MiRNAs and Baseline Asthma Daytime Symptoms in Two Pediatric Cohorts

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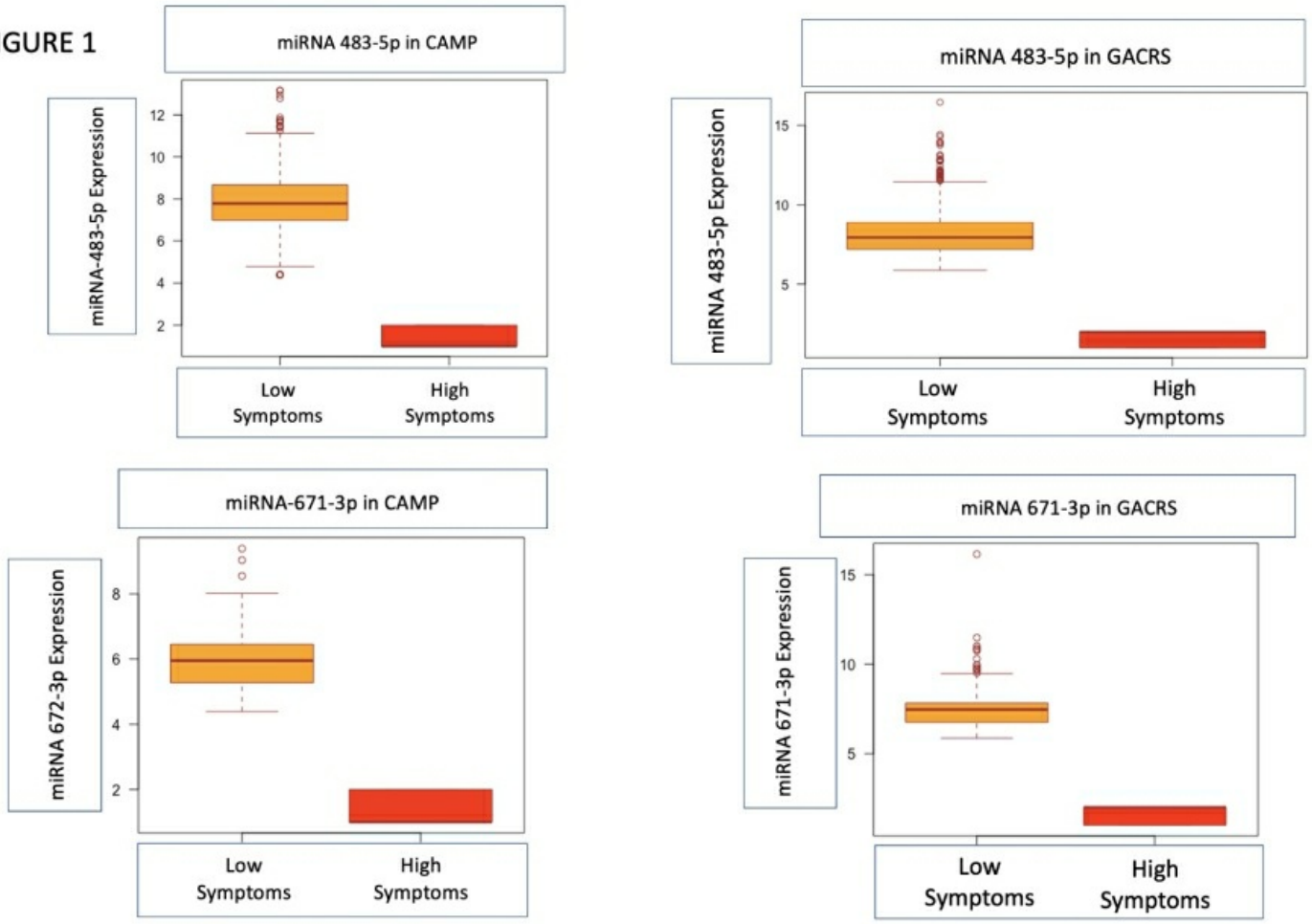
RATIONALE: Asthma is a complex disease influenced by environmental, behavioral, and genetic factors. Micro-RNAs (miRNAs) may be helpful as both biomarkers and therapeutic targets in childhood asthma. We hypothesized that miRNAs play a key regulatory role in daytime asthma symptoms in children. We tested this hypothesis in two independent cohorts of children with asthma. METHODS: For our analyses, miRNA was sequenced from serum of 492 children (ages 5-12 years) in the Childhood Asthma Management Program (CAMP) and 1159 children (ages 4-6 years) in the Genetics of Asthma in Costa Rica Study (GACRS). The subject recruitment and study procedures were previously reported in literature. Baseline daytime symptoms from both cohorts were derived from questionnaires obtained at the time of the serum samples. These were then dichotomized into low (0-1 symptoms per month) or high (symptoms once or more per week). Following quality control and filtering of the miRNAs to those present with >5 counts in at least 50% of the cohort, we performed differential gene expression analysis using Deseq2 analysis in R studio. A total of 255 miRNAs in CAMP and 304 miRNAs in GACRS and were analyzed; statistical significance was set at $p< 0.05$. Following differential expression analysis in the CAMP cohort, replication in GACRS for the significant miRNAs was analyzed by both p-values and direction of association between the two cohorts. RESULTS: After performing DeSeq2 analysis, we identified twenty-nine miRNAs associated with baseline daytime symptoms in the CAMP population. Of these highly expressed miRNAs in CAMP, we identified two miRNAs (hsa-miR-483-5p and hsa-miR-671-3p) as being significantly associated with daytime symptoms across both CAMP and GACRS subjects (Figure 1). Increased expressions of both hsa-miR-483-5p and hsa-miR-671-3p were associated with increased baseline daytime symptoms in the low and high symptoms groups across the two cohorts ($p=0.022$ in CAMP and $p=0.048$ in GACRS for hsa-miR-483-5p; $p=0.022$ in CAMP and $p=0.045$ in GACRS for hsa-miR-671-3p). CONCLUSIONS: We identified two circulating miRNAs associated with daytime symptoms in both the CAMP and GACRS populations. Based on our preliminary data, it appears that these miRNA (hsa-miR-483-5p and hsa-miR-671-3p) play a protective role in daytime symptoms across both CAMP and GACRS (figure 1); however, this will need further investigation and replication across additional cohorts. Additionally, we will need to analyze whether they can serve as targetable biomarkers for the development of therapy.

FIGURE 1



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