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*Review Article*

# The Role of Noncoding RNA in Airway Allergic Diseases through Regulation of T Cell Subsets

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Allergic rhinitis and asthma are common airway allergic diseases, the incidence of which has increased annually in recent years. The human body is frequently exposed to allergens and environmental irritants that trigger immune and inflammatory responses, resulting in altered gene expression. Mounting evidence suggested that epigenetic alterations were strongly associated with the progression and severity of allergic diseases. Noncoding RNAs (ncRNAs) are a class of transcribed RNA molecules that cannot be translated into polypeptides and consist of three major categories, microRNAs (miRNAs), long noncoding RNAs (lncRNAs), and circular RNAs (circRNAs). Previous studies showed that ncRNAs were involved in the physiopathological mechanisms of airway allergic diseases and contributed to their occurrence and development. This article reviews the current state of understanding of the role of noncoding RNAs in airway allergic diseases, highlights the limitations of recent studies, and outlines the prospects for further research to facilitate the clinical translation of noncoding RNAs as therapeutic targets and biomarkers.

## 1. Introduction

Airway allergic diseases, mainly asthma (AS) and allergic rhinitis (AR) are a group of chronic inflammatory diseases. Airway allergic diseases' main pathological features are the inflammatory response of the airway mucosa and airway tissue remodeling when individuals are exposed to airborne allergens, resulting in the involvement of multiple immune cells and the release of inflammatory mediators [1–3]. In recent years, the prevalence of allergic diseases has increased globally yearly, with the intensification of environmental pollution, which seriously adversely affects people's quality of life and learning [4, 5]. The occurrence of AS and AR results from a combination of factors, including individual differences, genetic inheritance, environmental exposure, and growth and development, all of which may be closely related to the onset of the disease. The key pathological features of both AS and AR, as heterogeneous chronic airway diseases, are recurrent inflammation, airway hyperresponsiveness, mucus hypersecretion, and reversible airway obstruction induced by the inflammatory cellular response [6–9].

Researchers agreed that abnormal activation and function of intrinsic immune cells and adaptive immune cells (T helper 2 (Th2) cells) play an extremely critical role in the pathogenesis of airway allergic diseases [10–12]. Prior publication suggested that Th2 cells in the airway epithelium could produce various type 2 cytokines (IL-4, IL-5, and IL-

13), which in turn promote eosinophil recruitment, while these cytokines play a key role in airway epithelial cell activation, chemoattraction of effector cells, regulation of airway smooth muscle, and remodeling of the epithelial matrix [13, 14]. In addition, the balance between Th17 cells and T regulatory cell (Tregs) cells is similarly thought to be associated with developing airway allergic diseases [15, 16]. Thus, tapping into the regulatory mechanisms of innate and adaptive immune cells from different perspectives is currently a hot spot and frontier in airway allergic disease research [17, 18] (Figure 1).

Th0 cell, T helper 0 cell; Th1 cell, T helper 1 cell; Th2 cell, T helper 2 cell; Treg cell, T regulatory cell; Th17 cell, T helper 17 cell; IL-4, Interleukin-4; IL-5, Interleukin-5; IL-13, Interleukin-13; IL-10, Interleukin-10; IL-12, Interleukin-12; IL-17A, Interleukin-17A; IFN-$\gamma$, Interferon-gamma; TGF-$\beta$, Transforming growth factor-beta.

In recent years, noncoding RNAs (ncRNAs), mainly miRNA, lncRNA, and circRNA, have been found to have a significant relationship with the occurrence and development of airway allergic diseases. [19, 20] Therefore, a deeper exploration of the role of ncRNAs in airway degeneration and related regulatory mechanisms is expected to provide new directions for the investigation of biomarkers for diagnosis, treatment, and prediction of disease prognosis. This review summarizes the role of ncRNAs in airway allergic diseases and investigates their regulatory mechanisms on T cells and their effects on downstream cytokines to better understand the pathogenesis of airway allergic diseases. (Figure 2).

ncRNA, noncoding RNA; miRNA, microRNA; lncRNA, long noncoding RNA; circRNA, circular RNA; Th1 cell, T helper 1 cell; Th2 cell, T helper 2 cell; Treg cell, T regulatory cell; Th17 cell, T helper 17 cell.

## 2. ncRNA and AS

*2.1. miRNA and AS.* Increasing attention has been paid to the linkage of epigenetic modifications in AS pathology and a series of results have been obtained. miRNAs, consisting of 22-24 single-stranded nucleotides, are an essential component of epigenetic regulation with crucial regulatory roles in immune cells [21, 22]. miRNA functions primarily as a repressor of gene expression at the posttranscriptional level by binding to complementary sequences in the target mRNA and without altering the genomic sequence [22–26]. Previous studies confirmed that miRNAs play an essential role in allergic diseases by influencing Th1/Th2 polarization and Tregs cell/Th17 cell imbalance, promoting epithelial chronic inflammation and tissue remodeling, and activating intrinsic immune cells [11, 27, 28]. Recently, researchers screened and validated various miRNAs that affected the development of AS by regulating immune cell function and promoting the release of inflammatory mediators [29–31]. Mattes et al. [32] reported that airway hyperactivity and inflammation might be reduced by inhibiting miR-126 expression, which could affect $CD4^+$ T cell differentiation towards Th2 and the release of inflammatory cytokines. As important inflammatory factors, interleukin-33 (IL-33) and IL-13 could activate Th2 cells, mast cells, dendritic cells, eosinophils, and basophils, which promote the development of AS disease [33, 34]. Thus, screening for miRNAs can bind to IL-33 or IL-13 mRNA, which inhibit the expression of IL-33 or IL-13, and further exploring the potential regulatory mechanisms would help alleviate the disease progression of AS. A recent study found that miR-200b and miR-200c were downregulated in alveolar lavage fluid-derived cells from AS patients and demonstrated their ability to bind to the 3′ nontranscribed region (UTR) of IL-33 mRNA and thus affect the expression level of IL-33 by in vitro and in vivo experiments [35]. In addition, the miRNA-let-7a family was shown to target the IL-13 mRNA, resulting in lower levels of IL-13 and alleviating airway inflammation [36]. Notably, matrix metallopeptidase-16 (MMP-16) can play an essential role in tissue remodeling and airway inflammation by activating proMMP-2 [37–40]. Lou et al. [41] showed that miR-192-5p plays an inhibitory role in airway remodeling and autophagy reduction in asthma patients by targeting MMP-16 and autophagy-related protein 7 (ATG7). In addition, phosphatase and tensin homolog (PTEN), and MAPK/STAT1 pathway are critical regulatory pathways in allergic diseases [42]. It was shown that overexpression of miR-19a in the airway enhanced Th2 cytokine production and reduced miR-19a levels in airway smooth muscle cells, which could promote airway remodeling by directly targeting PTEN and MAPK/STAT1 signaling pathways [43, 44]. Besides, a study by Zhang and colleagues [45] found that decreasing miR-221-3p expression in epithelial cells could reduce inflammation by upregulating anti-inflammatory chemokine ligand 17 (CXCL17), which in turn inhibited the expression of chemokine c-c motif ligand 24 (CCL24), CCL26 and osteochondral proteins because these cytokines act as a key role in the recruitment of eosinophils and macrophages to the airway [45–48]. Recently, there were also findings that miRNAs transported by extracellular vesicles of serum and immune cell origin could mediate intercellular communication and play a significant role in the development of AS by regulating immune cells [49–51]. Li et al. [52] found that macrophage-derived exosome transporting miR-21-5p could promote epithelial-mesenchymal transition of airway mucosal epithelial cells by targeting Smad7, consequently exacerbating airway inflammation and airway stenosis. In another study, researchers found that adipose mesenchymal stem cell-derived exosomal delivery miR-301a-3p targets the STAT3 pathway to regulate the involvement of airway smooth muscle cells in the disease development of AS. [53] Based on the above findings, miRNAs may be involved in the development and progression of AS by affecting intrinsic and adaptive immune functions and regulating the release of various inflammatory mediators and activating signaling pathways. These specific miRNAs may be used as therapeutic targets for AS. Additional miRNAs associated with AS are described in detail in Table 1.

