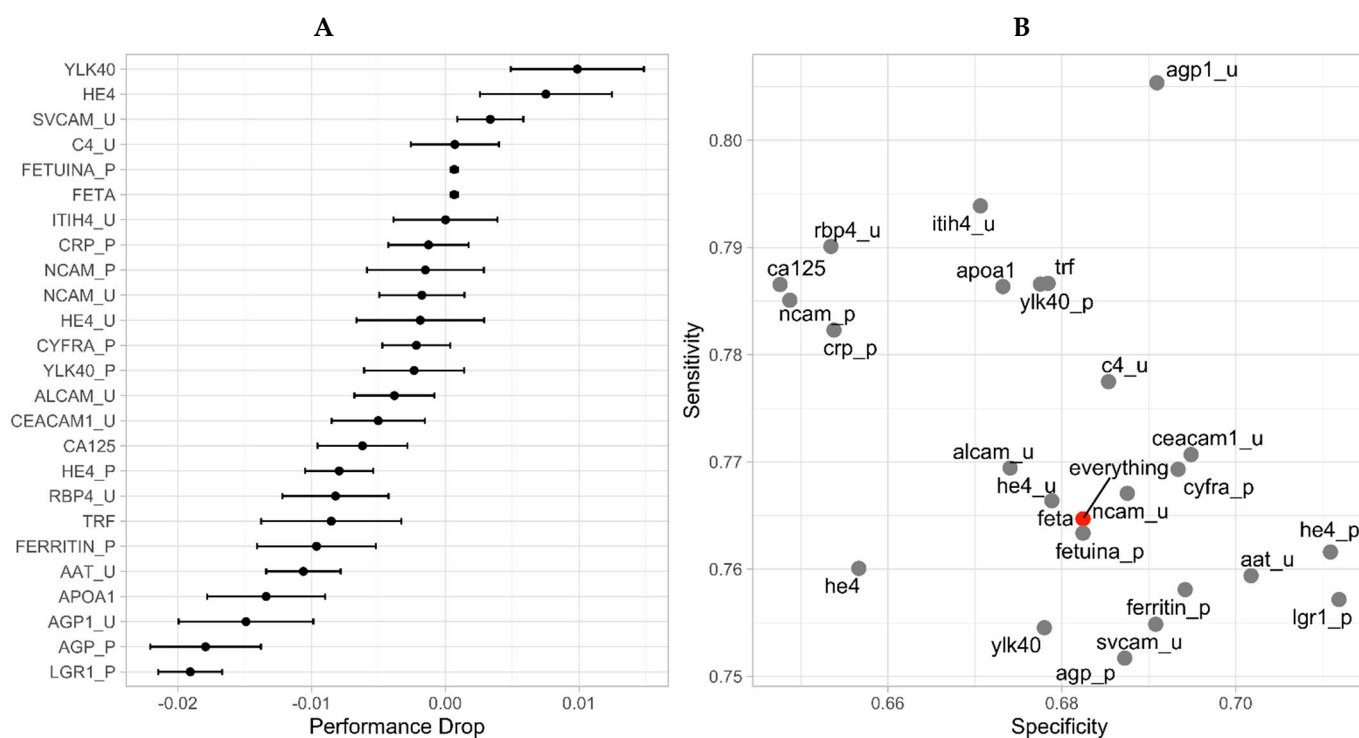
