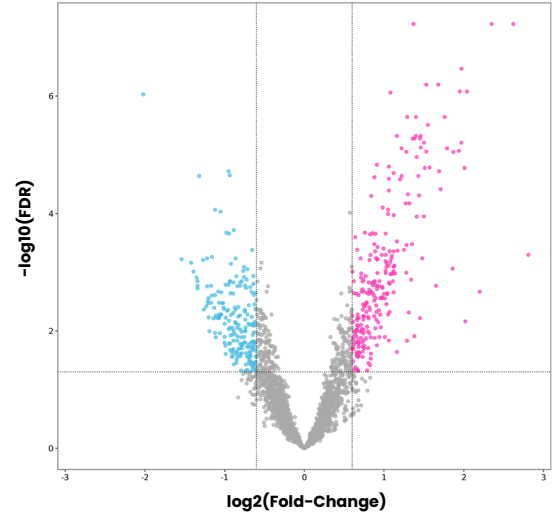


Enhanced Detection of Protein & RNA Markers in the Blood of NSCLC Patients

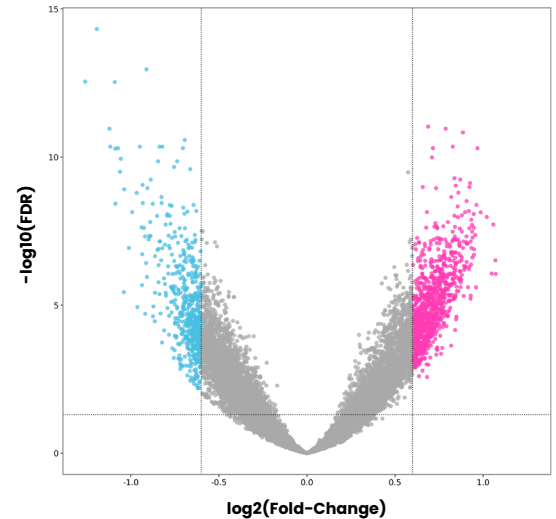
We have developed a highly sensitive, multi-omic EV subpopulation interrogation pipeline that robustly profiles tumor derived EVs (TDEVs) in biofluids utilizing FYR's novel EV enrichment technology called SPARCs.

	NSCLC	Healthy
N	49	45
Age		
<51	4	5
51-60	11	13
61-70	21	23
71-80	12	4
81-90	1	0
>90	0	0
Sex		
Male	28	26
Female	21	19
Race/Ethnicity		
Caucasian	49	37
Asian	0	2
Black	0	6
Staging		
Stage 1 (I, IA1, IA2, IA3, IB)	25	-
Stage 2 (IIA, IIB)	24	-
Subtype		
Adenocarcinoma (LUAD)	37	-
Squamous Cell Carcinoma (LUSC)	10	-
Adenosquamous	2	-
Specimen Providers	2	2
Smoking Status		
Unknown	-	8
Never used	17	23
Previous use	22	9
Current smoker	10	5

Differential Expression Analysis (Protein)

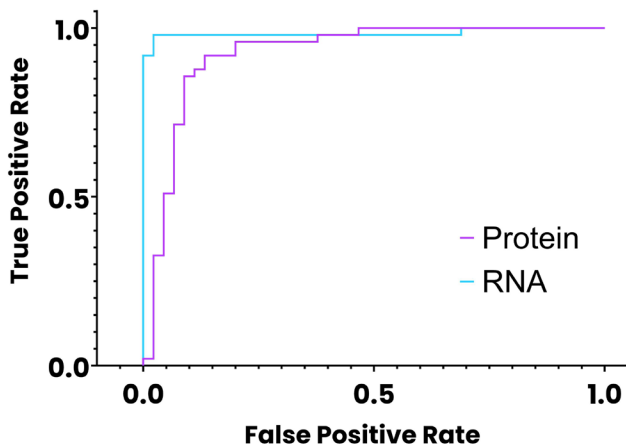


Differential Expression Analysis (RNA)



Differential expression analysis of NSCLC patients relative to healthy controls identified 250 significantly enriched proteins and 204 significantly depleted proteins using Tumor SPARCs and 897 significantly enriched RNAs and 516 significantly depleted RNAs using Tumor SPARCs

