

Exploration of hsa-mir-943 Function and Survival Impact in Uterine Cancers



Amber Hoskins, Elizabeth Miller, Elizabeth Schmidt, Mary Clayton, Rachel Frick, Riyaz Basha, PhD

BACKGROUND

- MicroRNAs (mRNAs) are small, non-coding RNAs that have been linked to cancer cell proliferation and prognosis due to their function in post-transcriptional gene regulation
- Thus, miRNAs have emerged as a novel biomarker to evaluate cancer prognosis based on differential expression
- In a genetic study of 69 individuals across 14 global population, hsa-miR-943 was identified as having population-differentiated genetic variation and previous linkage to cancer susceptibility as well as a higher-than-expected number of disease expression reports¹
- Expression of hsa-miR-943 has been reported across several tumor subtypes, including ovarian, lung, gastric, and prostate cancers, however a consistent expression pattern, functional mechanism, or prognostic value has not yet been established²
- Hsa-miR-943 is a relatively under-characterized miRNA in uterine cancers

METHODS

- Data on miRNA coding genes was obtained from The Cancer Genome Atlas (TCGA) via the University of Alabama at Birmingham Cancer data analysis portal (UALCAN)
- A comparison was made between the expression of hsa-mir-943 in UCEC vs USC
- Survival curves were obtained for UCEC and USC.
- Expression data for UCEC was extracted and evaluated for statistical significance
- Data related to miRNAs and associated gens came from TCGA accessed through UALCAN and survival curves were analyzed using Kaplan-Meier method with log-rank test. A p-value of 0.05 was used

Comparison of Top 100 Most Significant miRNA-Coding Genes Across 5 Women's Health Cancers				
Breast Invasive Carcinoma	Cervical Squamous Cell Carcinoma	Ovarian Serous Cysadenocarcinoma	Uterine Corpus Endometrial Carcinoma	Uterine Carcinosarcoma
hsa-mir-7706	hsa-mir-378d-2	hsa-mir-1301	hsa-mir-335	hsa-mir-181b-1
hsa-mir-125a	hsa-mir-502	hsa-mir-199a-1	hsa-mir-588	hsa-mir-190a
hsa-mir-5690	hsa-mir-3607	hsa-mir-3177	hsa-mir-1269a	hsa-mir-497
hsa-let-7e	hsa-mir-378c	hsa-mir-6834	hsa-mir-4723	hsa-mir-526b
hsa-mir-605	hsa-mir-600	hsa-mir-1245a	hsa-mir-7703	hsa-mir-4754
hsa-mir-181b-2	hsa-mir-7-3	hsa-mir-2276	hsa-mir-6871	hsa-mir-518e
hsa-mir-130b	hsa-mir-4680	hsa-mir-5008	hsa-mir-372	hsa-mir-1181
hsa-mir-503	hsa-mir-188	hsa-mir-4793	hsa-mir-598	hsa-mir-98
hsa-mir-186	hsa-mir-296	hsa-mir-6891	hsa-mir-6721	hsa-mir-943
hsa-mir-509-2	hsa-mir-6797	hsa-mir-1262	hsa-mir-760	hsa-mir-4735
hsa-mir-574	hsa-mir-6087	hsa-mir-6509	hsa-mir-320d-1	hsa-mir-767
hsa-mir-4664	hsa-mir-378d-1	hsa-mir-632	hsa-mir-211	hsa-mir-4515
hsa-mir-484	hsa-mir-599	hsa-mir-545	hsa-mir-499a	hsa-mir-29c
hsa-mir-3127	hsa-mir-532	hsa-mir-4525	hsa-mir-193a	hsa-mir-29b-2
hsa-mir-410	hsa-mir-128-1	hsa-mir-219a-1	hsa-mir-1249	hsa-mir-331
hsa-mir-495	hsa-mir-101-1	hsa-mir-6515	hsa-mir-548f-1	hsa-mir-616
hsa-mir-103a-2	hsa-mir-4491	hsa-mir-4647	hsa-mir-584	hsa-mir-130a
hsa-mir-6793	hsa-mir-216a	hsa-mir-199b	hsa-mir-137	hsa-mir-6798
hsa-mir-6802	hsa-mir-3178	hsa-mir-4709	hsa-mir-943	hsa-mir-519d
hsa-mir-19a	hsa-mir-2278	hsa-mir-451a	hsa-mir-379	hsa-mir-4286

Table 1. Comparison of Significant MiRNA-coding Genes in Gynecological and Breast Cancers

