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Identification of asthma associated microRNAs in bronchial biopsies

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Key message (max. 251/256 characters)

- Using small RNA sequencing on bronchial biopsies of asthma patients and healthy controls we identified microRNAs that are associated with clinical and inflammatory features of asthma and are potential regulators of asthma-associated gene expression.

Abstract (226/250 words) :

Changes in microRNA (miRNA) expression can contribute to the pathogenesis of many diseases, including asthma. We aimed to identify miRNAs that are differentially expressed between asthma patients and healthy controls and explored their association with clinical and inflammatory parameters of asthma.

Differentially expressed miRNAs were determined by small RNA sequencing on bronchial biopsies of 79 asthma patients and 82 healthy controls using linear regression models. Differentially expressed miRNAs were associated with clinical and inflammatory asthma features. Potential miRNA-mRNA interactions were analysed using mRNA data available from the same bronchial biopsies and enrichment of pathways was identified with Enrichr and g:Profiler.

In total 78 differentially expressed miRNAs were identified in bronchial biopsies of asthma patients compared to controls, of which 60 remained differentially expressed after controlling for smoke and inhaled corticosteroid treatment. We identified several asthma associated miRNAs, including miR-125b-5p and miR-223-3p, based on a significant association with multiple clinical and inflammatory asthma features and their negative correlation with genes associated with the presence of asthma. The most enriched biological pathway(s) affected by miR-125b-5p and miR-223-3p were inflammatory response and cilium assembly and organization. Of interest, we identified that lower expression of miR-26a-5p was linked to more severe eosinophilic inflammation as measured in blood, sputum as well as bronchial biopsies.

Collectively, we identified miR-125b-5p, miR-223-3p and miR-26a-5p, as potential regulators that could contribute to the pathogenesis of asthma.

Introduction

Asthma is a chronic inflammatory airway disease characterized by airway obstruction and airway hyperresponsiveness resulting in shortness of breath, cough, wheezing and chest tightness. Around 300 million people worldwide are affected by asthma [1]. Although asthma symptoms can be controlled by inhaled corticosteroids (ICS) and long-acting β-agonists, there is no cure available and optimal asthma control cannot be obtained in all patients with currently available treatments [1]. Therefore, there is a need to better understand the pathogenesis of asthma to identify new therapeutic targets and improve the management of asthma patients.

Genetics, epigenetics and microRNAs (miRNAs) are involved in the pathogenesis of asthma [2]. MiRNAs are small non-coding RNA molecules that target specific mRNAs leading to their degradation or translational repression. Several miRNAs can target the same mRNA and each miRNA can regulate hundreds of mRNAs [3]. Therefore, miRNAs have the potential to regulate many cellular functions including inflammation, cell differentiation and cell death [4]. MiRNAs can provide novel targets for new therapeutic treatment strategies, because miRNAs are small, highly conserved and have a specific sequence. As an example blocking the function of miR-155 with an miR-155 antagomir has been shown to overcome cancer cell drug resistance in a mouse model [5].

Several groups have investigated miRNA profiles in bronchial biopsies, brushings, blood and sputum of asthma patients compared to healthy controls [6–11]. However, generally small cohorts were used and most studies were based on microarray technology, which is less sensitive and specific compared to sequencing. In this study, we performed small RNA sequencing with matched RNA sequencing in the same bronchial biopsies of 79 well-characterized asthma patients and 82 matched healthy individuals. We aimed to identify miRNAs involved in the pathogenesis of asthma. We focussed on differentially expressed miRNAs and miRNA – mRNA correlations that are associated with clinical and inflammatory asthma features.

Material and Methods

Subjects characteristics

Asthma patients (n=79) had a doctor’s diagnosis of asthma and presence of bronchial hyperresponsiveness to adenosine 5’-monophosphate (AMP) or histamine. Healthy subjects (n=82) had normal pulmonary function, normal spirometry with forced expiratory volume in 1 second (FEV_1) >80% predicted and FEV_1/forced vital capacity (FVC) greater than the lower limit of normal, absence of reversibility (FEV_1% predicted to salbutamol <10%), no bronchial hyperresponsiveness (PC_{20} methacholine >16 mg/mL) and no respiratory symptoms [12]. Patients were included from three studies [12, 13], all carried out in the University Medical Center Groningen between 2001-2012 and approved by the local medical ethics committee (METc 2009/007, 2001/074 and 2004/271). All subjects provided their written informed consent.

Clinical measurements

Sputum induction, blood sampling, lung function and bronchial biopsies were performed in all subjects as previously described [12].

RNA isolation

Total RNA was extracted from frozen bronchial biopsies using the AllPrep DNA/RNA/miRNA Universal kit (Qiagen, Venlo, Netherlands), according to manufacturer’s instructions. Quality of RNA was assessed using Nanodrop-1000 and Labchip GX (PerkinElmer, Waltham, MA). Total RNA was extracted at the same time and asthma patients and controls were evenly distributed over batches of 12 samples based on disease/control-status, sex, age and smoking status.

MiRNA sequencing

Small RNA sequencing library preparation was performed using NEXTflex small-RNA-seq kit V3 (Bioo-Scientific Corporation, Austin, TX). Clean-up beads were used to eliminate small RNA fraction and quality control of RNA library was checked using LabChip GX (Perkin Elmer, Waltham, MA). Sequencing was performed using Illumina HiSeq 2500 (Illumina, San Diego, CA). Quality control of raw RNA sequencing data was performed using FastQC (version 0.11.5) and quality control of raw reads of adapter sequence was done using TrimGalore (version 0.3.7). NEXTFlex small-RNA-seq kit V3 processing was done using custom scripts documented in the GitHub repository. Alignment and quantification were performed using miRDeep2 (2.0.0.8) with Bowtie (v0.12.7). Also during the library preparation and sequencing, the samples were evenly distrusted over the batches based on disease/control-status, sex, age and smoking status.

mRNA sequencing

Sample preparation and mRNA sequencing was performed as previously described [14]. Library preparation for mRNA and miRNA sequencing was performed at the same time for asthma patients and healthy controls and samples were evenly distributed over the batches.

Statistical analyses of small RNA sequencing data

The (small) RNA sequencing data analyses were performed with R (version 3.5.3). MiRNAs with an average read count below 100 in asthma patients or healthy controls were filtered out. Differential expression of microRNAs was analysed with DESeq2 (version 1.24.0) adjusting for sex, age, smoking and library batch and corrected for multiple testing using Benjamini-Hochberg false discovery rate (FDR), FDR-values <0.05 were considered as statistically significant. Heatmap was generated and ordered from highest to lowest negative fold change miRNA in asthma patients compared to healthy controls. To exclude potential effects of ICS and smoke, a sensitivity analysis was performed in a subset of asthma patients (n=30) compared to healthy controls (n=42) excluding participants that smoke or use ICS.

Linear regression was performed to associate differentially expressed miRNAs with relevant clinical and inflammatory features of asthma; FEV_1 % predicted, PC_{20} AMP, eosinophil and neutrophil counts in blood, tissue and percentages of eosinophils and neutrophils in sputum in all asthma patients adjusting for age, sex, smoking status and ICS treatment.

To assess for miRNA-mRNA correlations, expression levels were log2-transformed into counts per million (logCPM). Pearson's correlations for miRNA-mRNA were calculated for miRNAs with one or more associations with asthma features, and genome wide gene expression data available in matched subjects (FDR-values <0.05 were considered statistically significant). Negatively correlated genes were checked for their association with asthma using the same statistical model in matched biopsies, these were defined as asthma genes. For those miRNAs, we checked for experimentally validated target genes in miRTarBase (v7.0) [15].

Gene ontology and pathway analyses

For each miRNA, the negatively or the positively and negatively correlated asthma-associated genes were analysed with Enricher [16, 17] and g:Profiler [18] to identify enriched biological processes (GO Biological Process 2018 in Enrichr and GO:BP releases/2020-12-15 in g:Profiler) and Reactome pathways (Reactome_2016 in Enrichr and Reactome_2020-12-15 in g:Profiler).

Results

Patients characteristics

The clinical characteristics of 79 asthma patients and 82 healthy controls are shown in **Table 1**. There were no significant differences between asthma patients and healthy controls with respect to sex and pack years. Asthma patients had significantly higher age, were less often current-smokers, had a lower FEV_1 % predicted and FEV_1/FVC, and more severe bronchial hyperresponsiveness to AMP.

Differentially expressed miRNAs in asthma patients compared to healthy controls

Of the 1860 miRNAs that were detected in bronchial biopsies, 136 miRNAs remained after filtering for low abundance. Of these 136, 78 miRNAs were differentially expressed in asthmatic patients compared to healthy controls, 48 having higher expression and 30 having lower expression in asthma (FDR p-value <0.05; **Figure 1a**). MiR-451a had the highest fold change, whereas miR-125b-5p had the lowest negative fold change in asthma. A volcano plot illustrates all differentially expressed miRNAs, with the top 5 most significant highest and lowest miRNAs indicated (FDR adjusted p-value <0.05; **Figure 1b**). To assess whether smoke and ICS treatment influenced the 78 differentially expressed miRNAs, we conducted a sensitivity analysis on a subgroup of individuals that did not smoke and did not use ICS. Of the 78 miRNAs that were differentially expressed between asthma patients and healthy controls in the complete cohort, 60 miRNAs remained significant in the same direction in the sensitivity analysis showing that our findings are robust (FDR adjusted p-value <0.05, **Figure 1c**). **Supplementary tables S1 and S2** present the full lists of significantly differentially expressed miRNAs in asthma patients compared to healthy controls, including and excluding smokers and ICS treated patients.

The expression of 25 differentially expressed miRNAs is associated with asthma features

To determine whether the 60 differentially expressed miRNAs in bronchial biopsies are relevant in asthma, we investigated the association of differentially expressed miRNAs with FEV_1 % predicted, PC_{20}AMP, eosinophil and neutrophil counts in blood, tissue and percentages of eosinophils and neutrophils in sputum of all asthma patients. We observed that 25 of the 60 differentially expressed miRNAs was associated with one or more clinical and inflammatory feature(s). **Figure 2** illustrates the association between miRNAs and features of asthma with T-values of the linear regression (p-value <0.05). Higher miR-21-5p expression in biopsies had the most significant association with more neutrophils in blood, and it was also associated with more neutrophils and eosinophils in tissue. Furthermore, miR-26a-5p had three significant associations with asthma features: lower miR-26a-5p expression was associated with higher eosinophil counts in blood, sputum and tissue. Moreover, higher expression levels of miR-223-3p were linked to higher eosinophils and neutrophils in tissue. Additionally, we observed that lower miR-125b-5p levels, the lowest negative fold change miRNA in asthma, was associated with lower FEV_1 % predicted and higher neutrophil levels in blood. For miR-451a, the miRNA with the highest fold change in asthma, we did not observe any associations with asthma features in our study.

Identification of key asthma-associated miRNA-mRNA targets

To investigate potential interactions between miRNA and mRNA expression, we correlated expression levels of the 25 miRNAs, that were associated with one or more clinical and inflammatory asthma feature(s), with mRNA sequencing data available from the same biopsies from all asthma patients and healthy controls. Hereby, we focused on the negatively correlated genes. The expression of 23 of the 25 miRNAs was negatively correlated with mRNA expression of one or more genes **(Table 2).** Thereafter, we investigated which of the negatively correlated genes were also associated with the presence of asthma. For miR-199b-

5p, miR-223-3p, miR-199b-3p, miR-142-5p, miR-181b-5p, miR-195-5p and miR-125b-5p, we observed that ~10% of the negatively correlated genes were also associated with asthma. A full list of negatively correlated genes per miRNA is provided in **Supplementary table S3.** As the expression of these 7 miRNAs (miR-199b-5p, miR-223-3p, miR-199b-3p, miR-142-5p, miR-181b-5p, miR-195-5p and miR-125-5p) was associated with one or more clinical and inflammatory asthma features and ~10% of their negatively correlated were associated with asthma genes, we selected those miRNAs as our candidate asthma miRNAs. For the five lower expressed miRNAs in asthma in our study, miR-199b-5p, miR-199b-3p, miR-181b-5p, miR-195-5p and miR-125b-5p, we observed that the genes *HBA1* and *RGS18* had the most significant negative correlation **(Figure 3a-b)**. *HBA1* and *RGS18* expression levels were higher in bronchial biopsies of asthma patients compared to healthy controls. Furthermore, for the two higher expressed asthma miRNAs in our study, miR-223-3p and miR-142-5p, we observed that *GREM2* and *RPS3AP5* are the most significant negatively correlated genes **(Figure 3c-d).** *GREM2* expression levels were lower in bronchial biopsies of asthma patients compared to healthy controls, while no expression differences were found for *RPS3AP5*. In addition, among the negatively correlated asthma-associated genes we identified 3 validated target genes for miR-199b-5p (*AGTRAP, RNF11* and *SNTB1),* 1 validated target gene for miR-125b-5p (S100A8) and 15 validated target genes for miR-223-3p (*ARL8B, ARTN, CAPRIN1, CDS1, CHMP2B, CHUK, MSMO1, NSUN3, PDZD8, SECISBP2L, TWF1, WASL, and ZBTB18).*

Enrichment of biological processes and pathways in negatively correlated asthma genes

To identify the potential mechanisms underlying the involvement of our 7 key candidate asthma miRNAs in disease pathogenesis, pathway enrichment analyses were performed on the negatively correlated asthma-associated genes, whereby we included all asthma patients and healthy controls. Gene ontology revealed in total 187 biological processes and 212 reactome pathways that were significantly enriched among the negatively correlated mRNA transcripts (FDR <0.05). The most significant biological process for miR-199b-5p and miR-223-3p was ‘cilium assembly’, for miR-181b-5p, miR-199b-3p and miR-195-5p ‘neutrophil degranulation’ and for miR-125b-5p ‘inflammatory response’. For miR-142-5p no significant enrichment was found using Enrichr, however using g:Profiler, four biological processes related to protein transport along microtubule were obtained. The top 5 pathways for each of the 6 asthma miRNAs are displayed in **Table 3a and 3b**; a list of all biological processes and reactome pathways is provided in **Supplementary tables S4** and **S5.** Additionally, we also performed pathway enrichment analyses on positively and negatively correlated asthma-associated genes. Using Enrichr, in total 56 biological processes and 51 pathways were significantly enriched among the positively and negatively correlated genes. The most significant biological process for miR-199b-5p and miR-223-3p remains “cilium assembly’, for miR-199b-3p ‘potassium ion transport, for miR-142-5p ‘neutrophil degranulation’ and for miR-181b-5p, miR-195-5p and miR-125b-5p no significant enriched biological processes were found. A full list of all biological processes and reactome pathways identified by Enrichr and g:Profiler is provided in **Supplementary tables S6** and **S7**.

Discussion

In this study, we identified 78 differentially expressed miRNAs in bronchial biopsies of asthma patients compared to healthy controls. Associations between miRNA expression and clinical and inflammatory asthma features identified seven candidate “asthma miRNAs”, i.e. miR-199b-5p, miR-223-3p, miR-199b-3p, miR-142-5p, miR-181b-5p, miR-195-5p and miR-125b-5p, that were significantly associated with one or more clinical and inflammatory asthma features as well as asthma-associated gene expression. The biological pathways affected by these miRNAs included cilium assembly/organization, neutrophil activation/degranulation and inflammatory response. Of interest, we identified that lower miR-26a-5p expression was strongly related to more eosinophilic inflammation.

The most significant lower expressed miRNA in asthma was miR-125b-5p, which was associated with more severe airflow obstruction and increased blood neutrophil counts. Enrichment of biological pathways revealed that miR-125b-5p is linked to inflammatory responses. Previously, *Liu* et al. showed that miR-125b-5p is also lower expressed in sputum of childhood asthma patients versus controls, especially in those with more severe eosinophilic inflammation [19]. Furthermore, in current smokers with or without chronic obstructive pulmonary disease, lower levels of miR-125b-5p were also linked with more airflow obstruction [20]. In our study, miR-125b-5p still remained lower expressed in asthma in the sensitivity analysis excluding smokers and patients that used ICS, indicating that in our cohort smoking had no major effect on the expression of miR-125b-5p. Additionally, functional studies demonstrated that intranasal administration of miR-125b can attenuate asthma features by reducing IL-4 and IL-13 levels, goblet cell differentiation and mucus production in a murine asthma model [19].

Since asthma patients had higher miR-223-3p levels and those levels were associated with higher tissue eosinophils and neutrophils and negatively correlated with asthma-associated genes, we suggest that miR-223-3p could play a role in the pathogenesis of asthma. In line with this, several studies showed higher levels of miR-223-3p in bronchial airway epithelial cells and sputum of asthma patients, especially in severe (neutrophilic) asthma patients [10, 21]. Furthermore, several studies demonstrated that overexpression of miR-223-3p reduced pro-inflammatory responses, while depletion of miR-223 enhanced inflammatory responses (reviewed in [22]). In our study higher levels of miR-223-3p in biopsies were strongly associated with lower *GREM2* expression. *GREM2*, which encodes for gremlin 2 and is lower expressed in asthma patients, is an antagonist of bone morphogenetic proteins [23]. Gremlin 2 is involved in abnormal tissue damage and repair responses, including lung fibrosis [24]. Additionally, the most significantly enriched biological processes in our study for miR-223-3p, is cilium assembly and organization. Cilium assembly and organization is important for the formation of cilia on bronchial epithelia cells, leading to mucociliary function and clearance of mucus and preventing infections and inflammation [25]. We also observed that miR-223-3p is enriched in several neutrophilic processes, which is in line with previous studies [10, 21]. However, in our study these processes do not belong to the top 50 most significantly enriched biological pathways, which can be due to the differences in source (biopsies versus sputum) and patient cohort (mild to moderate versus severe asthma patients). Overall, this indicates that miR-223-3p may contribute to aberrant airway inflammation and repair responses by regulating amongst others GREM2 expression, suggesting a mechanistic role of miR-223-3p in the asthma pathogenesis.

In addition, we identified miR-199b-5p, miR-181b-5p, miR-199b-3p and miR-195-5p as key candidate asthma miRNAs, since those miRNAs are associated with clinical and inflammatory asthma features and can play a potential role as regulators of asthma-associated gene expression. In this study, lower levels of miR-199b-5p, miR-181b-5p, miR-199b-3p and miR-195-5p were associated with higher levels of *HBA1* in bronchial biopsies of asthma patients. Erythrocyte precursors are the major producer of *HBA1,* which encodes for a subunit of the protein haemoglobin [26]. Additionally, lung epithelial cells can produce the haemoglobin subunit alpha [27]. As yet, little is known about the role of *HBA1* in clinical and inflammatory features of asthma. Furthermore, enrichment analyses with the negatively correlated asthma-associated genes of these miRNAs (miR-199b-5p, miR-181b-5p, miR-199b-3p and miR-195-5p) revealed that miR-199b-5p was involved in cilium assembly and organization and miR-181b-5p, miR-199b-3p and miR-195-5p were involved in neutrophil activation and degranulation. Regarding neutrophil activation and degranulation, neutrophilic inflammation is linked to severe, steroid-resistant asthma patients and to smoking asthmatics [28, 29]. Using both negatively and positively correlated asthma-associated genes for enrichment analyses, it remains that miR-199b-5p was involved in cilium assembly and organization. However, for miR-181b-5p and miR-195-5p no significant biological processes were found and miR-199b-3p revealed to be involved in potassium ion transport. Future functional studies should help elucidating the role of these miRNAs in cilium organization/assembly, neutrophil activation/degranulation and potassium ion transport.

Another miRNA of interest was miR-26a-5p. MiR-26a-5p expression was lower in asthma patients and associated with more severe eosinophilic inflammation as measured in blood, sputum as well as bronchial biopsies. Other studies have reported that miR-26a was lower expressed in bronchial epithelial brushings, serum and exosomes of bronchoalveolar lavage fluid derived from asthma patients compared to controls [8, 30, 31]. Furthermore, a previous study linked lower miR-26a expression in serum of asthma patients to lower levels of FEV_1 % predicted [31], however we did not observe this association for miR-26a-5p in bronchial biopsies. An *in vivo* mice study showed that miR-26a/b regulates allergic inflammation by reducing the levels of cyclo-oxygenase 2 [32]. While the expression of cyclo-oxygenase 2 is increased in airways of asthma patients [33], we did not observe differences in cyclo-oxygenase 2 expression in bronchial biopsies of asthma patients compared to healthy controls and also found no correlation between miR-26a-5p and cyclo-oxygenase 2. Altogether, these data indicate that there might be a potential role for miR-26a-5p in the pathogenesis of asthma, especially eosinophilic asthma.

Of interest, miR-451a was the miRNA with the highest fold change in bronchial biopsies of asthma patients, while no correlation was found with clinical features of asthma. This may suggest that the association of this miRNA with asthma is not driven by any of the well-known asthma features assessed in our study and may point towards a different underlying mechanism. Previous studies have shown decreased miR-451a expression in peripheral blood lymphocytes from asthmatic children [34] and that *in vivo* overexpression of miR-451a inhibits airway remodelling by targeting cadherin 11 [35], suggesting a potential role in (controlling) airway remodelling.

One of the main strengths of this study is the size of the cohort and the careful characterization of the subjects, which made it possible to make the association of miRNAs with clinical and inflammatory asthma features. Moreover, we had matched miRNA and mRNA data available from the same bronchial biopsies. Therefore we could directly correlate global miRNA and gene expression levels to identify miRNAs involved in the regulation of gene expression changes in asthma. One limitation of this study is the lack of suitable replication datasets to validate the differentially expressed miRNAs in asthma and their association with gene expression. There are only a few studies that determine miRNA expression in asthma patients, however to our knowledge no miRNA-mRNA data is available of bronchial biopsies.

In conclusion, we have profiled miRNA expression in bronchial biopsies from asthma patients and controls and identified several candidate “asthma miRNAs”, including miR-223-3p and miR-125b-5p, that were associated with multiple clinical and inflammatory asthma features and their negatively correlate genes are linked with the presence of asthma. Furthermore, miR-26a-5p is linked with inflammatory asthma features, especially eosinophilic inflammation. Therefore, these miRNAs are important candidates for future studies to unravel their mechanistic role in the pathogenesis of asthma.

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Table 1: Characteristics of asthma patients and healthy controls

	Including smokers and ICS treatment		**Excluding smokers and ICS treatment**	
	Asthma n=79	**Healthy controls n=82**	**Asthma n=30**	**Healthy controls n=42**
Age (years),	50 [38-56]	42 [23-56]#	53 [36-58]	38 [22-58]
Gender (female/male)$	39/40	36/46	19/11	19/23
Smoking status (n, %)$		#		
Non smoker	38 [48]	42 [51]	30 [100]	42 [100]
Ex-smoker	22 [28]	0 [0]		
Current smoker	19 [24]	40 [49]		
Pack years	11 [7-27]	16 [4-29]		
FEV$_1$ (% predicted) ~	82 [±17]	101 [±12]#	85[±15]	102 [±14]#
FEV$_1$/FVC~	70 [±11]	79 [±6]#	71 [±10]	80 [±7]#
Atopy, (yes/no/NA)$	58/17/4	30/51/1#	21/7/2	19/22/1#
PC$_{20}$ AMP, mg/ml*	39 [0.02-640]	543 [33-640]#	22 [0.02-640]	626 [270-640]#
PC$_{20}$ Methacholine, mg/ml*	-	38.9 [19.6-39.2]	-	38.6 [19.6-39.2]
ICS therapy (yes/no)$	33/46	0/82#	0/30	0/42

ICS dose, µg/day§	500 [250-800]	-	

Data are presented as median with interquartile range (IQR), unless stated otherwise; ~ mean with standard deviation, * geometric mean with range.§ beclomethasone equivalent. Mann-Whitney U test was performed, unless stated otherwise. $ Fisher's exact test was performed: # = $p<0.05$ vs asthma. FEV$_1$ (forced expiratory volume in 1 second); FVC (forced vital capacity); NA (not available); PC$_{20}$ (provocative concentration inducing a 20% fall in FEV$_1$); AMP (adenosine 5'-monophosphate); ICS (Inhaled corticosteroids). # = $p<0.05$ vs asthma

Table 2. Negatively correlated genes per miRNA

	Fold change (Log2) of differentially expression asthma versus healthy controls	Number of negatively correlated genes (FDR p<0.05)	Number of negatively correlated asthma genes	% Negatively correlated asthma genes
miR-199b-5p	-0.40	1773	920	51.89
miR-223-3p	0.80	8764	2641	30.13
miR-199b-3p	-0.37	165	33	20.00
miR-142-5p	0.68	1198	236	19.70
miR-181b-5p	-0.23	115	22	19.13
miR-195-5p	-0.49	310	54	17.42
miR-125b-5p	-0.53	202	20	9.90
miR-148b-3p	0.56	471	40	8.49
miR-30a-3p	-0.46	571	37	6.48
miR-99b-5p	-0.19	16	1	6.25
miR-34c-5p	1.03	92	2	2.17
miR-21-5p	0.47	509	9	1.77
miR-26a-5p	-0.26	516	9	1.74
miR-92b-3p	0.61	598	2	0.33
miR-125a-5p	-0.64	6417	21	0.33
let-7c-5p	-0.69	848	2	0.24
miR-200c	0.42	5255	6	0.11
let-7a-5p	-0.39	6789	1	0.01
miR-99a-5p	-0.30	1	0	0.00

miR-150-5p	-0.36	13	0	0
miR-1247-5p	-0.73	6	0	0
miR-347b-3p	0.47	1	0	0
miR-34c-3p	0.92	126	0	0

Differentially expressed miRNAs in asthma patients compared to healthy controls that have a correlation with clinical and inflammatory asthma feature(s). First column showed the fold change between asthma patients versus healthy controls (excluding subjects that smoked or used ICS), second column negatively correlated miRNA-mRNAs expression (all asthma and healthy subjects), third column overlap between the negatively correlated miRNA-mRNA expressions and genes that are differentially expressed in asthma patients, fourth column percentage of negatively correlated asthma-associated genes.