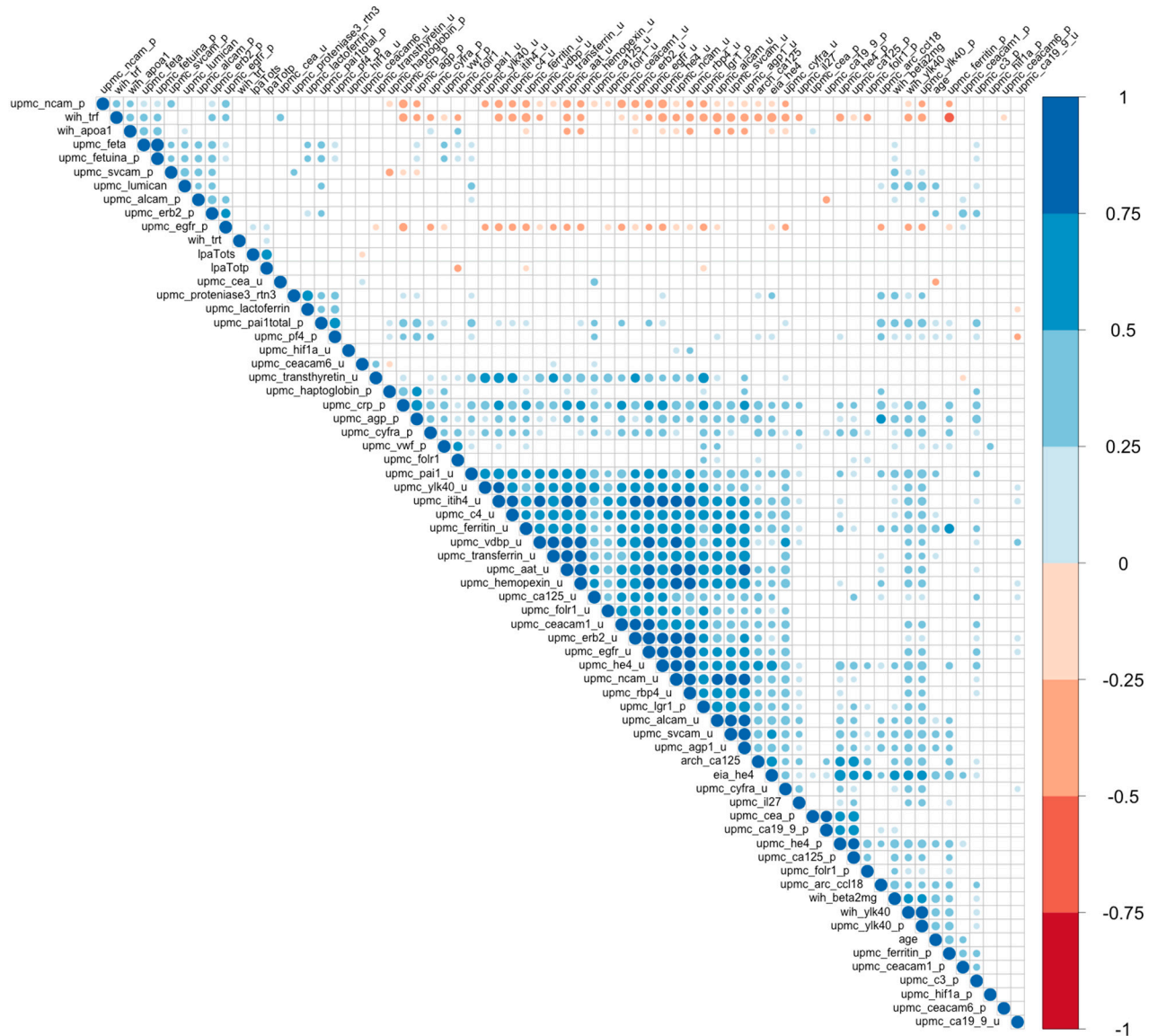