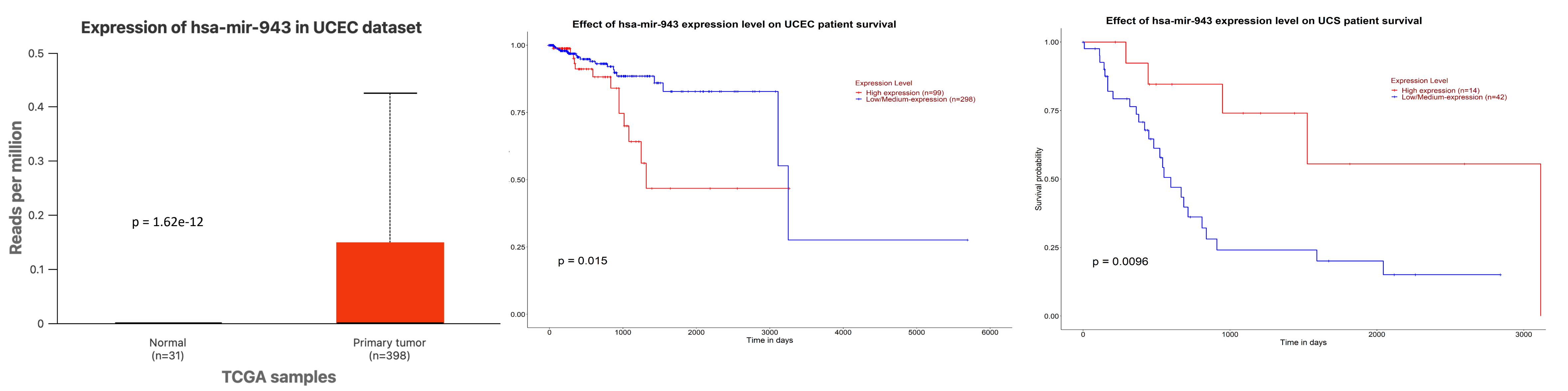


Figure 1. UCEC Expression data of hsa-mir-943 and Kaplan-Meier Survival Curves in UCEC and UCS based on hsa-mir-943 expression

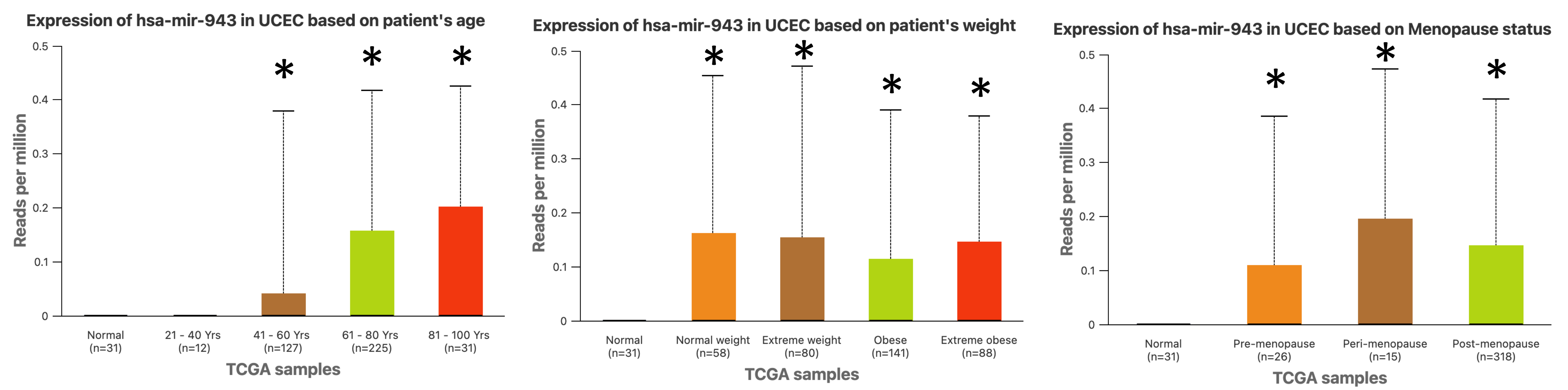


Figure 2. Expression differences of hsa-miR-943 based on Patient Age, Patient Weight, and Patient Menopausal Status in UCEC

* Indicates statistically significant in comparison to normal (p<0.05)

RESULTS AND CONCLUSIONS

- Table 1: Comparing 100 miRNA-coding genes found statistically significant in women's cancers, only one gene appears in more than 1 cancer: hsa-mir-943
- Figure 1: High expression of hsa-mir-943 (n=99) was associated with shorter survival time for UCEC compared to low/medium expression (n=298, p=0.015) demonstrating an oncogenic role. High expression of hsa-mir-943 (n=14) in UCS was associated with longer survival time compared to low/medium expression (n=42, p=0.0096) demonstrating a tumor suppressor role.
- Figure 2, Age: Categories seen as having a statistically significant increase of hsa-mir-943 expression compared to normal include 41-60 Yrs, 61-80 Yrs, and 81-100 Yrs
- Figure 2, Weight: Categories seen as having a statistically significant increase of hsa-mir-943 expression compared to normal include Normal Weight, Extreme Weight, Obese, and Extreme Obese
- Figure 2, Menopausal Status: Categories seen as having a statistically significant increase of hsa-mir-943 expression compared to normal include Pre Menopause, Peri Menopause, and Post Menopause
- Figure 2: hsa-mir-943 expression is highly variable based on several patient demographic factors

FUTURE DIRECTIONS

- Going forward, we would want to expand the sample size of UCS data regarding high hsa-mir-943 expression to further support our conclusion by increasing the sample size
- Currently, there is no clinical trial information specifically about hsa-mir-943 in uterine cancer specifically, so future clinical trials should expand to include miRNA information during trials and evaluations of trials

REFERENCES