Table 3a: Top 5 GO biological process of negatively correlated asthma genes per miRNA

	Pathway/term	**Adjusted P-value**
miR-199b-5p	cilium assembly (GO:0060271)	1.21E-17
	cilium organization (GO:0044782)	1.23E-17
	plasma membrane bounded cell projection assembly (GO:0120031)	1.19E-13
	organelle assembly (GO:0070925)	1.64E-11
	intraciliary transport (GO:0042073)	4.19E-09
miR-223-3p	cilium assembly (GO:0060271)	3.88E-11
	organelle assembly (GO:0070925)	4.60E-09
	plasma membrane bounded cell projection assembly (GO:0120031)	1.15E-08
	intraciliary transport involved in cilium assembly (GO:0035735)	5.37E-08
	intraciliary transport (GO:0042073)	2.55E-07
miR-199b-3p	neutrophil degranulation (GO:0043312)	1.66E-08
	neutrophil activation involved in immune response (GO:0002283)	1.66E-08
	neutrophil mediated immunity (GO:0002446)	1.66E-08
	inflammatory response (GO:0006954)	2.06E-04
	positive regulation of endopeptidase activity (GO:0010950)	3.73E-02
miR-181b-5p	neutrophil degranulation (GO:0043312)	1.75E-06
	neutrophil activation involved in immune response (GO:0002283)	1.75E-06
	neutrophil mediated immunity (GO:0002446)	1.75E-06
	inflammatory response (GO:0006954)	3.20E-04
miR-195-5p	neutrophil degranulation (GO:0043312)	4.39E-09

	neutrophil activation involved in immune response (GO:0002283)	4.39E-09
	neutrophil mediated immunity (GO:0002446)	4.39E-09
	inflammatory response (GO:0006954)	4.14E-05
	cellular defense response (GO:0006968)	1.45E-03
miR-125b-5p	inflammatory response (GO:0006954)	2.14E-04
	neutrophil degranulation (GO:0043312)	2.14E-04
	neutrophil activation involved in immune response (GO:0002283)	2.14E-04
	neutrophil mediated immunity (GO:0002446)	2.14E-04
	positive regulation of endopeptidase activity (GO:0010950)	7.56E-03

Table 3b: Top 5 Reactome pathways of negatively correlated asthma genes per miRNA

	Pathway/term	Adjusted P-value
miR-199b-5p	Assembly of the primary cilium Homo sapiens ((R-HSA-561783)	9.30E-16
	Intraflagellar transport Homo sapiens (R-HSA-5620924)	2.70E-11
	Organelle biogenesis and maintenance Homo sapiens (R-HSA-1852241)	7.81E-11
	Cargo trafficking to the periciliary membrane Homo sapiens (R-HSA-5620920)	8.92E-05
	BBSome-mediated cargo-targeting to cilium Homo sapiens (R-HSA-5620922)	1.10E-02
miR-223-3p	Assembly of the primary cilium Homo sapiens (R-HSA-5617833)	2.52E-13
	Membrane Trafficking Homo sapiens (R-HSA-199991)	1.36E-12
	Organelle biogenesis and maintenance Homo sapiens (R-HSA-1852241)	9.38E-12
	Vesicle-mediated transport Homo sapiens (R-HSA-5653656)	5.57E-10
	Intraflagellar transport Homo sapiens (R-HSA-5620924)	3.04E-09
miR-181b-5p	Immune System Homo sapiens (R-HSA-168256)	1.88E-02
	Immunoregulatory interactions between a Lymphoid and a non-Lymphoid cell Homo sapiens (R-HSA-198933)	4.09E-02

Figure Legends

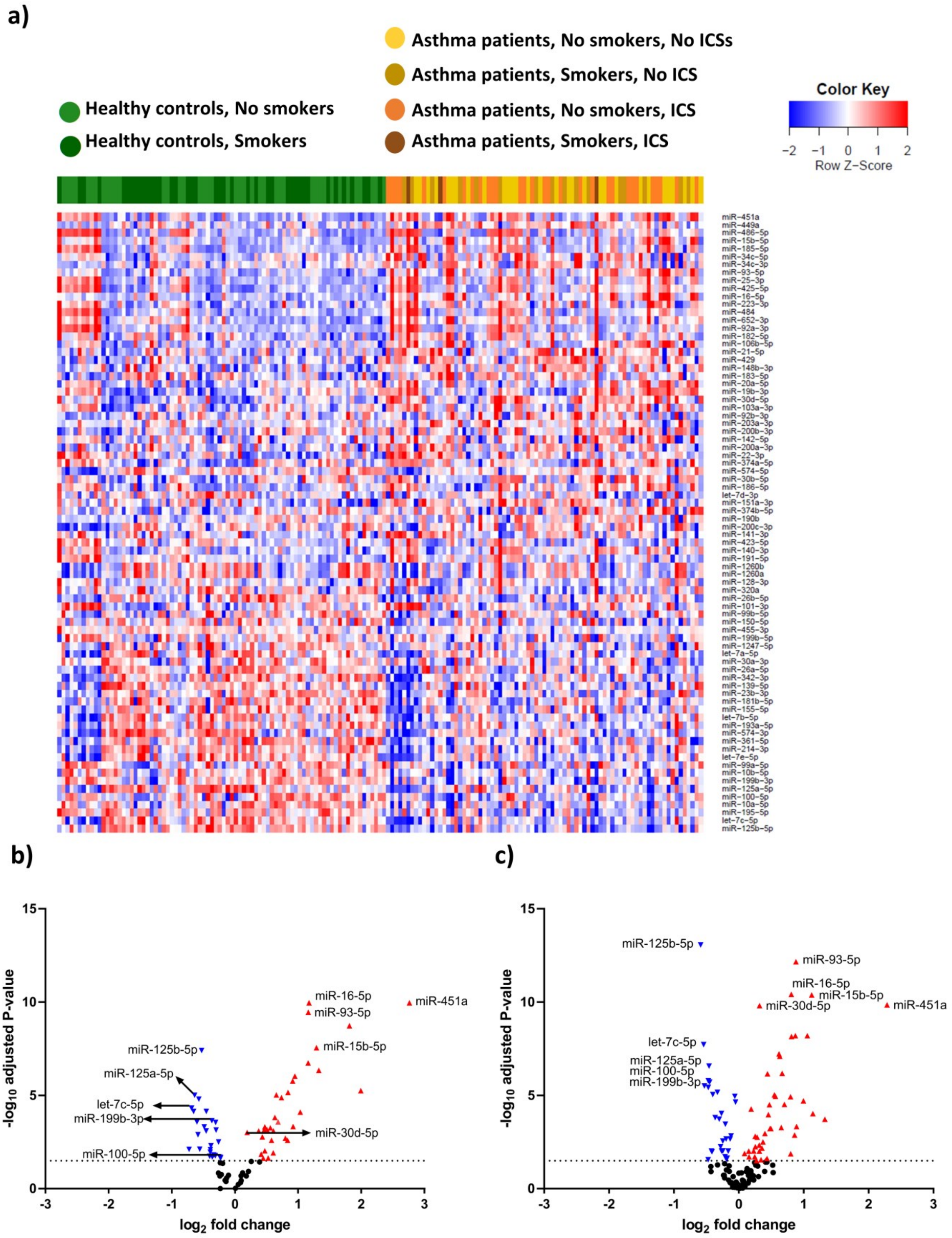

Figure 1: MicroRNAs (miRNAs) that were differentially expressed in bronchial biopsies of asthma patients compared to bronchial biopsies of healthy controls. a) Heatmap showing 78 differentially expressed miRNAs in asthma patients (n=79) compared to healthy controls (n=82); **b)** volcano plots showing differentially expressed miRNAs (FDR adjusted p-value <0.05) between asthma patients and healthy controls including smokers and ICS treatment. Top 5 up- and down-regulated miRNAs are highlighted; **c)** volcano plot showing the differentially expressed miRNAs (FDR adjusted p-value <0.05) between asthma patients (n=30) and healthy controls (n=42) excluded smokers and ICS treatment. ICS = inhaled corticosteroids

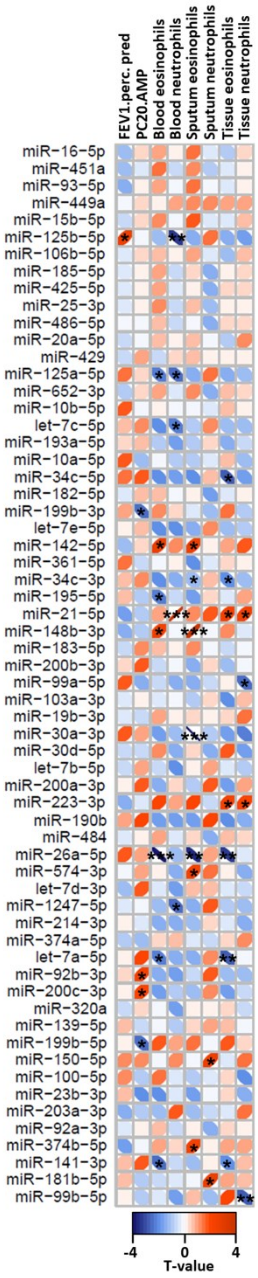

Figure 2: Linear regression between differentially expressed miRNAs in bronchial biopsies and clinical parameters. Positive associations are displayed in red and negative associations in blue colour (n=79, all asthma patients). * = p<0.05, ** = p<0.01, *** = p<0.001. FEV$_1$.perc.pred = forced expiratory volume in 1 s percentage predicted.

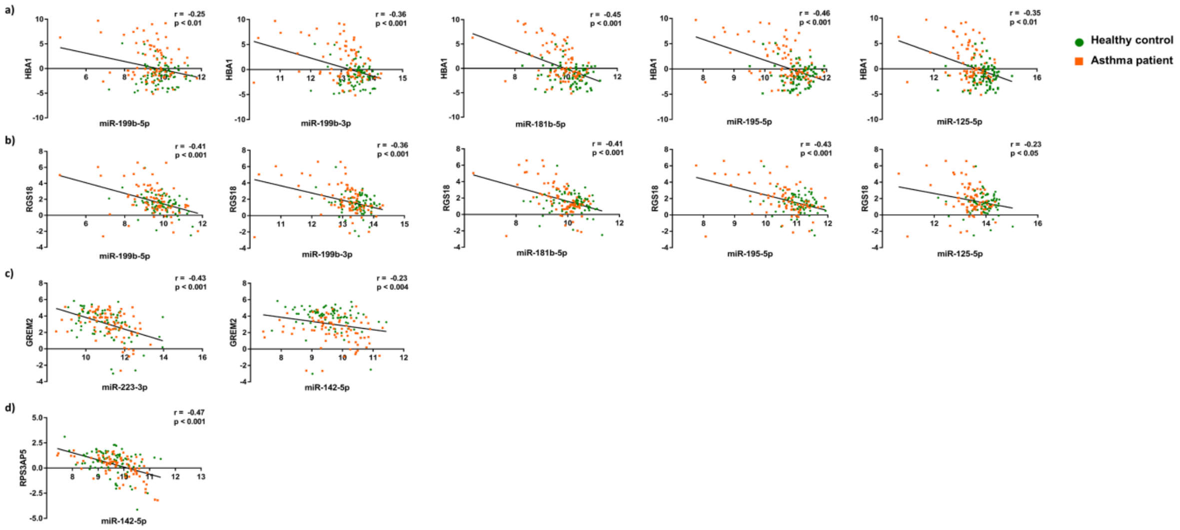

Figure 3: Correlation between asthma associated genes and miRNA expression. Pearson's correlation coefficient between **a)** *HBA1*, **b)** *RGS18,* **c)** *GREM2* and **d)** *RPS3AP5* expression correlated with miRNA expression in all subjects (n=79 asthma patients and n=82 healthy controls). Pearson's correlation coefficient (r) and p-value is given

Supplementary data: Identification of asthma associated microRNAs in bronchial biopsies

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Supplementary table 1: miRNAs upregulated in asthma patients compared to healthy controls, included and excluded smokers and ICS treatment

	Asthma vs healthy controls included smokers and ICS treatment			**Asthma vs healthy controls excluded smokers and ICS treatment**		
	Mean of normalized counts	**FC Log2**	**Adjusted p-value**	**Mean of normalized counts**	**FC Log2**	**Adjusted p-value**
miR-451a	30137	2.29	<0.001	29289	2.76	<0.001
miR-449a	385	1.33	<0.001	347	1.81	<0.001
miR-486-5p	45919	1.14	<0.001	31501	1.99	<0.001
miR-15b-5p	1823	1.12	<0.001	1878	1.29	<0.001
miR-185-5p	368	1.06	<0.001	321	1.33	<0.001
miR-34c-5p	1282	1.00	<0.001	1247	1.03	<0.001
miR-34c-3p	542	0.89	<0.001	537	0.92	<0.001
miR-93-5p	801	0.88	<0.001	840	1.16	<0.001
miR-25-3p	3637	0.87	<0.001	3382	0.91	<0.001
miR-425-5p	593	0.81	<0.001	531	0.95	<0.001
miR-16-5p	5020	0.81	<0.001	5483	1.17	<0.001
miR-223-3p	1887	0.80	<0.001	2065	0.80	<0.01
miR-484	615	0.70	<0.001	522	0.58	<0.01
miR-652-3p	283	0.67	<0.001	265	0.74	<0.001
miR-92a-3p	18239	0.65	<0.001	14711	0.45	<0.01
miR-182-5p	1010	0.63	<0.001	825	0.63	<0.001
miR-106b-5p	197	0.62	<0.001	222	1.16	<0.001
miR-21-5p	25592	0.56	<0.001	24262	0.47	<0.001
miR-429	738	0.55	<0.001	675	0.65	<0.001
miR-148b-3p	480	0.48	<0.001	455	0.56	<0.001
miR-183-5p	421	0.47	<0.001	364	0.51	<0.001
miR-20a-5p	265	0.46	<0.001	295	0.84	<0.001
miR-19b-3p	168	0.44	<0.001	187	0.61	<0.001
miR-30d-5p	6121	0.32	<0.001	6225	0.19	<0.001
miR-103a-3p	3117	0.19	<0.001	3228	0.38	<0.001
miR-92b-3p	2195	0.86	<0.01	1985	0.61	<0.01
miR-203a-3p	451	0.50	<0.01	325	0.52	<0.01
miR-200b-3p	8002	0.40	<0.01	7413	0.46	<0.001
miR-142-5p	562	0.37	<0.01	632	0.68	<0.001
miR-200a-3p	1404	0.36	<0.01	1260	0.43	<0.01
miR-22-3p	1043	0.32	<0.01	1029	0.09	**>0.05**
miR-374a-5p	405	0.31	<0.01	436	0.47	<0.01

Supplementary table 1 continued

	Asthma vs healthy controls included smokers and ICS treatment			Asthma vs healthy controls excluded smokers and ICS treatment		
	Mean of normalized counts	**FC Log2**	**Adjusted p-value**	**Mean of normalized counts**	**FC Log2**	**Adjusted p-value**
miR-574-3p	323	0.28	<0.01	292	-0.14	**>0.05**
miR-30b-5p	1425	0.26	<0.01	1421	0.10	**>0.05**
miR-186-5p	855	0.25	<0.01	900	0.12	**>0.05**
let-7d-3p	215	0.23	<0.01	234	-0.56	**<0.01**
miR-151a-3p	595	0.15	<0.01	610	0.10	**>0.05**
miR-374b-5p	422	0.16	<0.05	458	0.26	<0.05
miR-190b	211	0.80	<0.05	226	0.83	<0.01
miR-200c-3p	14888	0.43	<0.05	13044	0.42	<0.05
miR-141-3p	381	0.43	<0.05	333	0.39	<0.05
miR-423-5p	1305	0.41	<0.05	1168	-0.26	**>0.05**
miR-140-3p	1487	0.41	<0.05	1406	0.21	**>0.05**
miR-191-5p	5622	0.34	<0.05	5074	0.18	**>0.05**
miR-1260b	533	0.27	<0.05	509	-0.15	**>0.05**
miR-1260a	554	0.25	<0.05	534	-0.22	**>0.05**
miR-128-3p	351	0.24	<0.05	349	0.05	**>0.05**
miR-320a	3828	0.09	<0.05	3879	-0.34	**<0.05**

Supplementary table 2: miRNAs downregulated in asthma patients compared to healthy controls, included and excluded smokers and ICS treatment

	Asthma vs healthy controls included smokers and ICS treatment			Asthma vs healthy controls excluded smokers and ICS treatment		
	Mean of normalized counts	FC Log2	Adjusted p-value	Mean of normalized counts	FC Log2	Adjusted p-value
miR-125b-5p	7973	-0.59	<0.001	9157	-0.53	<0.001
let-7c-5p	7275	-0.54	<0.001	8426	-0.69	<0.001
miR-195-5p	1143	-0.53	<0.001	1290	-0.49	<0.001
miR-10a-5p	3169	-0.47	<0.001	3702	-0.45	<0.001
miR-100-5p	2584	-0.47	<0.001	2876	-0.24	<0.01
miR-125a-5p	11900	-0.46	<0.001	13862	-0.64	<0.001
miR-199b-3p	6078	-0.45	<0.001	6988	-0.37	<0.001
miR-10b-5p	1862	-0.40	<0.001	2246	-0.57	<0.001
miR-99a-5p	2976	-0.36	<0.001	3478	-0.30	<0.001
let-7e-5p	1829	-0.33	<0.001	2013	-0.60	<0.001
miR-214-3p	802	-0.30	<0.001	848	-0.39	<0.01
miR-361-5p	559	-0.27	<0.001	605	-0.31	<0.001
miR-574-3p	678	-0.21	<0.001	691	-0.38	<0.01
miR-193a-5p	145	-0.06	<0.001	149	-0.65	<0.001
let-7b-5p	20670	-0.05	<0.001	22519	-0.59	<0.01
miR-155-5p	1406	-0.42	<0.01	1637	-0.24	**>0.05**
miR-181b-5p	624	-0.28	<0.01	603	-0.23	<0.05
miR-23b-3p	8787	-0.26	<0.01	9153	-0.23	<0.05
miR-139-5p	479	-0.25	<0.01	541	-0.31	<0.05
miR-342-3p	1074	-0.25	<0.01	1173	-0.13	**>0.05**
miR-26a-5p	55527	-0.20	<0.01	60780	-0.26	<0.01
miR-30a-3p	604	-0.16	<0.01	665	-0.45	<0.001
let-7a-5p	62744	-0.13	<0.01	65528	-0.39	<0.05
miR-1247-5p	170	-0.12	<0.01	188	-0.73	<0.01
miR-199b-5p	546	-0.47	<0.05	624	-0.40	<0.05
miR-455-3p	117	-0.41	<0.05	121	-0.23	**>0.05**
miR-150-5p	2175	-0.22	<0.05	2512	-0.36	<0.05
miR-99b-5p	1314	-0.21	<0.05	1487	-0.19	<0.05
miR-101-3p	1273	-0.19	<0.05	1487	0.01	**>0.05**
miR-26b-5p	12756	-0.18	<0.05	13915	-0.10	**>0.05**

Supplementary table 3: All negatively correlated genes that were also associated with asthma

miRNA	Negatively correlated asthma-associated genes (bold = validated target gene of miRNA)						
miR-199b-5p	NCF2	RGS18	MEFV	VNN2	SIRPB2	SERPINA1	MGAM
	VIM-AS1	SMIM22	FPR1	SULT1B1	FAM65B	MNDA	FCGR3B
	S100A8	CDKN2D	TRIM36	KRT23	CSF3R	BPGM	CXCR2
	CXCR2	TUBB1	AGR3	C14orf142	CR1	HNF4G	BBS12
	ANXA3	FCGR2A	BNIP3L	RPA3	SELL	RP2	RAB20
	GCA	PRR15L	CCDC160	PCDHB1	DEFB1	DUSP4	CD200R1
	KLHDC9	COPRS	ITIH6	ZNF165	SCGB2A1	PI3	DUSP19
	HSPA6	CTSS	ENPP5	MCMDC2	DGAT2	ENPP4	C16orf54
	RHOU	DAPP1	RPP40	CDKN2B-AS1	RASEF	TMEM125	SMAP2
	UGT8	LINC01132	CFP	RPL26L1	CERKL	TTC30A	ARHGEF38
	C11orf70	S100A9	MLF1	C15orf65	DNER	LILRB2	TNFRSF10C
	CHST4	KIAA0895	MYCBP	MB	RMI1	CCDC34	TMPRSS7
	MORN2	FAM229B	CDKL2	C8orf37	SAP30	MSRB1	CDKN2B
	YOD1	RABL5	NME5	MRPL42	ARL6	MPZL3	TTC30B
	RNASE6	HILPDA	SLC11A1	IFT88	NCALD	ESRRG	PSENEN
	IPMK	STRADB	SPAG1	SRD5A2	LRP8	TMEM107	CCDC148
	SPAG16	PPP1R14C	APOO	ZMYND12	GALNT3	DRAM2	FSIP1
	NT5C3A	DNAJA1	MBOAT2	PPP1R42	MEIG1	SPATA4	EPB41L4B
	GRAMD1C	TIGD4	OR7E47P	WRB	ATP6V0A4	AKAP14	EMR3
	RASGEF1B	STX11	C6	SRD5A3	DDAH1	SCCPDH	CD24P4
	EFCAB10	SLC17A5	TFF3	MROH9	SMPD2	NAT1	LXN
	IQUB	HBA1	GABARAPL2	RRM2P3	INHBB	C15orf26	MNS1
	DNPH1	TSPAN13	GFM2	CCDC89	ATP6V1D	IFT57	EPCAM
	SPATA17	PIH1D2	SDR16C5	SOAT1	IGF2BP3	NUS1	FBXO36
	OCLN	EFCAB11	FSD1L	GAR1	DCAF12	MDH1B	RRAGD
	SPA17	MIPEP	TMPRSS3	RAB27B	PROM1	FAM151B	C9orf72
	ENO4	PGM2L1	TMEM45B	CDS1	GCNT4	PIH1D3	ABHD5
	DHX32	ZNF214	DYNLRB2	DNAJC6	VAMP8	ANKEF1	OSCP1
	LZTFL1	ZMAT2	CCDC181	FAM81A	C10orf107	ISCA1	SEC23B
	DCDC2	TMEM154	TSPAN19	LRRC34	GFPT1	C6orf57	CETN2
	IL13RA1	VSTM2L	DPEP2	TEX9	CCDC65	C12orf60	TRIP13
	GLT1D1	PHTF1	TTC9	SUSD1	CAPS2	STXBP4	CATSPERD
	RHPN2	FAM169A	IQCD	EFCAB7	EFHC2	UFC1	LRRIQ3
	CCDC176	CBY1	MAL2	TTC26	GLA	RPL7AP64	DNAAF2
	IFT52	TAT	ZBTB18	LRRC25	LINC00643	NMBR	TMC5
	SAMD15	ABHD6	CASC1	SGMS2	RALGPS2	PI4K2B	TCTEX1D1
	AGTPBP1	AK7	C11orf88	FECH	CHIC2	PPIL6	GLRX2
	CYSTM1	TCTEX1D2	DPH3	MDM1	AGR2	C21orf128	FAM174A
	ANKRD18CP	ERICH2	C9orf116	FCN1	CXorf57	LEKR1	IPO11

Supplementary table 3 continued

miRNA	**Negatively correlated asthma-associated genes** (bold = validated target gene of miRNA)						
miR-199b-5p	AGPAT9	C7orf57	FAM206A	WDR78	LCA5L	PFN2	AGPAT5
	LCLAT1	C12orf75	DYNLL1	IFT43	TTC39A	ECT2	C10orf115
	MACC1	C2orf73	WDR54	TLCD1	PECR	IQCK	LINC00332
	C7orf63	FAM167A	LINC00589	DYNLT1	LIPH	PLEKHB1	TMEM254
	IFT80	MRAP2	GIPC2	CEP41	CEP19	CPPED1	FMN1
	STMND1	B3GNT7	C3orf67	VPS25	TDRD7	LINC01171	SIGLEC9
	KBTBD4	ARPC3	CMPK2	B3GNT5	RPGR	CCDC39	HK3
	SMS	F2RL1	TCP11L2	LRRC6	ARL13B	KIF27	KLHL2
	SMIM14	CCDC138	PIFO	DNAL1	RPGRIP1L	TBC1D31	FGFBP2
	C1orf189	CEP97	SYNPR-AS1	FAM166B	ZC2HC1C	STOX1	GJB7
	ZNF487	GRM5	SLC2A12	**AGTRAP**	PELI1	ARL3	C4orf19
	EFCAB1	NME9	GALNT7	ENKUR	WDR63	SMKR1	**RNF11**
	C2orf70	TBC1D8B	SAMD9	WDR31	HIBADH	ROPN1L	CLDN16
	C5orf49	MXD1	TTC29	HSPB11	RNF141	DPCD	S100P
	C16orf80	PLS1	ANKRD66	IQCG	TMEM231	CDK7	PFDN6
	KLHDC7A	SLC27A2	MORN3	DYDC1	PACRG	TUBB2A	LINC01031
	SNX7	TP53RK	DYDC2	UEVLD	CCDC11	MRPS31	FAM183A
	TMEM232	DYX1C1	EIF2S2P4	TMF1	TAX1BP1	LRRC59	SYAP1
	HS6ST2	FAM47E	SOX9	**SNTB1**	CDC14A	ABCB10	AHSA1
	ARHGAP18	OMA1	C17orf97	RBM24	C9orf66	AGBL1	PYGL
	CDKL4	NHLRC4	RTDR1	POC1B	EDEM3	CD164	PEX7
	SNTN	SQLE	NPHP1	TBCA	ADIPOR1	ABHD17B	NEK11
	CASC2	SLC22A4	TC2N	TEX21P	SCIN	CCP110	LAMTOR2
	MICALCL	ZMPSTE24	LCA5	LILRA1	DZIP3	B9D1	HSDL2
	DAW1	ARMC3	UBXN10	CAPSL	AGPS	TOMM34	GLB1L
	TRMT1L	EIF1B	ANXA2P2	LINC00948	FOCAD	TMPRSS2	RAET1E
	GMDS	SOX2-OT	SPOPL	DYNC2LI1	FAM201A	ABCD3	CD59
	ANKRD42	KCNE3	ANKUB1	HSPH1	GLB1L2	MAP3K19	CCDC173
	NEBL	ADGB	EID2	KIAA0825	ZNF396	CXorf30	KLHL32
	CCT2	SYTL3	DUSP14	DYNLL1-AS1	PTBP3	WRAP53	CCDC153
	TUSC2	DALRD3	SLAIN2	CCDC96	PPM1H	KPNA3	EFHB
	AZIN1	FGF14	FBXO15	IBSP	CCDC104	FAM96B	KRT80
	CXorf22	HSP90AA1	CCDC170	SETD9	SYTL5	EPPIN	ALS2CR12
	MTMR2	HEATR5A	RNF6	FBXW9	RSPH4A	IQCH	HRK
	BCL2L1	WDR49	ARMC2	SLC9C2	PLCH1	C9orf24	KIF3A
	STPG1	FAM104B	WWC1	RAB11FIP4	C9orf43	GLRX5	NME7
	BASP1	PRICKLE2-AS3	COX17	CRY1	MCAT	TSPAN3	TMEM67
	RSAD2	KPNA7	NCF1	CYB5D1	CD164L2	PLEKHG7	ZBBX
	GTF2E2	HIST2H2BF	GDE1	CENPM	FAIM	C22orf15	AK9
	KIF6	FAM81B	CCDC113	CNOT11	SLFN13	WDR65	UBL3