*2.2. lncRNA and AS.* lncRNAs are composed of more than 200 nucleotides with tissue and cellular specificity, and their functions include epigenetic regulation and induction of

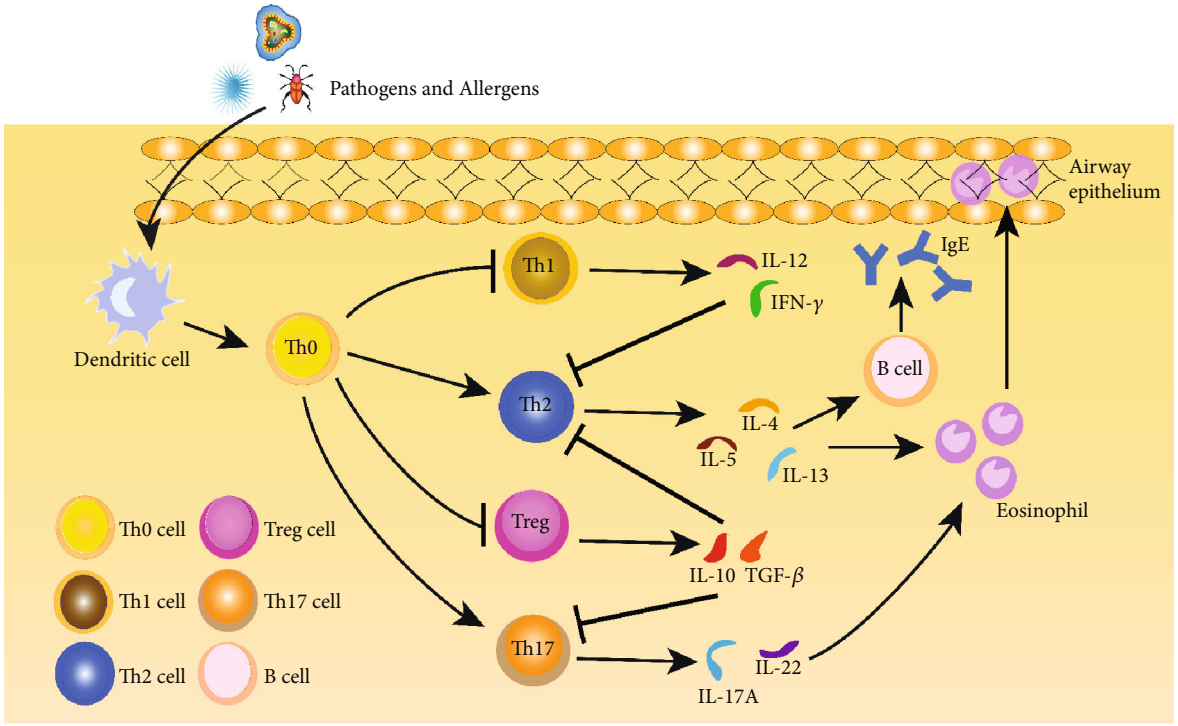


Figure 1: The interaction between innate and adaptive cells and type 2 inflammatory mediators underlies the pathophysiology of airway allergic disease. Disruption of the epithelium allows infiltration of viruses, bacteria, or allergens, activating innate and adaptive immune responses. Antigen presentation by dendritic cells activates the differentiation of naive T-helper cells (Th0 cell) to Th2 and Th17 cells and attenuates the differentiation to Th1 and Treg cells, immediately followed by the release of cytokines from Th2 and Th17 cells, leading to eosinophil recruitment, migration, and IgE production, and ultimately to the development of airway remodeling.

immune cell differentiation [22]. lncRNAs could facilitate or attenuate the translation of target mRNAs and even alter the stability of mRNAs and proteins through three main pathways: (1) acting as regulators of genomic transcription in the nucleus; (2) participating in posttranscriptional regulation in the cytoplasm; (3) secreting exosomes or other means to the outside of the cell and participating in cross-cellular talks [54–59]. lncRNAs were proven to play an integral role in the pathogenesis of AS by regulating the differentiation and apoptosis of hematopoietic stem cells, bone marrow cells, and the activation of monocytes, macrophages, and dendritic cells in immune regulation [60]. Previous studies demonstrated that lncRNAs could unlock the binding of miRNAs to the 3′ UTR of target genes by binding miRNAs as molecular sponges and then regulating the mRNA transcription of target genes in immune cells, ultimately affecting the release of inflammatory mediators and immune response [61]. Qiu et al. [62] found that lncRNA-MEG3 could act as competitive endogenous RNA to regulate the Tregs/Th17 balance in asthma patients by targeting miRNA-17, which could contribute to Th17 cell differentiation and affect disease progression. Additionally, Liang and Tang [63] found that lncRNA-MALAT1 could compete with miRNA-155 and subsequently alter the Th1/Th2 balance within $CD4^+$ T cells, impacting Th2 cytokine levels and the development of asthma. The nuclear factor-$\kappa$B (NF-$\kappa$B) signaling pathway, an essential signaling regulatory pathway, affects the transcription of proinflammatory cytokines such as interleukin-1$\beta$ (IL-1$\beta$), tumor necrosis factor-$\alpha$ (TNF-$\alpha$), and interleukin-6 (IL-6), all of which are closely associated with the development of AS [64, 65]. Moreover, increasing numbers of investigators are finding that multiple lncRNAs can be used as objective biomarkers for AS diagnosis, disease severity and prognosis assessment. Feng et al. [66] found that lncRNA-MEG3 was highly expressed in the serum of AS patients, and its elevated levels were correlated with the different inflammatory types and courses of AS. Xu et al. [67] found that lncRNA PCGEM1 could enhance the anti-inflammatory and respiratory protective effects of montelukast sodium in children with cough variant AS by blocking the activation of the NF-$\kappa$B signaling pathway. In another study, significant variability in lncRNA expression profiles was found, and lncPVT1 was tested as a predictor of the occurrence of airway remodeling in AS patients by collecting smooth muscle cells of airway origin from AS patients and normal controls for transcriptome sequencing [68]. A recent study found that the lncRNA-ANRIL/miR-125a axis was upregulated and positively correlated with disease severity in plasma samples collected from patients of varying severity, healthy subjects, and patients with worsening bronchial AS [69]. In another study, lncRNA GAS5 was identified as a potential biomarker for the early diagnosis of severe AS [70]. These studies suggested that lncRNAs were not only involved in the development of AS but that their expression levels could be closely related to the clinical severity of the disease. Importantly, exosome-carried lncRNAs have also

