MicroRNA of Exosomes in ccRCC Demonstrates Potential Biomarkers Between Aggressive and Indolent Disease

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Introduction

Clear cell renal cell carcinoma (ccRCC) remains an aggressive malignancy with known increasing incidence. Exosomes are small extracellular vesicles secreted from cancer cells, specifically ccRCC, and play important roles in cell signaling, and resistance to therapy. We collected serum exosomes from patients diagnosed with high and low risk ccRCC to identify an exosomal biomarker liked to worse prognosis.

Objectives:

1. Obtain miRNA expression profile of high-risk vs. low risk ccRCC
2. Evaluate pathways identified from these miRNA as novel therapeutic targets

Methods

- 59 patients met inclusion criteria confirmed pT1 or pT3 ccRCC
- TRPS technology measured exosome concentrations.
- miRNA sequencing was performed using Nanostring
- Pathway analysis was performed using Qiagen Ingenuity Pathway Analysis (IPA).

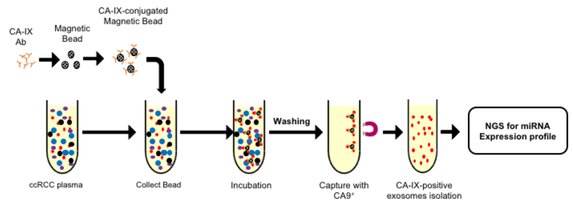
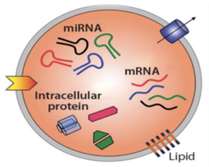


Figure 1: Methods. CA-IX-positive exosomes were isolated from plasma of ccRCC patients for expression profiling.

IPA®



Results

- High risk patients demonstrated increased exosome concentrations.
- Highest fold increased expression: mir-378, mir-1253, mir-1283, and mir-21-5p.
- Highest fold decrease expression: mir1909-3p, mir-1304-3p, mir-100-5p, and mir-876-3p.
- miRNAs interacts with mRNAs associated with ccRCC progression

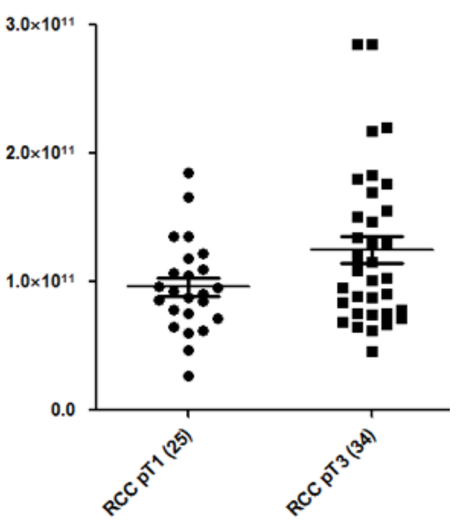


Figure 2: Exosome concentration. Number of exosomes are increased in the plasma of patients with higher risk kidney cancer.

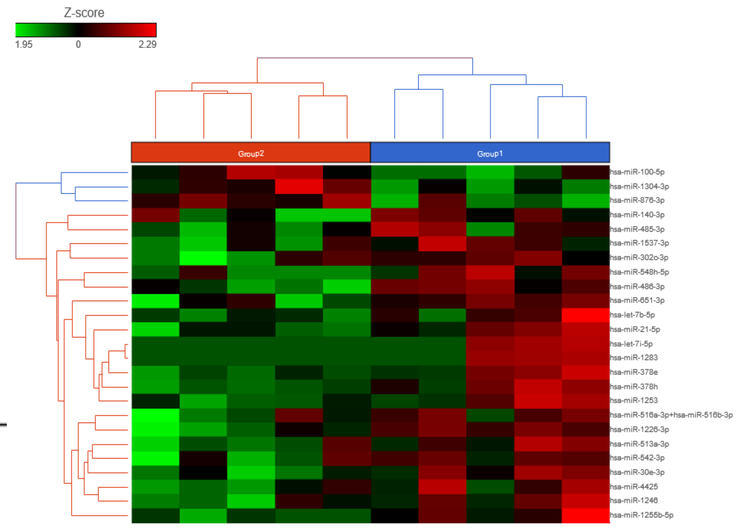


Figure 3: Heat Map comparing miRNA signatures between group 1 (pT1a) and group 2 (pT3)