Supplementary table 3 continued

miRNA	Negatively correlated asthma-associated genes (bold = validated target gene of miRNA)					
miR-199b-5p	KIF24	ECT2L	CPEB4	RUVBL1	CALM2	DNAL4	IFLTD1
	STS	KIAA1009	UGP2	TCTN2	CR1L	KDM1B	SESTD1
	NCEH1	DRC1	GALNT1	RAB3IP	STOML3	KIAA1407	PTGES3
	TCEB2	RFX3	POLR2I	EBNA1BP2	TPST1	TSG101	AP1M2
	KIF9	SLC44A4	UBB	PZP	APOBEC4	ACSBG1	MAPK8IP1
	LRP2BP	CAT	SPATA18	SRGAP3-AS2	WDR19	MKRN1	EGLN3
	MORF4L2	ATPIF1	PLAC8	TTC25	TCTN1	TNFAIP8L1	C4orf47
	UNC119B	SLC37A3	AXDND1	FAM216B	SHFM1	SSB	STYK1
	SMEK2	C1orf192	DIO1	MPP1	CNGA4	C20orf26	ANKDD1B
	C10orf67	LRP11	PPP4R4	CHDC2	RSPH3	STYXL1	BCCIP
	C7orf73	HSPA4L	PPID	STK33	S100A11	SLC25A14	MAPK10
	TSNAXIP1	CIB1	RGS22	CSNK1G1	NCF1B	PCYT1B	CGREF1
	DNAJC16	FBXL13	BBS7	RBM20	MEAF6	TRIM37	MPP7
	TMEM212	EHHADH	UBE3D	ABCC6P1	FAM154B	DPY19L2P2	TTC8
	MFSD6	COPB2	ARMC4	CCDC74A	WDR35	SERPINB1	CCDC41
	GOLPH3L	LINC00284	CDCP1	PPP1R7	TLR1	VEPH1	DDO
	BCL2A1	FOXA2	MKX	TSPAN6	DNAJC12	NDUFB3	IL1B
	HCK	C1GALT1C1	MPC2	COMMD8	NAMPTL	CNTF	NUS1P1
	LY75	MSMO1	DBI	MAD2L1	GMPR	C1orf141	ACSL1
	DPY30	C11orf74	TRMT10A	UBE2D1	FAM173B	VRK1	PLBD1
	DNMBP-AS1	CCDC110	MUC15	BANK1	CXXC4	C1D	UQCR10
	MRPL40	GOLM1	NDUFA1	TFF1	C21orf59	TEX26	ZBED5-AS1
	HSBP1	C6orf99	C17orf58	TMEM144	CD38	ICAM3	NAMPT
	TMEM70	CCDC67	BIK	COX16	C19orf38	HIST3H2A	NLRC4
	PNP	HSF2	HIGD1A	ROMO1	CETN3	NUDT16P1	CHMP5
	BOLA3	RGCC	PLEKHB2	TWF1	CCDC28A	JKAMP	FASTKD3
	C20orf195	TPMT	PDIA4	CP	B3GNT3	MAP9	LINC00326
	GTF3C6	AQP4	SLMO2	CEACAM6	VNN1	NOP10	TAF13
	YIPF5	PSMD10	CASP7	CDK5	CHMP2B	EPB42	COA3
	MTMR6	PRKAR1A	CMPK1	SLC35A2	PSMD14	SLC43A2	MRPS35
	NDUFAB1	ISCA2	JAGN1	PAPSS1	UBL5	SLC35A3	ABHD3
	PNMA1	ANG	GGCT	VNN3	PPIL1	PPP1R36	SLC22A16
	ATP6V1G1	C2orf40	CYB5R4	SRI	TWF1P1	NDUFB1	CHCHD2
	NOXRED1	FANCF	HCG14	DHRS7B	PROS1	CCNB1	DYNLT3
	ERH	TMEM66	NMI	IFT46	PSPH	FBXO8	PPP1CB
	LRRC63	KCNK1	TXNDC12	SCP2	UGCG	SLC1A2	KLHL13
	PGGT1B	C1orf168	AP1S3	RNFT2	TOMM22	CHUK	SNX3
	IARS2	C9orf135	COX5A	HNF1B	ETNK1	LIG4	MIR34C
	VDAC3	CASP8	DUSP10	GCLM	RTN4IP1	JRKL	BTBD1
	ATG5	MRPL44	FZD3	SPATA24	GYG2	JTB	TMEM68

Supplementary table 3 continued

miRNA	**Negatively correlated asthma-associated genes** (bold = validated target gene of miRNA)						
miR-199b-5p	TMEM17	ARF4	RRAD	SLC36A4	WDR86-AS1	TMEM41B	PLCL2
	NDUFC1	KIAA2022	PRR13	TIMM23	FAM177B	PSMB3	PRPS1
	CRNDE	ERBB4	TXLNB	ZNF295-AS1	VTA1	C5orf22	RNF2
	TIMM8B	OAS1	GNAI3	PNPLA8	TTC33	ADAMDEC1	NEIL3
	LSMD1	BLVRA	COPS8	ATP6V1A	AKIRIN1	OST4	SDCBP
	SH3BGRL2	HIST3H2BB	MED18	PTPLAD2	FAM227B	G3BP2	DPY19L1
	PARP15	NAALADL2	USP18	HTATIP2	H2AFJ	SCAMP1	ERO1L
	ZNF627	GPX1	TDP1	ENOPH1	LIMS1	MAPK6	RIBC2
	CMAHP	RPAP3	SOCS4	STAM2	SP140	PNPLA4	BLOC1S2
	CDK8	MTM1	TUBBP5	CLCN3	C5orf30	BROX	RHOBTB1
	CDC42	GOLPH3	C2orf69	NUBPL	PARK7	MTPN	MARCKS
	PPM1E	STK16	PPP4R2	IBTK	MARCH3	NUCB2	JAZF1
	ANKRD37	PWP1	POF1B	FAM221A			
miR-223-3p	EPHA7	GREM2	CCBE1	DIRAS3	PROX1	TMEM119	OMD
	GSTA2	RSPO1	PCDH10	TMEM100	SOSTDC1	TREM2	AJAP1
	PDGFRA	FAM180A	CDH2	LSAMP	CYP1B1-AS1	CCDC152	SCN7A
	FGF10-AS1	AKR1C3	FAT3	SFRP2	MAMDC2	ISM1	TRHDE
	OLFML3	ROBO2	LRP1B	CLDN8	ATRNL1	ADH1B	AOX1
	C11orf1	LUM	CES1	GSTA1	IGFBP6	CADM2	SV2A
	FGF10	IGSF1	PHEX	EDAR	C17orf58	PRDM6	ALDH1A1
	DOK6	CALCA	TENM3	SCN3A	AQP4	AKR1C2	RWDD4P2
	LINC00086	SRPX	NRCAM	WNT5A	CLMP	CYP1B1	CBR1
	TMEM132C	FKBP7	KIF5C	KIF1A	SCN2B	ADRB1	INMT
	CORIN	KIAA2022	TPH1	SEPP1	PMP2	RECK	LGR5
	CHGA	OSER1-AS1	BMP4	DKK3	FREM1	CXCL14	SPON1
	NDST4	FBLN1	OR51E1	ABCA8	TRIM16L	ADAMTS5	BOLA3
	NLGN1	RGN	FKBPL	KIT	TMEM70	RAB9A	AGPAT9
	BHLHE41	ASNA1	SCGB2A1	DNASE1L3	SLC2A12	TMEM86A	ADCYAP1R1
	KBTBD11	NQO1	ABCG2	NR2F1	GSTM5	GCLM	RWDD4
	PEX7	PCDH19	NR2F1-AS1	GBP6	B3GALT2	CETN3	SLC1A7
	GLO1	PID1	TNN	ARRDC4	PTPRD	PRDX1	SOD1
	PCSK2	CACNA1G	TMEM176A	EIF5AL1	MTTP	AKR1B10	MMP16
	COPG2	IGF1	ABI3BP	LINC00908	CCDC121	SFRP5	RYR1
	PDCL3	PKIB	CACNA2D3	SSTR1	NUDT16P1	MUC15	RPL10AP6
	CCL11	RFX8	GCLC	TMEM255A	PKMP3	HSPE1	MAD2L1
	HINT2	ASPA	GUCY1A3	USP51	LINC00087	SGCE	PCBD1
	RAB38	ACSS3	LINC00623	HCG11	RRM1	MPC2	FTH1P2
	NDUFA8	C5orf30	TMEM45B	SNRPC	ZNF540	SLC7A14	OLFML1
	FAM69A	SOWAHB	MRPL13	SLC26A9	PPP1R1A	GPX2	LRRTM4
	C1S	RPSAP15	FZD10-AS1	GLRX2	ARL3	PGRMC1	HTR7

Supplementary table 3 continued

miRNA	**Negatively correlated asthma-associated genes** (bold = validated target gene of miRNA)						
miR-223-3p	FGF13	BDH2	ERH	BMP5	HS6ST2	HMGN5	UBL3
	ABHD6	ST13P10	FBLN2	RPSAP58	TMEM59	MRPS9	CAPN9
	PLA2G5	KLHL13	EPHX1	YIPF5	VDAC3	FOPNL	PHYH
	MRPS36	ANXA2P2	LZIC	NKD2	PERP	MRPL36	C6orf57
	NAA20	OLFML2B	HTATIP2	CHMP5	DYNLT3	SNRNP25	MRAP2
	CTSK	CDH11	PFN2	SLC25A24	CXorf57	IL20RA	RAB30
	FAM3C	CAT	PTGR1	UCHL1	SAP18	HSDL2	MRPL47
	LRP4	GHR	C1QBP	**MSMO1**	STRAP	ANG	AR
	ENOPH1	SMKR1	MRPL40	CD163L1	CD24P4	DAD1	TRMT10A
	SCAMP1	C1GALT1C1	ACADM	LPHN2	LRP11	NDUFAB1	SERPINB7
	EID2	FAM96A	CYB5R1	SLC16A9	EDNRA	KATNAL1	FAM105A
	PSMD10	ISM1-AS1	PRTFDC1	PPID	VSTM2L	MLF1	PKIA
	CACNA2D4	FBXO8	ISOC1	TOMM22	TGFA	SYT1	MOSPD1
	HMGB1P5	ABHD17B	FBXO45	TMEM38A	AKR7A2	RRM2B	SLU7
	COX6A1	CPSF2	RPA3	SETD9	EPRS	TP53RK	GPN3
	SCG5	HGF	BCAS2	PSMB1	PIK3R1	WIBG	RRAGA
	RRAGC	ZDHHC15	NSMCE1	MUSK	PAPSS1	PPAP2B	FAM115C
	STK16	AP1M2	KLHDC9	BLVRA	COLEC12	ABHD2	TBPL1
	ITM2A	CCDC28A	ARHGAP42	POLR3K	VAMP7	SGIP1	ING2
	COX16	MRPS7	RAB2A	ADSS	COL6A3	ALCAM	ENPP4
	SDHB	OR7E47P	CHCHD5	GSR	SLC30A9	ABCA4	SLC30A5
	UQCR10	TRMT1L	TXN	NAT1	MRPS35	TSPAN6	COL5A2
	HIGD1A	C11orf45	COL1A2	THAP10	**TWF1**	TXNRD1	COMMD8
	CSRNP3	LGR6	CD9	TIMM10B	KLHL7	TSPAN1	CAPNS1
	MIR181A1HG	TMBIM6	BTF3L4	NSDHL	CXXC4	WDR72	CYP1A1
	VTA1	UEVLD	DSC3	ZMPSTE24	PARK7	CDKN2B	RNF175
	TMEM194A	HMGN3-AS1	DNM3OS	HNMT	HMGCR	DNTTIP2	SCN9A
	HAUS2	TMEM66	GTF2B	DHX40	FAM104B	MTX2	CMAS
	YWHAQ	TMED2	CMTM6	AHRR	COX5B	NDUFS5	TUSC3
	SRI	AXIN2	LGALS3	ZBTB33	SYBU	NARS	FAM198A
	SNTB1	SCCPDH	GSTP1	RRAGD	FAT4	UBL5	PRMT6
	PSMC2	NDUFB3	FGF14	CD164	BLOC1S2	MOCS3	UQCRQ
	SCRN1	TTC30B	NDUFA5	TOMM34	TMEM218	P4HA2	TTC8
	NUBPL	RAB4A	PDGFC	TSTD1	HAT1	DDO	HES2
	C15orf65	RPP40	FKBP4	SNORD108	SCP2	ZBTB7C	ZNF33B
	DIO3OS	DLAT	SOWAHC	SLC35A2	ANXA7	NRP1	MDH2
	IDH1	GSKIP	TSG101	SLC9A2	FAM66C	CHST9	USP46
	C1D	ENPP5	BRCC3	SGK3	RPSAP54	TMCO1	MTCH2
	COG6	MRPS10	RNF2	AAED1	CCDC25	ATP6V1G1	FRG1
	NUDT15	NUCB2	PIGX	PAAF1	TTC39A	SAP30	MTMR6

Supplementary table 3 continued

miRNA	Negatively correlated asthma-associated genes (bold = validated target gene of miRNA)						
miR-223-3p	PLS1	GSTA3	ABCA6	A2M	COX5A	CLDN11	SMIM14
	FAM20B	SUMO1	**WASL**	NDUFA1	PCDH9	MEAF6	GALC
	PALM2	HMGB2	MARVELD1	TM9SF2	MAP9	TTC33	KCMF1
	PCDH9	MEAF6	GALC	PALM2	HMGB2	MARVELD1	TM9SF2
	MAP9	TTC33	KCMF1	THSD4	TMEM50A	PDGFA	MYCBP
	UBE2N	ATPIF1	FAM84A	MOB1B	MAL2	HSBP1	TPMT
	HNRNPH2	TIPARP	SPR	KIFAP3	HILPDA	TFPI	SYPL1
	MYLIP	DGKE	PRPS1	DNMBP-AS1	BTBD1	NOP10	**ARTN**
	COL13A1	ISCA2	BRI3BP	CCNDBP1	ARL13B	ELOVL6	TENM1
	PPP1R3D	MAP1LC3B	TAF1B	S100A6	COL3A1	RDH10	KCTD12
	TSPAN13	KLHL4	IPMK	UGDH	SRP14	CEP97	**CDS1**
	ANKMY2	ETNK2	DUSP14	SLC16A2	LYRM7	CDK7	UTP18
	EIF1B	UBE2V2	MRC2	SNX3	ZKSCAN4	PTGES3	CHMP2A
	CEACAM6	COPZ1	GPR126	CRNDE	GNPAT	PSMD1	HADH
	CEBPG	DIMT1	RCAN3	ATP6V1F	PTS	PTGDS	HIATL1
	MPP7	P4HA1	RMND5A	**CHMP2B**	PSMB5	TP53INP1	WDR47
	SH3BGRL2	DPY30	HMCN1	YES1	TIPRL	CREBL2	TIMM8B
	SLC9A9	RPS10P7	DPP10	PAIP2	CASC4	GGCT	TMEM68
	TALDO1	WLS	IARS2	CCDC110	NUFIP1	PSMD14	SUMO2
	PRDX5	COA3	ARHGAP28	PRRG4	FZD3	FAM172A	ZFP91
	MAGED2	C1orf43	EIF4H	HSPA4	PLBD1	HCG14	SSB
	C16orf80	C1R	AMZ2	KLHL20	ALDH1A3	PWP1	MIF4GD
	FAM96B	PPP2CB	ZNF664	TMEM30B	PLA2G16	BROX	TMEM144
	MUC5AC	CALM2	VPS35	BLOC1S4	FANCF	LSM5	PPIL1
	GALNT3	CDK15	SEMA6D	KIAA1279	NEBL	RHOA	**CAPRIN1**
	FAM60A	PPP1CB	CHCHD2	LINC00092	SLC2A1	AGPS	DSP
	NELL1	GTF3C6	YWHAB	KDELR2	FBXO36	TUBA1A	CERS6
	KCTD18	PPP4R4	NDUFS6	PCCB	SLC27A2	NCKAP1	VPS25
	PLAA	PEG3	TKT	SESN1	C5orf22	CLDN16	ATP6V1A
	EPB41L4B	FAM173B	CTNNA1	RALBP1	SNX2	VPS4B	FLRT2
	ICMT	RAET1E	NAALAD2	YIPF6	CMPK1	NCEH1	EXPH5
	CALM1	ZFAND6	TXNDC12	ZNF578	CLPX	EPB41L2	ZNF485
	MORF4L1	TACO1	PROS1	ATP5E	ACOX2	CCT7	EMC8
	SNW1	GAN	ZDHHC13	EXTL2	AZIN1	PRICKLE1	NT5DC1
	ARL1	GTF2E1	UPK1B	PAPPA	PDSS2	AXL	LYRM2
	SUCLG2	UBE2L3	DRAM2	ASB7	SNX7	FTH1P8	IFT52
	CBFB	EDA2R	BCL2	NAV3	MORF4L2	C11orf74	COPS8
	EHHADH	UGT1A6	TRIM2	JRKL	SLCO2B1	APOO	ZMAT2
	ROPN1B	GOLT1A	HNRNPF	ACTR6	NPTN	GABARAPL2	HECTD1
	CCT5	HIST1H2BD	MRPL44	ZMAT3	ABI1	ZBED5-AS1	PSMB6

Supplementary table 3 continued

miRNA	**Negatively correlated asthma-associated genes** (bold = validated target gene of miRNA)						
miR-223-3p	CCT5	HIST1H2BD	MRPL44	ZMAT3	ABI1	ZBED5-AS1	PSMB6
	ANXA2	H3F3AP4	MTM1	DYNLT1	SLC35A3	DYNLL1	KCNMB2
	GOT2	DNPH1	BBS12	RNF138	COX6B1	RTFDC1	LIPH
	SMAD2	PPP6C	STARD13	UGT1A8	ZMYND12	PTPRN2	FREM2
	SLC25A4	MCM4	DYNC1LI1	GLCE	METTL15	BAG5	NME5
	PKHD1L1	CMTM4	CAB39	GLOD4	EPT1	NDUFC1	NTAN1
	GTF3A	PANK3	MAP3K2	ATP6V1H	**ARL8B**	SOX2-OT	GEMIN8P4
	MRPL42	TPRG1L	SERTAD2	SHFM1	PSMB3	TCP1	LRRC37A6P
	AP1AR	TRIM16	FAHD1	VEZF1	BRD7	PSMA5	LRRC2
	ABCD3	ZNF772	ZNF665	ATP6V1D	L3MBTL3	EMP2	ZNF354C
	BIRC6-AS1	COMMD7	RTCB	ARF5	SLMO2	PPP2R5E	JKAMP
	ALKBH3-AS1	LZTFL1	ARFIP1	ZNF677	ZC3H12B	MORF4L1P1	TWF1P1
	PIGT	TRAM1L1	MUCL1	KCNMB4	SH3RF1	LINC00667	VDAC1
	CLIC1	SOX21-AS1	ISCA1	PSMD4	SKP1	ZNF28	TMEM41B
	C6orf123	FCF1	CCNB1IP1	DNAJB4	RAD23B	RGCC	SPRY2
	AADAC	C8orf47	UBE2K	MEST	CDC5L	TUSC2	PGD
	DHRS9	SNRPD3	RFK	ZNF614	CETN2	ACBD3	TLN2
	FAM174A	HIBADH	BCL7A	RAB11A	ZNF627	APLF	LIN54
	KCNIP3	POLR2B	KLF5	WBSCR16	ANKRD66	FBXO17	MSH2
	SLC47A2	UQCRFS1	HMGCLL1	TMEM18	FASTKD3	DAZAP2	F2RL1
	CLTA	ANXA1	DARS2	SNAPC5	HSF2	SOCS4	RPL23AP82
	AAGAB	KIF5B	FRAS1	SERPINB5	SPRY1	DYNLRB2	SORT1
	FBXO28	AGR2	PRKCA	PSMD6	ADAM33	ERLIN1	MAGI3
	ADSSL1	ARCN1	IMPAD1	LCORL	CTTNBP2	NUS1	OBFC1
	TTC30A	HSPB11	ZC2HC1A	SLAIN2	DUSP19	LAMTOR5	UBE2M
	CDK5	ZNF285	FAM206A	ROMO1	UBE2A	HMGN3	SDR16C5
	EMC3	RNF6	EIF4A3	PPAP2A	SPTY2D1	BAI3	WRB
	SLC20A2	MERTK	CUL3	EBNA1BP2	EPCAM	SLC17A5	EZR
	PGGT1B	AP3M2	MBNL2	METTL21B	PROX2	SPPL2A	IBTK
	ERBB3	CD59	C2orf44	JAGN1	FAM169A	C1orf54	GOLGA5
	DYNC2LI1	KIAA1430	POU3F1	FOXRED2	ARIH1	G3BP2	SLC5A7
	CIPC	HAUS3	EVI5	RALGPS2	CLTC	PDCD1LG2	COPRS
	DYNC1I2	KCNB1	RMI1	WEE1	FMO3	BZW2	GFRA2
	ATG4A	IGFBP2	BLVRB	RASSF6	COX14	TAF13	MTIF3
	GLMN	PGM2	ALKBH5	RAB25	ABCB10	CCNC	ENOX1
	KBTBD4	ATG3	PIGH	AGPAT5	CCT6A	ARPC3	HADHA
	POF1B	UBE2H	NDUFS1	BANF1	KIAA1161	TIMM23	PDCD6IP
	RPF2	VAMP8	RNF11	PDE11A	C5orf15	DBI	C2orf69
	NDUFB10	GRIK2	BBS7	ARL6	HSD17B11	MAGED1	PA2G4
	KLHL32	ITGB8	RALA	MAPK6	GALNT1	DPY19L1	KLHDC8B

Supplementary table 3 continued

miRNA	**Negatively correlated asthma-associated genes** (bold = validated target gene of miRNA)						
miR-223-3p	CCT3	IDE	DACT2	AMIGO1	CTSF	FGD5-AS1	SLC25A12
	NUGGC	RALB	TEAD1	BCAS1	UFC1	JMY	TTC9
	DYNLRB1	MORN2	GALNT5	ZFYVE21	GNAI3	AKAP3	SBNO1
	THRB	C7orf73	CHMP4B	DACH1	MARCKS	ANKEF1	MBOAT2
	CCNA2	PAG1	TBCA	C2orf40	ENO4	STYK1	EHBP1
	PAWR	ZNF302	S100A10	RAB34	PNPLA8	MRPL18	RAB10
	UBE2E3	TSPAN15	ADAT2	BUD31	RND2	FAM227B	SFTA1P
	DHRS7B	DNAJC27	ZNF530	KLHL8	OGFOD2	AMPD1	ATP9A
	PPP2CA	GBAS	FILIP1	LINC00517	SIAH2	CLCN3	DPH3
	C15orf56	CFH	KLHL5	ULK2	COX8A	OCLN	ZNF311
	IRAK1BP1	RPP38	MRPL51	SMEK2	RNF20	PRKD3	EFCAB11
	ELF1	FXYD3	EXD2	ATP6AP1	PEX13	KLHDC10	LMO7
	PTGES3P1	RNF219	TCP11L2	SNTN	SAMM50	DCTN4	COPS6
	CD109	NRL	SLC2A10	C2orf73	HSPA4L	KPNA4	RYBP
	DCP1B	VAPA	NAA35	KTN1	CAP2	PRKAR2A	ZNF14
	CPEB1	GDF9	LCA5	LRTOMT	SOX2	CDC42	DCUN1D1
	AEBP2	SFMBT1	SMS	ZNF529	ACPP	ALDH3B2	ENSA
	TUBA1C	RLIM	SUDS3	ACSM3	PDP2	PI4K2B	BBS4
	FAM114A1	ZNF471	VRK1	ADAM10	NAALADL2	VSIG2	PSMD2
	FAIM	STAM2	HSPA1A	TCEANC2	EIF4HP1	DDHD2	TTC5
	NEDD1	ADAM9	RP2	RNASEH1-AS1	PRKAR1A	IFT46	FASTKD5
	DNAJC18	ATXN7L3B	HOXB6	RTN4	MPP5	XRCC4	FTH1P7
	PIP4K2C	IPP	C10orf118	ERP44	FBXL5	CDK8	RRAGB
	SCRN3	TFF3	LXN	SCEL	CPEB2	UGCG	TSPAN3
	PIH1D2	IFT20	MRPL54	RFTN2	RBM24	NUTF2	MB
	SQLE	STEAP2	FIS1	UBE2D1	CPSF3	PARG	TRAPPC8
	RNF141	RPL17P11	CUL5	TAX1BP1	CCT2	UHMK1	OTUD7B
	GEMIN2	CREB3	NUDT5	B3GNT5	CAPZA1	HSP90AA1	KPNA3
	ZNF45	SEC23B	MORN5	GLS2	HN1L	SUGT1	LYRM1
	CCDC104	SYTL2	GFM1	NDUFB1	FGFR4	ZNF106	YPEL5
	BRAP	CCSAP	DIAPH2	SAMD8	TXLNB	FAM8A4P	COPA
	LSMD1	MRPS34	PCDHGA4	NFATC4	RHOU	NBR1	SMARCA5
	GPKOW	RB1	CSF1R	CNTF	ZNF221	RPS6KA3	JTB
	C1orf186	C12orf49	KIAA0895	IPO11	ANXA4	WDR92	GPLD1
	DNAJC6	AGFG1	LRRC49	SLK	GPX4	RUVBL1	SPATA6
	DNAJC3	COBL	SSU72	UNC119B	GLA	UHRF1BP1L	RBM27
	PLEKHB2	NIPAL2	RAB5A	ATG5	CTBS	ESYT2	FGF14-AS1
	RUNX1T1	RAB6A	LY75	REPS1	MTMR2	PSMC3	FAM183A
	IFT57	COPB2	MACC1	ZBTB21	ZFAND5	BCL2L13	MANBAL
	PNPLA4	RANBP1	SDHA	FOLR2	CLU	FAM229B	RPL4P5