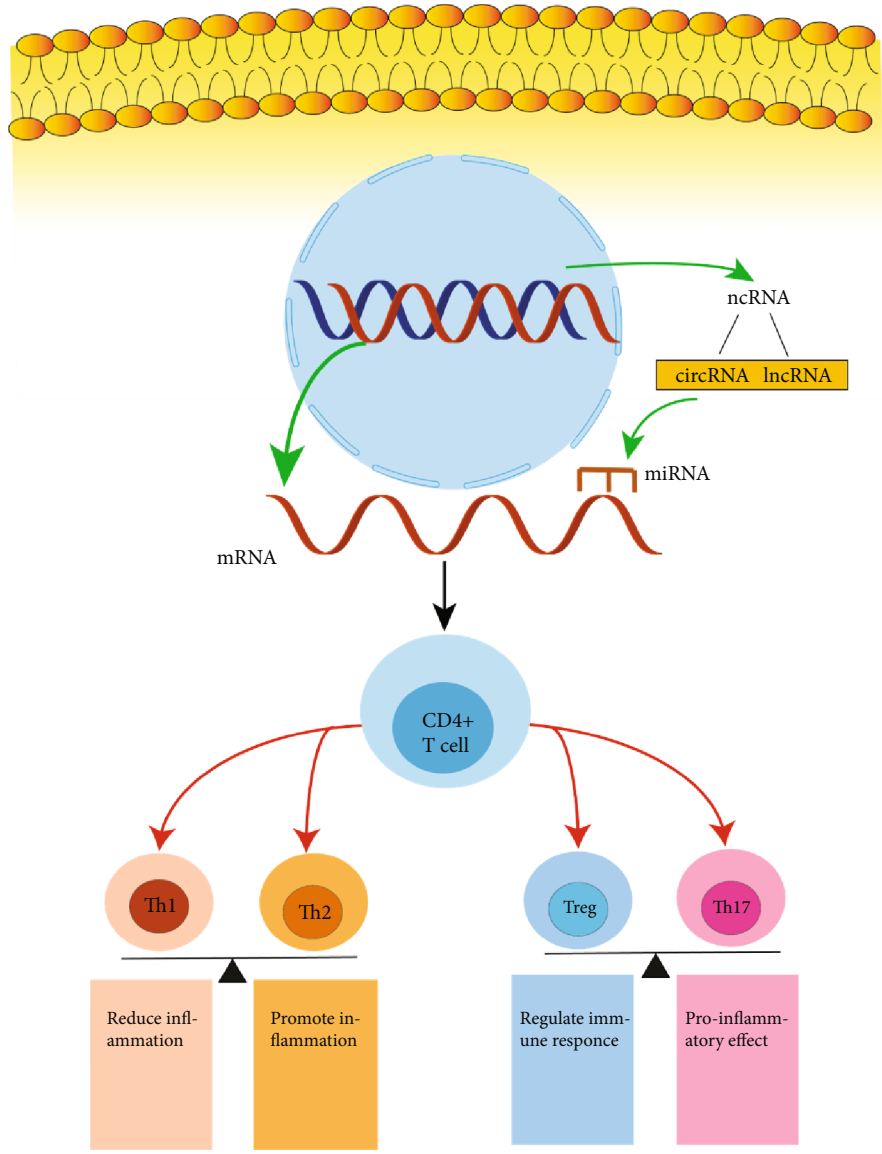


Figure 2: ncRNA regulates the mechanism of $CD4^+$ T cell differentiation. ncRNA affects miRNA level via molecular sponge action, which can influence $CD4^+$ T cell differentiation by binding to mRNA encoding $CD4^+$ T cell genes, resulting in an imbalance between Th1 and Th2, Th17 and Treg. Thereby, exacerbating or reducing airway remodeling, inflammatory mediators release, and inflammatory responses.

been shown to be involved in the development of AS [71, 72]. Zhang et al. [73] found that activated neutrophil-derived exosomes transporting the lncRNA CRNDE effectively promote differentiation and migration of airway smooth muscle cells, which were closely associated with disease progression and airway remodeling in AS. Other lncRNAs associated with AS disease are detailed in Table 1. Therefore, it is expected that new ideas for the precise treatment of AS can be provided by targeting and regulating specific lncRNAs and downstream signaling pathways, and the related molecular mechanisms are yet to be further explored in-depth.

*2.3. circRNA and AS.* CircRNA is a newly discovered endogenously expressed ncRNA characterized by a loop structure without $5'$-$3'$ polarity and a polyphyletic acid tail [74–76]. CircRNA has been shown to be involved in pathophysiological processes in various diseases, such as diabetes, cardiovascular diseases, neurological diseases, and tumors [77–81], and can similarly act as miRNA sponges to regulate gene expression [82, 83]. Several studies have found that circRNAs could be involved in developing AS by regulating innate and adaptive immune responses in recent years [22, 84]. A recent study found that hsa_circ_0005519 could regulate the expression of IL-6 and IL-13 in $CD4^+$ T cells by targeting hsa-let-7a-5p, which influenced the development of AS [82]. In another study, circHIPK3 was shown to influence the pathological process of AS by regulating the miR-326/STIM1 axis regulating the proliferation of airway smooth muscle cells [85]. In particular, circRNA levels were found to be a potential objective assessment marker for diagnosing AS and disease severity [86]. Huang et al. [86] found

Table 1: The expression and mechanisms of ncRNAs in asthma.

| ncRNA | Expression level | Signaling pathways or targets | Function |
|---|---|---|---|
| miRNA-1248 | Upregulation | Unknown | Elevate Th2 cytokine levels [87] |
| miRNA-126 | Upregulation | DNMT1 | Promote inflammation [88] |
| miRNA-21 | Upregulation | PI3K/Akt, IL13R$\alpha$1, STAT6 | Modulate ASMCs proliferation, migration, and modulate IL-12 [89, 90] |
| miRNA-21 | Upregulation | STAT4 | Decrease IL-12 levels [90] |
| miRNA-98 | Upregulation | Unknown | Suppress the expression of TSP1 [91] |
| miRNA-155 | Upregulation | PGE2 | Enhance COX2 expression [92] |
| miR-371 miR-138 miR-544 miR-145 miR-214 | Upregulation | Runx3 | Balance Th1/Th2 [93] |
| miRNA-16 | Upregulation | ADRB2 | Predictive biomarker of therapeutic response [94] |
| miRNA-146a-5p | Upregulation | 5-LO | Attenuate inflammation [95] |
| miRNA-30a | Upregulation | ATG5 | Decrease inflammation [96] |
| miRNA-126 | Downregulation | GATA3 | Diminish Th2 response [32] |
| miRNA-200 | Downregulation | Unknown | Inhibit IL-33 levels [35] |
| miRNA-let-7a | Upregulation | Unknown | Decrease IL-33 levels [36] |
| miR-192-5p | Upregulation | MMP-16, ATG7 | Enhance airway remodeling and autophagy [41] |
| miR-19a | Upregulation | PTEN, MAPK/STAT1 | Enhance airway remodeling and Th2 [43, 44] |
| miR-221-3p | Upregulation | CXCL17 | Aggravate inflammation [45] |
| miRNA-221 | Downregulation | Unknown | Reduce airway inflammation [97] |
| miR-142-3p | Downregulation | WNT | Regulate proliferation and differentiation of ASMCs [98] |
| miRNA-34a | Downregulation | FoxP3 | Attenuate inflammation [99] |
| miRNA-410 | Downregulation | Unknown | Decrease IL-4/IL13levels [100] |
| miR-218-5p | Downregulation | CTNND2 | Suppress chemokine expression [101] |
| miRNA-192 | Downregulation | CXCR5 | Suppresses T helper cell [102] |
| miRNA-485 | Downregulation | TGF-$\beta$/Smads | Decrease smurf2 levels [103] |
| miR-21-5p | Downregulation | Smad7 | Promote epithelial-mesenchymal transition [52] |
| miR-301a-3p | Downregulation | STAT3 | Activate smooth muscle cells [53] |
| lncRNA-MEG3 | Upregulation | miRNA-17/ ROR$\gamma$t | Regulate Treg/Th17 balance [62] |
| lncRNA-MALAT1 | Upregulation | miRNA-155 | Promote Th2 inflammation [63] |
| lncRNA PCGEM1 | Upregulation | NF-$\kappa$B | Ameliorate inflammation [67] |
| lncRNA CRNDE | Upregulation | Unknown | Enhance airway remodeling [73] |
| lncRNA-BAZ2B | Upregulation | Unknown | Promote M2 macrophage activation [104] |
| lncRNA-000127 | Upregulation | Unknown | Promote Th2 inflammation [105] |
| lncRNA-TCF7 | Upregulation | TIMMDC1/Akt | Promote the growth and migration of ASMCs [106] |
| lncRNA-PVT1 | Upregulation | miRNA-149, miR-15a-5p, miR-29c-3p | Exacerbate inflammation and impact Th1/Th2 imbalance [107, 108] |
| lncRNA-PVT1 | Upregulation | miR-590-5p/FSTL1 | Attenuate airway remodeling [68, 109] |
| lncRNA-ANRIL | Upregulation | miRNA-125a | Exacerbate severity and inflammation [69] |
| lncRNA-Malat1 | Upregulation | miR-150-eIF4E/Akt | Exacerbate inflammation [110] |
| lncRNA-NEAT1 | Upregulation | microRNA-124 | Increase inflammation [111] |
| lncRNA- n337374 | Upregulation | CD86 and ERK | Ameliorate inflammation [112] |
| lncRNA-BCYRN1 | Upregulation | Receptor potential 1 | Promote inflammation [113] |
| lncRNA-TUG1 | Upregulation | microRNA181b/HMGB1 | Promote inflammation [114, 115] |
| lncRNA- LASI | Upregulation | MUC5AC | Promote inflammation [115] |
| lncRNA-H19 | Downregulation | PI3K/Akt/NF-kB, miR21/PTEN/Akt | Attenuate inflammation [116, 117] |