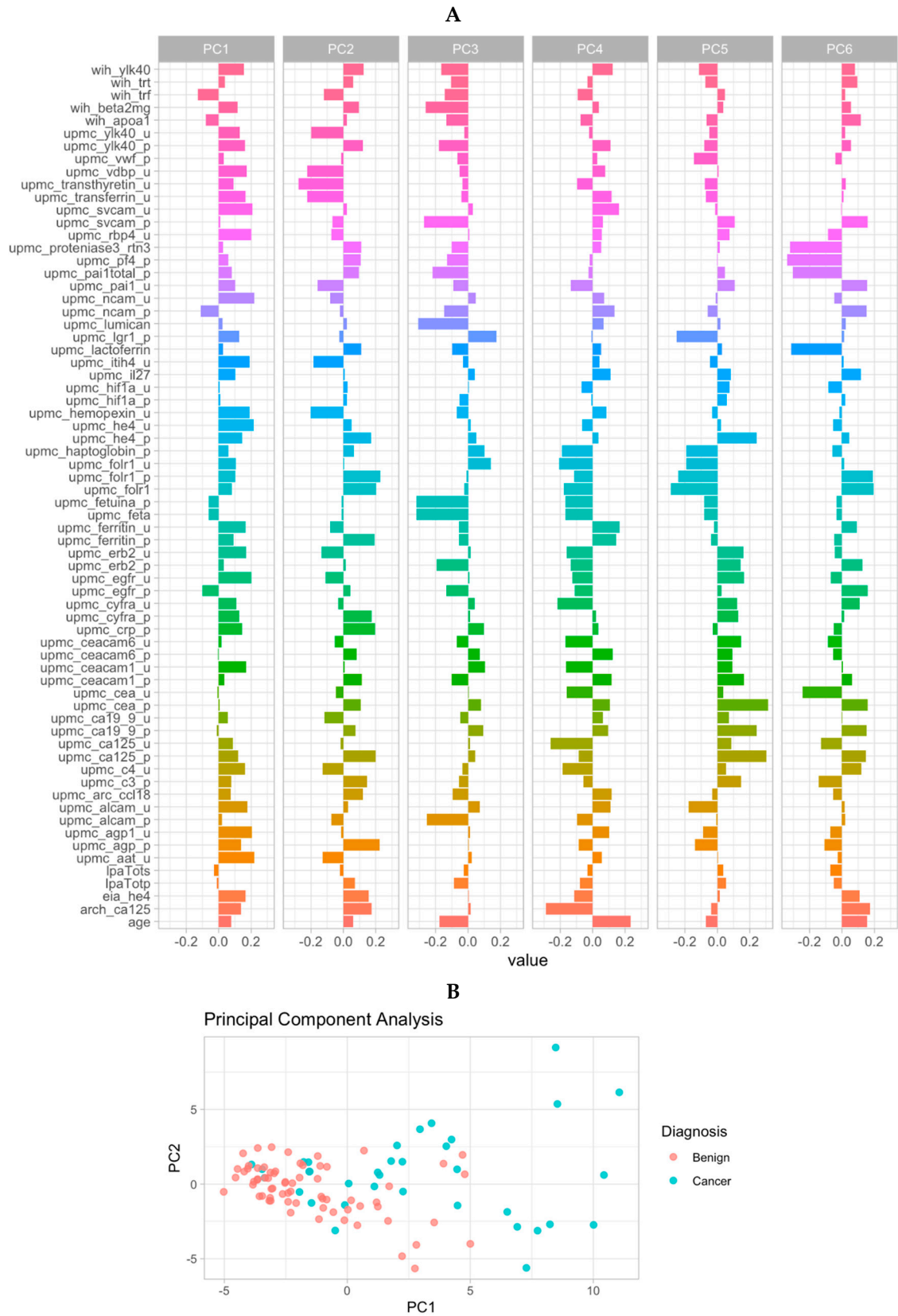
**Figure S1.** Univariate analysis of non-parametric Mann-Whitney test.  $p$ -values are corrected with False Discovery Rate (FDR) correction. Biomarkers with corrected  $p$ -value  $< 0.01$  are labeled.