Supplementary table 3 continued

miRNA	**Negatively correlated asthma-associated genes** (bold = validated target gene of miRNA)						
miR-223-3p	EDRF1-AS1	SDC4	PSPH	PDE7B	PPP4R2	**PDZD8**	GNG5
	H2AFJ	STOX1	XRN2	TMEM150C	EIF3EP1	PRR15L	CKAP5
	SLC37A2	TCP11L1	PTBP3	RAB14	TUFM	TES	EXOC8
	DYRK2	NAPG	CDK14	FAM76A	MSH3	BSPRY	CCDC138
	TM4SF1	FAM32A	INPP4B	NUP62CL	CCDC23	**CHUK**	MFSD9
	NEURL3	WASF3	METTL9	INTS10	RAC1	VCP	PXK
	SORCS2	SOAT1	CD2AP	NBPF16	TMCO3	UGP2	MRPL37
	WDR31	ZNF396	SULT1C4	AGR3	FAM161A	UBE2B	TBC1D8B
	S100A14	C1orf110	NME7	ENAH	GLTP	TIPIN	EIF3C
	MARVELD2	DNAJC10	YWHAZ	SIX4	ELK3	C10orf131	POLR3F
	MRPS31	PARP4	STRBP	ADAMTS9-AS2	SPSB1	ATP1A1	ATP8B1
	RPN1	GFPT1	PRSS12	DHRS4-AS1	SLC25A13	MTFR1	DLG3
	VANGL1	PAICS	SERPINB6	GPD2	DAAM1	MNAT1	GOLGA6L4
	YWHAE	GNS	DCBLD2	PAPD5	TFG	SEPHS2	IDS
	FLRT3	EXOSC4	FAM98B	GLE1	LSM1	CSNK2A1	FAM83D
	DENND5B	CTSH	PALD1	CLINT1	TXNL4A	MAPK1	HSPA8
	SSBP1	C1orf192	FAM43A	UBXN10-AS1	LINC00675	INTS4L1	IK
	OMA1	SPATA7	WDR35	BCCIP	ARHGAP18	WDR54	SPAG9
	C11orf95	MIPEP	C9orf116	SPCS2P4	ADH6	SH3GLB1	DDHD1
	LRIG3	ERGIC3	RAB7A	EAF1	C12orf75	CDKL2	CIR1
	LARP4	C8orf37	KDM1B	PIGU	RAB1A	LIG4	TRIP11
	CTNNAL1	C1orf210	MBP	SMAD7	COL21A1	RAP2C	EEA1
	NR2F6	ZNF57	ZNF74	CEP44	RNASEL	GNB1	MRFAP1
	GTF3C3	MBD2	LRRC34	GDAP2	DENND2C	DNAL1	CSTB
	DENND4C	MTURN	CT62	NCSTN	MFSD6	PHAX	THAP6
	ZNF214	TMPRSS2	WRNIP1	GFM2	UBXN4	SEC61B	CA5B
	PIWIL4	PRPF19	TMEM56	DOCK3	SGMS2	ZDHHC5	GPR180
	KCNC1	TARSL2	UGT8	KIAA0232	PRKAR2A-AS1	TNKS	RIMKLA
	USP7	**SECISBP2**L	RTN4IP1	CDH1	LCLAT1	AIG1	PPM1G
	STXBP4	PPP1R7	SLC36A4	CRY1	MICU1	CCNY	DDX6
	ETV1	SRGAP3-AS2	KHDRBS1	EFCAB7	WDR3	PDK1	SCYL2
	LRBA	PFDN2	RPAP3	PPP1R14C	CLTB	TRIM36	CCDC91
	EIF3J	TUBB4B	FER1L6	GTF3C4	SLC9A4	EDEM3	CAMK1D
	ERO1L	FANCE	RPL26L1	MED28	RASAL2	GLRX3	UNC13B
	UBQLN1	NUDT19	TACSTD2	RAD50	ZNF33A	TCF12	FLVCR1
	TRAPPC3	ETNK1	BTBD3	LAMB1	MTERFD2	DNAAF2	LRP8
	PPAP2C	RTCA	CAST	RPP14	EML1	GOLPH3L	RABL5
	LCOR	F11R	ARPC1A	SSNA1	TMEM17	KPNB1	WDR78
	PELI1	ZNF649	FAR1	C19orf12	PSMD13	MAPK10	PTMA
	SYS1	ACBD7	GFPT2	CNOT6	PDIA3P1	AP1G1	DAB2

Supplementary table 3 continued

miRNA	**Negatively correlated asthma-associated genes** (bold = validated target gene of miRNA)						
miR-223-3p	PSEN1	NUS1P1	IQGAP1	C9orf106	RHBDD2	MTX1	CYSTM1
	HDHD2	PAK2	RRP36	SPINT2	RAB5B	SERGEF	AKIRIN1
	TCAIM	GIPC2	SLC13A3	CTSC	AQP4-AS1	C1orf194	FAM84B
	AHSA1	MREG	EI24	FYCO1	TECR	SLC43A1	PAF1
	SERF2	ARSE	STEAP1	KCTD11	COPG1	SLC35B3	LEAP2
	KRAS	C2CD5	RAB6B	TTC3	HK1	ASXL2	EGLN3
	FAM177A1	MRPL48	FGF14-IT1	FBXO11	STAM	FAM179B	PRTG
	ALDH3B1	SLC10A5	UBC	STX12	FAM184A	PPP2R5C	CDC20
	TUBB2A	PLAC8	TTC26	CWF19L1	FAM213B	GPR160	PSMB2
	ODC1	ZNF573	SHMT1	STK24	SERBP1	TNFSF15	GAR1
	C5orf49	CAMSAP1	HIST3H2A	INTS2	CALR	GOLPH3	DZIP3
	C10orf107	MIPOL1	PRDX2	SPATS2L	ARFGEF1	GLIPR1L1	RNF130
	LINC00883	IGHG1	FA2H	EIF2S2	AHCTF1	SPAG7	**ZBTB18**
	ELAVL1	MTPN	STOML3	LIMS1	SRFBP1	LINC00475	PTCH1
	NAA15	RNF167	SETMAR	SNX14	KCNJ5	SEC23IP	SLC35B1
	VCPIP1	MAP2K4	RQCD1	RSPH4A	C14orf142	CCDC90B	USP8
	PIN4	CHIC2	KLF10	GALNT7	DDX52	ABCA12	TUBA1B
	YWHAG	PPP2R4	TMEM254	TRIM13	LSM4	TRIM37	KIF11
	NSMAF	RAB27B	SLC23A2	TPST1	STIP1	MARVELD3	CERKL
	KPNA6	SRPK2	CCDC160	HRASLS2	MID1IP1	ABAT	SRP68
	FEM1C	STAU1	HIST1H2BE	FRK	RTN3	PTTG1IP	HIPK3
	OSBPL3	KLHL35	TMF1	PPP1CA	DCAF6	C9orf85	HIPK1
	EPHA5	RASEF	SPAG16	DALRD3	TET1	MAP7	CACUL1
	ZNF204P	GOSR1	IL33	SYNGR1	IL22RA1	BCAR3	LGALSL
	AP3B1	ANKRD16	TTC39C	CGNL1	TBC1D2B	TPPP3	ARHGAP32
	AFTPH	ETF1	GRAMD1C	ITM2C	RAB20	BRCA1	ABHD17C
	ZNF227	AIFM2	ZFP82	CLCC1	TBP	UBB	HEATR5A
	HIST1H2BH	DYNC1H1	THAP3	TPGS2	TRIP12	ZNF141	OSTF1
	TTC19	UBAP1	CAMK2D	PNMA1	VPS41	TJP2	CYCS
	LRRC59	PABPC4L	HSPA1B	LINC00094	GARS	ACTR2	CNOT11
	WNT9A	NOLC1	TADA3	GRIA2	ESRP1	DKK1	PDIA4
	MS4A8	TSPYL4	YPEL2	CFDP1	PIBF1	ALDOA	ZNF559
	MAN1C1	ZFP3	EIF4G2	AK7	MIR155HG	ATP1B1	CDHR1
	PSMC4	DDB2	KIF2A	KDM7A	DDAH1	TULP3	SLC16A10
	CHCHD7	LAMTOR2	TOR3A	SULT1E1	GTF2E2	ACVR1C	CCL22
	LAMC2	RB1CC1	UXS1	TFDP1	RGS13	CITED2	C10orf76
	SLC44A4	NDUFB7	SFTA3	SPRTN	FLNB	S100A11	PPP2R2A
	ERI1	TP53BP2	DCAF16	LRRIQ3	ZKSCAN1	CES2	LRRC1
	NSUN3	PRKX	CDKN2AIPNL	AVEN	KIF3B	ABCC3	TJP1
	CCDC181	CCDC39	SPTLC2	HMMR	CNOT1	GRHL3	DNAJC16

Supplementary table 3 continued

miRNA	Negatively correlated asthma-associated genes (bold = validated target gene of miRNA)						
miR-223-3p	MIR34C	DDX21	YWHAH	MKX	TFCP2	AKIP1	C11orf88
	NBAS	OLFM2	TCEB2	ACTR3	CPEB4	ERBB2IP	NRG4
	RHOBTB1	CDK1	SLC16A12	MTMR12	ALYREF	AJUBA	ARPC5L
	PLD3	PSMD12	HMOX2	MYO1D	RAB3IP	EFCAB2	CTSV
	NEK1	PIP4K2B	UBE2G1	IGFBP3	ENKUR	PRPF40A	LINC00467
	PKIG	OPA1	KCTD1	DAW1	FTL	CHMP1B2P	SLC25A42
	THRAP3	NEK4	AGBL3	GLRX5	MMACHC	KLF15	COLCA2
	ARF6	ANXA3	UNC80	HSD11B1	PTPLAD2	NCOA2	KHNYN
	PIFO	PBRM1	C18orf25	GSK3B	CDH13	C12orf5	PHLPP1
	XPR1	KLHL2	NUP50	NCR3LG1	DHX32	MNS1	STYXL1
	MRPL23	ZSCAN12P1	NDUFA10	OSBPL11	PCDHGB6	GSN	FAM81B
	EFTUD2	TAF5L	ABHD3	WDR45B	UGGT1	TBC1D32	C9orf72
	PPL	USP12	SOX21	MCCC2	ZIK1	ANKDD1B	AKAP14
	HNRNPC	CMKLR1	DHX29	FAM218A	MYO5B	USP6NL	GAPVD1
	POLR2J	FOCAD	C3orf67	RFT1	ATP6V0D1	CNTD1	SMYD2
	UBXN2A	SIGLEC8	NPPC	LMAN2	SATB1	COA4	ZNF345
	TRAPPC1	KIAA1549	LACE1	TMEM131	TAB3	GNAQ	MCM2
	TMEM40	KPNA2	FIBP	LRRFIP2	IL13RA1	WNT11	CCDC58
	C16orf62	CTBP1-AS2	AKAP9	LDLRAD1	WSB2	UGT1A2P	FANCM
	GOLGB1	PITPNA	MARCH6	PPP1R15B	ARF1	TDRD7	CNTN2
	NID2	OAZ1	STX18	C9orf69	LMTK2	CDC14A	ZSWIM5
	ATP2B1	RIPK4	HHAT	GNL2	PPTC7	AMY2B	GPR155
	ST6GALNAC2	ZNF582	PACRG	HIST2H2BE	SLC25A14	PCDHGA5	CDC16
	SF3B2	KIF3A	HDLBP	TTC22	C12orf60	SHOC2	HSD17B13
	ARF4	IFT74	TK2	SLC23A1	CCR2	USP10	GOLM1
	FAN1	EIF4E3	GALNT12	STAU2	ZFYVE16	PRKDC	FTOP1
	DHX57	CADPS	ARSJ	ZNF19	MXI1	C6orf106	ZNF576
	KIAA1211L	CKLF	CYB5D1	ALS2	UBXN7	PLIN3	CLIC6
	CCDC6	LAS1L	PNPT1	C11orf70	ZNF577	CCDC34	MTSS1
	ATP8A1	PDLIM4	LRRC8B	KIAA1755	PCM1	FBXO16	PCP4L1
	NFX1	PPP1R42	C14orf93	SPOPL	DEFB1	PECR	ST3GAL5
	ASNS	IQCB1	RAB28	C11orf49	DNAL4	ZNF682	ERBB4
	RINT1	SAMD12	TRIM45	CDY4P	TNFRSF21	TMEM125	DIO1
	ANKRD28	SLC29A3	ATP6V0B	SS18	CCDC113	DNAJA4	TMOD3
	RFWD3	SDCBP	CHMP1B	OXTR	HECA	IKZF2	PPP4C
	SEPT1	ZFP28	C1orf141	ZNF521	CAPSL	MIEN1	SGPP2
	BDKRB2	PPP3CC	GTF3C1	TC2N	LARP7	KIAA1244	GPR156
	ZNF280D	PPP1R11	SESTD1	PLEKHA2	NELFE	TOB2	DDI2
	PHYHD1	ACLY	RN7SL648P	CAPN2	CHRNA9	NKAP	IFT80
	PPP1R36	C7	ARHGEF25	PSMD11	HEATR3	ABI2	CBY1

Supplementary table 3 continued

miRNA	**Negatively correlated asthma-associated genes** (bold = validated target gene of miRNA)						
miR-223-3p	EFCAB10	PREX2	DNER	RAD18	ZNF417	GPATCH2L	TMPRSS13
	APITD1	HIST3H2BB	EFHC2	LIFR	PCID2	DNAJB2	MFN1
	FBXO15	TOE1	PCOLCE	PPP1R14B	GCC2	EMP1	SYAP1
	UBQLN2	STOML1	MMP19	S100P	SCNM1	COX17	FCGR2B
	SLC9B1	MTR	ZNF274	CCDC89	FECH	ADORA2B	GDE1
	AHNAK2	ARFIP2	NUFIP2	PCYT1B	RPS4XP16	CHP1	C15orf26
	HOXB-AS2	ERO1LB	MDM1	ELOVL5	LEPREL4	NCALD	CSTA
	SPATA13	ZNF165	ZNF445	KDM5B	PITHD1	MICE	DCDC2
	TMEM232	IGSF8	HNF4G	HMG20A	NDRG4	TRAC	KIRREL
	CASC1	SPA17	TMEM219	KCNK1	POC1B	NT5C3A	PPP4R1
	TNIK	RALGAPB	UBR1	POLD2	AMMECR1	PDLIM1	NPTXR
	IPO9	DRG2	GPRASP1	OAF	LRP6	NUP98	NRD1
	C9orf152	CASP7	MORC3	ABCC4	PIH1D3	ZC3HAV1	DRC1
	EVC2	SEC14L3	UBE2R2	DPCD	IMMP2L	PRR15	MYB
	DAPP1	PSMC5	ZNF549	SPRYD3	CDKL1	ZNF419	FBLN7
	SPATA18	COL4A6	CORO2B	FAM216B	RIOK3	ARHGAP11A	POT1-AS1
	CRHR1-IT1	TTBK2	EXOC4	DYRK1A	AMOT	EIF4G3	ZNF157
	CHD1L	TMCC1	GRIA3	ST6GALNAC6	SLC37A3	PDLIM5	C11orf53
	PBLD	TOP2A	FAM120A	S100A16	ACO2	DNAJC5B	IFIT1
	PLEKHB1	MAP3K5	STPG1	EIF5A	PSMF1	SLC9C1	HHLA2
	BAG1	XCR1	DYNC2H1	ZDHHC9	NIPBL	SCIN	NUP153
	NT5DC3	ANXA11	RCOR1	HMGN2P5	MAP6	NPEPPS	PCYT2
	SCAMP2	WBSCR22	HEBP2	WNT2B	PFDN6	RSAD1	DFNB59
	ZNF763	GPBP1	RFX3	SMIM22	YTHDF1	ABCC9	TNS3
	CCDC170	DAP	IGHG3	CEP41	NBPF24	RAB1B	C19orf70
	C9orf78	ACER2	WDR1	AFAP1L2	RCBTB2	HN1	KHDRBS2
	C12orf10	DNAJA1	RHOD	GPX1	SLC38A4	FAHD2A	SYTL3
	C19orf43	WDR17	SEMA5A	ZNF667-AS1	GALK2	IDH3A	LINC00896
	SHROOM3	RBKS	GALNT6	LCA5L	LUZP2	MLEC	ZNF432
	CCDC65	GNE	RNPEP	RNF165	PPFIBP2	CACHD1	CXCR6
	PLP2	CCDC102B	RUVBL2	ANKRD42	NOXRED1	TMUB2	ELMO1-AS1
	PAPOLA	VWDE	TMED11P	BECN1	CASC2	C21orf59	RPL7L1
	STX19	SHQ1	TSPAN9	H3F3A	PDCD6	FANCB	SLC50A1
	IL1R2	MBOAT1	SSTR2	HSPH1	MEG8	SEPW1	ATP2B4
	ATP8B2	GLB1L	AGBL5	TMEM39A	GSPT1	PLOD2	WDR45
	LTA4H	CXXC5	EXOSC6	ASXL3	METTL17	TDP1	LRRC4C
	UNC93B1	C1QA	ADIPOR1	IVNS1ABP	ZNF551	SLC22A4	PAXBP1-AS1
	HDGF	CKB	OSCP1	ZNF362	MTMR4	PPME1	WHSC1L1
	OTUD4	CDIP1	SCAF11	TTYH2	NAB2	ZNF275	FMO2
	FAM154B	CLOCK	EVC	MPZL3	UBE2Q2P1	WNK1	RSG1

Supplementary table 3 continued

miRNA	**Negatively correlated asthma-associated genes** (bold = validated target gene of miRNA)					
miR-223-3p	HSPA5	C12orf4	KRT8	LPAR6	ANXA2P1	CLDN7	PRODH
	MID1	FCHSD2	CCDC153	SLC9A3R1	CDKL5	LHPP	LYSMD4
	SLC25A26	CTNND1	UAP1	SLC2A9	C5orf42	CCDC146	TSHR
	C14orf37	TRO	FSD1L	RC3H1	UGT1A4	PACRGL	FMN1
	MAT2A	CLDN4	DOCK10	MIAT	SF3B4	BDH1	OSGEP
	NAP1L4	PRR13	TUBA4B	PHTF1	ZC2HC1C	WDR19	OMG
	LDLRAD4	HIST1H4K	FAM149A	TCTN2	PTPRG	TEKT1	UBXN10
	MCAT	LRRC8A	ECT2L	RNF169	CCDC163P	AGPAT2	RNF17
	BTBD9	ABCA9	ARFGAP3	GCNT4	ZNF267	SIX1	IQCH
	EIF4ENIF1	KIAA2018	CDYL	SMEK1	MYO6	IFT88	ZFAND4
	SPATA17	WIPF3	SMAGP	SERINC5	KIAA1958	FAM126B	PICALM
	CCNT2-AS1	RN7SKP64	ZNF232	PCYT1A	SRD5A2	LRIG2	ECT2
	MYO1B	CMPK2	BID	RHBDL2	PANK2	ABCB4	TBC1D4
	B3GNT3	C17orf67	SLC35E1	EIF2AK2	ZNF589	C20orf85	MYO1E
	GEMIN4	CFL1	PMF1	LAMB2	TSPAN5	DUSP22	LPIN2
	PSMG3	DLG1	ZKSCAN7	MIR645	LETMD1	MT1E	BPGM
	VPS52	KDM4D	IFNGR2	NR1H3	ATR	CHN2	SWAP70
	CC2D2A	SAMD9	ZNF594	MCMDC2	APPL2	EPAS1	KRT80
	ATP2A2	DNTTIP1	FANCC	SPG11	PAMR1	NUDC	SRD5A3
	IDH2	RBM47	CHST6	TEX9	RMDN3	TTC23	DNAJB1
	WNK3	GPATCH2	AREL1	MLH3	UBE3D	MIR374B	FAM160A1
	CAPS2	TBCB	DPAGT1	CYB5R4	TOP1	NSFL1C	MYEF2
	TM9SF1	RRN3P1	MKRN1	ZNF713	GRAMD3	TMEM105	SPATA13-AS1
	ZSCAN12	IQCG	RAB11FIP1	LRP10	FAM86C2P	ZNF792	MIR421
	ZDHHC16	NPHP1	NHSL1	GLIPR2	MGA	RAET1G	NBEA
	CCP110	CD38	ATRIP	IFFO2	CHMP4A	PCDHGB2	ANKUB1
	PKD1L3	IFT43	TRAF3IP1	PPM1H	PPIL6	SYTL5	BRWD3
	KANSL3	HSD17B1	CSNK1A1	B9D1	ACTG1	MAP1A	UBA1
	CPNE1	EFNB3	XKR9	RHPN2	LINC01171	YPEL1	EPHB6
	ADAMTSL2	MAP1LC3B2	DRAP1	PNKD	CLIP1	GJC2	SPAG6
	ZMYND10	PRICKLE2-AS3	ZBTB47	STOM	ZNF641	WDR20	SLC1A1
	S100PBP	RPGRIP1L	ZDHHC23	KPNA1	TSEN15P2	CTSS	PVRL4
	CENPF	CHD1	TNNI1	SNHG1	C3orf52		
miR-199b-3p	RGS18	FCGR3B	HBA1	MEFV	SULT1B1	TUBB1	FPR1
	TNFRSF10C	EMR3	CR1L	CSF3R	CR1	S100A8	C19orf38
	MNDA	VNN2	CXCR2	NRGN	SIRPB2	HK3	BCL2A1
	SLC11A1	SELL	GLT1D1	LRRC25	LILRA1	VEPH1	FCN1
	TFF1	FGFBP2	DGAT2	HSPA6	CGREF1		
miR-142-5p	SOWAHA	MUC15	SCGB2A1	DKK1	HCG14	SLC9A2	C15orf65
	HS6ST2	PCDH10	NDST4	NMBR	WDR72	AGPAT9	GLRX2

Supplementary table 3 continued

miRNA	Negatively correlated asthma-associated genes (bold = validated target gene of miRNA)						
miR-142-5p	C6	SOWAHB	SLC2A12	C11orf53	ANXA2P2	LINC00643	GSTA1
	NUDT16P1	GBP6	DIRAS3	F2RL1	PDCL3	PLA2G5	CLDN16
	HIST3H2A	MLF1	GEMIN8P4	MRPL42	COPG2	GCLM	TRMT10A
	MAL2	C11orf74	LINC01171	SDR16C5	ENPP5	TMEM45B	RGN
	CDH2	LRRTM4	KIF1A	SERPINB5	FAM104B	SEPP1	ZNF157
	NME5	NDUFB3	MYCBP	DYNLT3	BBS12	C1D	EDAR
	MRAP2	DUSP19	MB	SLC27A2	APOO	KLHL13	HSPA4L
	CBR1	CCDC152	MPC2	ELOVL6	IPMK	TREM2	ARL3
	RPL26L1	RHOU	SMKR1	NQO1	ACOT4	FAM180A	AP1M2
	IL20RA	TRIM36	ENPP4	PPP4R4	FAM174A	HSDL2	NAT1
	SOSTDC1	PEX7	OCLN	CD24P4	AKR1C2	RPP40	LRRIQ3
	FBXO36	LINC01014	SETD9	ZMYND12	C14orf142	UBL3	VSTM2L
	ANKRD66	PLS1	PCDH9	CXXC4	CDS1	PTGR1	ABHD17B
	ABHD6	PPP1R14C	STOX1	C11orf88	RPA3	AGR3	PRRG4
	HES2	CXorf57	SOX2-OT	SNX7	CETN2	C8orf47	LINC00908
	EIF4HP1	TTC30B	FAT3	COPRS	FOXA2	SLMO2	RHOD
	KLHL32	GPR115	PIH1D3	C16orf80	C9orf116	HIBADH	RPL7AP64
	PCDHB1	AKR1B10	TIPARP	FGF14	BLVRA	DCDC2	EPB41L4B
	EHHADH	RBM24	KLHDC9	SNTB1	TP53RK	FAM96B	HSD17B13
	ZBED5-AS1	C10orf107	PFN2	PRDX1	B3GNT5	AGPAT5	NAA20
	PCDHA4	C5orf49	TPH1	CERS6	FGFBP1	DUSP14	MBOAT2
	MRPL36	PRDX5	C2orf40	C11orf70	DNMBP-AS1	NDUFAB1	EID2
	TRHDE	MORN2	C12orf75	SCCPDH	PRMT6	PNPLA4	CDKL2
	SNTN	BRI3BP	TRMT1L	ZNF396	GREM2	NSMCE1	SAP30
	MRPL44	TM4SF1	RABL5	LINC00589	ARHGAP42	SRI	C8orf37
	LZTFL1	LSAMP	TXN	TTC30A	DYNLRB2	ZMPSTE24	KBTBD4
	VAMP8	CRNDE	HN1L	NDUFA1	TMEM38A	CDKN2B	CALCA
	CA9	UFC1	MALRD1	MEIG1	COX5A	SNORD108	DEFB1
	CDK7	AK7	SCAMP1	FAM183A	ZNF165	EFHC2	LIPH
	UGDH	SUMO1	AOX1	DBI	CATSPERD	FCF1	SYPL1
	ARL13B	MORN5	CHGA	RMI1	SCEL	SRGAP3-AS2	CDH13
	EFCAB10	RBKS	SQLE	STMND1	TOMM34		
miR-181b-5p	HBA1	TUBB1	RGS18	FCGR3B	TNFRSF10C	SULT1B1	MNDA
	EMR3	SELL	HK3	CSF3R	CXCR2	FPR1	FCN1
	SLC11A1	LILRA1	NRGN	MEFV	ITGA2B	LRRC25	VEPH1
	LILRA6						
miR-195-5p	HBA1	RGS18	FCGR3B	SULT1B1	TUBB1	NRGN	CR1L
	TNFRSF10C	MEFV	GLT1D1	CXCR2	C19orf38	CXCR2P1	CSF3R
	S100A8	VNN2	SLC11A1	EMR3	FPR1	HK3	MNDA
	LILRA6	FGFBP2	FAM27E3	ITIH6	LUCAT1	FCN1	ABCC6P1

Supplementary table 3 continued

miRNA	**Negatively correlated asthma-associated genes** (bold = validated target gene of miRNA)						
miR-195-5p	LILRA1	LRRC25	NFE4	SELL	HOXB1	CR1	DGAT2
	VNN1	MINOS1P3	FAM220CP	IL1B	SPATS1	LILRB2	NCF1C
	NCF2	ITGA2B	SIRPB2	DUXAP1	MGAM	BCL2A1	SERPINA1
	ANKRD18CP	PLCH1-AS1	TPT1P12	VEPH1	IBSP		
miR-125b-5p	HBA1	NRGN	FCGR3B	**S100A8**	GLT1D1	TNFRSF10C	TUBB1
	MEFV	SILT1B1	CR1	C15ORF48	LRRC25	CR1L	FCN1
	FGFBP2	CSF3R	FPR1	CXCR2	EMR2	RGS18	

Genes are ranked (left to right) from most to least significant negatively correlated asthma-associated genes.

