FYR

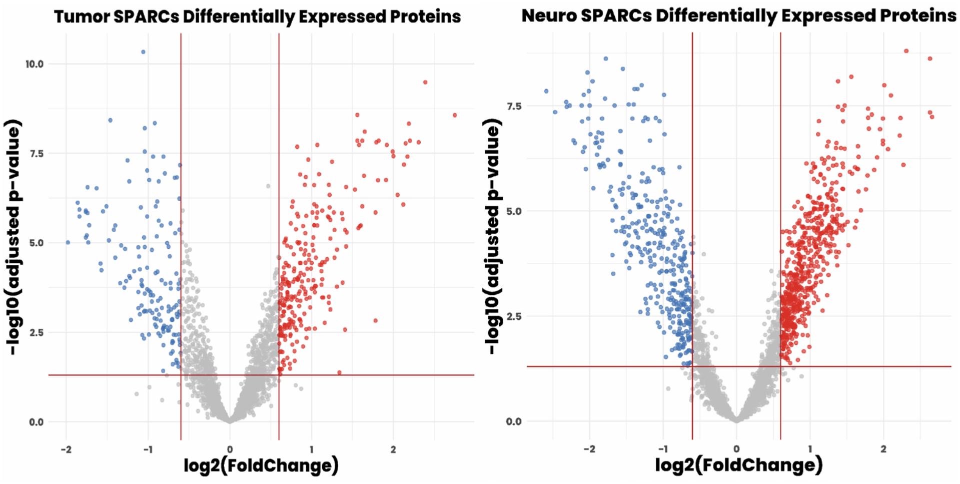
Utilization of Tumor-derived Extracellular Vesicles for Patient Stratification and Biomarker Discovery

Study Design

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

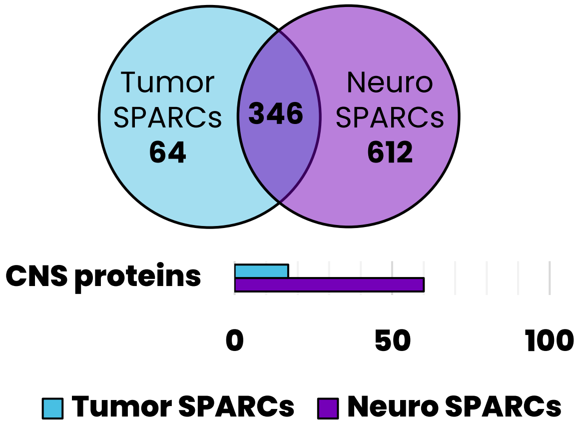
	N	Specimen Providers	Age				Sex		Race/Ethnicity		
			<51	51-60	61-70	71-80	Male	Female	White	Asian	Black
Glioma	**52**	2	18	14	18	2	23	29	51	1	0
Benign	**15**	1	6	3	5	1	2	13	15	0	0
Healthy	**38**	2	13	12	11	2	21	17	34	0	4

Brain Tumor Plasma Proteomic Signatures & Biomarker Discovery



Volcano plots with differentially expressed proteins (DEPs) enriched by Tumor or Neuro SPARCs. padj<0.05 and $\log_2$ fold-change ±0.6.

Brain Tumor vs. Healthy DEPs



Differential expression analysis of brain tumor (malignant and benign) patients relative to healthy controls identified 256 significantly enriched proteins and 154 significantly depleted proteins using Tumor SPARCs and 598 significantly enriched proteins and 360 significantly depleted proteins using Neuro SPARCs

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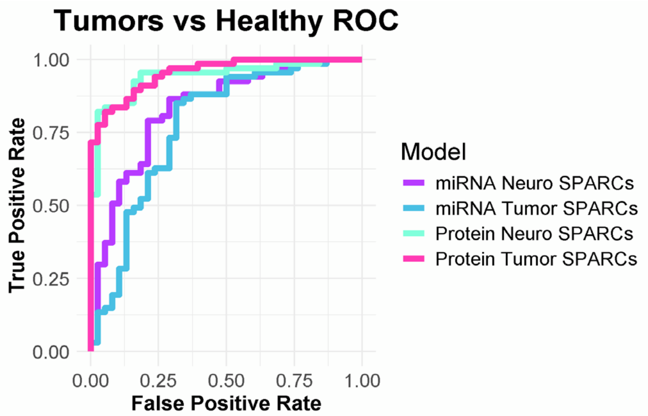
Objective: *Distinction of brain tumors (malignant and benign) from healthy patients.*

	Protein Tumor SPARCs	Protein Neuro SPARCs	miRNA Tumor SPARCs	miRNA Neuro SPARCs
AUC	0.98	0.96	0.80	0.83
Accuracy	0.87	0.88	0.77	0.74
Sensitivity	0.82	0.82	0.47	0.56
Specificity	0.95	0.97	0.89	0.89
Features	16	17	13	17

Performance metrics for leading models. Models optimized for maximum specificity.



