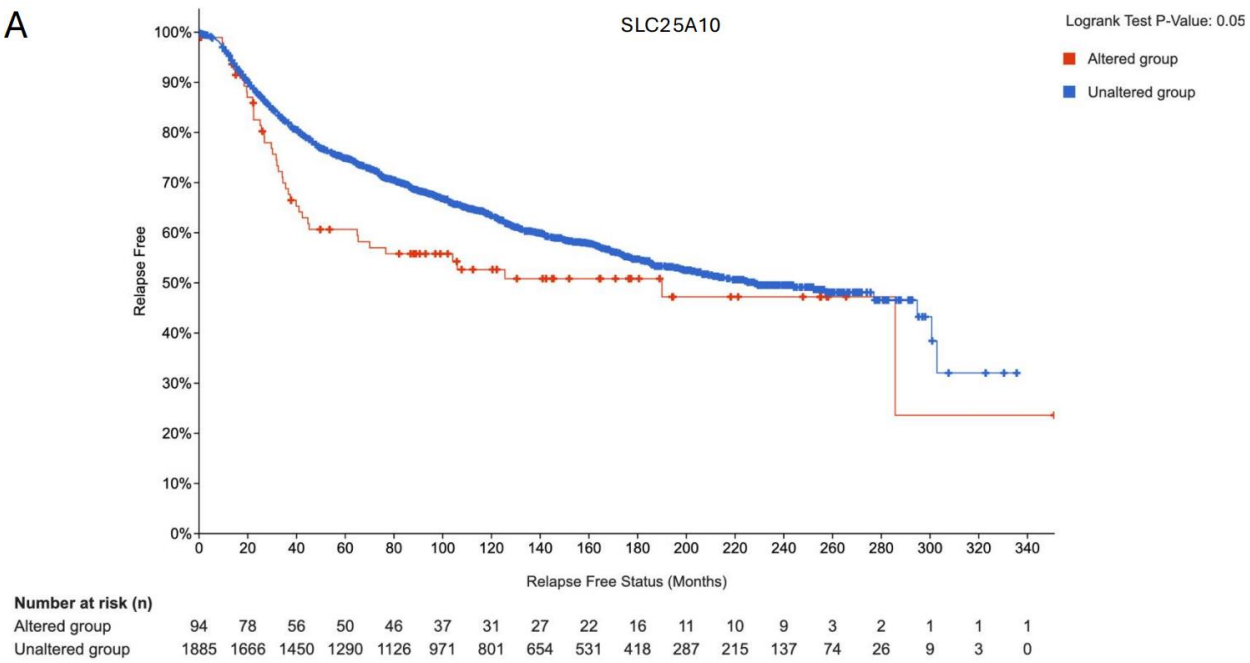
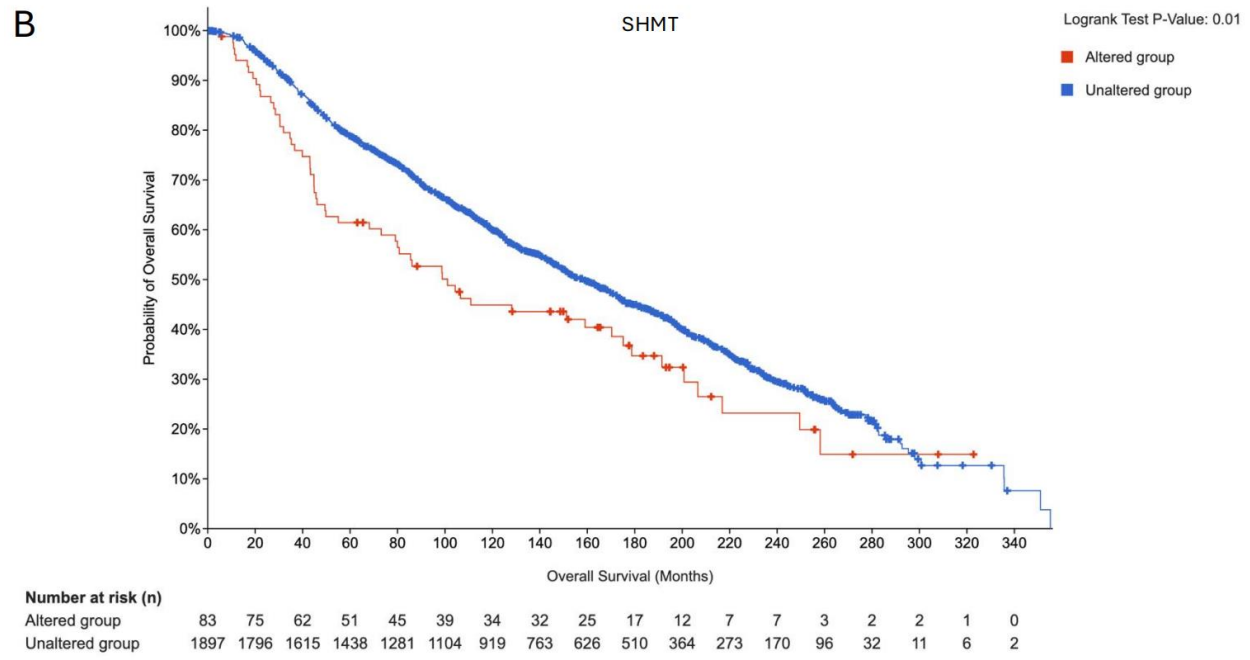
Supplementary Material

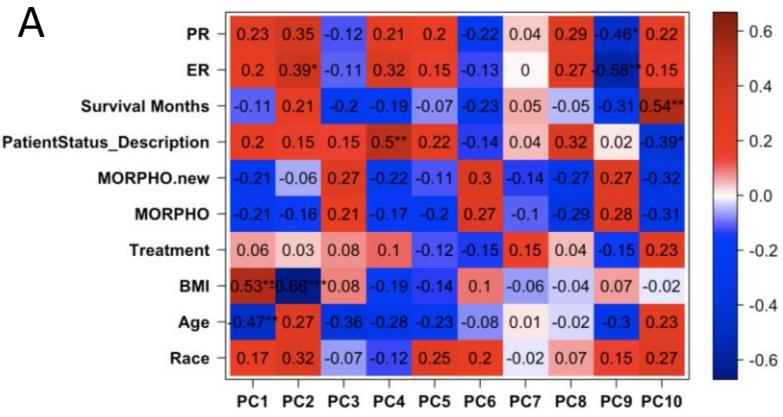
Characteristic	Sub-characteristic	N=15	
Race		13	
	White		
	Black		
	Native American		
Gender	**Female**	15	
Age	**(range; years)**	38 to 78	
Morphology			
	Infiltrating Ductal Carcinoma, NOS	5	
