



Serum miRNAs are crucial for prediction of Asthma Exacerbations in Costa Rica

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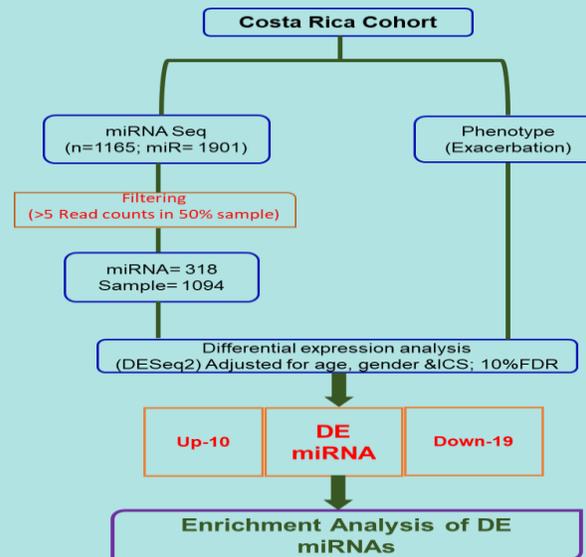
Rationale

- Asthma is chronic inflammation of the airways characterized by airway obstruction due to both smooth muscle hyperresponsiveness and inflammation.
- Asthma affects >350 million people worldwide.
- It is the leading chronic condition that occurs results in hospitalization and school absences in children.
- MicroRNAs (miRNAs) are small non-coding RNAs that regulate their target mRNAs post-transcriptionally through degradation or translational repression.
- miRNAs have emerged as vital molecules in asthma.
- However, the investigation of circulating miRNAs association with significant clinical events including exacerbations has not been carried out previously.

Objective

- The purpose of this study was to determine the association between circulating miRNAs & asthma exacerbation.
- miRNAs regulate gene expression, particularly inflammatory pathways
- Airway inflammation is a primary driver of the asthma exacerbation.
- Our primary outcome was severe asthma exacerbations, defined as >2 emergency room or urgent care visits in GACRS.

Methods



Results

- We identified 10 upregulated & 19 downregulated miRNAs among 29 differentially expressed miRNAs between frequent exacerbation (n=778) & infrequent exacerbation subjects (n=316).
- To check the ability of 4 DE replicated miRs to predict Asthma exacerbations, we used a linear regression model and obtained an AUC of 63%, indicating a predictive performance statistically better than random guessing.
- Enrichment analysis showed the most enriched pathway cluster was PI3AKT, Ras, RAP and MAPK signaling pathway.

Table 1. Significant up- and down-regulated miRNAs between infrequent exacerbators and frequent exacerbators

