Identification of a saliva exosomal RNA signature for Sjogren's syndrome

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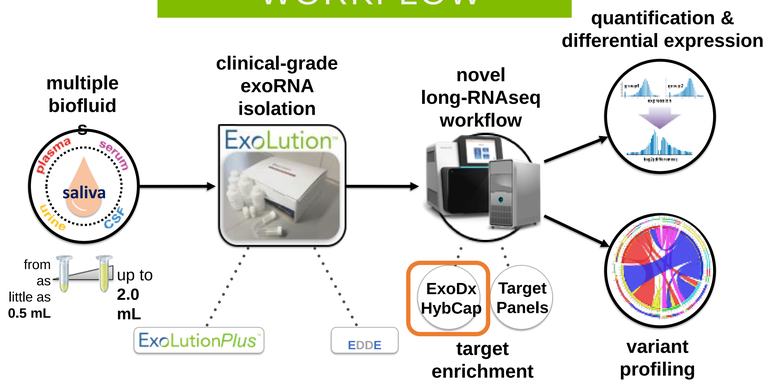
INTRODUCTION

Sjogren's syndrome (SS) is a systemic autoimmune disease in which inflammation progressively damages the moisture producing glands of the afflicted. Four million Americans are estimated to be suffering from the disease, 90% of which are women with an average age of 40. Overlapping symptoms with other health conditions and co-morbidities make SS particularly difficult to diagnose, with average time to diagnosis of 3 years. A non-invasive saliva exosomal RNA (exoRNA) based test capable of diagnosis would be highly desirable.

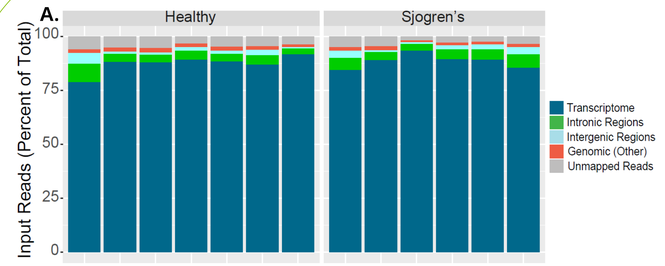
Saliva exoRNA profiling has been heavily limited by the large contamination from the oral microbiome. Here, we present results from our optimized RNASeq workflow which selectively enriches human salivary exoRNA & efficiently depletes microbial contamination. By applying this workflow, we further identify a preliminary gene signature which could potentially provide a non-invasive molecular means of diagnosing Sjogren's syndrome.

WORKFLOW

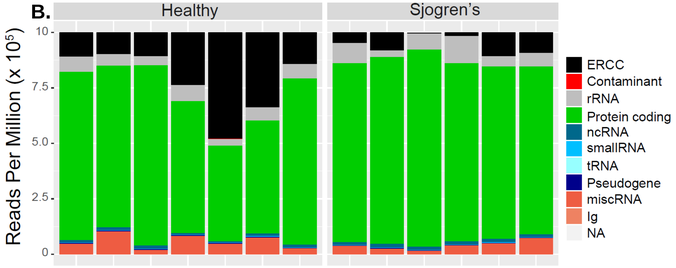


ExosomeDx's proprietary isolation and analysis pipeline enables studies of differential gene expression and variant profiling from exosomes. Here, we developed and utilized ExoDx HybCap to profile saliva exosomes from six SS patients and seven healthy controls.

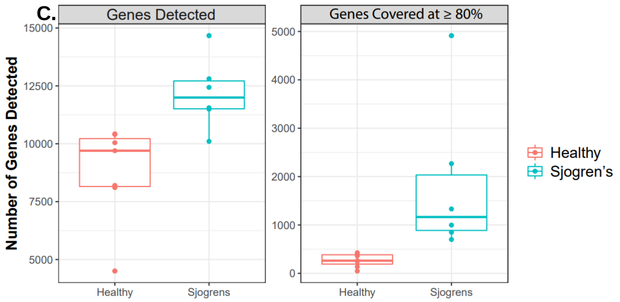
RESULTS



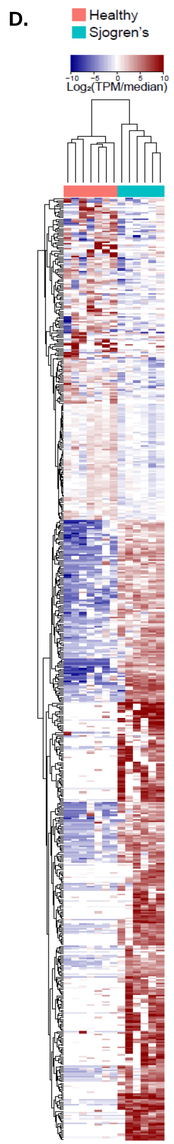
Over 75% reads aligned to human transcriptome with highly efficient depletion of microbial reads (unmappable). This is in stark contrast with <20% human reads reported in current literature.

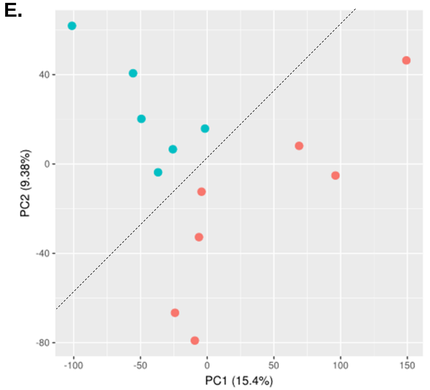


Biotype distribution demonstrates over 75% of reads mapping to mRNAs & ncRNAs, with highly efficient depletion of rRNAs.



At a sequencing depth of just 10M reads, over 10,000 protein coding genes are detected from saliva exosomes. Significant proportion of these genes have more than 80% gene body coverage.





D. Heatmap representation of differentially expressed genes between healthy and Sjogren's samples. Differential expression analysis identified 438 genes upregulated and 198 genes downregulated in saliva exoRNA from Sjogren's patients compared to healthy controls.

E. Principal component analysis (PCA) using saliva exoRNA expression levels show clear separation of healthy and Sjogren's syndrome samples.

CONCLUSIONS

- ExoDx Hyb-cap workflow enables saliva-based liquid biopsy for biomarker discovery that was previously not feasible.
- Selective enrichment of human exoRNA detects over 10,000 mRNAs & over 1000 ncRNAs, enabling informative differential expression analysis.
- The gene signature identified in this ongoing study may lead to non-invasive diagnosis of Sjogren's syndrome.

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