	Invasive Carcinoma	3	
	Invasive Carcinoma, NOS	3	
	Metaplastic Carcinoma, NOS	2	
	Cancer and carcinoma	2	
Receptor status		**Yes**	**No**
	ER	12	3
	PR	11	4
	HER-2	0	15
Treatments		**Baseline**	**Baseline and Progression**
	Eribulin	1	4
	Paclitaxel	4	0
	Capecitabine	1	2
	Paclitaxel/Eribulin	0	1
	Capecitabine/Paclitaxel	0	1
	Capecitabine/Eribulin		
Survival	**(range; months)**	20 to 250	

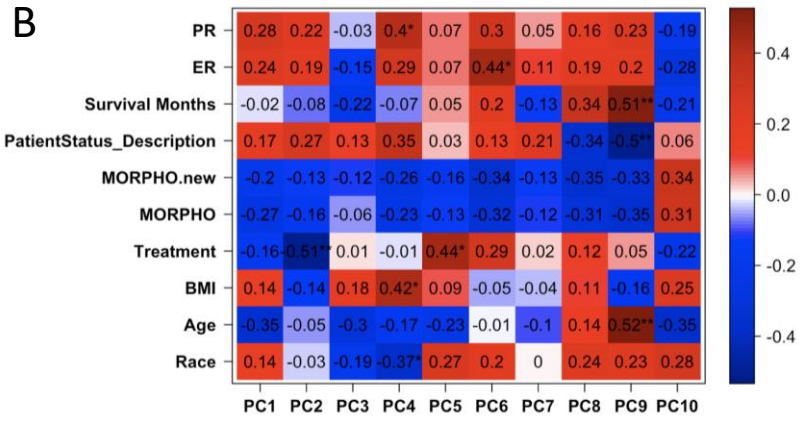
Supplementary Table 1. Patient/Sample Demographics

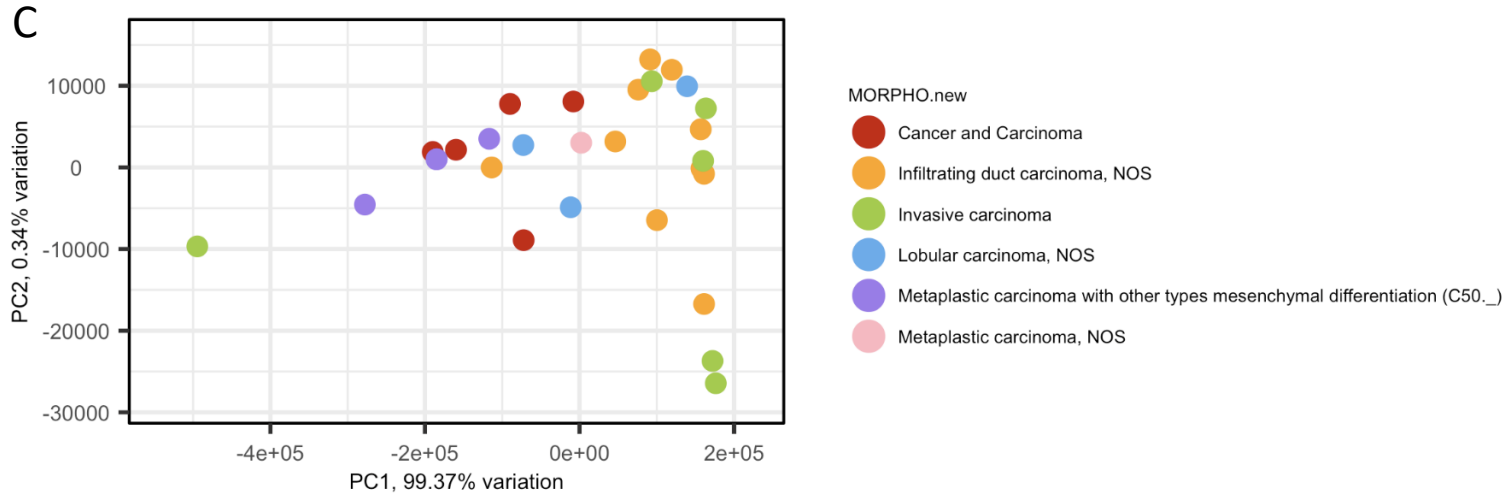


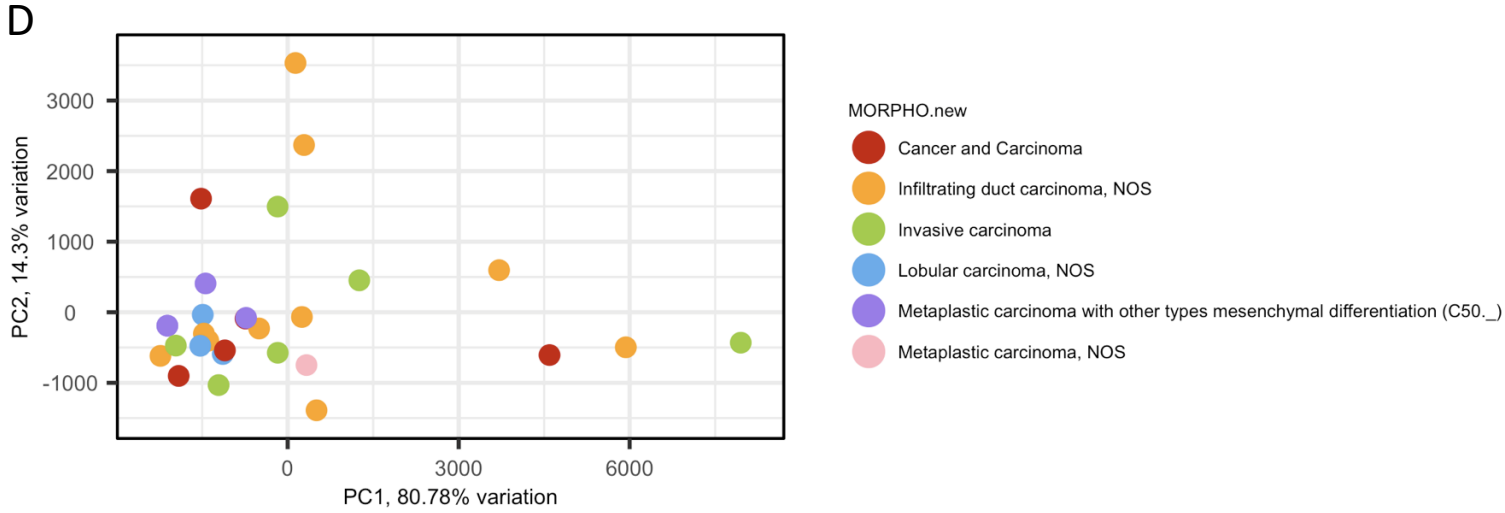


Supplementary Figure 1: A. Differences in Relapse Free Survival