Table 1: Continued.

| ncRNA | Expression level | Signaling pathways or targets | Function |
|---|---|---|---|
| lncRNA-AK169641 | Downregulation | Unknown | Increase eosinophils infiltration [118] |
| lncRNA-TUG1 | Downregulation | miR-29c/B7-H3 | Promote Th2 cell differentiation [20] |
| lncRNA-AK085-865 | Downregulation | Unknown | Ameliorate inflammation [119] |
| lncRNA-BCYRN1 | Downregulation | miRNA-150 | Inhibit the proliferation of ASMCs [113] |
| lncRNA-LINCPINT | Downregulation | miRNA-265p/PTEN | Retard the abnormal growth of ASMCs [120] |
| circRNA-0005519 | Upregulation | miRNA-7a-5p | Increase IL-6/IL-13levels [82] |
| circRNA-HIPK3 | Upregulation | miR-326/STIM1; miR-375/MMP-16 | Modulate the proliferation of AMSCs [85, 121] |
| circRNA-0002594 | Upregulation | Unknown | Upregulate in $CD4^+$ T cells [86] |
| CircRNA-ZNF652 | Upregulation | miR-452-5p/JAK2 | Promote the goblet cell metaplasia [122] |
| circRNA-ERBB2 | Downregulation | miR-98-5p/IGF1R | Increase infiltration [123] |

that upregulation of hsa_circ_0002594 was positively correlated with exhaled nitric oxide levels, and its expression was positively correlated with the patient's family history, positive skin prick test (SPT), and Th2 cytokine expression levels. To date, only a few circRNA mechanisms of action in AS have been initially explored (Table 1), and there are no studies on the expression profile and mechanisms of exosomal-derived circRNAs in pathological specimens from AS patients.

## 3. ncRNA and AR

*3.1. miRNA and AR.* Although some scholars have observed some similarities between AR and AS in terms of disease onset and immune response and proposed the concept of "one airway, one disease", significant differences still exist in the pathological mechanisms and targets of intervention between the two diseases. Moreover, differentially expressed miRNAs could be involved in the development of AR by affecting the function of innate and adaptive immune cells and the level of inflammatory mediators [124–126]. A previous study found that modulation of miRNA-let-7e and miR-let-7 overlap could effectively regulate the expression levels of various inflammatory factors in AR mouse models and nasal mucosal epithelial cell models [36, 127]. In addition, Gao and Yu [128] found that miRNA-16 inhibited IL-13-induced inflammatory cytokine secretion and mucus production in nasal epithelial cells by suppressing the I$\kappa$B kinase $\beta$/NF-$\kappa$B pathway, which could promote Th2 cell differentiation. Recent studies have identified multiple miRNAs that could be involved in PM2.5-induced AR inflammation by inhibiting autophagy and regulating the AKT/mTOR pathway, which could prompt Treg/Th17 cell imbalance [124, 125]. In addition, various miRNAs were confirmed to be correlated with the diagnosis, disease severity, and treatment efficacy of AR [129]. Previous studies reported that serum miRNA-223 levels in AR patients were higher than normal controls and positively correlated with serum eosinophil cationic protein, eosinophil count, and total nasal symptom score (TNSS), suggesting that miRNA-223 has been involved in AR eosinophilic inflammation and disease progression [130, 131]. Interestingly, miRNA expression profiles were associated with the efficacy of AR-specific immunotherapy, where patients received treatment with significant changes in multiple miRNA expression levels [132, 133]. Other miRNAs associated with AR disease are detailed in Table 2. In conclusion, miRNAs can be involved in AR pathogenesis by regulating immune cell activity and releasing inflammatory factors. Further exploration of their potential mechanisms could provide a theoretical basis for future precision treatment of AR.

*3.2. lncRNA and AR.* Many previous studies confirmed that lncRNAs have a variety of important biological activities, including DNA damage, programmed cell death, development, inflammation, tumorigenesis, and immune response [134, 135]. In recent years, researchers focused on the differential expression levels of lncRNAs in nasal mucosal tissues of AR patients and mouse models and their involvement in disease development by affecting different downstream signaling pathways [134, 136, 137]. Yue et al. [138] demonstrated that lncRNA00632 inhibited Th2 cell differentiation and IL-13 release by adsorbing miRNA-498, indicating a protective role of lnc00632 in AR. The JAK signaling pathway is a critical cytokine signaling pathway [139, 140]. In contrast, the Th2-associated cytokines IL-4, 5, and 13 are associated with activating the JAK2 and STAT6 signaling pathways, respectively [141, 142]. Liu et al. [143] identified lncANRIL as a potential new target for the treatment of AR by knocking down lncANRIL to modulate the miR-15a-5p/JAK2 signaling axis and consequently inhibit the secretion of IL-13. Moreover, the literature has reported that lncRNA expression profiles in immune cells of AR patients and animal models are equally cell-specific [144, 145]. Ma

Table 2: The expression and mechanisms of ncRNAs in AR.