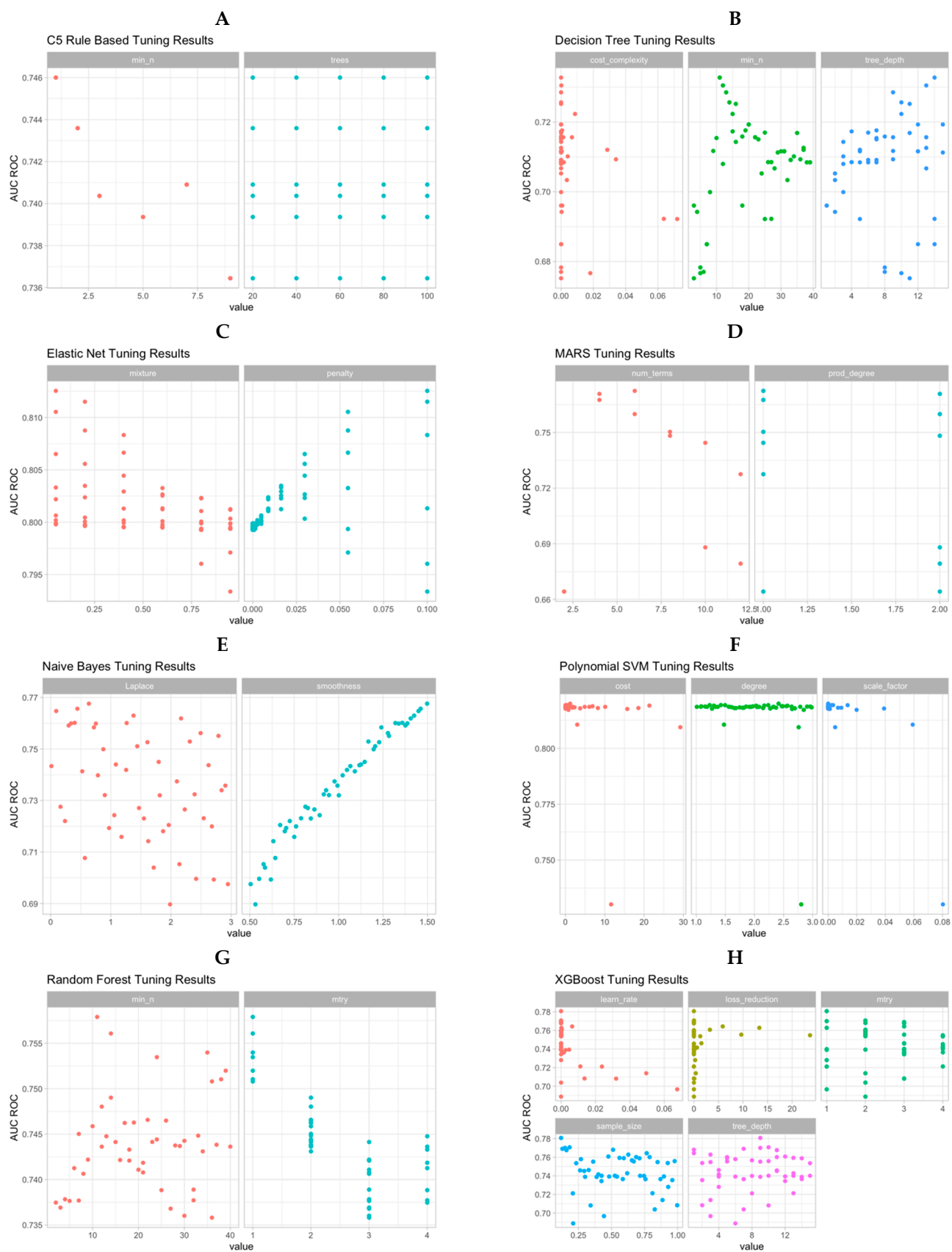
**Figure S2.** Logistic Regression model of 25 statistically significant variables. **(A)** Positive values indicate improved model performance (ROC AUC) with biomarker exclusion from the logistic regression model. The mean performance drop is represented by the circle; standard error is indicated by the error bars. **(B)** Specificity versus sensitivity dot plot. Labels indicate when that biomarker is excluded from the logistic regression model.