between "altered" group with upregulated gene (SLC25A10) associated with therapeutic resistance and "unaltered" group lacking upregulated genes associated with therapeutic resistance. B. Differences in Overall Survival between "altered" group with upregulated gene (SHMT2) associated with therapeutic resistance and "unaltered" group lacking upregulated genes associated with therapeutic resistance.

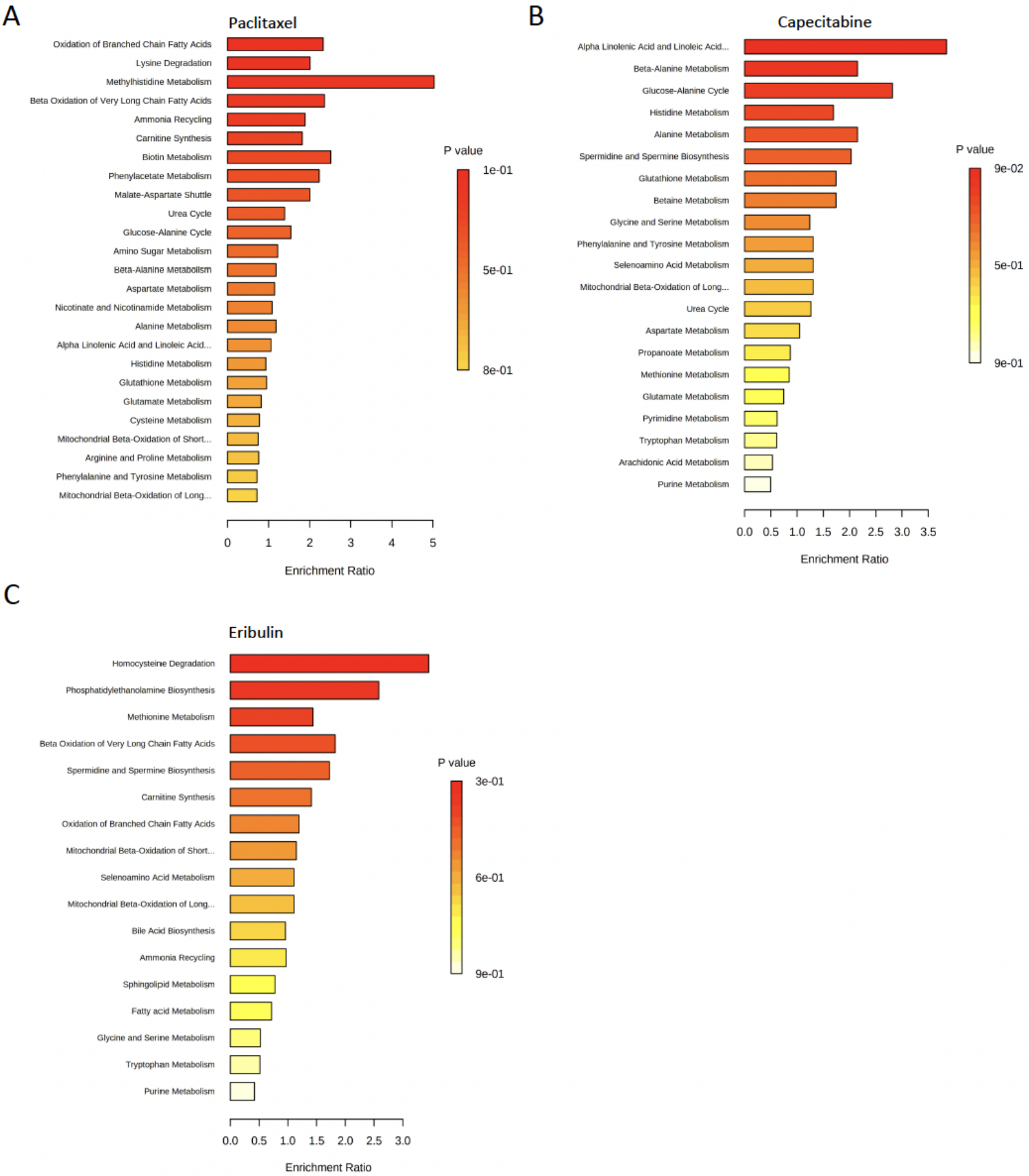




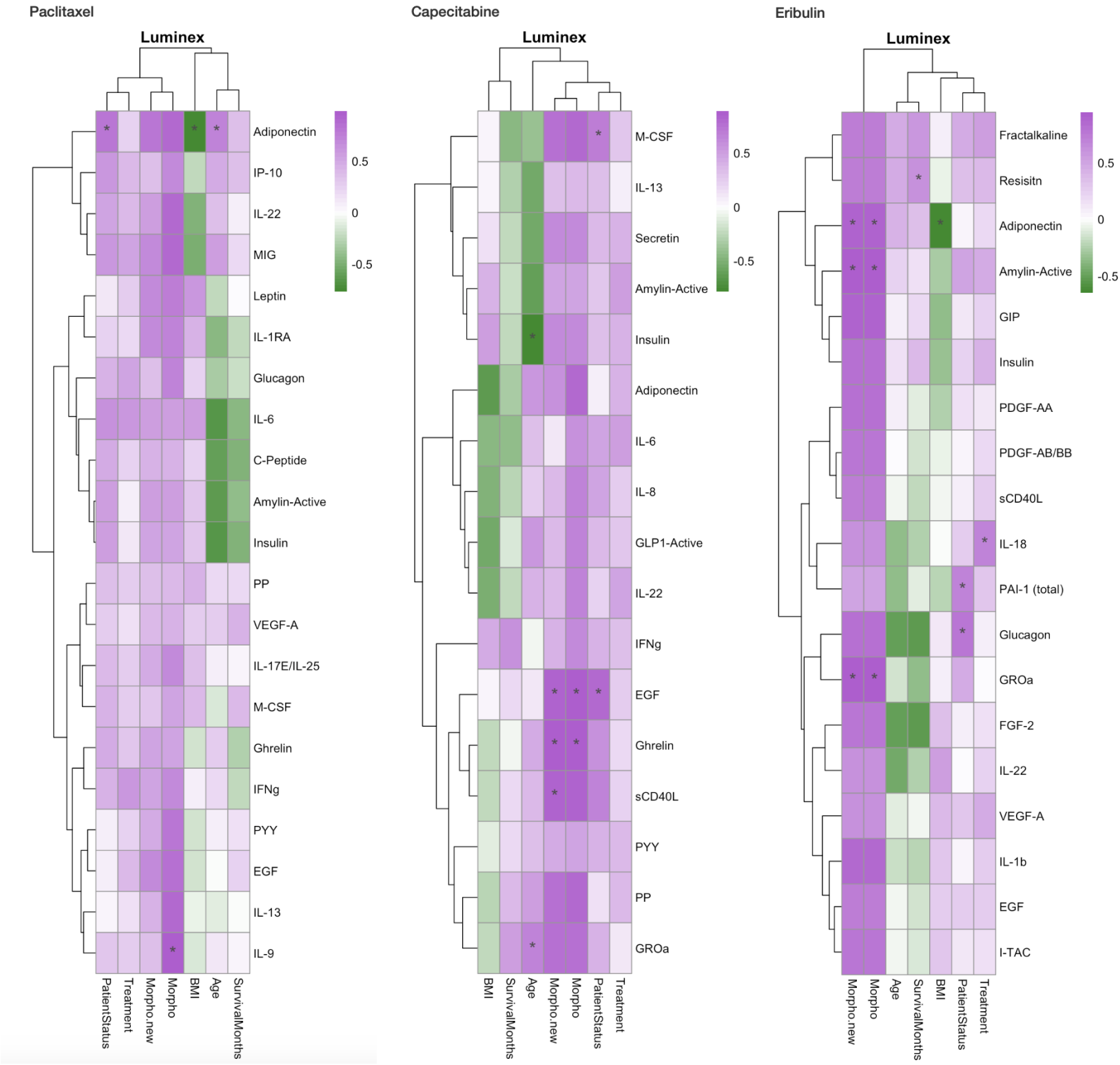




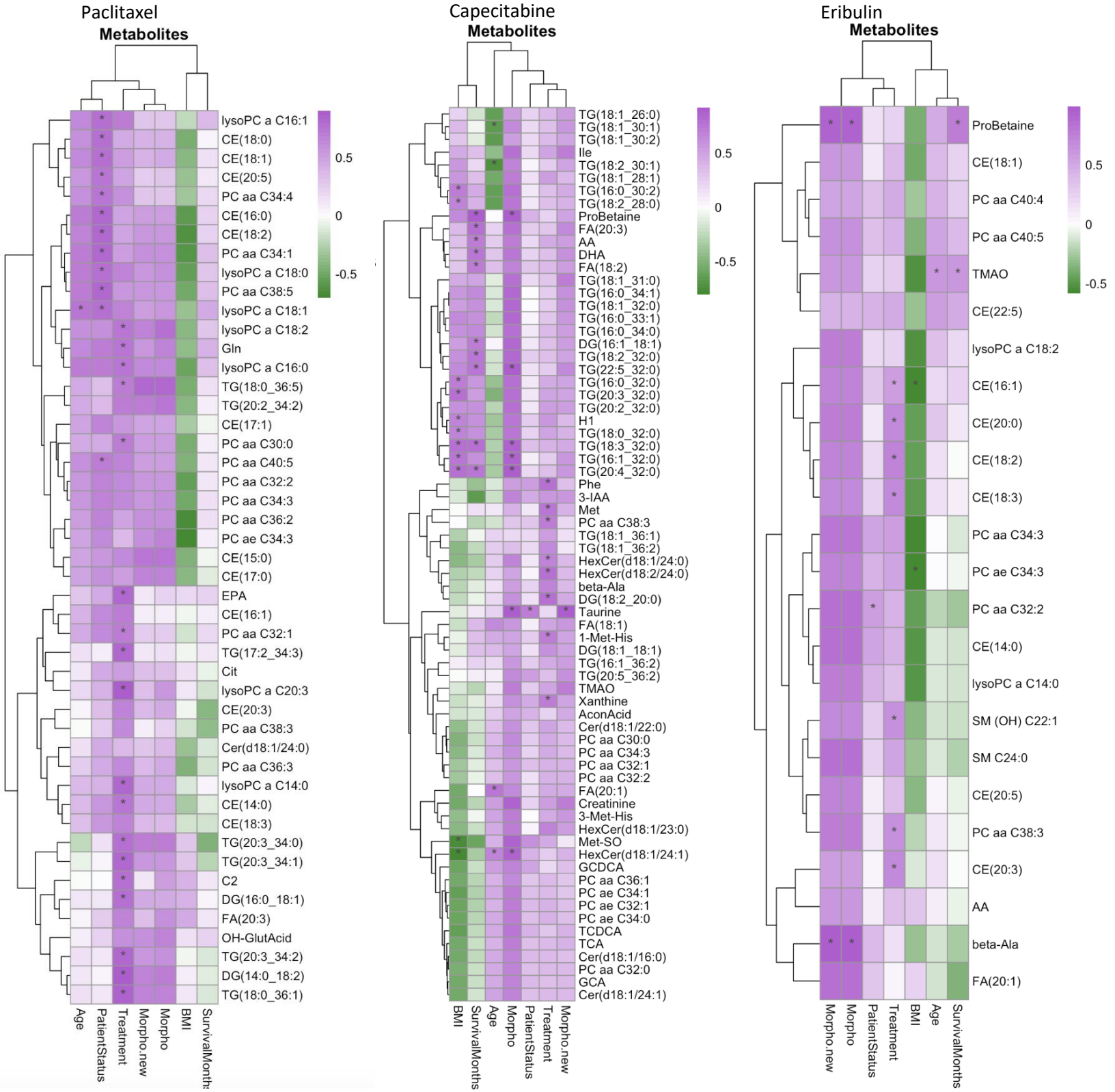
Supplementary Figure 2. Selecting Relevant Clinical Co-Variates to Adjust the Model for Differential Abundance Assessment. (A) Luminex and (B) Metabolomics principal component analysis to assess which clinical factors contribute to the largest amount of variability, and to the most significant extent. (A) BMI and Age were found to be significantly associated with a high amount of variability in Luminex data, and were, therefore, built into the model as co-variates. (B) While no clinical factors were found to be associated with PC1 in the metabolomics data, for consistency, models were adjusted based on age and BMI. Representative principal component analysis plots show no separation of patients by morphology based on (C) Luminex or (D) Metabolomics data.