| ncRNA | Expression level | Signaling pathways or target | Function |
|---|---|---|---|
| miRNA-223 | Upregulation | Unknown | Promote inflammation [130] |
| miRNA-155 | Upregulation | Unknown | Regulate Th2 factors [160] |
| miRNA-202-5P | Upregulation | MATN2 | Promote M2 polarization [161] |
| miRNA-202-5p | Upregulation | MATN2 | Promote Tregs polarization [162] |
| miRNA-17-5P | Upregulation | ABCA1/CD69 | Aggravate seasonal AR [163] |
| miRNA-375 | Upregulation | JAK2/STAT3 | Ameliorate AR [164] |
| miRNA-223-3p | Upregulation | INPP4A | Enhance eosinophil infiltration [165] |
| miRNA-let-7a | Upregulation | OPEN | Regulate Th2 cells [166] |
| miRNA-17-92 | Upregulation | Unknown | Exacerbate AR Inflammation [167] |
| miRNA-15a-5p | Downregulation | ADRB2 | Inhibit IL-13 levels [168] |
| miRNA-155 | Downregulation | SOCS1and SIRT1 | Promote Tregs differentiation [169] |
| miRNA-181a | Downregulation | PI3K/AKT | Upregulate IL-10 and TGF-$\beta$ [169] |
| miRNA-146a | Downregulation | TLR4/TRAF6/NF-$\kappa$B | Regulate Th2 cells [170] |
| miRNA-466a-3p | Downregulation | GATA3 | Attenuate inflammation [171] |
| miRNA-345-5p | Downregulation | TLR4/NF-$\kappa$B | Increase anti-inflammatory factors [172] |
| miRNA-29 | Downregulation | CD276 | Reduce IL-4, IL-6 level [173] |
| miRNA-133b | Downregulation | Nlrp3 | Ameliorate allergic inflammation [174] |
| miRNA-106b | Downregulation | Egr-2 | Regulate Th2 polarisation [175] |
| miRNA-143 | Downregulation | IL13Ra1 | Inhibit inflammation [176] |
| miRNA-30a-5p | Downregulation | SOCS3 | Involved in AR pathogenesis [177] |
| miRNA-135a | Downregulation | Unknown | Regulate Th1/Th2 imbalance [11] |
| miRNA-let-7e | Downregulation | SOCS4 | Anti-inflammatory [127, 128] |
| miRNA-16 | Downregulation | I$\kappa$B kinase $\beta$/NF-$\kappa$B | Inhibit IL-13 secretion [128] |
| miRNA-487b | Downregulation | IL-33/ST2 | Inhibit IL-13 secretion [178] |
| lncRNA SNHG16 | Upregulation | miR-106b-5p/JAK1/STAT3 | Promote inflammation [179] |
| lncRNAGABPA-9 : 1, NR103763, CCL21, APOA2, RAD9B-1 : 4 | Upregulation | Unknown | Involved in AR pathogenesis [134] |
| lncRNA-ANRIL | Upregulation | miR-15a-5p/JAK2 | Suppress inflammation [143] |
| lncRNA-NEAT1 | Upregulation | miR-21, miR-125a | Affect allergy inflammation [180] |
| lncRNA-GAS-5 | Downregulation | EZH2 and T-bet | Promote Th2 differentiation [181] |
| lncRNA-GAS-5 | Downregulation | miR-21 and miR-140 | Affect Th1/Th2 imbalance [182] |
| lncRNAFOXD3-AS1 | Downregulation | Unknown | Inhibit Th2 immunoreaction [183] |
| LncRNATCONS_00147848 | Downregulation | JAK/STAT3 | Reduce inflammatory response [184] |
| lncRNA-000632 | Downregulation | miRNA-498 | Inhibit IL-13[143] |
| circRNA-HIPK3 | Upregulation | miRNA-495 | Promote Th2 differentiation [158] |
| circRNA-ARRDC3 | Downregulation | miR-375/KLF4 | Promote inflammatory [185] |
| circRNA-0000520 | Downregulation | miR-556-5p/NLRP3 | Attenuate inflammatory [186] |

et al. [146] found that the expression profiles of lncRNAs were significantly cell-specific and involved multiple signaling pathways associated with AR disease development by comparing the expression profiles of lncRNAs in $CD4^+$ T cells from AR mouse models and control mice by sequencing. In parallel, some lncRNAs have been proven to be potential biomarkers for assessing AR severity and prognosis. In a recent study, histopathological specimens revealed that lncRNA-NEAT1 expression was significantly upregulated in the nasal mucosa of AR patients and positively correlated with disease symptom scores and inflammatory cytokine levels, suggesting that it could be used as a biomarker to assess the severity of AR disease [140]. Moreover, a recent study found that circulating-derived lncRNAs also

play an essential role in the pathogenesis of AR [147–149]. Wang et al. [148] found that the exosome-derived lncRNA NEAT1 regulates the microRNA-511/NR4A2 signaling axis and then participates in the disease development of AR. The above studies suggested that both nasal mucosal and circulating sources of lncRNAs could be involved in developing AR disease through different pathways. The potential regulatory mechanisms need to be explored in further studies. Additional lncRNAs associated with AR disease are detailed in Table 2.

*3.3. circRNA and AR.* circRNA, an emerging endogenous ncRNA, also plays a critical role in the immune and inflammatory responses [150, 151]. Chen et al. [152] identified circRNA expression profiles in the nasal mucosa of AR mice using RNA sequencing and found 51 circRNAs upregulated and 35 circRNAs downregulated, with some circRNAs involved in activating T and B cells. In another study, investigators analyzed circRNAs in the nasal mucosa of AR patients and controls using high-throughput sequencing. They explored the possible role and mechanism of the circRNA-miRNA-mRNA interaction network in AR pathology by bioinformatic analysis [153]. A previous study confirmed that GATA3 plays a crucial role in developing Th2 cells and two innate lymphocytes [154], whose signaling is a key process inducing Th2 cell development [155, 156]. GATA3 could induce chromatin remodeling at Th2-related loci and enhance Th2 cytokine production [157]. A new study revealed that circHIPK3 was highly expressed in the nasal mucosa of AR mice, and it acted as a sponge for miR-495 and deregulated the transcriptional repression of GATA3, promoting $CD4^+$ T cells to Th2 and secreting cytokines that exacerbate d ovalbumin-induced nasal symptoms [158]. Investigators identified an essential regulatory role for circARRDC3/miR-375/KLF4z in developing IL-13-induced inflammation in nasal mucosal epithelial cells by accelerating Th2 differentiation [159]. Currently, studies on the role and mechanism of circRNA in AR are less circRNA expression in AR nasal mucosa and peripheral blood. The related mechanism of action remains to be further explored.

## 4. Conclusion and Perspective

As the most common airway allergic diseases, AS and AR seriously affect patients' quality of life and impose a substantial economic burden on society. Therefore, it is of great clinical value to explore their pathogenesis and treatment precisely. In recent years, ncRNAs have been used as a new biomarker for disease treatment research, especially lncRNAs and circRNAs are the current hot spots in epigenetic research. However, circRNAs have been relatively poorly explored in AS and AR. In this review, most miRNAs, lncRNAs, and circRNAs currently have essential roles in developing AS and AR from three initial aspects, respectively. miRNAs can participate in the pathogenesis of AS and AR by targeting target genes to inhibit their expression in innate and adaptive immune cells. At the same time, lncRNAs and circRNAs are mainly involved in the development and progression of AS and AR by binding to the corresponding miRNAs through the ceRNA mechanism to relieve the inhibitory effect of the latter on target genes and regulate immune cells through downstream signaling pathways. The role of circulating ncRNAs, especially exosomal-transported ncRNAs, is gradually coming into the view of researchers in AS and AR, and whether they can be used as objective biomarkers for diagnosis, disease symptom assessment, and prognosis prediction is still under investigation. Follow-up studies should explore the role and mechanism of ncRNAs in the development and progression of AS and AR from multiple perspectives to provide new ideas for future diagnosis, treatment, and prognosis of the diseases.

## Conflicts of Interest

The authors have declared that there is no competing interest in this study.

## Authors' Contributions

Shenghao Cheng and Qingping Tang wrote and revised the manuscript. Shaobing Xie, Sihui Wen, and Hua Zhang draw the figures. Zhihai Xie and Weihong Jiang designed the study and reviewed the manuscript.

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## References

[1] Y. Li, W. Wang, and S. Ying, "Factors affecting the migration of ILC2s in allergic disease," *Cellular & Molecular Immunology*, vol. 18, no. 8, pp. 2069-2070, 2021.

[2] N. Oikonomou, M. J. Schuijs, A. Chatzigiagkos et al., "Airway epithelial cell necroptosis contributes to asthma exacerbation in a mouse model of house dust mite-induced allergic inflammation," *Mucosal Immunology*, vol. 14, no. 5, pp. 1160–1171, 2021.

[3] M. J. Sun, Z. Teng, P. S. Fan, X. G. Chen, and Y. Liu, "Bridging micro/nano-platform and airway allergy intervention," *Journal of Controlled Release*, vol. 341, pp. 364–382, 2022.

[4] J. Bousquet, J. M. Anto, C. Bachert et al., "Allergic rhinitis," *Nature Reviews Disease Primers*, vol. 6, no. 1, p. 95, 2020.

[5] R. García-Almaraz, N. Reyes-Noriega, B. E. del-Río-Navarro et al., "Prevalence and risk factors associated with allergic rhinitis in Mexican school children: global asthma network phase I," *World Allergy Organization Journal*, vol. 14, no. 1, article 100492, 2021.

