDORSE scores.

Boxplots showing ENDORSE predicted risk scores in METABRIC that were significantly different in mean values (false discovery rate-adjusted $P < 0.05$) in samples grouped by copy number amplification status of cancer genes. The colored boxes display interquartile range with median, while the whiskers show 1.5 × interquartile range. The numbers of wild type (no gain) and mutated (copy number amplified) tumors serving as independent biological replicates are annotated below the boxplots for each gene.