**Figure S3.** Pairwise Spearman rank coefficient of all numerical variables. Non-significant correlations are left white. Negative correlations are indicated in red. Positive correlations are indicated in blue.



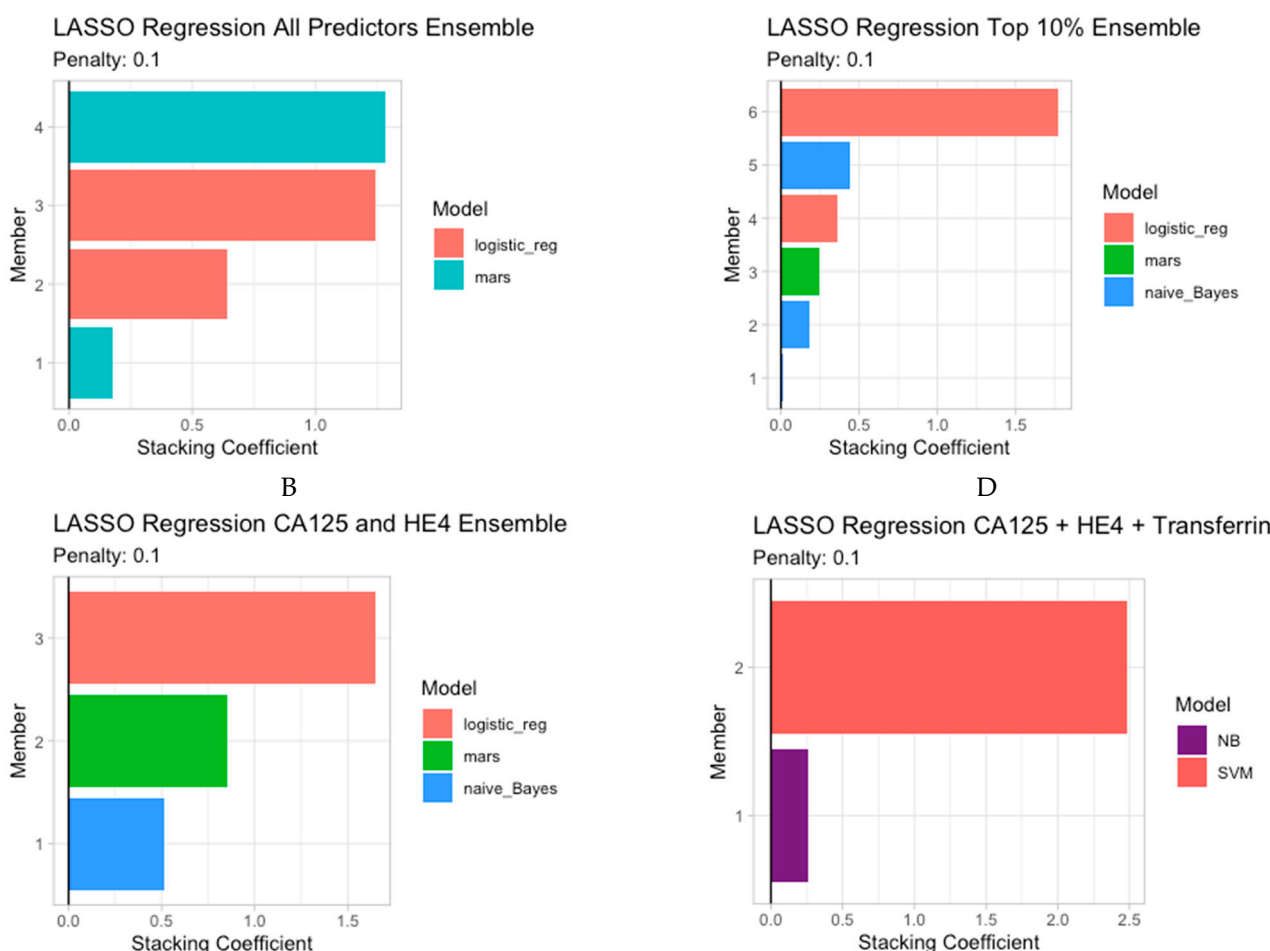
**Figure S4.** (A) Principal Component Analysis of all numerical variables. (B) First principal component ( $x$ -axis) plotted against the second principal component ( $y$ -axis), beginning to separate the benign from cancer samples.