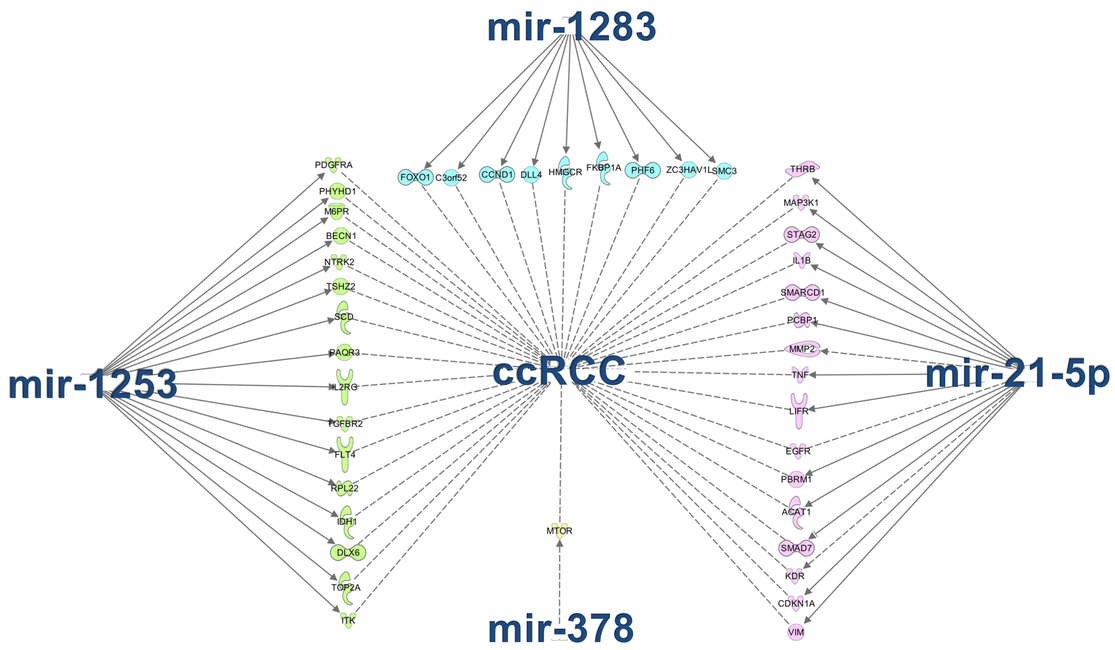


Figure 4: **miRNA association.** Decreased miRNA expression associated with High Risk ccRCC

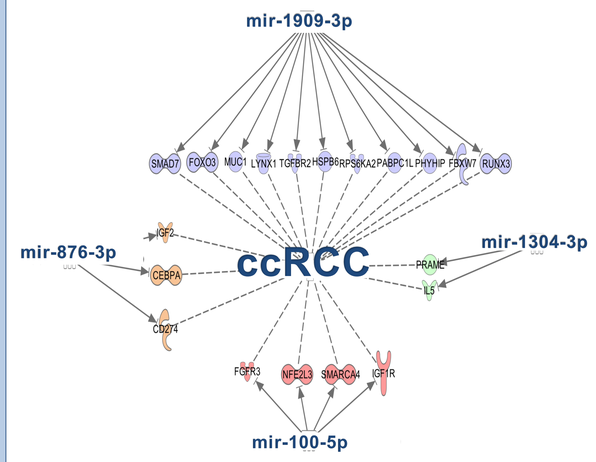


Figure 5: **miRNA association.** Increased miRNA expression associated with High Risk ccRCC

Conclusions

- **These findings suggest that high risk renal malignancies demonstrate a unique exosomal signature which can be used to as target for anticancer agents.**
- **Further validation of these markers may create blood-based markers for ccRCC aggressiveness.**
- **Analyses of pathways highlight several potential novel therapeutic treatment pathways.**

Acknowledgments

- Department Editor: Jessica Daigle
- Thank you to Tulane University School of Medicine for funding the license that allowed us to use IPA.
- FUNDING: Aspire Program/Debakey Scholars, Carol-Lavin Bernik Grant