	baseMean	log2FC	pvalue	padj
hsa-miR-30a-3p	1.43E+02	-1.25286	1.08E-10	1.44E-08
hsa-miR-500b-3p	1.81E+02	-1.00606	6.83E-13	1.82E-10
hsa-miR-411-5p	1.40E+02	-0.7959	1.57E-05	8.40E-04
hsa-miR-766-3p	7.96E+01	-0.7334	1.06E-04	3.15E-03
hsa-miR-3131	7.87E+01	-0.68029	3.00E-03	4.22E-02
hsa-miR-483-5p	6.35E+02	-0.64017	5.89E-05	2.24E-03
hsa-miR-98-5p	5.95E+02	-0.63722	2.71E-06	2.39E-04
hsa-miR-326	1.58E+02	-0.63403	1.74E-03	2.73E-02
hsa-miR-1-3p	2.58E+03	-0.58073	1.93E-04	4.68E-03
hsa-miR-1290	1.10E+02	-0.46007	4.96E-04	9.93E-03
hsa-miR-148a-5p	1.66E+02	-0.4453	1.03E-02	9.79E-02
hsa-miR-7706	1.51E+02	-0.44387	5.35E-03	6.49E-02
hsa-miR-409-5p	5.86E+02	-0.3449	4.24E-03	5.67E-02
hsa-miR-1271-5p	6.03E+02	-0.31445	2.71E-03	4.02E-02
hsa-miR-99a-5p	8.87E+04	-0.21566	7.49E-04	1.33E-02
hsa-miR-500a-3p	3.99E+03	-0.19627	7.67E-03	8.53E-02
hsa-miR-10a-5p	1.56E+05	-0.18285	8.80E-03	9.04E-02
hsa-miR-10b-5p	2.28E+05	-0.18031	1.07E-02	9.81E-02
hsa-miR-24-3p	2.04E+04	-0.13488	9.25E-03	9.15E-02
hsa-miR-21-5p	2.71E+04	0.16217	6.35E-03	7.37E-02
hsa-miR-25-3p	1.06E+04	0.209544	8.54E-03	9.04E-02
hsa-miR-28-3p	4.20E+03	0.260048	2.93E-04	6.52E-03
hsa-miR-101-3p	2.81E+04	0.312038	7.60E-05	2.54E-03
hsa-miR-103a-3p	2.42E+03	0.366806	1.58E-04	4.21E-03
hsa-miR-443b-5p	3.82E+02	0.397657	4.51E-03	5.73E-02
hsa-miR-342-5p	8.36E+02	0.522224	1.92E-05	8.53E-04
hsa-miR-3158-3p	8.08E+01	0.658961	1.41E-03	2.35E-02
hsa-miR-125b-5p	6.01E+01	0.781527	5.21E-04	9.93E-03
hsa-miR-1307-5p	2.95E+02	0.851277	3.58E-06	2.39E-04

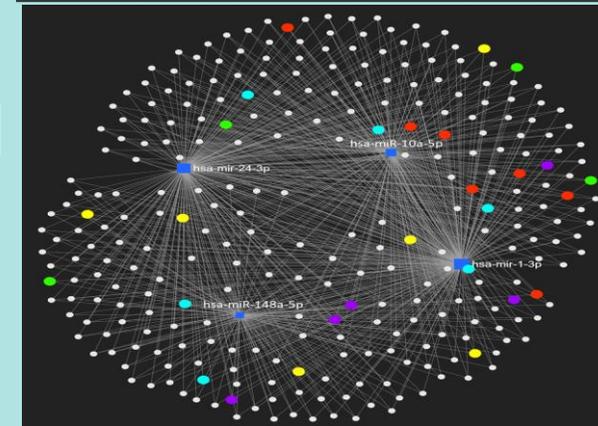
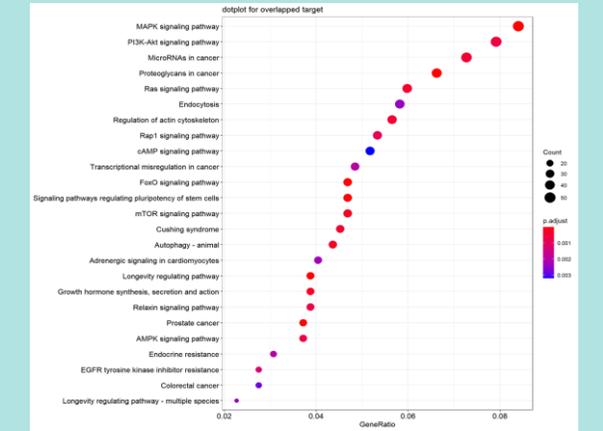


Figure 1. Network between DE miRNA and putative target genes from miRNet. Sky-blue color squares represent the miRNAs and different color circles represents the target genes involved in different essential pathways implicated in Asthma.

Figure 2. Functional enrichment of putative target genes of DE miRNAs from KEGG



Conclusion

Results show that 29 DE miRNAs were linked with asthma exacerbation in our discovery cohort and involved in 4 main asthma-related pathways: PI3AKT, Ras, RAP and MAPK signaling pathway.

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