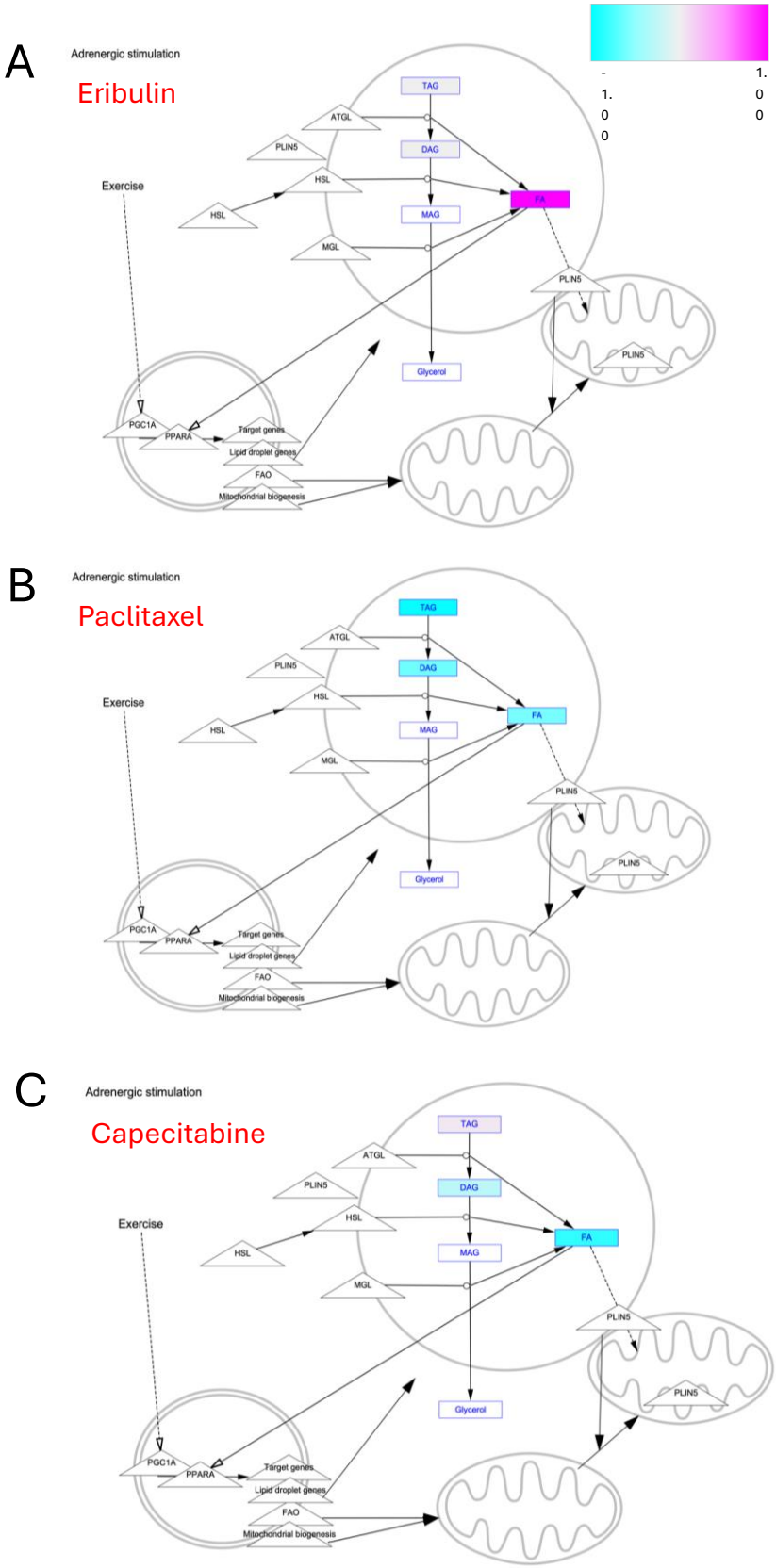
Supplementary Figure 3. Metabolite Set Enrichment Analysis. Metabolite set enrichment analysis of the differentially abundant metabolites revealed different metabolic pathways in (A) Paclitaxel, (B) Capecitabine, and (C) Eribulin.



Supplementary Figure 4. Clinical Correlations with Immune Factors. Pooling both baseline and progression, heatmaps display Spearman correlation between the top immune factors and several clinical factors for Paclitaxel (left), Capecitabine (center), and Eribulin (right). * p <0.05 for correlation between top immune factors and clinical factors.



Supplementary Figure 5. Clinical Correlations with Metabolomics. Pooling both baseline and progression, heatmaps display Spearman correlation between the top metabolic factors and several clinical factors for Paclitaxel (left), Capecitabine (center), and Eribulin (right). * p <0.05 for correlation between top differential metabolites and clinical factors.



Supplementary Figure 6: Schematic representation of metabolic alterations associated with resistance of Paclitaxel (A), Eribulin (B) and Capecitabine (C).