Identification of Plasma-Derived, EV-Based Biomarkers for Glioblastoma

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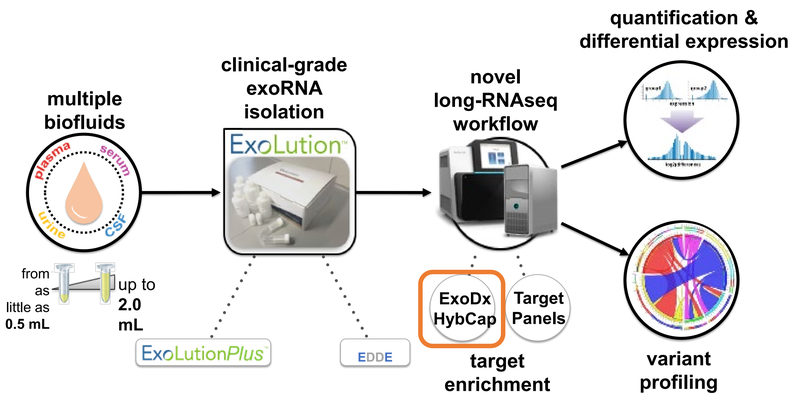
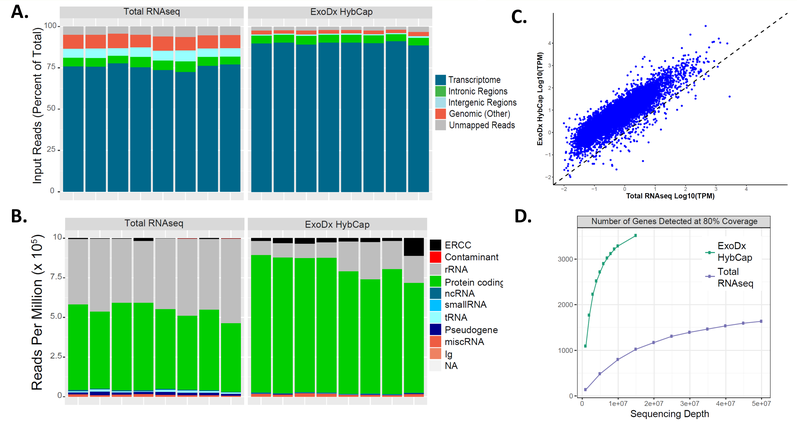
Introduction

Glioblastoma (GBM) is the most malignant and aggressive primary brain cancer in adults, with an incidence of 3.2 per 100,000 people. Currently, diagnosis is only performed via histopathological investigation of a tissue sample from a GBM lesion, complemented with molecular identification of select biomarkers. MRI is the standard of care for follow-up and monitoring of treatment response but suffers from an imagery read only. Therefore, development of a "liquid biopsy" to obtain molecular, disease-relevant information from body fluids is highly desirable. We present the results of our profiling of extracellular vesicle (EV)-derived mRNAs from the plasma of GBM patients and control individuals via ExoDx HybCap.

ExoDx Proprietary NGS Pipeline and HybCap



ExosomeDx's proprietary isolation and analysis platforms enable studies of differential gene expression and variant profiling from EVs. Here, we developed and utilized ExoDx HybCap to profile plasma EVs from GBM patients and healthy controls.



ExoDx HybCap improves on our previous long RNAseq performance by (A) increasing the number of reads in the transcriptome and (B) reducing background rRNA reads. As a result, (C) we detect most genes at higher TPM and (D) improve gene body coverage at lower sequencing depths.

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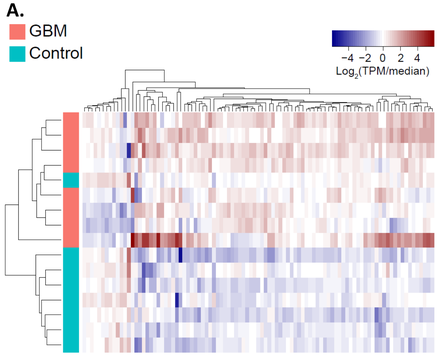
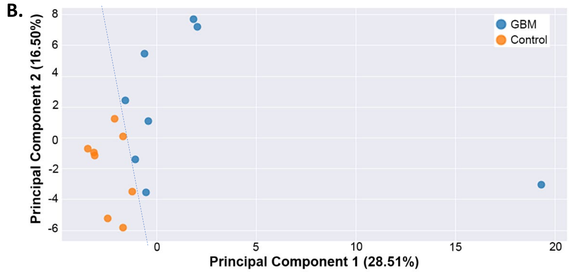
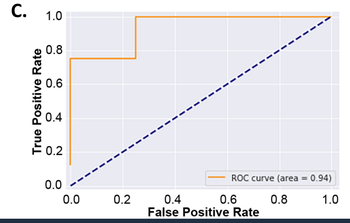
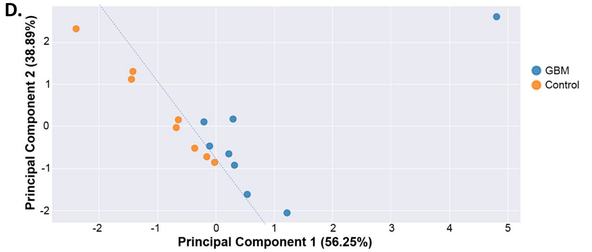


(A) Initial profiling of plasma EVs from 8 GBM patients and 8 controls matched for age and sex determined 95 differentially expressed genes.





In order to validate the 95 gene signature, we performed the same experiment with 8 more GBM patients and matched controls. We then determined that the initial 95 gene signature was able to (B) segregate the validation set (PCA analysis) with (C) excellent discrimination between GBM and control (ROC curve).



We next used a random forest feature selection algorithm to reduce the 95 gene signature down to a 4 gene signature that (D) could still separate the validation data set. (E) This newly-identified 4 gene signature has an even better discrimination. Work is now underway to test this signature via qPCR assay.

Conclusions

- ExosomeDx proprietary EV isolation and long RNA profiling via ExoDx HybCap enable informative biomarker discovery via differential gene expression.
- Profiling plasma-derived EVs from GBM patients and controls resulted in a 95 gene signature that was further reduced to 4 genes using feature selection.
- Further validation work is underway.

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