[6] J. Weidner, S. Bartel, A. Kılıç et al., "Spotlight on microRNAs in allergy and asthma," *Allergy*, vol. 76, no. 6, pp. 1661–1678, 2021.

[7] L. R. Stolzenburg and A. Harris, "The role of microRNAs in chronic respiratory disease: recent insights," *Biological Chemistry*, vol. 399, no. 3, pp. 219–234, 2018.

[8] A. Gajewski, R. Szewczyk, M. L. Kowalski, M. Chalubinski et al., "The effect of human microbiome on the regulation of T2-type immune response in relation to the development of allergies and asthma," *Alergia Astma Immunologia*, vol. 25, no. 2, pp. 55–58, 2020.

[9] D. T. Umetsu and R. H. DeKruyff, "The regulation of allergy and asthma," *Immunological Reviews*, vol. 212, pp. 238–255, 2006.

[10] J. L. Ingram and M. Kraft, "IL-13 in asthma and allergic disease: asthma phenotypes and targeted therapies," *Journal of Allergy and Clinical Immunology*, vol. 130, no. 4, pp. 829–842, 2012.

[11] Y. Luo, Y. Deng, Z. Tao et al., "Regulatory effect of microRNA-135a on the Th1/Th2 imbalance in a murine model of allergic rhinitis," *Experimental and Therapeutic Medicine*, vol. 8, no. 4, pp. 1105–1110, 2014.

[12] N. Garg and J. I. Silverberg, "Association between childhood allergic disease, psychological comorbidity, and injury requiring medical attention," *Annals of Allergy Asthma & Immunology*, vol. 112, no. 6, pp. 525–532, 2014.

[13] D. Robinson, M. Humbert, R. Buhl et al., "Revisiting type 2-high and type 2-low airway inflammation in asthma: current knowledge and therapeutic implications," *Clinical and Experimental Allergy*, vol. 47, no. 2, pp. 161–175, 2017.

[14] W. W. Busse, M. Kraft, K. F. Rabe et al., "Understanding the key issues in the treatment of uncontrolled persistent asthma with type 2 inflammation," *European Respiratory Journal*, vol. 58, no. 2, article 2003393, 2021.

[15] M. A. Hofmann, J. W. Fluhr, C. Ruwwe-Glösenkamp, K. Stevanovic, K. C. Bergmann, and T. Zuberbier, "Role of IL-17 in atopy-a systematic review," *Clinical and Translational Allergy*, vol. 11, no. 6, article e12047, 2021.

[16] J. H. Kappen, S. R. Durham, H. I. '. Veen, and M. H. Shamji, "Applications and mechanisms of immunotherapy in allergic rhinitis and asthma," *Therapeutic Advances in Respiratory Disease*, vol. 11, no. 1, pp. 73–86, 2017.

[17] X. Hou, H. Wan, X. Ai et al., "Histone deacetylase inhibitor regulates the balance of Th17/Treg in allergic asthma," *The Clinical Respiratory Journal*, vol. 10, no. 3, pp. 371–379, 2016.

[18] P. Um-Bergström, M. Pourbazargan, B. Brundin et al., "Increased cytotoxic T-cells in the airways of adults with former bronchopulmonary dysplasia," *The European Respiratory Journal*, vol. 60, no. article 2102531, 2022.

[19] M. P. Roffel, I. M. Boudewijn, J. L. van Nijnatten et al., "Identification of asthma associated microRNAs in bronchial biopsies," *The European Respiratory Journal*, vol. 59, no. 3, 2021.

[20] H. Sun, T. Wang, W. Zhang et al., "LncRNATUG1 facilitates Th2 cell differentiation by targeting the miR-29c/B7-H3 axis on macrophages," *Frontiers in Immunology*, vol. 12, article 631450, 2021.

[21] Y. Yang, W. Yujiao, W. Fang et al., "The roles of miRNA, lncRNA and circRNA in the development of osteoporosis," *Biological Research*, vol. 53, no. 1, p. 40, 2020.

[22] S. Ghafouri-Fard, H. Shoorei, M. Taheri, and M. Sanak, "Emerging role of non-coding RNAs in allergic disorders," *Biomedicine & Pharmacotherapy*, vol. 130, article 110615, 2020.

[23] H. Ding, Y. L. Wu, Y. X. Wang, and F. F. Zhu, "Characterization of the microRNA expression profile of cervical squamous cell carcinoma metastases," *Asian Pacific Journal of Cancer Prevention*, vol. 15, no. 4, pp. 1675–1679, 2014.

[24] H. Guo, N. T. Ingolia, J. S. Weissman, and D. P. Bartel, "Mammalian microRNAs predominantly act to decrease target mRNA levels," *Nature*, vol. 466, no. 7308, pp. 835–840, 2010.

[25] M. Losko, J. Kotlinowski, and J. Jura, "Long noncoding RNAs in metabolic syndrome related disorders," *Mediators of Inflammation*, vol. 2016, Article ID 5365209, 12 pages, 2016.

[26] J. A. Vidigal and A. Ventura, "The biological functions of miRNAs: lessons from in vivo studies," *Trends in Cell Biology*, vol. 25, no. 3, pp. 137–147, 2015.

[27] J. A. Cañas, J. M. Rodrigo-Muñoz, B. Sastre, M. Gil-Martinez, N. Redondo, and V. Del Pozo, "MicroRNAs as potential regulators of immune response networks in asthma and chronic obstructive pulmonary disease," *Frontiers in Immunology*, vol. 11, 2021.

[28] X. Y. Jiang, "The emerging role of microRNAs in asthma," *Molecular and Cellular Biochemistry*, vol. 353, no. 1-2, pp. 35–40, 2011.

[29] Y. Guo, X. Yuan, L. Hong et al., "Promotor hypomethylation mediated upregulation of miR-23b-3p targets PTEN to promote bronchial epithelial-mesenchymal transition in chronic asthma," *Frontiers in Immunology*, vol. 12, article 771216, 2022.

[30] Y. Guan, Y. Ma, Y. Tang, X. Liu, Y. Zhao, and L. An, "MiRNA-221-5p suppressed the Th17/Treg ratio in asthma via RORγt/Foxp3 by targeting SOCS1," *Allergy, Asthma and Clinical Immunology*, vol. 17, no. 1, p. 123, 2021.

[31] A. Wardzyńska, M. Pawełczyk, J. Rywaniak et al., "MicroRNA expression profile in peripheral blood mononuclear cells of asthmatic patients and healthy individuals: the effect of age and ex vivo rhinovirus exposure," *Clinical and Experimental Allergy*, vol. 52, no. 3, pp. 461–464, 2022.

[32] J. Mattes, A. Collison, M. Plank, S. Phipps, and P. S. Foster, "Antagonism of microRNA-126 suppresses the effector function of TH2 cells and the development of allergic airways disease," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 106, no. 44, pp. 18704–18709, 2009.

[33] K. Shinoda, A. Choe, K. Hirahara et al., "Nematode ascarosides attenuate mammalian type 2 inflammatory responses," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 119, no. 9, 2022.

[34] G. Zhu, H. Cai, L. Ye et al., "Small proline-rich protein 3 regulates IL-33/ILC2 axis to promote allergic airway inflammation," *Frontiers in Immunology*, vol. 12, article 758829, 2022.

[35] X. Tang, F. Wu, J. Fan, Y. Jin, J. Wang, and G. Yang, "Post-transcriptional regulation of interleukin-33 expression by microRNA-200 in bronchial asthma," *Molecular Therapy*, vol. 26, no. 7, pp. 1808–1817, 2018.

[36] M. Kumar, T. Ahmad, A. Sharma et al., "Let-7 microRNA-mediated regulation of IL-13 and allergic airway inflammation," *Journal of Allergy and Clinical Immunology*, vol. 128, no. 5, pp. 1077–1085, 2011.