Supplementary Table 4. Gene ontology and pathway analyses using Enrichr

Table 4a: Biological processes of negatively correlated asthma genes per miRNA

	Pathway/term	Overlap	Adjusted P-value
miR-199b-5p	cilium assembly (GO:0060271)	57/288	1.21E-17
	cilium organization (GO:0044782)	46/192	1.23E-17
	plasma membrane bounded cell projection assembly (GO:0120031)	46/241	1.19E-13
	organelle assembly (GO:0070925)	55/376	1.64E-11
	intraciliary transport (GO:0042073)	17/46	4.19E-09
	intraciliary transport involved in cilium assembly (GO:0035735)	15/40	4.69E-08
	neutrophil degranulation (GO:0043312)	46/479	7.89E-04
	neutrophil activation involved in immune response (GO:0002283)	46/483	8.65E-04
	neutrophil mediated immunity (GO:0002446)	46/487	8.93E-04
	protein transport along microtubule (GO:0098840)	7/16	8.93E-04
	axoneme assembly (GO:0035082)	8/24	1.78E-03
	regulation of cilium movement (GO:0003352)	5/8	2.23E-03
	axonemal dynein complex assembly (GO:0070286)	9/33	2.56E-03
	protein complex localization (GO:0031503)	7/22	7.46E-03
	ciliary basal body-plasma membrane docking (GO:0097711)	14/96	2.16E-02
	regulation of cilium assembly (GO:1902017)	7/27	2.78E-02
	regulation of organelle assembly (GO:1902115)	9/47	3.88E-02
	nucleoside diphosphate phosphorylation (GO:0006165)	4/8	3.94E-02
miR-223-3p	cilium assembly (GO:0060271)	88/288	3.88E-11
	organelle assembly (GO:0070925)	100/376	4.60E-09
	plasma membrane bounded cell projection assembly (GO:0120031)	72/241	1.15E-08
	intraciliary transport involved in cilium assembly (GO:0035735)	23/40	5.37E-08
	intraciliary transport (GO:0042073)	24/46	2.55E-07
	cilium organization (GO:0044782)	58/192	3.76E-07
	regulation of cellular amine metabolic process (GO:0033238)	24/51	2.27E-06
	regulation of cellular amino acid metabolic process (GO:0006521)	24/51	2.27E-06
	regulation of G2/M transition of mitotic cell cycle (GO:0010389)	47/149	2.27E-06
	regulation of canonical Wnt signaling pathway (GO:0060828)	60/213	2.27E-06
	regulation of cellular ketone metabolic process (GO:0010565)	26/61	5.34E-06
	protein ubiquitination (GO:0016567)	111/506	1.05E-05
	Wnt signaling pathway. planar cell polarity pathway (GO:0060071)	32/88	1.05E-05
	negative regulation of canonical Wnt signaling pathway (GO:0090090)	45/148	1.08E-05
	regulation of establishment of planar polarity (GO:0090175)	32/89	1.25E-05
	proteasome-mediated ubiquitin-dependent protein catabolic process (GO:0043161)	72/291	1.64E-05
	positive regulation of canonical Wnt signaling pathway (GO:0090263)	37/113	1.64E-05
	ubiquitin-dependent protein catabolic process (GO:0006511)	81/341	1.64E-05
	protein polyubiquitination (GO:0000209)	70/283	2.27E-05

Table 4a (continued)

	Pathway/term	Overlap	Adjusted P-value
miR-223-3p	positive regulation of ubiquitin-protein ligase activity involved in regulation of mitotic cell cycle transition (GO:0051437)	28/76	3.39E-05
	regulation of ubiquitin-protein ligase activity involved in mitotic cell cycle (GO:0051439)	27/72	3.51E-05
	positive regulation of ubiquitin protein ligase activity (GO:1904668)	29/82	5.18E-05
	regulation of transcription from RNA polymerase II promoter in response to hypoxia (GO:0061418)	28/78	5.56E-05
	regulation of mitotic cell cycle phase transition (GO:1901990)	50/184	5.61E-05
	proteasomal protein catabolic process (GO:0010498)	60/237	5.67E-05
	anaphase-promoting complex-dependent catabolic process (GO:0031145)	28/79	6.69E-05
	NIK/NF-kappaB signaling (GO:0038061)	28/80	8.69E-05
	regulation of hematopoietic stem cell differentiation (GO:1902036)	27/76	9.45E-05
	negative regulation of ubiquitin protein ligase activity (GO:1904667)	27/77	1.18E-04
	regulation of hematopoietic progenitor cell differentiation (GO:1901532)	27/77	1.18E-04
	negative regulation of Wnt signaling pathway (GO:0030178)	47/174	1.18E-04
	Golgi vesicle transport (GO:0048193)	65/271	1.19E-04
	negative regulation of cell cycle G2/M phase transition (GO:1902750)	25/69	1.36E-04
	positive regulation of protein ubiquitination involved in ubiquitin-dependent protein catabolic process (GO:2000060)	29/87	1.41E-04
	regulation of stem cell differentiation (GO:2000736)	29/88	1.78E-04
	regulation of transcription from RNA polymerase II promoter in response to stress (GO:0043618)	30/93	1.91E-04
	negative regulation of G2/M transition of mitotic cell cycle (GO:0010972)	23/62	2.03E-04
	retrograde vesicle-mediated transport. Golgi to ER (GO:0006890)	27/80	2.23E-04
	regulation of mRNA stability (GO:0043488)	37/128	2.35E-04
	positive regulation of telomerase RNA localization to Cajal body (GO:1904874)	10/15	2.64E-04
	cellular protein localization (GO:0034613)	73/327	3.61E-04
	non-canonical Wnt signaling pathway (GO:0035567)	36/127	4.89E-04
	negative regulation of mitotic cell cycle phase transition (GO:1901991)	26/79	5.14E-04
	positive regulation of Wnt signaling pathway (GO:0030177)	38/140	7.94E-04
	multivesicular body assembly (GO:0036258)	14/30	8.03E-04
	SCF-dependent proteasomal ubiquitin-dependent protein catabolic process (GO:0031146)	24/72	8.57E-04
	protein modification by small protein removal (GO:0070646)	60/261	8.78E-04
	protein deubiquitination (GO:0016579)	59/257	1.06E-03
	virion assembly (GO:0019068)	10/17	1.08E-03
	neutrophil activation involved in immune response (GO:0002283)	97/483	1.08E-03
	multivesicular body organization (GO:0036257)	14/31	1.14E-03
	neutrophil degranulation (GO:0043312)	96/479	1.26E-03
	autophagosome organization (GO:1905037)	20/56	1.29E-03
	ether lipid metabolic process (GO:0046485)	7/9	1.53E-03

Table 4a (continued)

	Pathway/term	Overlap	Adjusted P-value
miR-223-3p	antigen processing and presentation of exogenous peptide antigen via MHC class I. TAP-dependent (GO:0002479)	24/75	1.57E-03
	interleukin-1-mediated signaling pathway (GO:0070498)	28/95	1.82E-03
	macroautophagy (GO:0016236)	31/110	1.82E-03
	regulation of telomerase RNA localization to Cajal body (GO:1904872)	10/18	1.83E-03
	vesicle budding from membrane (GO:0006900)	8/12	1.95E-03
	G2/M transition of mitotic cell cycle (GO:0000086)	34/126	1.95E-03
	autophagosome assembly (GO:0000045)	20/58	2.02E-03
	ciliary basal body-plasma membrane docking (GO:0097711)	28/96	2.06E-03
	neutrophil mediated immunity (GO:0002446)	96/487	2.06E-03
	cell cycle G2/M phase transition (GO:0044839)	34/127	2.19E-03
	protein complex localization (GO:0031503)	11/22	2.35E-03
	cellular protein complex assembly (GO:0043623)	37/144	2.57E-03
	protein transport (GO:0015031)	69/326	2.57E-03
	antigen processing and presentation of exogenous peptide antigen via MHC class I (GO:0042590)	24/78	2.62E-03
	regulation of mitotic spindle assembly (GO:1901673)	10/19	2.87E-03
	'de novo' posttranslational protein folding (GO:0051084)	13/30	2.90E-03
	respiratory electron transport chain (GO:0022904)	27/94	3.33E-03
	stimulatory C-type lectin receptor signaling pathway (GO:0002223)	32/121	4.23E-03
	viral life cycle (GO:0019058)	29/107	5.57E-03
	chaperone mediated protein folding requiring cofactor (GO:0051085)	11/24	5.67E-03
	endosomal transport (GO:0016197)	51/229	5.90E-03
	regulation of protein localization to Cajal body (GO:1904869)	6/8	6.39E-03
	positive regulation of protein localization to Cajal body (GO:1904871)	6/8	6.39E-03
	innate immune response activating cell surface receptor signaling pathway (GO:0002220)	32/124	6.47E-03
	proteolysis involved in cellular protein catabolic process (GO:0051603)	26/93	6.68E-03
	regulation of spindle assembly (GO:0090169)	11/25	8.18E-03
	intra-Golgi vesicle-mediated transport (GO:0006891)	13/33	8.18E-03
	negative regulation of programmed cell death (GO:0043069)	80/408	8.40E-03
	cellular response to hypoxia (GO:0071456)	33/132	9.18E-03
	positive regulation of protein localization to membrane (GO:1905477)	26/95	9.18E-03
	Rab protein signal transduction (GO:0032482)	21/70	9.25E-03
	regulation of organelle assembly (GO:1902115)	16/47	1.03E-02
	positive regulation of clathrin-dependent endocytosis (GO:2000370)	5/6	1.03E-02
	regulation of extracellular exosome assembly (GO:1903551)	5/6	1.03E-02
	regulation of cell death (GO:0010941)	26/96	1.04E-02
	positive regulation of exocytosis (GO:0045921)	13/34	1.05E-02
	regulation of primary metabolic process (GO:0080090)	34/139	1.06E-02
	positive regulation of protein insertion into mitochondrial membrane involved in apoptotic signaling pathway (GO:1900740)	12/30	1.08E-02

Table 4a (continued)

	Pathway/term	**Overlap**	**Adjusted P-value**
miR-223-3p	regulation of protein insertion into mitochondrial membrane involved in apoptotic signaling pathway (GO:1900739)	12/30	1.08E-02
	response to unfolded protein (GO:0006986)	15/43	1.11E-02
	positive regulation of exosomal secretion (GO:1903543)	8/15	1.11E-02
	mitochondrial respiratory chain complex assembly (GO:0033108)	26/97	1.16E-02
	intracellular protein transport (GO:0006886)	69/347	1.28E-02
	regulation of mitotic spindle organization (GO:0060236)	13/35	1.34E-02
	apical junction assembly (GO:0043297)	13/35	1.34E-02
	ubiquitin-dependent ERAD pathway (GO:0030433)	18/58	1.39E-02
	post-Golgi vesicle-mediated transport (GO:0006892)	18/58	1.39E-02
	viral budding (GO:0046755)	10/23	1.46E-02
	Ras protein signal transduction (GO:0007265)	48/223	1.56E-02
	positive regulation of establishment of protein localization to mitochondrion (GO:1903749)	28/110	1.61E-02
	regulation of macroautophagy (GO:0016241)	29/116	1.74E-02
	protein transport along microtubule (GO:0098840)	8/16	1.74E-02
	regulation of exosomal secretion (GO:1903541)	8/16	1.74E-02
	negative regulation of apoptotic process (GO:0043066)	90/485	1.84E-02
	mitochondrial ATP synthesis coupled electron transport (GO:0042775)	23/85	1.95E-02
	vesicle-mediated transport (GO:0016192)	78/410	1.97E-02
	fatty acid catabolic process (GO:0009062)	19/65	2.03E-02
	tumor necrosis factor-mediated signaling pathway (GO:0033209)	30/123	2.07E-02
	nucleotide-sugar metabolic process (GO:0009225)	7/13	2.16E-02
	positive regulation of mitochondrial outer membrane permeabilization involved in apoptotic signaling pathway (GO:1901030)	13/37	2.17E-02
	negative regulation of cell death (GO:0060548)	22/81	2.29E-02
	modification-dependent protein catabolic process (GO:0019941)	33/141	2.37E-02
	regulation of autophagosome assembly (GO:2000785)	12/33	2.37E-02
	modulation by symbiont of host cellular process (GO:0044068)	5/7	2.37E-02
	cellular lipid biosynthetic process (GO:0097384)	5/7	2.37E-02
	protein localization to plasma membrane (GO:0072659)	31/130	2.37E-02
	ESCRT complex disassembly (GO:1904896)	6/10	2.40E-02
	ESCRT III complex disassembly (GO:1904903)	6/10	2.40E-02
	postreplication repair (GO:0006301)	15/47	2.51E-02
	chaperone-mediated protein complex assembly (GO:0051131)	8/17	2.51E-02
	regulation of cellular response to stress (GO:0080135)	26/104	2.84E-02
	regulation of proteasomal ubiquitin-dependent protein catabolic process (GO:0032434)	23/88	2.86E-02
	smoothened signaling pathway (GO:0007224)	11/30	3.41E-02
	mitotic cell cycle phase transition (GO:0044772)	46/221	3.49E-02
	cell-cell junction assembly (GO:0007043)	21/79	3.64E-02
	protein localization to cell periphery (GO:1990778)	28/117	3.65E-02

Table 4a (continued)

	Pathway/term	Overlap	Adjusted P-value
miR-223-3p	metaphase plate congression (GO:0051310)	14/44	3.65E-02
	nuclear envelope reassembly (GO:0031468)	8/18	3.76E-02
	negative regulation of response to endoplasmic reticulum stress (GO:1903573)	9/22	3.78E-02
	positive regulation of ATPase activity (GO:0032781)	12/35	3.83E-02
	protein stabilization (GO:0050821)	34/152	4.00E-02
	cell part morphogenesis (GO:0032990)	6/11	4.14E-02
	regulation of inclusion body assembly (GO:0090083)	6/11	4.14E-02
	intrinsic apoptotic signaling pathway in response to oxidative stress (GO:0008631)	6/11	4.14E-02
	protein polymerization (GO:0051258)	14/45	4.40E-02
	phagosome acidification (GO:0090383)	10/27	4.78E-02
	negative regulation of cAMP-dependent protein kinase activity (GO:2000480)	5/8	4.78E-02
	actin polymerization or depolymerization (GO:0008154)	12/36	4.78E-02
miR-199b-3p	neutrophil degranulation (GO:0043312)	11/479	1.66E-08
	neutrophil activation involved in immune response (GO:0002283)	11/483	1.66E-08
	neutrophil mediated immunity (GO:0002446)	11/487	1.66E-08
	inflammatory response (GO:0006954)	6/252	2.06E-04
	positive regulation of endopeptidase activity (GO:0010950)	2/24	3.73E-02
miR-181b-5p	neutrophil degranulation (GO:0043312)	8/479	1.75E-06
	neutrophil activation involved in immune response (GO:0002283)	8/483	1.75E-06
	neutrophil mediated immunity (GO:0002446)	8/487	1.75E-06
	inflammatory response (GO:0006954)	5/252	3.20E-04
miR-195-5p	neutrophil degranulation (GO:0043312)	14/479	4.39E-09
	neutrophil activation involved in immune response (GO:0002283)	14/483	4.39E-09
	neutrophil mediated immunity (GO:0002446)	14/487	4.39E-09
	inflammatory response (GO:0006954)	8/252	4.14E-05
	cellular defense response (GO:0006968)	4/56	1.45E-03
	leukocyte aggregation (GO:0070486)	2/7	1.15E-02
	pantothenate metabolic process (GO:0015939)	2/8	1.31E-02
	positive regulation of adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains (GO:0002824)	2/10	1.83E-02
miR-125b-5p	inflammatory response (GO:0006954)	5/252	2.14E-04
	neutrophil degranulation (GO:0043312)	6/479	2.14E-04
	neutrophil activation involved in immune response (GO:0002283)	6/483	2.14E-04
	neutrophil mediated immunity (GO:0002446)	6/487	2.14E-04
	positive regulation of endopeptidase activity (GO:0010950)	2/24	7.56E-03
	pattern recognition receptor signaling pathway (GO:0002221)	2/48	2.46E-02
	neutrophil chemotaxis (GO:0030593)	2/53	2.46E-02

Table 4a (continued)

	Pathway/term	Overlap	Adjusted P-value
miR-125b-5p	granulocyte chemotaxis (GO:0071621)	2/56	2.46E-02
	neutrophil migration (GO:1990266)	2/58	2.46E-02

Table 4b: Reactome pathways of negatively correlated asthma genes per miRNA

	Pathway/term	Overlap	Adjusted P-value
miR-199b-5p	Assembly of the primary cilium Homo sapiens (R-HSA-5617833)	43/187	9.30E-16
	Intraflagellar transport Homo sapiens (R-HSA-5620924)	18/41	2.70E-11
	Organelle biogenesis and maintenance Homo sapiens (R-HSA-1852241)	49/326	7.81E-11
	Cargo trafficking to the periciliary membrane Homo sapiens (R-HSA-5620920)	13/51	8.92E-05
	BBSome-mediated cargo-targeting to cilium Homo sapiens (R-HSA-5620922)	7/23	1.10E-02
	Anchoring of the basal body to the plasma membrane Homo sapiens (R-HSA-5620912)	14/97	2.30E-02
	Endosomal Sorting Complex Required For Transport (ESCRT) Homo sapiens (R-HSA-917729)	7/28	3.10E-02
	HSF1 activation Homo sapiens (R-HSA-3371511)	7/29	3.43E-02
miR-223-3p	Assembly of the primary cilium Homo sapiens (R-HSA-5617833)	69/187	2.52E-13
	Membrane Trafficking Homo sapiens (R-HSA-199991)	116/420	1.36E-12
	Organelle biogenesis and maintenance Homo sapiens (R-HSA-1852241)	95/326	9.38E-12
	Vesicle-mediated transport Homo sapiens (R-HSA-5653656)	122/492	5.57E-10
	Intraflagellar transport Homo sapiens (R-HSA-5620924)	24/41	3.04E-09
	G2/M Transition Homo sapiens (R-HSA-69275)	55/173	3.97E-08
	Mitotic G2-G2/M phases Homo sapiens (R-HSA-453274)	55/175	5.53E-08
	Hedgehog 'off' state Homo sapiens (R-HSA-5610787)	37/99	1.94E-07
	Regulation of ornithine decarboxylase (ODC) Homo sapiens (R-HSA-350562)	24/50	4.06E-07
	Signaling by Hedgehog Homo sapiens (R-HSA-5358351)	44/136	8.46E-07
	Cyclin E associated events during G1/S transition Homo sapiens (R-HSA-69202)	28/68	1.12E-06
	Regulation of activated PAK-2p34 by proteasome mediated degradation Homo sapiens (R-HSA-211733)	23/49	1.12E-06
	Vif-mediated degradation of APOBEC3G Homo sapiens (R-HSA-180585)	24/53	1.21E-06
	Apoptosis Homo sapiens (R-HSA-109581)	49/163	1.21E-06
	Dectin-1 mediated noncanonical NF-kB signaling Homo sapiens (R-HSA-5607761)	26/61	1.21E-06
	Cyclin A:Cdk2-associated events at S phase entry Homo sapiens (R-HSA-69656)	28/69	1.21E-06
	Regulation of Apoptosis Homo sapiens (R-HSA-169911)	23/50	1.21E-06
	SCF-beta-TrCP mediated degradation of Emi1 Homo sapiens (R-HSA-174113)	24/54	1.21E-06
	AUF1 (hnRNP D0) binds and destabilizes mRNA Homo sapiens (R-HSA-450408)	24/54	1.21E-06
	Degradation of AXIN Homo sapiens (R-HSA-4641257)	24/54	1.21E-06
	G2/M Checkpoints Homo sapiens (R-HSA-69481)	46/150	1.21E-06
	NIK. noncanonical NF-kB signaling Homo sapiens (R-HSA-5676590)	25/58	1.22E-06
	PCP/CE pathway Homo sapiens (R-HSA-4086400)	33/91	1.25E-06

Table 4b (continued)

	Pathway/term	Overlap	Adjusted P-value
miR-223-3p	Vpu mediated degradation of CD4 Homo sapiens (R-HSA-180534)	23/51	1.36E-06
	Programmed Cell Death Homo sapiens (R-HSA-5357801)	49/166	1.36E-06
	HIV Infection Homo sapiens (R-HSA-162906)	60/222	1.36E-06
	GLI3 is processed to GLI3R by the proteasome Homo sapiens (R-HSA-5610785)	25/59	1.36E-06
	Degradation of GLI2 by the proteasome Homo sapiens (R-HSA-5610783)	25/59	1.36E-06
	The role of GTSE1 in G2/M progression after G2 checkpoint Homo sapiens (R-HSA-8852276)	25/59	1.36E-06
	Cdc20:Phospho-APC/C mediated degradation of Cyclin A Homo sapiens (R-HSA-174184)	28/71	1.36E-06
	TP53 Regulates Metabolic Genes Homo sapiens (R-HSA-5628897)	31/84	1.54E-06
	APC:Cdc20 mediated degradation of cell cycle proteins prior to satisfation of the cell cycle checkpoint Homo sapiens (R-HSA-179419)	28/72	1.83E-06
	Intra-Golgi and retrograde Golgi-to-ER traffic Homo sapiens (R-HSA-6811442)	51/179	2.00E-06
	Degradation of beta-catenin by the destruction complex Homo sapiens (R-HSA-195253)	30/82	2.91E-06
	APC/C:Cdc20 mediated degradation of mitotic proteins Homo sapiens (R-HSA-176409)	28/74	3.10E-06
	Cell Cycle Checkpoints Homo sapiens (R-HSA-69620)	51/182	3.10E-06
	CDK-mediated phosphorylation and removal of Cdc6 Homo sapiens (R-HSA-69017)	22/50	3.10E-06
	Ubiquitin-dependent degradation of Cyclin D1 Homo sapiens (R-HSA-69229)	22/50	3.10E-06
	Ubiquitin-dependent degradation of Cyclin D Homo sapiens (R-HSA-75815)	22/50	3.10E-06
	Regulation of APC/C activators between G1/S and early anaphase Homo sapiens (R-HSA-176408)	29/79	3.74E-06
	Activation of APC/C and APC/C:Cdc20 mediated degradation of mitotic proteins Homo sapiens (R-HSA-176814)	28/75	3.97E-06
	Autodegradation of the E3 ubiquitin ligase COP1 Homo sapiens (R-HSA-349425)	22/51	4.35E-06
	Asymmetric localization of PCP proteins Homo sapiens (R-HSA-4608870)	25/63	4.35E-06
	Hh mutants that don't undergo autocatalytic processing are degraded by ERAD Homo sapiens (R-HSA-5362768)	23/55	4.35E-06
	SCF(Skp2)-mediated degradation of p27/p21 Homo sapiens (R-HSA-187577)	24/59	4.35E-06
	G1/S Transition Homo sapiens (R-HSA-69206)	36/112	4.99E-06
	Mitotic G1-G1/S phases Homo sapiens (R-HSA-453279)	41/136	4.99E-06
	Hedgehog 'on' state Homo sapiens (R-HSA-5632684)	30/85	4.99E-06
	APC/C-mediated degradation of cell cycle proteins Homo sapiens (R-HSA-174143)	30/85	4.99E-06
	Regulation of mitotic cell cycle Homo sapiens (R-HSA-453276)	30/85	4.99E-06
	Antigen processing: Ubiquitination & Proteasome degradation Homo sapiens (R-HSA-983168)	65/260	4.99E-06