**Figure S5.** Model-specific hyperparameter tuning results of the three-variable biomarker panel across the training dataset. (A) C5.0 Rule-based; (B) Decision Tree; (C) Elastic Net; (D) Multivariate regression spline (MARS); (E) Naïve Bayes; (F) Polynomial Support Vector Machine; (G) Random Forest; (H) Extreme Gradient Boosted Trees (XGBoost). The Neural Net classifier was not tuned across a grid of parameters.

A

B



**Figure S6.** Lasso Regression results of the four ensemble stacks. (A) All predictors. (B) Top10% of predictors as defined by largest Gini impurity. (C) CA125 + HE4. (D) CA125 + HE4 + Transferrin.

**Table S1.** Demographic and biomarker variables.

Variables	
Age	CEACAM-1 (U)
Menopausal status	CEACAM-6 (U)
CA125	Ferritin (U)
HE4	NCAM (U)
YKL-40	sVCAM (U)
Transferrin	PAI-1 (U)
ApoA1	YKL40 (U)
Beta2 Microglobulin	FOLR1 (U)
Transferrin	FETA
LPA (S)	IL-27
LPA (P)	Lumican
HE4 (P)	ARC/CCL18
Cyfra (P)	Proteinase 3/RTN3
CA125 (P)	CRP (P)
CEA (P)	Fetuin A (P)
ErbB2 (P)	AGP (P)
EGFR (P)	Haptoglobin (P)
CA 19-9 (P)	PF4 (P)
HIF-1a (P)	vWF (P)
ALCAM (P)	C3 (P)

CEACAM-1 (P)	FOLR1
CEACAM-6 (P)	LRG1 (U)
Ferritin (P)	ITIH4 (U)
NCAM (P)	C4 (U)
sVCAM (P)	AAT (U)
PAI-1 (total) (P)	AGP-1 (U)
YKL40 (P)	Hemopexin (U)
FOLR1 (P)	RBP-4 (U)
HE4 (U)	Transferrin (U)
Cyfra (U)	Transthyretin (U)
CA125 (U)	VDBP (U)
CEA (U)	Lactoferrin
ErbB2 (U)	ALCAM (U)
EGFR (U)	CEACAM-1 (U)
CA 19-9 (U)	CEACAM-6 (U)
HIF-1a (U)	Ferritin (U)
ALCAM (U)	

**Table S2.** Histopathology of benign and malignant tumors.

### **Malignancies**

#### **Epithelial Ovarian Cancer**

Serous	28
Endometrioid	2
Mucinous	8
Clear Cell	6
Mixed Serous and Endometrioid	2
Germ Cell Tumor	2
LMP Serous	2
LMP Mucinous	2
Uterine Malignancy	3
Metastatic to the Ovary	6

### **Benign Tumors**

Serous Cystadenoma and Cystadenofibroma	20
Mucinous	16
Endometriosis	13
Teratoma	9
Fibroma / Fibrothecoma	7
Brenner Tumor	0
Simple / Hemorrhagic Cysts	11
Leiomyoma	1
Endometrial Polyp	1
Endometrial Hyperplasia	1
<b>Total Number of Malignant and Benign Tumors</b>	<b>140</b>

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**Table S3.** Tri-variable ensemble stack statistics from the testing dataset.

<b>Model</b>	<b>AUC</b>	<b>Accuracy</b>	<b>Sensitivity</b>	<b>Specificity</b>	<b>PPV</b>	<b>NPV</b>
Ensemble	0.951	97.1%	93.3%	100.0%	100.0%	95.0%
SVM	0.951	94.1%	93.3%	94.7%	93.3%	94.7%
NB	0.867	82.4%	73.3%	89.5%	84.6%	81.0%