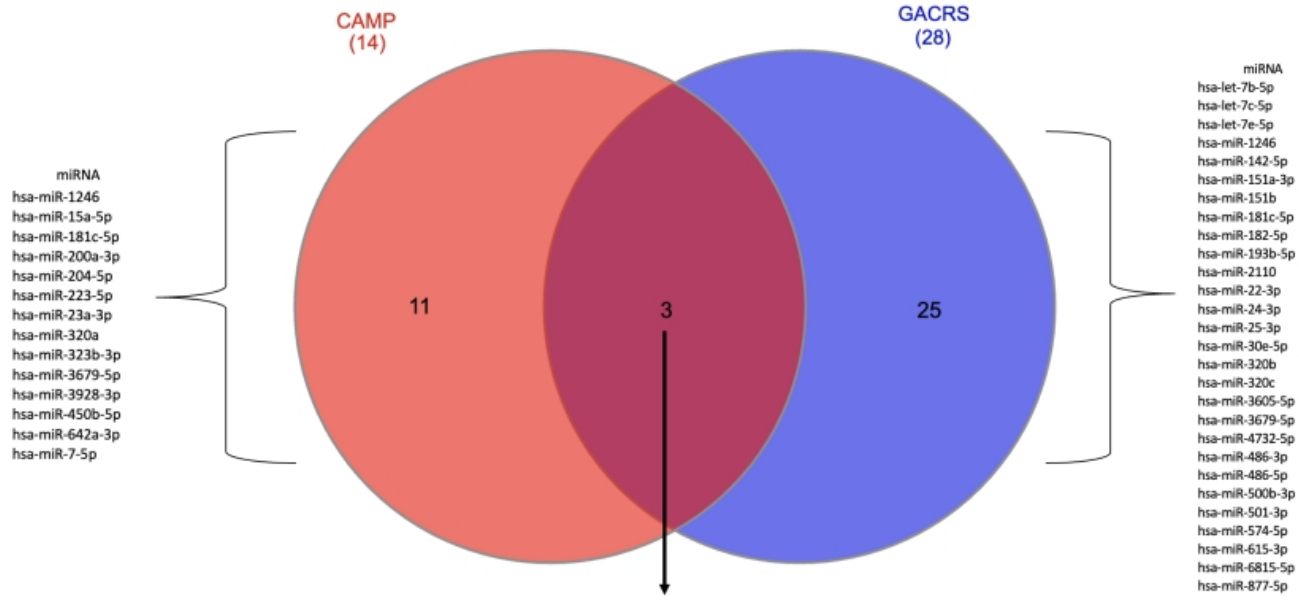
Microrna and Short-Acting Beta-2 Agonist Usage in Asthma

R. Wong[1], B. Desai[2], U. Srivastava[3], A. Kho[4], S. T. Weiss[5], J. C. Celedon[6], M. McGeachie[5], K. Tantisira[1]; [1]Division of Pediatric Respiratory Medicine, University of California San Diego - Rady Children's Hospital, San Diego, CA, United States, [2]Division of Pulmonology and Critical Care, University of California San Diego, San Diego, CA, United States, [3]Division of Pediatric Respiratory Medicine, University of California San Diego, San Diego, CA, United States, [4]Computational Health Informatics, Boston Children's Hospital, Boston, MA, United States, [5]Channing Division of Network Medicine, Brigham and Women's Hospital, Boston, MA, United States, [6]Division of Pediatric Pulmonary Medicine, University of Pittsburgh Medical Center - Children' Hospital of Pittsburgh, Pittsburgh, PA, United States.

Corresponding author's email: riwong@health.ucsd.edu

Rationale: MicroRNAs (miRNAs) are small non-coding segments that can target downstream pathways, which may influence the pathogenesis of intermediate phenotypes in diseases like asthma. GINA guidelines stratify asthma diagnosis and control by several clinical phenotypes. We hypothesized that miRNA expression can worsen asthma symptom control, leading to increased short acting beta agonist (SABA) use. We tested this hypothesis in two independent cohorts of children with asthma, the Childhood Asthma Management Program (CAMP) and the Genetics of Asthma in Costa Rica Study (GACRS). Methods: Banked serum miRNAs sequences were utilized from 491 CAMP and 1159 GACRS participants. After quality control and filtration of low-quality miRNA counts, differential gene expression using DESeq in R was conducted on 255 miRNAs in CAMP and 304 miRNAs in GACRS. Cross-cohort analysis focused on differential gene expression by SABA use frequency. Data was extracted from their respective studies using questionnaires obtained at the time of sampling and categorized by frequency of SABA use. In both CAMP and GACRS, the frequency of SABA use was dichotomized as “little to no use” (defined as less than once per week) versus “increased use” (defined as greater than or equal to once per week). Statistical significance was defined as a p-value <0.05. Results: We identified 14 miRNAs in CAMP and 28 miRNAs in GACRS that were differentially expressed by increased SABA use at P <0.05. Of these, three miRNAs were differentially expressed in both cohorts: hsa-miR-1246, hsa-miR-3679-5p, and hsa-miR-181c-5p. Increased miRNA expression in hsa-miR-3679-5p was associated with increased SABA use in both cohorts. With regard to increased SABA use, hsa-miR-1246 had decreased expression in CAMP and increased expression in GACRS. Conversely, hsa-miR-181c-5p had increased expression in CAMP and reduced expression in GACRS. Conclusion: Three miRNAs were differentially expressed by frequency of SABA use in two cohorts of children with asthma, with one of these miRNAs (hsa-miR-3679-5p) having the same direction of association in both cohorts. Our results suggest that altered expression of hsa-miR-3679-5p may contribute to β2-adrenergic responsiveness. Alternatively, our findings may be mediated by another variable that influences frequency of SABA use. Further analyses focused on utility of these miRNAs as biomarkers and gene ontology/pathway enrichment are underway. These may further inform the role of the miRNAs in airway biology and/or neurobehavioral symptoms pathogenesis.



miRNA	Expression (Log 2 Fold Change)*	P-value	Study
hsa-miR-1246	-0.387	0.008	CAMP
hsa-miR-1246	0.302	0.024	GACRS
hsa-miR-181c-5p	0.538	0.019	CAMP
hsa-miR-181c-5p	-0.564	0.010	GACRS
hsa-miR-3679-5p	0.519	0.007	CAMP
hsa-miR-3679-5p	0.590	0.009	GACRS

*Log 2-fold change: Ratio of gene expression in logarithmic base 2 scale

This abstract is funded by: NIH: R01 HL16257, R01 HL161362, R01 HL127332, R01 HL 139634, R01 HL 155742

Am J Respir Crit Care Med 2023;207:A3609
Internet address: www.atsjournals.org **Online Abstracts Issue**