Table 4b (continued)

	Pathway/term	**Overlap**	**Adjusted P-value**
miR-223-3p	p53-Independent DNA Damage Response Homo sapiens (R-HSA-69610)	22/52	5.22E-06
	p53-Independent G1/S DNA damage checkpoint Homo sapiens (R-HSA-69613)	22/52	5.22E-06
	Ubiquitin Mediated Degradation of Phosphorylated Cdc25A Homo sapiens (R-HSA-69601)	22/52	5.22E-06
	Degradation of DVL Homo sapiens (R-HSA-4641258)	23/56	5.24E-06
	Regulation of mRNA stability by proteins that bind AU-rich elements Homo sapiens (R-HSA-450531)	30/86	5.98E-06
	Cross-presentation of soluble exogenous antigens (endosomes) Homo sapiens (R-HSA-1236978)	21/49	7.17E-06
	Hh mutants abrogate ligand secretion Homo sapiens (R-HSA-5387390)	23/57	7.29E-06
	Host Interactions of HIV factors Homo sapiens (R-HSA-162909)	39/129	7.65E-06
	Golgi-to-ER retrograde transport Homo sapiens (R-HSA-8856688)	35/110	7.65E-06
	Transcriptional Regulation by TP53 Homo sapiens (R-HSA-3700989)	80/348	7.89E-06
	Switching of origins to a post-replicative state Homo sapiens (R-HSA-69052)	26/70	8.15E-06
	Orc1 removal from chromatin Homo sapiens (R-HSA-68949)	26/70	8.15E-06
	APC/C:Cdc20 mediated degradation of Securin Homo sapiens (R-HSA-174154)	25/66	8.66E-06
	Autodegradation of Cdh1 by Cdh1:APC/C Homo sapiens (R-HSA-174084)	24/62	9.06E-06
	Cellular responses to stress Homo sapiens (R-HSA-2262752)	83/367	9.17E-06
	Stabilization of p53 Homo sapiens (R-HSA-69541)	22/54	9.32E-06
	Regulation of RAS by GAPs Homo sapiens (R-HSA-5658442)	25/67	1.14E-05
	Degradation of GLI1 by the proteasome Homo sapiens (R-HSA-5610780)	23/59	1.28E-05
	Removal of licensing factors from origins Homo sapiens (R-HSA-69300)	26/72	1.39E-05
	HSF1 activation Homo sapiens (R-HSA-3371511)	15/29	1.49E-05
	Hedgehog ligand biogenesis Homo sapiens (R-HSA-5358346)	24/64	1.62E-05
	Class I MHC mediated antigen processing & presentation Homo sapiens (R-HSA-983169)	71/305	1.81E-05
	Signaling by Wnt Homo sapiens (R-HSA-195721)	69/295	2.10E-05
	E(R-Phagosome pathway Homo sapiens (R-HSA-1236974)	24/65	2.16E-05
	MAPK6/MAPK4 signaling Homo sapiens (R-HSA-5687128)	30/92	2.29E-05
	Activation of NF-kappaB in B cells Homo sapiens (R-HSA-1169091)	24/66	2.89E-05
	TCF dependent signaling in response to WNT Homo sapiens (R-HSA-201681)	51/199	3.00E-05
	Regulation of DNA replication Homo sapiens (R-HSA-69304)	26/75	3.02E-05
	Cell Cycle. Mitotic Homo sapiens (R-HSA-69278)	97/462	3.09E-05
	CDT1 association with the CDC6:ORC:origin complex Homo sapiens (R-HSA-68827)	22/58	3.27E-05
	APC/C:Cdh1 mediated degradation of Cdc20 and other APC/C:Cdh1 targeted proteins in late mitosis/early G1 Homo sapiens (R-HSA-174178)	25/71	3.29E-05
	Cell Cycle Homo sapiens (R-HSA-1640170)	114/566	3.29E-05

Table 4b (continued)

	Pathway/term	**Overlap**	**Adjusted P-value**
miR-223-3p	Metabolism Homo sapiens (R-HSA-1430728)	319/1908	3.47E-05
	Assembly of the pre-replicative complex Homo sapiens (R-HSA-68867)	24/67	3.57E-05
	p53-Dependent G1/S DNA damage checkpoint Homo sapiens (R-HSA-69580	23/63	3.88E-05
	p53-Dependent G1 DNA Damage Response Homo sapiens (R-HSA-69563)	23/63	3.88E-05
	Infectious disease Homo sapiens (R-HSA-5663205)	77/348	4.26E-05
	Antigen processing-Cross presentation Homo sapiens (R-HSA-1236975)	27/82	5.30E-05
	G1/S DNA Damage Checkpoints Homo sapiens (R-HSA-69615)	23/65	6.94E-05
	Respiratory electron transport Homo sapiens (R-HSA-611105)	28/88	7.32E-05
	Metabolism of polyamines Homo sapiens (R-HSA-351202)	27/84	8.58E-05
	CLEC7A (Dectin-1) signaling Homo sapiens (R-HSA-5607764)	30/99	1.01E-04
	Attenuation phase Homo sapiens (R-HSA-3371568)	13/26	1.01E-04
	COPI-dependent Golgi-to-ER retrograde traffic Homo sapiens (R-HSA-6811434)	26/81	1.26E-04
	The citric acid (TCA) cycle and respiratory electron transport Homo sapiens (R-HSA-1428517)	40/153	1.81E-04
	Anchoring of the basal body to the plasma membrane Homo sapiens (R-HSA-5620912)	29/97	1.81E-04
	Cargo trafficking to the periciliary membrane Homo sapiens (R-HSA-5620920)	19/51	1.81E-04
	COPI-mediated anterograde transport Homo sapiens (R-HSA-6807878)	25/78	1.85E-04
	Translocation of GLUT4 to the plasma membrane Homo sapiens (R-HSA-1445148)	21/60	1.95E-04
	Endosomal Sorting Complex Required For Transport (ESCRT) Homo sapiens (R-HSA-917729)	13/28	2.62E-04
	Cooperation of Prefoldin and TriC/CCT in actin and tubulin folding Homo sapiens (R-HSA-389958)	14/32	2.88E-04
	M Phase Homo sapiens (R-HSA-68886)	60/268	3.03E-04
	TNFR2 non-canonical NF-kB pathway Homo sapiens (R-HSA-5668541)	28/95	3.20E-04
	Formation of tubulin folding intermediates by CCT/TriC Homo sapiens (R-HSA-389960)	12/25	3.48E-04
	Chk1/Chk2(Cds1) mediated inactivation of Cyclin B:Cdk1 complex Homo sapiens (R-HSA-75035)	8/12	3.54E-04
	Activation of BAD and translocation to mitochondria Homo sapiens (R-HSA-111447)	9/15	3.61E-04
	Cellular response to heat stress Homo sapiens (R-HSA-3371556)	28/96	3.81E-04
	DNA Replication Pre-Initiation Homo sapiens (R-HSA-69002)	25/82	4.33E-04
	M/G1 Transition Homo sapiens (R-HSA-68874)	25/82	4.33E-04
	Synthesis of DNA Homo sapiens (R-HSA-69239)	28/97	4.56E-04
	Gene Expression Homo sapiens (R-HSA-74160)	269/1631	4.83E-04
	Beta-catenin independent WNT signaling Homo sapiens (R-HSA-3858494)	37/144	4.88E-04
	HSF1-dependent transactivation Homo sapiens (R-HSA-3371571)	14/34	5.87E-04

Table 4b (continued)

	Pathway/term	Overlap	Adjusted P-value
miR-223-3p	Respiratory electron transport. ATP synthesis by chemiosmotic coupling. and heat production by uncoupling proteins. Homo sapiens (R-HSA-163200)	30/109	6.34E-04
	Mitotic Anaphase Homo sapiens (R-HSA-68882)	42/173	6.34E-04
	Downstream TCR signaling Homo sapiens (R-HSA-202424)	28/99	6.47E-04
	BBSome-mediated cargo-targeting to cilium Homo sapiens (R-HSA-5620922	11/23	7.03E-04
	Mitotic Metaphase and Anaphase Homo sapiens (R-HSA-2555396)	42/174	7.12E-04
	ER to Golgi Anterograde Transport Homo sapiens (R-HSA-199977)	34/131	7.45E-04
	Regulation of HSF1-mediated heat shock response Homo sapiens (R-HSA-3371453)	24/80	7.47E-04
	Prefoldin mediated transfer of substrate to CCT/TriC Homo sapiens (R-HSA-389957)	12/27	7.75E-04
	Generic Transcription Pathway Homo sapiens (R-HSA-212436)	145/812	8.12E-04
	RHO GTPase Effectors Homo sapiens (R-HSA-195258)	56/255	8.12E-04
	C-type lectin receptors (CLRs) Homo sapiens (R-HSA-5621481)	32/123	1.10E-03
	RHO GTPases Activate WASPs and WAVEs Homo sapiens (R-HSA-5663213)	14/36	1.12E-03
	Axon guidance Homo sapiens (R-HSA-422475)	98/515	1.12E-03
	TCR signaling Homo sapiens (R-HSA-202403)	31/118	1.13E-03
	Separation of Sister Chromatids Homo sapiens (R-HSA-2467813)	39/162	1.24E-03
	S Phase Homo sapiens (R-HSA-69242)	32/124	1.24E-03
	Golgi Associated Vesicle Biogenesis Homo sapiens (R-HSA-432722)	18/54	1.24E-03
	RHO GTPases activate IQGAPs Homo sapiens (R-HSA-5626467)	7/11	1.45E-03
	Budding and maturation of HIV virion Homo sapiens(R-HSA-162588)	11/25	1.60E-03
	Activation of BH3-only proteins Homo sapiens (R-HSA-114452)	12/29	1.63E-03
	DNA Replication Homo sapiens (R-HSA-69306)	28/105	1.71E-03
	trans-Golgi Network Vesicle Budding Homo sapiens(R-HSA-199992)	21/70	1.84E-03
	Clathrin derived vesicle budding Homo sapiens (R-HSA-421837)	21/70	1.84E-03
	Asparagine N-linked glycosylation Homo sapiens (R-HSA-446203)	55/259	2.12E-03
	Regulation of PLK1 Activity at G2/M Transition Homo sapiens (R-HSA-2565942)	24/87	2.72E-03
	Macroautophagy Homo sapiens (R-HSA-1632852)	20/67	2.74E-03
	Downstream signaling events of B Cell Receptor (BCR) Homo sapiens (R-HSA-1168372)	43/192	2.97E-03
	G2/M DNA damage checkpoint Homo sapiens (R-HSA-69473)	22/78	3.35E-03
	Post-translational protein modification Homo sapiens(R-HSA-597592)	96/521	3.77E-03
	Signaling by Insulin receptor Homo sapiens (R-HSA-74752)	62/311	5.07E-03
	Adaptive Immune System Homo sapiens (R-HSA-1280218)	132/762	5.29E-03
	Metabolism of lipids and lipoproteins Homo sapiens (R-HSA-556833)	116/659	6.09E-03

Table 4b (continued)

	Pathway/term	Overlap	Adjusted P-value
miR-223-3p	Folding of actin by CCT/TriC Homo sapiens (R-HSA-390450)	6/10	6.28E-03
	AURKA Activation by TPX2 Homo sapiens (R-HSA-8854518)	20/72	7.16E-03
	Phospholipid metabolism Homo sapiens (R-HSA-1483257)	36/161	8.45E-03
	FCERI mediated NF-kB activation Homo sapiens (R-HSA-2871837)	27/111	9.40E-03
	Mitochondrial translation Homo sapiens (R-HSA-5368287)	23/90	1.04E-02
	Loss of Nlp from mitotic centrosomes Homo sapiens(R-HSA-380259)	19/69	1.04E-02
	Loss of proteins required for interphase microtubule organization?from the centrosome Homo sapiens (R-HSA-380284)	19/69	1.04E-02
	Lysosome Vesicle Biogenesis Homo sapiens (R-HSA-432720)	12/35	1.05E-02
	Fanconi Anemia Pathway Homo sapiens (R-HSA-6783310)	12/35	1.05E-02
	DNA Repair Homo sapiens (R-HSA-73894)	56/285	1.18E-02
	Glycerophospholipid biosynthesis Homo sapiens (R-HSA-1483206)	25/102	1.20E-02
	Processing of DNA double-strand break ends Homo sapiens (R-HSA-5693607)	21/81	1.32E-02
	Peroxisomal lipid metabolism Homo sapiens (R-HSA-390918)	10/27	1.33E-02
	MHC class II antigen presentation Homo sapiens (R-HSA-2132295)	25/103	1.37E-02
	VEGFA-VEGFR2 Pathway Homo sapiens (R-HSA-4420097)	61/320	1.55E-02
	Signalling to RAS Homo sapiens (R-HSA-167044)	49/246	1.64E-02
	ISG15 antiviral mechanism Homo sapiens (R-HSA-1169408)	19/72	1.67E-02
	Antiviral mechanism by IFN-stimulated genes Homo sapiens (R-HSA-1169410)	19/72	1.67E-02
	Transport to the Golgi and subsequent modification Homo sapiens (R-HSA-948021)	35/162	1.67E-02
	Metabolism of proteins Homo sapiens (R-HSA-392499)	174/1074	1.69E-02
	MAPK family signaling cascades Homo sapiens (R-HSA-5683057)	55/284	1.69E-02
	Signaling by VEGF Homo sapiens (R-HSA-194138)	62/328	1.69E-02
	MAPK1/MAPK3 signaling Homo sapiens (R-HSA-5684996)	48/241	1.70E-02
	GRB2 events in EGFR signaling Homo sapiens (R-HSA-179812)	47/235	1.70E-02
	SHC1 events in EGFR signaling Homo sapiens (R-HSA-180336)	47/235	1.70E-02
	SOS-mediated signalling Homo sapiens (R-HSA-112412)	47/235	1.70E-02
	SHC1 events in ERBB4 signaling Homo sapiens (R-HSA-1250347)	47/235	1.70E-02
	RAF/MAP kinase cascade Homo sapiens (R-HSA-5673001)	47/235	1.70E-02
	EPHB-mediated forward signaling Homo sapiens (R-HSA-3928662)	13/42	1.70E-02
	FRS-mediated FGFR2 signaling Homo sapiens (R-HSA-5654700)	47/236	1.81E-02
	FRS-mediated FGFR4 signaling Homo sapiens (R-HSA-5654712)	47/236	1.81E-02
	FRS-mediated FGFR3 signaling Homo sapiens (R-HSA-5654706)	47/236	1.81E-02
	FRS-mediated FGFR1 signaling Homo sapiens (R-HSA-5654693)	47/236	1.81E-02
	Mitochondrial translation elongation Homo sapiens (R-HSA-5389840)	21/84	1.89E-02
	EPH-Ephrin signaling Homo sapiens (R-HSA-2682334)	23/95	1.89E-02
	Disease Homo sapiens (R-HSA-1643685)	122/725	1.91E-02
	Formation of Incision Complex in GG-NER Homo sapiens (R-HSA-5696395)	13/43	2.04E-02

Table 4b (continued)

	Pathway/term	Overlap	Adjusted P-value
miR-223-3p	Iron uptake and transport Homo sapiens (R-HSA-917937)	13/43	2.04E-02
	IGF1R signaling cascade Homo sapiens (R-HSA-2428924)	55/288	2.08E-02
	Signaling by Type 1 Insulin-like Growth Factor 1 Receptor (IGF1R) Homo sapiens (R-HSA-2404192)	55/288	2.08E-02
	IRS-related events triggered by IGF1R Homo sapiens (R-HSA-2428928)	55/288	2.08E-02
	Interleukin receptor SHC signaling Homo sapiens (R-HSA-912526)	48/245	2.20E-02
	ARMS-mediated activation Homo sapiens (R-HSA-170984)	47/239	2.21E-02
	Signalling to p38 via RIT and RIN Homo sapiens (R-HSA-187706)	47/239	2.21E-02
	Frs2-mediated activation Homo sapiens (R-HSA-170968)	47/240	2.39E-02
	IRS-mediated signalling Homo sapiens (R-HSA-112399)	54/284	2.41E-02
	Signaling by Rho GTPases Homo sapiens (R-HSA-194315)	67/367	2.41E-02
	Retrograde transport at the Trans-Golgi-Network Homo sapiens (R-HSA-6811440)	14/49	2.41E-02
	Complex I biogenesis Homo sapiens (R-HSA-6799198)	14/49	2.41E-02
	Signalling to ERKs Homo sapiens (R-HSA-187687)	49/253	2.44E-02
	Heme degradation Homo sapiens (R-HSA-189483)	4/6	2.49E-02
	VEGFR2 mediated cell proliferation Homo sapiens (R-HSA-5218921)	48/248	2.67E-02
	RHO GTPases activate PKNs Homo sapiens (R-HSA-5625740)	16/60	2.70E-02
	Prolonged ERK activation events Homo sapiens (R-HSA-169893)	47/242	2.70E-02
	Interleukin-3. 5 and GM-CSF signaling Homo sapiens (R-HSA-512988)	50/261	2.74E-02
	Insulin receptor signalling cascade Homo sapiens (R-HSA-74751)	54/287	2.86E-02
	ABC-family proteins mediated transport Homo sapiens (R-HSA-382556)	13/45	2.86E-02
	Signaling by ERBB2 Homo sapiens (R-HSA-1227986)	13/45	2.86E-02
	Signaling by Leptin Homo sapiens (R-HSA-2586552)	47/243	2.86E-02
	Cell-cell junction organization Homo sapiens (R-HSA-421270)	16/61	3.11E-02
	HIV Life Cycle Homo sapiens (R-HSA-162587)	30/141	3.36E-02
	Cyclin A/B1 associated events during G2/M transition Homo sapiens (R-HSA-69273)	8/22	3.38E-02
	Post-chaperonin tubulin folding pathway Homo sapiens (R-HSA-389977)	8/22	3.38E-02
	Signaling by the B Cell Receptor (BCR) Homo sapiens (R-HSA-983705)	45/233	3.42E-02
	Interleukin-2 signaling Homo sapiens (R-HSA-451927)	48/252	3.44E-02
	Signaling by EGFR Homo sapiens (R-HSA-177929)	64/355	3.55E-02
	Gap junction degradation Homo sapiens (R-HSA-190873)	5/10	3.55E-02
	Activation of Ca-permeable Kainate Receptor Homo sapiens (R-HSA-451308)	5/10	3.55E-02
	Ionotropic activity of Kainate Receptors Homo sapiens (R-HSA-451306)	5/10	3.55E-02
	Mitochondrial translation initiation Homo sapiens (R-HSA-5368286)	20/84	3.55E-02

Table 4b (continued)

	Pathway/term	**Overlap**	**Adjusted P-value**
miR-223-3p	Mitochondrial translation termination Homo sapiens (R-HSA-5419276)	20/84	3.55E-02
	NCAM signaling for neurite out-growth Homo sapiens (R-HSA-375165)	50/266	3.68E-02
	AMER1 mutants destabilize the destruction complex Homo sapiens (R-HSA-4839748)	6/14	3.68E-02
	Truncations of AMER1 destabilize the destruction complex Homo sapiens (R-HSA-5467348)	6/14	3.68E-02
	truncated APC mutants destabilize the destruction complex Homo sapiens (R-HSA-4839744)	6/14	3.68E-02
	AXIN missense mutants destabilize the destruction complex Homo sapiens (R-HSA-5467340)	6/14	3.68E-02
	AXIN mutants destabilize the destruction complex. activating WNT signaling Homo sapiens (R-HSA-4839735)	6/14	3.68E-02
	APC truncation mutants have impaired AXIN binding Homo sapiens (R-HSA-5467337)	6/14	3.68E-02
	Synthesis of Prostaglandins (PG) and Thromboxanes (TX) Homo sapiens (R-HSA-2162123)	6/14	3.68E-02
	Centrosome maturation Homo sapiens (R-HSA-380287)	19/79	3.69E-02
	Recruitment of mitotic centrosome proteins and complexes Homo sapiens (R-HSA-380270)	19/79	3.69E-02
	Nonhomologous End-Joining (NHEJ) Homo sapiens (R-HSA-5693571)	14/52	3.70E-02
	Diseases of signal transduction Homo sapiens (R-HSA-5663202)	53/288	4.32E-02
	NrCAM interactions Homo sapiens (R-HSA-447038)	4/7	4.47E-02
	Citric acid cycle (TCA cycle) Homo sapiens (R-HSA-71403)	7/19	4.77E-02
	G1 Phase Homo sapiens (R-HSA-69236)	11/38	4.77E-02
	Cyclin D associated events in G1 Homo sapiens (R-HSA-69231)	11/38	4.77E-02
miR-181b-5p	Immune System Homo sapiens (R-HSA-168256)	8/1547	1.88E-02
	Immunoregulatory interactions between a Lymphoid and a non-Lymphoid cell Homo sapiens (R-HSA-198933)	3/157	4.09E-02

Supplementary Table 5. Gene ontology and pathway analyses using g:Profiler

Table 5a: Biological processes of negatively correlated asthma genes per miRNA

	Pathway/term	Overlap	Adjusted P-value
miR-199b-5p	cilium organization (GO:0044782)	74 / 414	6.09E-29
	cilium assembly (GO:0060271)	69 / 394	3.46E-26
	cell projection assembly (GO:0030031)	74 / 611	4.84E-18
	microtubule-based movement (GO:0007018)	55 / 383	8.59E-18
	plasma membrane bounded cell projection assembly (GO:0120031)	72 / 596	2.11E-17
	intraciliary transport (GO:0042073)	22 / 53	3.48E-15
	organelle assembly (GO:0070925)	86/ 907	1.45E-14
	protein transport along microtubule (GO:0098840)	23 / 68	1.27E-13
	microtubule-based protein transport (GO:0099118)	23 / 68	1.27E-13
	microtubule-based transport (GO:0099111)	35 / 201	5.47E-13
	microtubule-based process (GO:0007017)	81 / 888	1.84E-12
	cilium movement (GO:0003341)	28 / 168	2.14E-09
	neutrophil degranulation (GO:0043312)	18 / 484	2.42E-09
	neutrophil activation involved in immune response (GO:0002283)	18 / 487	2.69E-09
	neutrophil mediated immunity (GO:0002446)	18 / 498	3.93E-09
	neutrophil activation (GO:0042119)	18 / 500	4.20E-09
	granulocyte activation (GO:0036230)	18 / 507	5.31E-09
	intraciliary transport involved in cilium assembly (GO:0035735)	16 / 40	8.26E-09
	leukocyte degranulation (GO:0043299)	18 / 539	1.48E-08
	myeloid cell activation involved in immune response (GO:0002275)	18 / 549	2.02E-08
	myeloid leukocyte mediated immunity (GO:0002444)	18 / 556	2.49E-08
	axoneme assembly (GO:0035082)	19 / 76	3.36E-08
	myeloid leukocyte activation (GO:0002274)	18 / 673	5.79E-07
	axonemal dynein complex assembly (GO:0070286)	13/37	6.96E-07
	cilium-dependent cell motility (GO:0060285)	21 / 128	1.29E-06
	cilium or flagellum-dependent cell motility (GO:0001539)	21 / 128	1.29E-06
	leukocyte activation involved in immune response (GO:0002366)	18 / 719	1.69E-06
	protein localization to cilium (GO:0061512)	16 / 64	1.69E-06
	cell activation involved in immune response (GO:0002263)	18 / 726	1.85E-06
	transport along microtubule (GO:0010970)	24 / 166	1.88E-06
	extracellular transport (GO:0006858)	13 / 38	4.71E-06
	regulated exocytosis (GO:0045055)	18 / 799	9.12E-06
	microtubule bundle formation (GO:0001578)	19 / 107	1.80E-05
	epithelial cilium movement involved in extracellular fluid movement (GO:0003351)	12 / 35	2.08E-05
	leukocyte mediated immunity (GO:0002443)	18 / 891	5.05E-05
	exocytosis (GO:0006887)	18 / 921	8.43E-05
	cytoskeleton-dependent intracellular transport (GO:0030705)	19 / 204	1.08E-04
	determination of left/right symmetry (GO:0007368)	19 / 612	2.53E-04

Table 5a (continued)