[37] W. L. Zhang, Y. F. Chen, H. Z. Meng et al., "Role of miR-155 in the regulation of MMP-16 expression in intervertebral disc degeneration," *Journal of Orthopaedic Research*, vol. 35, no. 6, pp. 1323–1334, 2017.

[38] Y. Kuwabara, T. Kobayashi, C. N. D'Alessandro-Gabazza et al., "Role of matrix metalloproteinase-2 in eosinophil-mediated airway remodeling," *Frontiers in Immunology*, vol. 9, 2018.

[39] H. M. Yin, S. Zhang, Y. Sun et al., "MicroRNA-34/449 targets IGFBP-3 and attenuates airway remodeling by suppressing Nur77-mediated autophagy," *Cell Death & Disease*, vol. 8, no. 8, article e2998, 2017.

[40] J. Lee and H. S. Kim, "The role of autophagy in eosinophilic airway inflammation. immune," *Network*, vol. 19, no. 1, 2019.

[41] L. Lou, M. Tian, J. Chang, F. Li, and G. Zhang, "MiRNA-192-5p attenuates airway remodeling and autophagy in asthma by targeting MMP-16 and ATG7," *Biomedicine & Pharmacotherapy*, vol. 122, 2020.

[42] Q. Z. Sun, L. Liu, J. Mandal et al., "PDGF-BB induces PRMT1 expression through ERK1/2 dependent STAT1 activation and regulates remodeling in primary human lung fibroblasts," *Cellular Signalling*, vol. 89, article 110114, 2022.

[43] Q. Z. Sun, L. Liu, H. Wang et al., "Constitutive high expression of protein arginine methyltransferase 1 in asthmatic airway smooth muscle cells is caused by reduced microRNA-19a expression and leads to enhanced remodeling," *Journal of Allergy and Clinical Immunology*, vol. 140, no. 2, pp. 510–524.e3, 2017.

[44] L. J. Simpson, S. Patel, N. R. Bhakta et al., "A microRNA upregulated in asthma airway T cells promotes $T_H2$ cytokine production," *Nature Immunology*, vol. 15, no. 12, pp. 1162–1170, 2014.

[45] K. Zhang, Y. Liang, Y. Feng et al., "Decreased epithelial and sputum miR-221-3p associates with airway eosinophilic inflammation and CXCL17 expression in asthma," *American Journal of Physiology-Lung Cellular and Molecular Physiology*, vol. 315, no. 2, pp. L253–L264, 2018.

[46] W. Y. Lee, C. J. Wang, T. Y. Lin, C. L. Hsiao, and C. W. Luo, "CXCL17, an orphan chemokine, acts as a novel angiogenic and anti-inflammatory factor," *American Journal of Physiology-Endocrinology and Metabolism*, vol. 304, no. 1, pp. E32–E40, 2013.

[47] A. M. Burkhardt, K. P. Tai, J. P. Flores-Guiterrez et al., "CXCL17 is a mucosal chemokine elevated in idiopathic pulmonary fibrosis that exhibits broad antimicrobial activity," *Journal of Immunology*, vol. 188, no. 12, pp. 6399–6406, 2012.

[48] M. T. Pisabarro, B. Leung, M. Kwong et al., "Cutting edge: novel human dendritic cell- and monocyte-attracting chemokine-like protein identified by fold recognition methods," *Journal of Immunology*, vol. 176, no. 4, pp. 2069–2073, 2006.

[49] Y. Yang, L. Yuan, X. Du et al., "Involvement of epithelia-derived exosomes in chronic respiratory diseases," *Biomedicine & Pharmacotherapy*, vol. 143, article 112189, 2021.

[50] W. Pei, X. Li, R. Bi et al., "Exosome membrane-modified M2 macrophages targeted nanomedicine: treatment for allergic asthma," *Journal of Controlled Release*, vol. 338, pp. 253–267, 2021.

[51] Y. Yu, Y. Zhou, C. di et al., "Increased airway epithelial cell-derived exosomes activate macrophage-mediated allergic inflammation via CD100 shedding," *Journal of Cellular and Molecular Medicine*, vol. 25, no. 18, pp. 8850–8862, 2021.

[52] X. Li, N. Yang, Q. Cheng, H. Zhang, F. Liu, and Y. Shang, "MiR-21-5p in macrophage-derived exosomes targets Smad7 to promote epithelial-mesenchymal transition of airway epithelial cells," *Journal of Asthma and Allergy*, vol. 14, pp. 513–524, 2021.

[53] C. Y. Feng, S. Y. Bai, M. L. Li et al., "Adipose-derived mesenchymal stem cell-derived exosomal miR-301a-3p regulates airway smooth muscle cells during asthma by targeting STAT3," *Journal of Asthma and Allergy*, vol. 15, pp. 99–110, 2022.

[54] C. R. Lin and L. Q. Yang, "Long noncoding RNA in cancer: wiring signaling circuitry," *Trends in Cell Biology*, vol. 28, no. 4, pp. 287–301, 2018.

[55] J. Beermann, M. T. Piccoli, J. Viereck, and T. Thum, "Non-coding RNAs in development and disease: background, mechanisms, and therapeutic approaches," *Physiological Reviews*, vol. 96, no. 4, pp. 1297–1325, 2016.

[56] T. Qin, J. Li, and K. Q. Zhang, "Structure, regulation, and function of linear and circular long non-coding RNAs," *Frontiers in Genetics*, vol. 11, 2020.

[57] S. Geisler and J. Coller, "RNA in unexpected places: long non-coding RNA functions in diverse cellular contexts," *Nature Reviews Molecular Cell Biology*, vol. 14, no. 11, pp. 699–712, 2013.

[58] J. H. Yoon, K. Abdelmohsen, S. Srikantan et al., "LincRNA-p21 suppresses target mRNA translation," *Molecular Cell*, vol. 50, no. 2, pp. 303–303, 2013.

[59] C. G. Gong and L. E. Maquat, "lncRNAs transactivate STAU1-mediated mRNA decay by duplexing with 3 ' UTRs via Alu elements," *Nature*, vol. 470, no. 7333, pp. 284–288, 2011.

[60] M. R. Hadjicharalambous and M. A. Lindsay, "Long non-coding RNAs and the innate immune response," *Non-Coding RNA*, vol. 5, no. 2, 2019.

[61] X. Y. Zhang, X. Y. Tang, N. Li et al., "GAS5 promotes airway smooth muscle cell proliferation in asthma via controlling miR-10a/BDNF signaling pathway," *Life Sciences*, vol. 212, pp. 93–101, 2018.

[62] Y. Y. Qiu, Y. Wu, M. J. Lin, T. Bian, Y. L. Xiao, and C. Qin, "LncRNA-MEG3 functions as a competing endogenous RNA to regulate Treg/Th17 balance in patients with asthma by targeting microRNA-17/ RORγt," *Biomedicine & Pharmacotherapy*, vol. 111, pp. 386–394, 2019.

[63] Z. J. Liang and F. L. Tang, "The potency of lncRNA MALAT1/miR-155/CTLA4 axis in altering Th1/Th2 balance of asthma," *Bioscience Reports*, vol. 40, 2020.

[64] T. H. Mogensen, "Pathogen recognition and inflammatory signaling in innate immune defenses," *Clinical Microbiology Reviews*, vol. 22, no. 2, 2009.

[65] S. Roy, K. Manna, T. Jha, and K. D. Saha, "Chrysin-loaded PLGA attenuates OVA-induced allergic asthma by modulating TLR/NF-κB/NLRP3 axis," *Nanomedicine-Nanotechnology Biology and Medicine*, vol. 30, p. 102292, 2020.

