

MicroRNAs and Frequency of Nighttime Symptoms in Asthma

Richard Wong, DO¹; Brinda Desai, MD²; Upasna Srivastava, PhD¹; Alvin T Kho, PhD^{3,4,5}; Scott T Weiss, MD⁴; Juan C Celedón, MD, DrPH⁶; Michael J McGeachie, PhD^{3,4}; Kelan Tantisira, MD, MPH¹

1. University of California San Diego, Rady Children's Hospital, Division of Pediatric Respiratory Medicine, San Diego, CA, USA
2. University of California San Diego, Division of Pulmonology and Critical Care, San Diego, CA, USA
3. Channing Division of Network Medicine, Brigham and Women's Hospital, 181 Longwood Avenue, Boston, MA, 02115, USA.
4. Harvard Medical School, 25 Shattuck Street, Boston, MA, 02115, USA.
5. Computational Health Informatics Program, Boston Children's Hospital, 320 Longwood Avenue, Boston, MA, 02115, USA.
6. Division of Pediatric Pulmonary Medicine, UPMC Children's Hospital of Pittsburgh, University of Pittsburgh, Pittsburgh, PA.

Rationale:

MicroRNAs (miRNAs) are small non-coding segments that can target downstream pathways that can influence symptoms in diseases like asthma. GINA guidelines stratify asthma diagnosis and control on several clinical phenotypes including frequency of nighttime symptoms. We hypothesized that miRNA expression can influence asthma symptom control resulting in a child's increased nighttime symptoms in two independent clinical cohorts, the Childhood Asthma Management Program (CAMP) and Genetics of Asthma in Costa Rica (GACRS).

Methods:

Banked serum miRNAs sequences were utilized from 491 CAMP and 1159 GACRS participants. Differential gene expression using DESeq in R was conducted on 255 miRNAs in CAMP and 304 miRNAs in GACRS. Differential gene expression analysis was conducted comparing patients with different frequency of night time symptoms. This analysis dichotomized nighttime symptom control based on awakening frequency due to symptoms. GACRS defined "Controlled" as absence of any nighttime symptoms in the past year. CAMP defined "Controlled" as symptoms occurring less than once weekly per month. Statistical significance was defined as a p-value of 0.05.

Results:

In assessing differential gene expression with frequency of nighttime symptoms, we identified 2 common miRNAs among 25 miRNAs in CAMP and 30 miRNAs in GACRS that had $p < 0.05$. These miRNAs were hsa-miR-181a-5p and hsa-miR-24-3p. Decreased miRNA expression in hsa-miR-24-3p was observed with increased nighttime awakenings due to asthma symptoms both cohorts. Hsa-181a-5p had different levels of gene expression when evaluating increased nighttime asthma symptoms. On gene target enrichment analysis, ErbB signaling pathway had highest expression (2.7-Fold Enrichment) and was the most statistically significant (FDR 1.3E-05)

Conclusion:

We have identified 2 miRNAs that were differentially expressed in two independent asthma cohorts when evaluating nighttime awakenings due to asthma symptoms. During the gene target enrichment analysis, the top pathway identified, ErbB, was also the top pathway in a separate analysis evaluating SABA-usage frequency. These results may suggest that altered levels of miRNAs may play a role in the pathogenesis of uncontrolled asthma due to its pathway involvement in altered epithelial differentiation, remodeling, and airway inflammation, which can contribute to nighttime awakenings.

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