	Pathway/term	Overlap	Adjusted P-value
miR-199b-5p	cell projection organization (GO:0030030)	96 / 1627	3.09E-04
	cilium movement involved in cell motility (GO:0060294)	16 / 117	5.73E-04
	determination of bilateral symmetry (GO:0009855)	19 / 134	7.90E-04
	specification of symmetry (GO:0009799)	19 / 135	8.91E-04
	immune effector process (GO:0002252)	13 / 1310	1.27E-03
	plasma membrane bounded cell projection organization (GO:0120036)	92 / 1586	1.34E-03
	immune response (GO:0006955)	21 / 2326	3.89E-03
	protein localization to ciliary membrane (GO:1903441)	6 / 12	4.07E-03
	flagellated sperm motility (GO:0030317)	14 / 106	5.61E-03
	sperm motility (GO:0097722)	14 / 106	5.61E-03
	ciliary basal body-plasma membrane docking (GO:0097711)	14 / 95	8.62E-03
	vesicle-mediated transport (GO:0016192)	15 / 2193	1.28E-02
	leukocyte activation (GO:0045321)	12 / 1346	1.37E-02
	immune system process (GO:0002376)	23 / 3322	1.76E-02
	secretion by cell (GO:0032940)	12 / 1396	2.01E-02
	microtubule cytoskeleton organization (GO:0000226)	48 / 617	2.37E-02
	export from cell (GO:0140352)	12 / 1450	2.99E-02
	organelle organization (GO:0006996)	248 / 4115	3.01E-02
	cell activation (GO:0001775)	12 / 1540	4.55E-02
	autocrine signaling (GO:0035425)	3 / 8	4.90E-02
	intraciliary retrograde transport (GO:0035721)	12 / 1538	2.12E-02
	cerebrospinal fluid circulation (GO:0090660)	5 / 9	2.15E-02
	smoothened signaling pathway (GO:0007224)	17 / 149	2.17E-02
	inner dynein arm assembly (GO:0036159)	5 / 15	2.22E-02
	neutrophil aggregation (GO:0070488)	2/2	3.31E-02
	defense response (GO:0006952)	14 / 1831	3.51E-02
	cellular component assembly (GO:0022607)	188 /3030	4.76E-02
miR-223-3p	microtubule-based protein transport (GO:0099118)	36/68	1.68E-10
	protein transport along microtubule (GO:0098840)	36/68	1.68E-10
	intraciliary transport (GO:0042073)	31/53	2.51E-10
	cytoskeleton-dependent intracellular transport (GO:0030705)	68/207	4.93E-09
	protein localization (GO:0008104)	508/2789	8.16E-09
	intraciliary transport involved in cilium assembly (GO:0035735)	25/40	9.80E-09
	organelle assembly (GO:0070925)	201/904	1.19E-08
	macromolecule localization (GO:0033036)	576/3238	1.22E-08
	microtubule-based transport (GO:0099111)	66/201	2.35E-08
	transport along microtubule (GO:0010970)	58/166	2.78E-08
	oxidation-reduction process (GO:0055114)	51/744	3.66E-08
	cilium organization (GO:0044782)	109/414	6.57E-08
	protein transport (GO:0015031)	278/1946	2.16E-07

Table 5a (continued)

	Pathway/term	Overlap	Adjusted P-value
miR-223-3p	cilium assembly (GO:0060271)	103/394	3.93E-07
	cell projection assembly (GO:0030031)	143/611	5.08E-07
	peptide transport (GO:0015833)	281/1989	5.68E-07
	amide transport (GO:0042886)	285/2024	5.80E-07
	intracellular transport (GO:0046907)	301/1777	6.13E-07
	plasma membrane bounded cell projection assembly (GO:0120031)	140/596	6.20E-07
	establishment of protein localization (GO:0045184)	275/2044	9.31E-07
	cellular protein localization (GO:0034613)	376/2024	1.12E-06
	nitrogen compound transport (GO:0071705)	350/2347	2.14E-06
	cellular macromolecule localization (GO:0070727)	379/2035	2.27E-06
	glutathione metabolic process (GO:0006749)	13/52	2.78E-06
	cellular localization (GO:0051641)	430/3562	8.05E-06
	cellular component biogenesis (GO:0044085)	545/3276	8.59E-06
	organic substance transport (GO:0071702)	403/2790	9.96E-06
	cellular protein catabolic process (GO:0044257)	129/818	1.01E-05
	organelle organization (GO:0006996)	612/4115	1.31E-05
	vesicle organization (GO:0016050)	68/343	1.39E-05
	proteolysis involved in cellular protein catabolic process (GO:0051603)	144/756	1.40E-05
	cellular component assembly (GO:0022607)	521/3030	2.18E-05
	regulation of cellular amino acid metabolic process (GO:0006521)	27/64	2.35E-05
	anion transport (GO:0006820)	415/2914	3.32E-05
	small molecule metabolic process (GO:0044281)	146/1929	3.59E-05
	microtubule-based movement (GO:0007018)	95/383	3.67E-05
	organic acid metabolic process (GO:0006082)	95/1094	3.94E-05
	energy derivation by oxidation of organic compounds (GO:0015980)	50/291	8.92E-05
	intracellular protein transport (GO:0006886)	210/1195	1.55E-04
	Golgi vesicle transport (GO:0048193)	79/383	1.66E-04
	proteasome-mediated ubiquitin-dependent protein catabolic process (GO:0043161)	73/435	1.90E-04
	macroautophagy (GO:0016236)	65/312	2.03E-04
	microtubule-based process (GO:0007017)	180/888	2.45E-04
	carboxylic acid metabolic process (GO:0019752)	88/1027	2.45E-04
	Wnt signaling pathway. planar cell polarity pathway (GO:0060071)	35/110	2.47E-04
	oxoacid metabolic process (GO:0043436)	90/1060	3.04E-04
	establishment of tissue polarity (GO:0007164)	39/129	3.13E-04
	establishment of planar polarity (GO:0001736)	39/129	3.13E-04
	regulation of animal organ morphogenesis (GO:2000027)	44/189	4.15E-04
	cellular respiration (GO:0045333)	37/194	4.82E-04
	protein catabolic process (GO:0030163)	142/983	4.84E-04
	cell projection organization (GO:0030030)	298/1627	5.07E-04

Table 5a (continued)

	Pathway/term	Overlap	Adjusted P-value
miR-223-3p	tube development (GO:0035295)	20/1128	5.12E-04
	cell adhesion (GO:0007155)	25/1494	5.13E-04
	anaphase-promoting complex-dependent catabolic process (GO:0031145)	29/84	5.15E-04
	electron transport chain (GO:0022900)	20/187	5.63E-04
	biological adhesion (GO:0022610)	25/1501	5.63E-04
	mitochondrion organization (GO:0007005)	79/570	6.12E-04
	tissue development (GO:0009888)	24/2161	6.29E-04
	modification-dependent protein catabolic process (GO:0019941)	104/664	6.35E-04
	regulation of establishment of planar polarity (GO:0090175)	35/114	6.78E-04
	organelle localization (GO:0051640)	143/676	6.83E-04
	ubiquitin-dependent protein catabolic process (GO:0006511)	103/657	7.01E-04
	establishment of localization in cell (GO:0051649)	363/2840	8.24E-04
	G2/M transition of mitotic cell cycle (GO:0000086)	54/261	9.35E-04
	proteasomal protein catabolic process (GO:0010498)	98/495	9.41E-04
	cellular aldehyde metabolic process (GO:0006081)	14/64	1.35E-03
	plasma membrane bounded cell projection organization (GO:0120036)	289/1586	1.35E-03
	modification-dependent macromolecule catabolic process (GO:0043632)	121/675	1.36E-03
	regulation of transcription from RNA polymerase II promoter in response to hypoxia (GO:0061418)	27/78	1.38E-03
	anatomical structure morphogenesis (GO:0009653)	35/2865	1.45E-03
	regulation of cellular amine metabolic process (GO:0033238)	29/85	1.71E-03
	cellular catabolic process (GO:0044248)	312/2350	1.82E-03
	generation of precursor metabolites and energy (GO:0006091)	53/548	1.92E-03
	hormone metabolic process (GO:0042445)	23/231	1.93E-03
	cellular ketone metabolic process (GO:0042180)	34/273	2.00E-03
	vesicle-mediated transport (GO:0016192)	307/2193	2.02E-03
	morphogenesis of a polarized epithelium (GO:0001738)	45/151	2.38E-03
	respiratory electron transport chain (GO:0022904)	26/118	2.54E-03
	antigen processing and presentation (GO:0019882)	49/234	2.69E-03
	primary alcohol metabolic process (GO:0034308)	12/95	2.89E-03
	animal organ morphogenesis (GO:0009887)	15/1106	2.92E-03
	antigen processing and presentation of exogenous peptide antigen (GO:0002478)	45/174	2.93E-03
	regulation of organelle organization (GO:0033043)	207/1224	2.99E-03
	response to toxic substance (GO:0009636)	20/249	3.12E-03
	tertiary alcohol metabolic process (GO:1902644)	6/20	3.33E-03
	autophagosome assembly (GO:0000045)	33/98	3.87E-03
	cell cycle G2/M phase transition (GO:0044839)	55/280	4.26E-03
	tube morphogenesis (GO:0035239)	17/975	4.37E-03

Table 5a (continued)

	Pathway/term	Overlap	Adjusted P-value
miR-223-3p	antigen processing and presentation of exogenous antigen (GO:0019884)	46/182	4.45E-03
	morphogenesis of an epithelial bud (GO:0060572)	42461	4.93E-03
	bone development (GO:0060348)	11/212	5.04E-03
	mitochondrial ATP synthesis coupled electron transport (GO:0042775)	20/99	5.56E-03
	regulation of canonical Wnt signaling pathway (GO:0060828)	10/302	5.79E-03
	membrane organization (GO:0061024)	149/968	6.41E-03
	multivesicular body assembly (GO:0036258)	11/30	6.56E-03
	ATP synthesis coupled electron transport (GO:0042773)	20/100	6.58E-03
	negative regulation of extrinsic apoptotic signaling pathway (GO:2001237)	14/109	6.89E-03
	cellular detoxification (GO:1990748)	13/113	6.92E-03
	morphogenesis of an epithelial fold (GO:0060571)	6/26	7.78E-03
	antigen processing and presentation of peptide antigen (GO:0048002)	47/192	9.05E-03
	vasculature development (GO:0001944)	17/847	9.16E-03
	multivesicular body organization (GO:0036257)	11/31	9.61E-03
	protein polyubiquitination (GO:0000209)	63/344	9.81E-03
	regulation of organelle assembly (GO:1902115)	52/194	1.03E-02
	retrograde vesicle-mediated transport. Golgi to endoplasmic reticulum (GO:0006890)	26/87	1.05E-02
	autophagosome organization (GO:1905037)	33/102	1.09E-02
	regulation of hematopoietic stem cell differentiation (GO:1902036)	25/76	1.19E-02
	establishment of protein localization to mitochondrial membrane (GO:0090151)	18/53	1.27E-02
	positive regulation of telomerase RNA localization to Cajal body (GO:1904874)	10/15	1.32E-02
	cellular response to toxic substance (GO:0097237)	13/120	1.38E-02
	digestive tract morphogenesis (GO:0048546)	18050	1.49E-02
	heterophilic cell-cell adhesion via plasma membrane cell adhesion molecules (GO:0007157)	18172	1.61E-02
	ossification (GO:0001503)	26/428	1.65E-02
	neutrophil mediated immunity (GO:0002446)	84/498	1.69E-02
	negative regulation of synapse assembly (GO:0051964)	3/8	1.79E-02
	cellular hormone metabolic process (GO:0034754)	7/137	1.85E-02
	mitochondrial respiratory chain complex assembly (GO:0033108)	19/105	1.87E-02
	regulation of developmental process (GO:0050793)	32/2648	1.89E-02
	epithelium development (GO:0060429)	17/1361	2.00E-02
	canonical Wnt signaling pathway (GO:0060070)	10/347	2.03E-02
	establishment of vesicle localization (GO:0051650)	54/215	2.08E-02
	venous blood vessel morphogenesis (GO:0048845)	2/9	2.15E-02
	regulation of postsynapse organization (GO:0099175)	7/92	2.28E-02
	regulation of cellular ketone metabolic process (GO:0010565)	50/195	2.41E-02
	anatomical structure development (GO:0048856)	53/6210	2.45E-02

Table 5a (continued)

	Pathway/term	Overlap	Adjusted P-value
miR-223-3p	protein localization to organelle (GO:0033365)	170/1014	2.48E-02
	transport (GO:0006810)	614/5259	2.53E-02
	negative regulation of canonical Wnt signaling pathway (GO:0090090)	29/188	2.59E-02
	regulation of G2/M transition of mitotic cell cycle (GO:0010389)	48/202	2.63E-02
	positive regulation of canonical Wnt signaling pathway (GO:0090263)	22/154	2.86E-02
	positive regulation of organelle organization (GO:0010638)	102/620	3.12E-02
	response to acid chemical (GO:0001101)	14/142	3.21E-02
	catabolic process (GO:0009056)	348/2746	3.27E-02
	organ induction (GO:0001759)	4/25	3.33E-02
	antigen processing and presentation of exogenous peptide antigen via MHC class I. TAP-dependent (GO:0002479)	24/75	3.35E-02
	antigen processing and presentation of exogenous peptide antigen via MHC class I (GO:0042590)	25/80	3.42E-02
	mitochondrial translation (GO:0032543)	26/136	3.45E-02
	odontogenesis (GO:0042476)	7/136	3.73E-02
	bud elongation involved in lung branching (GO:0060449)	5/7	4.06E-02
	ion transport (GO:0006811)	418/3689	4.25E-02
	detoxification (GO:0098754)	17/134	4.28E-02
	regulation of multicellular organismal process (GO:0051239)	33/2894	4.43E-02
	neutrophil activation involved in immune response (GO:0002283)	81/487	4.48E-02
	non-canonical Wnt signaling pathway (GO:0035567)	38/151	4.81E-02
	regulation of Wnt signaling pathway (GO:0030111)	10/383	4.89E-02
	cellular macromolecule catabolic process (GO:0044265)	174/1237	4.94E-02
miR-199b-3p	neutrophil degranulation (GO:0043312)	11 / 484	2.45E-07
	neutrophil activation involved in immune response (GO:0002283)	11 / 487	2.62E-07
	neutrophil mediated immunity (GO:0002446)	11 / 498	3.32E-07
	neutrophil activation (GO:0042119)	11 / 500	3.46E-07
	granulocyte activation (GO:0036230)	11 / 504	4.01E-07
	leukocyte degranulation (GO:0043299)	11 / 539	7.65E-07
	myeloid cell activation involved in immune response (GO:0002275)	11 / 549	9.29E-07
	myeloid leukocyte mediated immunity (GO:0002444)	11 / 556	1.06E-06
	myeloid leukocyte activation (GO:0002274)	11 / 673	7.81E-06
	leukocyte activation involved in immune response (GO:0002366)	11 / 719	1.55E-05
	cell activation involved in immune response (GO:0002263)	11 / 723	1.64E-05
	regulated exocytosis (GO:0045055)	11 / 799	4.58E-05
	leukocyte mediated immunity (GO:0002443)	11 / 891	1.39E-04
	exocytosis (GO:0006887)	11 / 921	1.94E-04
	immune effector process (GO:0002252)	12 / 1310	7.99E-04
	leukocyte activation (GO:0045321)	11/1346	8.17E-03
	regulation of immune system process (GO:0002682)	9/998	9.07E-03
	immune system process (GO:0002376)	13/2326	9.17E-03

Table 5a (continued)

	Pathway/term	Overlap	Adjusted P-value
miR-199b-3p	secretion by cell (GO:0032940)	11/1396	1.16E-02
	export from cell (GO:0140352)	11/1450	1.66E-02
	complement receptor mediated signaling pathway (GO:0002430)	2/12	2.31E-02
	cell activation (GO:0001775)	11/1510	2.43E-02
	secretion (GO:0046903)	11/1538	2.89E-02
miR-142-5p	protein transport along microtubule (GO:0098840)	7/68	1.65E-02
	microtubule-based protein transport (GO:0099118)	7/68	1.65E-02
	oxidation-reduction process (GO:0055114)	24/744	3.97E-02
	intraciliary transport (GO:0042073)	6/53	4.62E-02
miR-181b-5p	neutrophil degranulation (GO:0043312)	8 / 484	4.85E-07
	neutrophil activation involved in immune response (GO:0002283)	8 / 487	5.09E-07
	neutrophil mediated immunity (GO:0002446)	8 / 498	6.08E-07
	neutrophil activation (GO:0042119)	8 / 500	6.27E-07
	granulocyte activation (GO:0036230)	8 / 507	7.00E-07
	leukocyte degranulation (GO:0043299)	8 / 539	1.14E-06
	myeloid cell activation involved in immune response (GO:0002275)	8 / 549	1.31E-06
	myeloid leukocyte mediated immunity (GO:0002444)	8 / 556	1.45E-06
	myeloid leukocyte activation (GO:0002274)	8 / 673	6.51E-06
	leukocyte activation involved in immune response (GO:0002366)	8 / 719	1.09E-05
	cell activation involved in immune response (GO:0002263)	8 / 723	1.14E-05
	regulated exocytosis (GO:0045055)	9 / 799	1.56E-05
	exocytosis (GO:0006887)	9 / 921	5.32E-05
	leukocyte mediated immunity (GO:0002443)	8 / 891	5.81E-05
	immune effector process (GO:0002252)	8 / 1310	1.12E-03
	leukocyte activation (GO:0045321)	8 / 1346	1.38E-03
	secretion (GO:0046903)	9/1396	1.82E-03
	export from cell (GO:0140352)	8/1450	2.43E-03
	cell activation (GO:0001775)	8/1510	3.30E-03
	secretion (GO:0046903)	8/1538	3.79E-03
	vesicle-mediated transport (GO:0016192)	9/2193	4.72E-03
	regulation of immune response (GO:0050776)	7/998	4.98E-03
	regulation of immune system process (GO:0002682)	9/1625	6.42E-03
	immune system process (GO:0002376)	12/3322	6.66E-03
	immune response (GO:0006955)	10/2326	7.47E-03
miR-195-5p	neutrophil degranulation (GO:0043312)	14/484	1.36E-08
	neutrophil activation involved in immune response (GO:0002283)	14/487	1.48E-08
	neutrophil mediated immunity (GO:0002446)	14/498	2.00E-08
	neutrophil activation (GO:0042119)	14/500	2.11E-08
	granulocyte activation (GO:0036230)	14/507	2.54E-08
	leukocyte degranulation (GO:0043299)	14/539	5.72E-08

Table 5a (continued)

	Pathway/term	Overlap	Adjusted P-value
miR-195-5p	myeloid cell activation involved in immune response (GO:0002275)	14/549	7.30E-08
	myeloid leukocyte mediated immunity (GO:0002444)	14/556	8.63E-08
	regulated exocytosis (GO:0045055)	15/799	9.23E-07
	myeloid leukocyte activation (GO:0002274)	14/673	1.06E-06
	leukocyte activation involved in immune response (GO:0002366)	14/719	2.48E-06
	cell activation involved in immune response (GO:0002263)	14/723	2.67E-06
	leukocyte mediated immunity (GO:0002443)	15/891	4.12E-06
	exocytosis (GO:0006887)	15/921	6.46E-06
	immune effector process (GO:0002252)	16/1310	1.01E-04
	secretion by cell (GO:0032940)	16/1396	2.43E-04
	export from cell (GO:0140352)	16/1450	4.08E-04
	immune response (GO:0006955)	20/2326	4.33E-04
	cell activation (GO:0001775)	16/1510	7.09E-04
	secretion (GO:0046903)	16/1538	9.09E-04
	leukocyte activation (GO:0045321)	15/1346	9.66E-04
	regulation of immune response (GO:0050776)	11/998	6.45E-03
	immune system process (GO:0002376)	22/3322	7.60E-03
	cellular defense response (GO:0006968)	4/53	8.65E-03
	regulation of immune system process (GO:0002682)	14/1625	1.13E-02
	vesicle-mediated transport (GO:0016192)	17/2193	2.10E-02
	defense response (GO:0006952)	14/1831	3.21E-02
miR-125b-5p	neutrophil degranulation (GO:0043312)	6/484	8.36E-03
	neutrophil activation involved in immune response (GO:0002283)	6/487	8.67E-03
	neutrophil mediated immunity (GO:0002446)	6/498	9.85E-03
	neutrophil activation (GO:0042119)	6/500	1.01E-02
	granulocyte activation (GO:0036230)	6/507	1.09E-02
	leukocyte degranulation (GO:0043299)	6/539	1.55E-02
	myeloid cell activation involved in immune response (GO:0002275)	6/549	1.72E-02
	myeloid leukocyte activation (GO:0002274)	6/556	1.85E-02

Table 5b: Reactome pathways of negatively correlated asthma genes per miRNA

	Pathway/term	**Overlap**	**Adjusted P-value**
miR-199b-5p	Cilium Assembly (R-HSA-5617833)	44 / 201	1.22E-11
	Intraflagellar transport (R-HSA-5620924)	20 / 54	8.97E-09
	Organelle biogenesis and maintenance (R-HSA-1852241)	46 / 293	6.54E-07
	Neutrophil degranulation (R-HSA-6798695)	17 / 474	1.57E-05
	Innate Immune System (R-HSA-168249)	19 / 1073	4.18E-04
	Immune System (R-HSA-168256)	25 / 2116	2.18E-02
	Cargo trafficking to the periciliary membrane (R-HSA-5620920)	12 / 51	2.96E-02
miR-223-3p	Intraflagellar transport (R-HSA-5620924)	30/54	5.77E-04
	Regulation of Apoptosis (R-HSA-169911)	26/53	5.34E-03
	Regulation of ornithine decarboxylase (R-HSA-350562)	25/51	8.40E-03
	Negative regulation of NOTCH4 signaling (R-HSA-9604323)	25/53	1.99E-02
	Regulation of activated PAK-2p34 by proteasome mediated degradation (R-HSA-211733)	24/50	2.05E-02
	AUF1 (hnRNP D0) binds and destabilizes mRNA (R-HSA-450408)	25/54	3.00E-02
	Cilium Assembly (R-HSA-5617833)	74/201	3.06E-02
	Metabolism of polyamines (R-HSA-351202)	26/58	4.15E-02
	SCF-beta-TrCP mediated degradation of Emi1 (R-HSA-174113)	25/55	4.43E-02
	Degradation of AXIN (R-HSA-4641257)	25/55	4.43E-02
	Ubiquitin-dependent degradation of Cyclin D (R-HSA-75815)	24/52	4.69E-02
	Vpu mediated degradation of CD4 (R-HSA-180534)	24/52	4.69E-02
miR-199b-3p	Neutrophil degranulation (R-HSA-6798695)	11 / 474	8.03E-06
	Innate Immune System (R-HSA-168249)	10 / 1073	3.73E-03
	Immune System (R-HSA-168256)	14/2116	3.70E-02
miR-181b-5p	Neutrophil degranulation (R-HSA-6798695)	8 / 474	5.90E-06
	Immune System (R-HSA-168256)	13 / 2116	4.08E-04
	Innate Immune System (R-HSA-168249)	9 / 1071	2.05E-03
miR-195-5p	Neutrophil degranulation (R-HSA-6798695)	14/474	1.47E-06
	Innate Immune System (R-HSA-168249)	17/1073	2.40E-04
	Immune System (R-HSA-168256)	22/2116	4.29E-03
miR-125b-5p	Neutrophil degranulation (R-HSA-6798695)	6 / 474	2.75E-02

Supplementary Table 6. Gene ontology and pathway analyses using Enrichr

Table 6a: Biological processes of positively and negatively correlated asthma genes per miRNA

	Pathway/term	**Overlap**	**Adjusted P-value**
miR-199b-5p	cilium assembly (GO:0060271)	84/288	9,90E-36
	cilium organization (GO:0044782)	60/192	1,31E-27
	plasma membrane bounded cell projection assembly (GO:0120031)	59/241	3,63E-21
	organelle assembly (GO:0070925)	70/376	8,68E-18
	intraciliary transport (GO:0042073)	23/46	1,14E-16
	intraciliary transport involved in cilium assembly (GO:0035735)	21/40	6,75E-16
	protein transport along microtubule (GO:0098840)	11/16	1,04E-10
	axoneme assembly (GO:0035082)	13/24	1,47E-10
	cilium-dependent cell motility (GO:0060285)	12/24	2,56E-09
	cilium movement (GO:0003341)	16/49	1,14E-08
	protein complex localization (GO:0031503)	11/22	1,20E-08
	axonemal dynein complex assembly (GO:0070286)	13/33	2,03E-08
	ciliary basal body-plasma membrane docking (GO:0097711)	22/96	3,43E-08
	neutrophil degranulation (GO:0043312)	53/479	9,81E-06
	neutrophil activation involved in immune response (GO:0002283)	53/483	1,24E-05
	neutrophil mediated immunity (GO:0002446)	53/487	1,56E-05
	motile cilium assembly (GO:0044458)	6/13	5,21E-05
	epithelial cilium movement (GO:0003351)	6/15	1,37E-04
	positive regulation of telomerase RNA localization to Cajal body (GO:1904874)	6/15	1,37E-04
	intraciliary retrograde transport (GO:0035721)	5/10	1,44E-04
	smoothened signaling pathway (GO:0007224)	8/30	2,75E-04
	chaperone-mediated protein complex assembly (GO:0051131)	6/17	3,06E-04
miR-223-3p	cilium assembly (GO:0060271)	79/288	4,85E-24
	cilium organization (GO:0044782)	55/192	2,66E-17
	organelle assembly (GO:0070925)	78/376	4,81E-16
	intraciliary transport (GO:0042073)	26/46	4,81E-16
	intraciliary transport involved in cilium assembly (GO:0035735)	24/40	1,25E-15
	plasma membrane bounded cell projection assembly (GO:0120031)	59/241	1,57E-15
	protein transport along microtubule (GO:0098840)	11/16	2,19E-07
	protein complex localization (GO:0031503)	12/22	1,39E-06
	ciliary basal body-plasma membrane docking (GO:0097711)	22/96	1,41E-04
	axoneme assembly (GO:0035082)	10/24	5,50E-04
	neutrophil degranulation (GO:0043312)	61/479	5,50E-04
	neutrophil activation involved in immune response (GO:0002283)	61/483	6,63E-04
	neutrophil mediated immunity (GO:0002446)	61/487	8,01E-04
	smoothened signaling pathway (GO:0007224)	10/30	4,31E-03