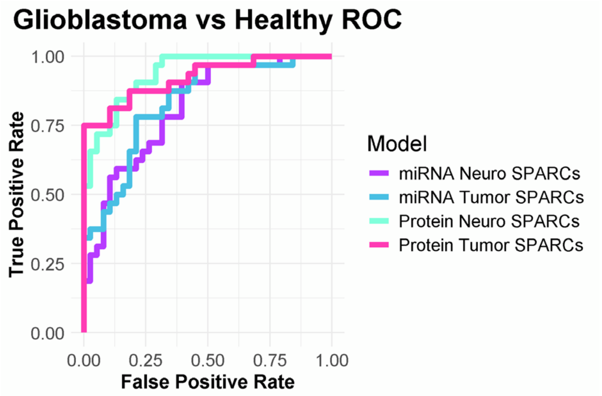
ROC curve comparison of leading models by method and analyte.

Utilization of Tumor-derived Extracellular Vesicles for Patient Stratification and Biomarker Discovery

Objective: *Distinction of glioblastomas from healthy patients.*

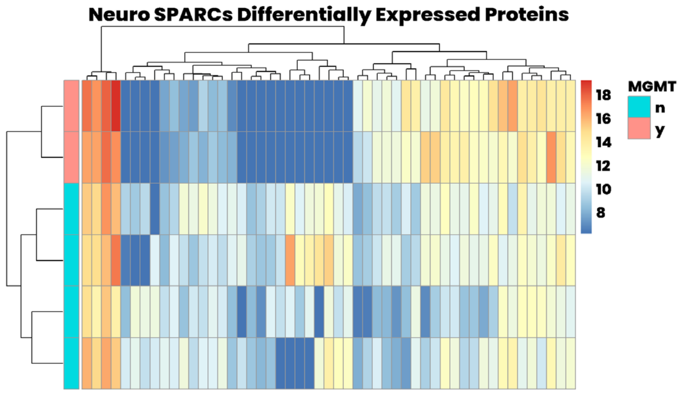
	Protein Tumor SPARCs	Protein Neuro SPARCs	miRNA Tumor SPARCs	miRNA Neuro SPARCs
AUC	0.93	0.94	0.86	0.83
Accuracy	0.89	0.84	0.79	0.74
Sensitivity	0.75	0.72	0.78	0.56
Specificity	1	0.95	0.79	0.89
Features	11	16	17	18

Performance metrics for leading models. Models optimized for maximum specificity.



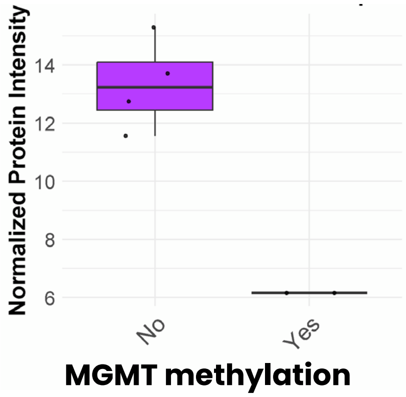
ROC curve comparison of leading models by method and analyte.

Subtyping Pilot: Tissue MGMT Status



Hierarchical clustering heatmap comparing n=4 non-MGMT methylated GBMs, with n=2 MGMT methylated GBMs.

DNA repair marker



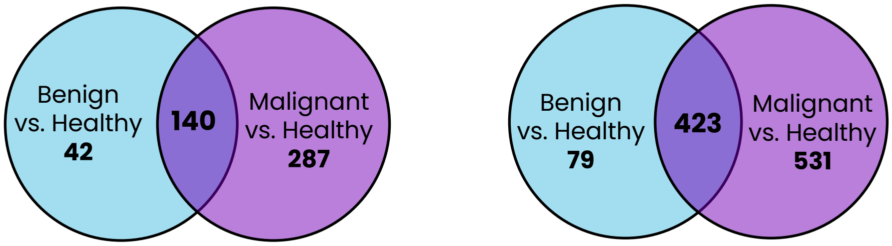
Box plot depicting significant differential expression of a biologically relevant marker.

For n=6 glioblastoma patient plasma specimens, matched tissue was assayed for MGMT promoter methylation status using PCR. Neuro SPARCs proteomic profiles provide preliminary evidence supporting the ability of BDEV subpopulations to identify novel liquid biomarkers for MGMT methylation status.

Benign Tumor Discrimination

Tumor SPARCs DEPs

Neuro SPARCs DEPs



Venn diagrams showing DEP count comparisons at p.adj<0.05 and $\log_2$ fold-change ±0.6 of benign vs. healthy and malignant vs. healthy patient populations in both tumor and neuro SPARCs.

Differential expression analysis comparing benign vs. healthy and malignant vs. healthy shows that while malignant disease displayed more significant DEPS, benign disease also demonstrated a unique DEP signature in TDEVs and BDEVs.