ROC Curves

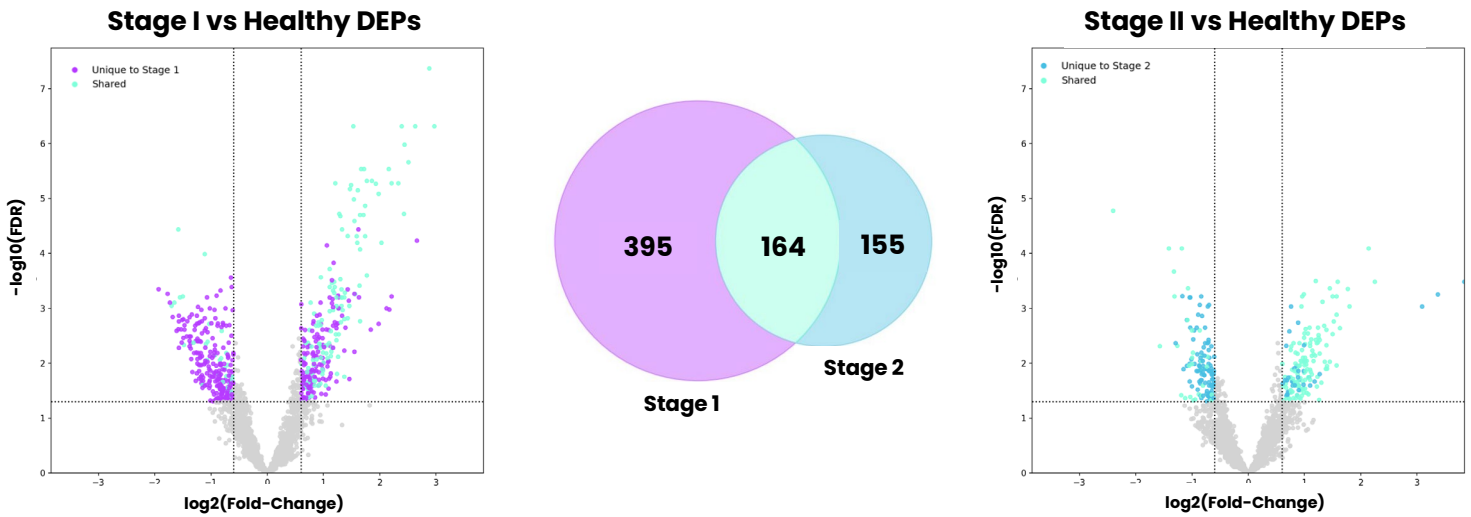


ML Model Performance Metrics

	Protein	RNA
AUC	0.93	0.98
Combined Sensitivity	0.92	0.98
Stage I Sensitivity	0.92	0.96
Stage 2 Sensitivity	0.92	1
Specificity	0.87	0.98
No of Features	9	24

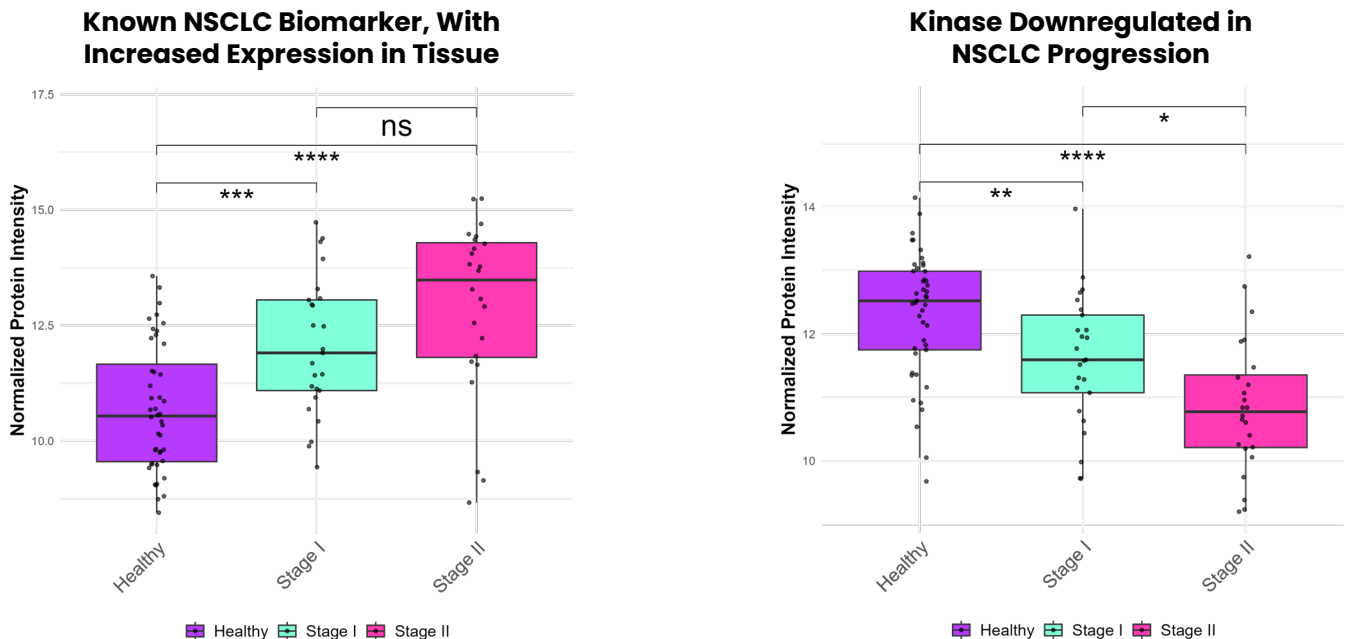
EVO Enables Detection of Unique Signatures of Stage I and Stage II NSCLC

Differentially Expressed Proteins shared by both Stage I and Stage II have a strong enrichment of markers and mechanisms related to the immune response (neutrophils), cytoplasmic translation, and ribosomes, as well as a strong dysregulation of metabolic processing and mitochondrial function.



EVO Enables Detection of Known NSCLC Markers Progressive Across Stages

Published NSCLC markers known to increase or decrease through cancer progression based on tissue data are captured by SPARCs, highlighting the possibility of liquid biopsy-based progression monitoring.



Box plots of biomarkers known to change during NSCLC progression. $p \leq 0.05$ (*), $p \leq 0.01$ (**), $p \leq 0.001$ (***), and $p \leq 0.0001$ (****).