Table 6a continued

	Pathway/term	Overlap	Adjusted P-value
miR-223-3p	positive regulation of telomerase RNA localization to Cajal body (GO:1904874)	7/15	6,00E-03
	virion assembly (GO:0019068)	7/15	1,42E-02
	chaperone-mediated protein complex assembly (GO:0051131)	7/15	1,42E-02
	regulation of telomerase RNA localization to Cajal body (GO:1904872)	7/18	2,01E-02
	cellular protein complex assembly (GO:0043623)	23/144	2,01E-02
	multivesicular body assembly (GO:0036258)	9/30	2,01E-02
	cilium-dependent cell motility (GO:0060285)	8/24	2,01E-02
	small nucleolar ribonucleoprotein complex assembly (GO:0000491)	5/9	2,24E-02
	multivesicular body organization (GO:0036257)	9/31	2,33E-02
	postreplication repair (GO:0006301)	11/47	3,55E-02
	intraciliary retrograde transport (GO:0035721)	5/10	3,63E-02
	regulation of extracellular exosome assembly (GO:1903551)	4/6	3,63E-02
	positive regulation of exosomal secretion (GO:1903543)	6/15	3,63E-02
	G2/M transition of mitotic cell cycle (GO:0000086)	20/126	4,05E-02
	cell cycle G2/M phase transition (GO:0044839)	20/127	4,35E-02
	regulation of exosomal secretion (GO:1903541)	6/16	4,93E-02
miR-199b-3p	potassium ion transport (GO:0006813)	10/61	3,73E-02
miR-142-5p	neutrophil degranulation (GO:0043312)	30/479	2,72E-05
	neutrophil activation involved in immune response (GO:0002283)	30/483	2,72E-05
	neutrophil mediated immunity (GO:0002446)	30/487	2,72E-05

Table 6b: Reactome pathways of positively and negatively correlated asthma genes per miRNA

	Pathway/term	Overlap	Adjusted P-value
miR-199b-5p	Assembly of the primary cilium (R-HSA-5617833)	59/187	2,11E-24
	Intraflagellar transport (R-HSA-5620924)	24/41	8,94E-17
	Organelle biogenesis and maintenance (R-HSA-1852241)	65/326	1,23E-15
	Cargo trafficking to the periciliary membrane (R-HSA-5620920)	16/51	5,63E-06
	Anchoring of the basal body to the plasma membrane (R-HSA-5620912)	22/97	8,64E-06
	BBSome-mediated cargo-targeting to cilium (R-HSA-5620922)	10/23	5,12E-05
	Cooperation of Prefoldin and TriC/CCT in actin and tubulin folding (R-HSA-389958)	09/32	1,07E-02
	Prefoldin mediated transfer of substrate to CCT/TriC (R-HSA-389957)	08/27	1,58E-02
	HSF1 activation (R-HSA-3371511)	08/29	2,44E-02
	Formation of tubulin folding intermediates by CCT/TriC (R-HSA-389960)	07/25	4,95E-02
miR-223-3p	Assembly of the primary cilium (R-HSA-5617833)	60/187	4,58E-22
	Intraflagellar transport (R-HSA-5620924)	25/41	1,20E-16
	Organelle biogenesis and maintenance (R-HSA-1852241)	69/326	6,57E-15
	Anchoring of the basal body to the plasma membrane (R-HSA-5620912)	23/97	3,12E-05
	Cargo trafficking to the periciliary membrane (R-HSA-5620920)	15/51	2,08E-04
	BBSome-mediated cargo-targeting to cilium (R-HSA-5620922)	10/23	2,08E-04
	Cooperation of Prefoldin and TriC/CCT in actin and tubulin folding (R-HSA-389958)	11/32	8,13E-04
	Prefoldin mediated transfer of substrate to CCT/TriC (R-HSA-389957)	10/27	8,93E-04
	Membrane Trafficking (R-HSA-199991)	53/420	1,43E-03
	Formation of tubulin folding intermediates by CCT/TriC (R-HSA-389960)	9/25	2,75E-03
	Post-chaperonin tubulin folding pathway (R-HSA-389977)	8/22	6,08E-03
	Vesicle-mediated transport (R-HSA-5653656)	57/492	6,08E-03
	HSF1 activation (R-HSA-3371511)	9/29	8,07E-03
	Hedgehog 'off' state (R-HSA-5610787)	18/99	9,33E-03
	G2/M Transition (R-HSA-69275)	26/173	9,33E-03
	Mitotic G2-G2/M phases (R-HSA-453274)	26/175	1,06E-02
	Attenuation phase (R-HSA-3371568)	8/26	1,63E-02
	Activation of BAD and translocation to mitochondria (R-HSA-111447)	6/15	1,90E-02
	Signaling by Hedgehog (R-HSA-5358351)	21/136	2,20E-02
	Transcriptional Regulation by TP53 (R-HSA-3700989)	41/348	2,55E-02
	Protein folding (R-HSA-391251)	17/101	2,55E-02
	Apoptotic cleavage of cell adhesion proteins (R-HSA-351906)	5/11	2,55E-02
	Activation of BH3-only proteins (R-HSA-114452)	8/29	2,76E-02
	Cellular response to heat stress (R-HSA-3371556)	16/96	3,49E-02
	Cell Cycle (R-HSA-1640170)	59/566	3,49E-02

Table 6b (continued)

	Pathway/term	**Overlap**	**Adjusted P-value**
miR-223-3p	Chk1/Chk2(Cds1) mediated inactivation of Cyclin B:Cdk1 complex (R-HSA-75035)	5/12	3,49E-02
	Centrosome maturation (R-HSA-380287)	14/79	3,51E-02
	Recruitment of mitotic centrosome proteins and complexes (R-HSA-380270)	14/79	3,51E-02
	Regulation of HSF1-mediated heat shock response (R-HSA-3371453)	14/80	3,85E-02
	Golgi-to-ER retrograde transport (R-HSA-8856688)	17/110	4,84E-02
miR-199b-3p	Potassium Channels (R-HSA-1296071)	13/99	9,59E-03
miR-142-5p	Cargo trafficking to the periciliary membrane (R-HSA-5620920)	5/51	2,78E-06
	Assembly of the primary cilium (R-HSA-5617833)	17/187	5,28E-05
	BBSome-mediated cargo-targeting to cilium (R-HSA-5620922)	7/23	5,28E-05
	Prefoldin mediated transfer of substrate to CCT/TriC (R-HSA-389957)	6/27	2,27E-03
	Organelle biogenesis and maintenance (R-HSA-1852241)	19/326	4,27E-03
	Cooperation of Prefoldin and TriC/CCT in actin and tubulin folding (R-HSA-389958)	6/32	4,27E-03
	Formation of tubulin folding intermediates by CCT/TriC (R-HSA-389960)	5/25	1,23E-02
	Detoxification of Reactive Oxygen Species (R-HSA-3299685)	5/33	4,21E-02
	Lysosome Vesicle Biogenesis (R-HSA-432720)	5/35	4,58E-02
	Transcriptional Regulation by TP53 (R-HSA-3700989)	17/348	4,58E-02

Supplementary Table 7. Gene ontology and pathway analyses using g:Profiler

Table 7a: Biological processes of positively and negatively correlated asthma genes per miRNA

	Pathway/term	Overlap	Adjusted P-value
miR-199b-5p	cilium organization (GO:0044782)	116/440	2,47E-42
	cilium assembly (GO:0060271)	108/418	2,83E-38
	cell projection assembly (GO:0030031)	115/630	2,42E-26
	plasma membrane bounded cell projection assembly (GO:0120031)	114/616	4,90E-26
	microtubule-based movement (GO:0007018)	81/385	2,23E-23
	organelle assembly (GO:0070925)	136/921	3,91E-22
	intraciliary transport (GO:0042073)	28/53	1,17E-18
	microtubule-based process (GO:0007017)	132/927	1,91E-17
	microtubule-based transport (GO:0099111)	50/196	6,70E-16
	axoneme assembly (GO:0035082)	32/82	4,36E-15
	intraciliary transport involved in cilium assembly (GO:0035735)	21/40	2,14E-13
	cilium movement (GO:0003341)	42/172	7,25E-12
	cell projection organization (GO:0030030)	164/1636	1,71E-10
	microtubule bundle formation (GO:0001578)	32/113	1,76E-10
	plasma membrane bounded cell projection organization (GO:0120036)	159/1596	7,49E-10
	cilium or flagellum-dependent cell motility (GO:0001539)	32/133	9,76E-10
	cilium-dependent cell motility (GO:0060285)	32/133	9,76E-10
	protein localization to cilium (GO:0061512)	22/62	4,22E-09
	axonemal dynein complex assembly (GO:0070286)	17/39	8,55E-09
	leukocyte degranulation (GO:0043299)	19/538	1,20E-08
	extracellular transport (GO:0006858)	17/37	1,25E-08
	transport along microtubule (GO:0010970)	34/162	1,35E-08
	myeloid cell activation involved in immune response (GO:0002275)	19/552	1,87E-08
	neutrophil degranulation (GO:0043312)	18/483	1,95E-08
	myeloid leukocyte mediated immunity (GO:0002444)	19/558	2,26E-08
	neutrophil activation involved in immune response (GO:0002283)	18/488	2,32E-08
	epithelial cilium movement involved in extracellular fluid movement (GO:0003351)	16/34	3,36E-08
	neutrophil mediated immunity (GO:0002446)	18/500	3,46E-08
	neutrophil activation (GO:0042119)	18/502	3,70E-08
	granulocyte activation (GO:0036230)	18/509	4,65E-08
	cytoskeleton-dependent intracellular transport (GO:0030705)	37/200	8,15E-08
	myeloid leukocyte activation (GO:0002274)	19/671	5,30E-07
	leukocyte activation involved in immune response (GO:0002366)	19/726	1,85E-06
	cell activation involved in immune response (GO:0002263)	19/727	2,03E-06
	motile cilium assembly (GO:0044458)	16/47	4,16E-06
	microtubule cytoskeleton organization (GO:0000226)	80/663	5,66E-06
	determination of left/right symmetry (GO:0007368)	22/128	6,60E-06
	regulated exocytosis (GO:0045055)	19/790	8,00E-06

Table 7a (continued)

	Pathway/term	Overlap	Adjusted P-value
miR-199b-5p	exocytosis (GO:0006887)	20/906	1,24E-05
	determination of bilateral symmetry (GO:0009855)	22/136	2,12E-05
	specification of symmetry (GO:0009799)	22/137	2,44E-05
	ciliary basal body-plasma membrane docking (GO:0097711)	22/95	2,49E-05
	outer dynein arm assembly (GO:0036158)	10/22	3,94E-05
	cilium movement involved in cell motility (GO:0060294)	24/120	4,39E-05
	leukocyte mediated immunity (GO:0002443)	19/888	5,32E-05
	sperm motility (GO:0097722)	22/109	1,44E-04
	flagellated sperm motility (GO:0030317)	22/109	1,44E-04
	organelle localization by membrane tethering (GO:0140056)	29/174	3,25E-04
	vesicle-mediated transport (GO:0016192)	28/2193	9,58E-04
	membrane docking (GO:0022406)	29/183	9,80E-04
	non-motile cilium assembly (GO:1905515)	15/58	9,82E-04
	smoothened signaling pathway (GO:0007224)	25/141	1,17E-03
	secretion by cell (GO:0032940)	21/1351	1,91E-03
	protein-containing complex localization (GO:0031503)	37/289	2,11E-03
	immune effector process (GO:0002252)	19/1135	2,41E-03
	protein localization to ciliary membrane (GO:1903441)	6/12	3,00E-03
	export from cell (GO:0140352)	21/1413	3,95E-03
	secretion (GO:0046903)	21/1492	9,39E-03
	immune response (GO:0006955)	21/2544	9,74E-03
	left/right pattern formation (GO:0060972)	6/21	1,02E-02
	leukocyte activation (GO:0045321)	12/1341	2,08E-02
	cellular component assembly (GO:0022607)	229/3104	2,13E-02
	establishment of left/right asymmetry (GO:0061966)	3/3	2,23E-02
	inner dynein arm assembly (GO:0036159)	7/16	2,27E-02
	cerebrospinal fluid circulation (GO:0090660)	5/10	2,62E-02
	autocrine signaling (GO:0035425)	3/8	3,06E-02
	organelle organization (GO:0006996)	292/4136	3,08E-02
	cytoskeleton organization (GO:0007010)	122/1473	3,21E-02
	RNA localization to nucleus (GO:0090685)	7/19	4,31E-02
	telomerase RNA localization (GO:0090672)	7/19	4,31E-02
	telomerase RNA localization to Cajal body (GO:0090671)	7/19	4,31E-02
	RNA localization to Cajal body (GO:0090670)	7/19	4,31E-02
	neutrophil aggregation (GO:0070488)	2/2	4,93E-02
miR-223-3p	cilium organization (GO:0044782)	102/440	2,17E-24
	cilium assembly (GO:0060271)	95/418	7,55E-22
	organelle assembly (GO:0070925)	152/921	1,42E-20
	intraciliary transport (GO:0042073)	31/53	2,79E-19
	cell projection assembly (GO:0030031)	112/630	6,62E-17

Table 7a (continued)

	Pathway/term	Overlap	Adjusted P-value
miR-223-3p	intraciliary transport involved in cilium assembly (GO:0035735)	25/40	8,44E-17
	plasma membrane bounded cell projection assembly (GO:0120031)	110/616	1,04E-16
	microtubule-based transport (GO:0099111)	55/196	3,10E-16
	microtubule-based process (GO:0007017)	142/927	2,16E-15
	microtubule-based movement (GO:0007018)	77/385	5,69E-14
	cytoskeleton-dependent intracellular transport (GO:0030705)	52/200	1,15E-13
	transport along microtubule (GO:0010970)	45/162	1,03E-12
	cell projection organization (GO:0030030)	191/1636	1,32E-09
	plasma membrane bounded cell projection organization (GO:0120036)	187/1596	1,76E-09
	organelle organization (GO:0006996)	383/4136	7,65E-07
	cellular component assembly (GO:0022607)	301/3104	1,31E-06
	protein localization (GO:0008104)	144/2670	1,08E-05
	macromolecule localization (GO:0033036)	203/3148	1,12E-05
	neutrophil mediated immunity (GO:0002446)	48/500	2,13E-05
	cellular localization (GO:0051641)	281/3519	3,71E-05
	exocytosis (GO:0006887)	73/906	3,97E-05
	microtubule cytoskeleton organization (GO:0000226)	87/663	4,91E-05
	neutrophil degranulation (GO:0043312)	46/483	5,64E-05
	neutrophil activation (GO:0042119)	53/502	5,65E-05
	myeloid cell activation involved in immune response (GO:0002275)	50/552	6,91E-05
	extracellular vesicle biogenesis (GO:0140112)	9/23	7,67E-05
	neutrophil activation involved in immune response (GO:0002283)	46/488	7,71E-05
	leukocyte degranulation (GO:0043299)	49/538	8,05E-05
	granulocyte activation (GO:0036230)	53/509	8,99E-05
	myeloid leukocyte mediated immunity (GO:0002444)	50/558	9,76E-05
	cellular component biogenesis (GO:0044085)	312/3377	1,08E-04
	vesicle-mediated transport (GO:0016192)	142/2193	1,47E-04
	ciliary basal body-plasma membrane docking (GO:0097711)	22/95	1,76E-04
	secretion by cell (GO:0032940)	95/1351	2,08E-04
	membrane docking (GO:0022406)	32/183	2,78E-04
	organelle localization by membrane tethering (GO:0140056)	31/174	2,83E-04
	protein localization to cell periphery (GO:1990778)	24/339	3,33E-04
	regulation of protein localization to cell periphery (GO:1904375)	14/128	3,60E-04
	establishment of localization in cell (GO:0051649)	176/2778	3,61E-04
	cell redox homeostasis (GO:0045454)	6/43	3,70E-04
	exosomal secretion (GO:1990182)	8/20	3,80E-04
	organelle localization (GO:0051640)	73/657	3,88E-04
	export from cell (GO:0140352)	94/1413	4,51E-04
	extracellular exosome biogenesis (GO:0097734)	8/21	5,96E-04

Table 7a (continued)

	Pathway/term	Overlap	Adjusted P-value
miR-223-3p	protein-containing complex localization	42/289	8,69E-04
	protein localization to cilium	17/62	1,51E-03
	secretion	99/1492	1,67E-03
	regulation of exosomal secretion	7/17	1,88E-03
	regulation of protein localization to plasma membrane	12/107	2,19E-03
	regulation of organelle assembly	31/192	2,27E-03
	cellular protein catabolic process	38/822	2,93E-03
	establishment of protein localization	101/1866	3,41E-03
	regulation of protein localization to membrane	16/203	4,18E-03
	intracellular transport	148/1723	4,19E-03
	multivesicular body assembly	7/30	4,23E-03
	protein localization to plasma membrane	20/287	4,88E-03
	multivesicular body organization	7/31	5,37E-03
	transport	287/5214	7,89E-03
	axoneme assembly	19/82	8,05E-03
	cellular protein localization	119/1842	8,21E-03
	cytoskeleton organization	149/1473	8,71E-03
	protein localization to membrane	35/698	9,07E-03
	protein transport	114/1754	1,04E-02
	myeloid leukocyte activation	51/671	1,07E-02
	establishment of localization	293/5364	1,13E-02
	positive regulation of protein localization to cell periphery	9/71	1,15E-02
	cellular macromolecule localization	119/1856	1,18E-02
	regulated exocytosis	59/790	1,20E-02
	protein catabolic process	41/983	1,42E-02
	positive regulation of exosomal secretion	6/15	1,51E-02
	leukocyte activation involved in immune response	43/723	1,57E-02
	cell activation involved in immune response	43/727	1,80E-02
	maintenance of DNA repeat elements	4/6	2,02E-02
	positive regulation of ATPase activity	13/60	2,10E-02
	regulation of organelle organization	115/1228	2,74E-02
	localization within membrane	39/775	2,78E-02
	smoothened signaling pathway	25/141	2,84E-02
	positive regulation of viral release from host cell	5/15	3,14E-02
	cellular catabolic process	75/2381	3,46E-02
	chaperone-mediated protein complex assembly	6/23	3,57E-02
	positive regulation of telomerase RNA localization to Cajal body	7/15	3,76E-02
	positive regulation of protein localization to plasma membrane (GO:1903078)	8/64	4,41E-02
	protein localization to ciliary membrane (GO:1903441)	6/12	4,63E-02

Table 7a (continued)

	Pathway/term	Overlap	Adjusted P-value
miR-223-3p	post-Golgi vesicle-mediated transport (GO:0006892)	16/144	4,94E-02
	regulation of extracellular exosome assembly (GO:1903551)	4/6	4,99E-02
miR-199b-3p	anatomical structure morphogenesis (GO:0009653)	24/2816	7,00E-03
	cell development (GO:0048468)	22/2122	7,35E-03
	cell morphogenesis (GO:0000902)	25/1045	7,52E-03
	cell adhesion (GO:0007155)	33/1502	1,51E-02
	biological adhesion (GO:0022610)	33/1509	1,66E-02
	negative regulation of cell projection organization (GO:0031345)	8/192	2,85E-02
	negative regulation of neuron projection development (GO:0010977)	7/142	3,46E-02
miR-142-5p	exocytosis (GO:0006887)	43/906	4,96E-05
	myeloid cell activation involved in immune response (GO:0002275)	15/552	6,91E-05
	neutrophil degranulation (GO:0043312)	8/483	7,83E-05
	neutrophil activation involved in immune response (GO:0002283)	8/488	8,48E-05
	neutrophil mediated immunity (GO:0002446)	8/500	1,02E-04
	neutrophil activation (GO:0042119)	8/502	1,06E-04
	granulocyte activation (GO:0036230)	8/509	1,18E-04
	cell redox homeostasis (GO:0045454)	8/43	1,20E-04
	leukocyte degranulation (GO:0043299)	30/538	1,47E-04
	regulated exocytosis (GO:0045055)	9/790	2,16E-04
	myeloid leukocyte mediated immunity (GO:0002444)	8/558	2,39E-04
	leukocyte activation involved in immune response (GO:0002366)	16/723	3,85E-04
	cell activation involved in immune response (GO:0002263)	16/727	4,15E-04
	myeloid leukocyte activation (GO:0002274)	15/671	8,66E-04
	extracellular vesicle biogenesis (GO:0140112)	6/23	3,87E-03
	immune effector process (GO:0002252)	8/1135	4,11E-03
	secretion by cell (GO:0032940)	51/1351	7,14E-03
	leukocyte mediated immunity (GO:0002443)	8/888	8,05E-03
	secretion (GO:0046903)	57/1492	9,93E-03
	cellular defense response (GO:0006968)	5/53	9,93E-03
	export from cell (GO:0140352)	52/1413	1,50E-02
	regulation of immune system process (GO:0002682)	10/1734	1,79E-02
	vesicle-mediated transport (GO:0016192)	71/2193	2,91E-02
	cell activation (GO:0001775)	8/1507	3,42E-02
	exosomal secretion (GO:1990182)	5/20	3,69E-02
	regulation of antigen processing and presentation (GO:0002577)	3/21	3,74E-02
	immune system process (GO:0002376)	13/3438	3,84E-02
	extracellular exosome biogenesis (GO:00977340)	5/21	4,78E-02
miR-181b-5p	flavonoid metabolic process (GO:0009812)	4/17	4,84E-05
	xenobiotic metabolic process (GO:0006805)	6/116	1,04E-03
	cellular response to xenobiotic stimulus (GO:0071466)	6/121	1,34E-03

Table 7a (continued)

	Pathway/term	Overlap	Adjusted P-value
miR-181b-5p	flavonoid metabolic process (GO:0009812)	4/17	4,84E-05
	xenobiotic metabolic process (GO:0006805)	6/116	1,04E-03
	cellular response to xenobiotic stimulus (GO:0071466)	6/121	1,34E-03
	response to xenobiotic stimulus (GO:0009410)	9/129	1,42E-03
	flavonoid glucuronidation (GO:0052696)	2/9	4,98E-03
	primary alcohol catabolic process (GO:0034310)	3/16	5,13E-03
	xenobiotic glucuronidation (GO:0052697)	2/11	7,60E-03
	regulation of mitotic spindle assembly (GO:1901673)	6/19	1,54E-02
	secretion (GO:0046903)	89/1492	1,55E-02
	cellular glucuronidation (GO:0052695)	2/20	2,62E-02
	uronic acid metabolic process (GO:0006063)	2/25	4,14E-02
	glucuronate metabolic process (GO:0019585)	2/25	4,14E-02
miR-195-5p	negative regulation of cell projection organization (GO:0031345)	7/192	1,89E-02
	anatomical structure morphogenesis (GO:0009653)	35/2816	2,12E-02
	cell morphogenesis (GO:0000902)	19/1045	2,38E-02
	cell adhesion (GO:0007155)	32/1502	2,64E-02
	biological adhesion (GO:0022610)	32/1509	2,90E-02
	neuron projection development (GO:0031175)	13/1021	3,58E-02
	negative regulation of neuron projection development (GO:0010977)	6/142	3,78E-02
	homophilic cell adhesion via plasma membrane adhesion molecules (GO:0007156)	9/167	4,67E-02
miR-125b-5p	neuron projection development (GO:0031175)	11/1021	7,01E-03
	animal organ morphogenesis (GO:0009887)	10/1079	9,49E-03
	cell development (GO:0048468)	15/2122	1,27E-02
	neuron development (GO:0048666)	11/1159	2,37E-02
	anatomical structure morphogenesis (GO:0009653)	17/2816	2,97E-02
	oligodendrocyte progenitor proliferation (GO:0070444)	2/8	3,87E-02
	regulation of oligodendrocyte progenitor proliferation (GO:0070445)	2/8	3,87E-02

Table 7b: Reactome pathways of positevly and negatively correlated asthma genes per miRNA

	Pathway/term	Overlap	Adjusted P-value
miR-199b-5p	Cilium Assembly (R-HSA-5617833)	62/201	7,17E-15
	Intraflagellar transport (R-HSA-5620924)	27/54	5,60E-12
	Organelle biogenesis and maintenance (R-HSA-1852241)	67/293	4,95E-09
	Neutrophil degranulation (R-HSA-6798695)	17/476	8,21E-05
	Innate Immune System (R-HSA-168249)	19/1090	1,30E-03
	Cargo trafficking to the periciliary membrane (R-HSA-5620920)	16/51	3,91E-03
	BBSome-mediated cargo-targeting to cilium (R-HSA-5620922)	10/23	7,89E-03
	Anchoring of the basal body to the plasma membrane (R-HSA-5620912)	22/96	4,04E-02
	Immune System (R-HSA-168256)	25/2038	4,54E-02
miR-223-3p	Intraflagellar transport (R-HSA-5620924)	30/54	9,29E-13
	Cilium Assembly (R-HSA-5617833)	62/201	1,59E-12
	Organelle biogenesis and maintenance (R-HSA-1852241)	67/293	3,01E-06
	Cargo trafficking to the periciliary membrane (R-HSA-5620920)	13/51	8,23E-05
	BBSome-mediated cargo-targeting to cilium (R-HSA-5620922)	8/23	9,18E-04
	Prefoldin mediated transfer of substrate to CCT/TriC (R-HSA-389957)	9/28	8,30E-03
	Formation of tubulin folding intermediates by CCT/TriC (R-HSA-389960)	8/26	3,52E-02
	Cooperation of Prefoldin and TriC/CCT in actin and tubulin folding (R-HSA-389958)	9/33	3,58E-02
miR-199b-3p	Activated NTRK2 signals through PLCG1 (R-HSA-9026527)	3/4	2,55E-02
miR-142-5p	Cargo trafficking to the periciliary membrane (R-HSA-5620920)	11/51	5,87E-04
	Neutrophil degranulation (R-HSA-679869)	8/476	8,47E-04
	BBSome-mediated cargo-targeting to cilium (R-HSA-5620922)	7/23	4,57E-03
	Cilium Assembly (R-HSA-5617833)	19/201	4,34E-02
miR-181b-5p	Glucuronidation (R-HSA-156588)	2/25	2,79E-02