[66] Y. Feng, C. Yang, and W. Yan, "Expression of lncRNA MEG3 in asthma with different phenotypes and its relationship with course of disease," *Experimental and Therapeutic Medicine*, vol. 19, no. 3, pp. 2211–2217, 2020.

[67] Z. X. Xu, L. Meng, and Y. Xie, "lncRNA PCGEM1 strengthens anti-inflammatory and lung protective effects of montelukast sodium in children with cough-variant asthma," *Brazilian Journal of Medical and Biological Research*, vol. 53, no. 7, article e9271, 2020.

[68] P. J. Austin, E. Tsitsiou, C. Boardman et al., "Transcriptional profiling identifies the long non-coding RNA plasmacytoma variant translocation (PVT1) as a novel regulator of the asthmatic phenotype in human airway smooth muscle," *Journal of Allergy and Clinical Immunology*, vol. 139, no. 3, pp. 780–789, 2017.

[69] S. L. Ye, S. Zhu, and L. J. Feng, "LncRNA ANRIL/miR-125a axis exhibits potential as a biomarker for disease exacerbation, severity, and inflammation in bronchial asthma," *Journal of Clinical Laboratory Analysis*, vol. 34, no. 3, 2020.

[70] D. Wu, B. Gu, Y. Qian et al., "Long non-coding RNA growth arrest specific-5: a potential biomarker for early diagnosis of severe asthma," *Journal of Thoracic Disease*, vol. 12, no. 5, pp. 1960–1971, 2020.

[71] C. Poulet, M. S. Njock, C. Moermans et al., "Exosomal long non-coding RNAs in lung diseases," *International Journal of Molecular Sciences*, vol. 21, no. 10, 2020.

[72] Y. Li, Z. Yin, J. Fan, S. Zhang, and W. Yang, "The roles of exosomal miRNAs and lncRNAs in lung diseases," *Signal Transduction and Targeted Therapy*, vol. 4, p. 47, 2019.

[73] X. Y. Zhang, Z. C. Chen, N. Li et al., "Exosomal transfer of activated neutrophil-derived lncRNA CRNDE promotes proliferation and migration of airway smooth muscle cells in asthma," *Human Molecular Genetics*, vol. 31, no. 4, pp. 638–650, 2022.

[74] B. Chen and S. L. Huang, "Circular RNA: an emerging noncoding RNA as a regulator and biomarker in cancer," *Cancer Letters*, vol. 418, pp. 41–50, 2018.

[75] S. B. Qu, Z. Liu, X. Yang et al., "The emerging functions and roles of circular RNAs in cancer," *Cancer Letters*, vol. 414, pp. 301–309, 2018.

[76] T. B. Hansen, T. I. Jensen, B. H. Clausen et al., "Natural RNA circles function as efficient microRNA sponges," *Nature*, vol. 495, no. 7441, pp. 384–388, 2013.

[77] L. Kumar, Shamsuzzama, P. Jadiya, R. Haque, S. Shukla, and A. Nazir, "Functional characterization of novel circular RNA molecule, circzip-2 and its synthesizing gene zip-2 in C. elegans model of Parkinson's disease," *Molecular Neurobiology*, vol. 55, no. 8, pp. 6914–6926, 2018.

[78] G. Jiang, Y. Ma, T. An et al., "Relationships of circular RNA with diabetes and depression," *Scientific Reports*, vol. 7, 2017.

[79] Y. M. Wang, Y. Mo, Z. Gong et al., "Circular RNAs in human cancer," *Molecular Cancer*, vol. 16, no. 1, p. 25, 2017.

[80] S. L. Mehta, G. Pandi, and R. Vemuganti, "Circular RNA expression profiles alter significantly in mouse brain after transient focal ischemia," *Stroke*, vol. 48, no. 9, 2017.

[81] Z. Y. Zhong, M. Huang, M. Lv et al., "Circular RNA MYLK as a competing endogenous RNA promotes bladder cancer progression through modulating VEGFA/VEGFR2 signaling pathway," *Cancer Letters*, vol. 403, pp. 305–317, 2017.

[82] Z. Huang, Y. Cao, M. Zhou et al., "Hsa circ 0005519 increases IL-13/IL-6 by regulating hsa-let-7a-5p in CD4(+) T cells to affect asthma," *Clinical and Experimental Allergy*, vol. 49, no. 8, pp. 1116–1127, 2019.

[83] Y. X. Zhong, Y. du, X. Yang et al., "Circular RNAs function as ceRNAs to regulate and control human cancer progression," *Molecular Cancer*, vol. 17, no. 1, p. 79, 2018.

[84] D. Chen, W. Wu, L. Yi et al., "A potential circRNA-miRNA-mRNA regulatory network in asthmatic airway epithelial cells identified by integrated analysis of microarray datasets," *Frontiers in Molecular Biosciences*, vol. 8, article 703307, 2021.

[85] J. L. Lin, X. K. Feng, and J. Zhang, "Circular RNA circHIPK3 modulates the proliferation of airway smooth muscle cells by miR-326/STIM1 axis," *Life Sciences*, vol. 255, 2020.

[86] Z. Huang, B. Fu, X. Qi et al., "Diagnostic and therapeutic value of Hsa_circ_0002594 for T helper 2-mediated allergic asthma," *International Archives of Allergy and Immunology*, vol. 182, no. 5, pp. 388–398, 2021.

[87] R. P. L. Panganiban, M. H. Pinkerton, S. Y. Maru, S. J. Jefferson, A. N. Roff, and F. T. Ishmael, "Differential microRNA expression in asthma and the role of miR-1248 in regulation of IL-5," *American Journal of Clinical and Experimental Immunology*, vol. 1, no. 2, pp. 154–165, 2012.

[88] M. Zhao, Y. P. Li, X. R. Geng et al., "Expression level of MiRNA-126 in serum exosomes of allergic asthma patients and lung tissues of asthmatic mice," *Current Drug Metabolism*, vol. 20, no. 10, pp. 799–803, 2019.

[89] Y. Liu, K. Yang, H. Shi et al., "MiR-21 modulates human airway smooth muscle cell proliferation and migration in asthma through regulation of PTEN expression," *Experimental Lung Research*, vol. 41, no. 10, pp. 535–545, 2015.

[90] T. X. Lu, A. Munitz, and M. E. Rothenberg, "MicroRNA-21 is up-regulated in allergic airway inflammation and regulates IL-12p35 expression," *Journal of Immunology*, vol. 182, no. 8, pp. 4994–5002, 2009.

[91] L. Chen, J. Xu, X. Chu, and C. Ju, "MicroRNA-98 interferes with thrombospondin 1 expression in peripheral B cells of patients with asthma," *Bioscience Reports*, vol. 37, no. 4, 2017.

[92] B. S. Comer, B. Camoretti-Mercado, P. C. Kogut, A. J. Halayko, J. Solway, and W. T. Gerthoffer, "Cyclooxygenase-2 and microRNA-155 expression are elevated in asthmatic airway smooth muscle cells," *American Journal of Respiratory Cell and Molecular Biology*, vol. 52, no. 4, pp. 438–447, 2015.

[93] Y. Y. Qiu, Y. W. Zhang, X. F. Qian, and T. Bian, "miR-371, miR-138, miR-544, miR-145, and miR-214 could modulate Th1/Th2 balance in asthma through the combinatorial regulation of Runx3," *American Journal of Translational Research*, vol. 9, no. 7, pp. 3184–3199, 2017.

[94] B. Yu, L. Yao, C. Liu, L. Tang, and T. Xing, "Upregulation of microRNA16 alters the response to inhaled beta-agonists in patients with asthma through modulating expression of ADRB2," *Molecular Medicine Reports*, vol. 19, no. 5, pp. 4027–4034, 2019.

[95] D. Fussbroich, C. Kohnle, T. Schwenger et al., "A combination of LCPUFAs regulates the expression of miRNA-146a-5p in a murine asthma model and human alveolar cells," *Prostaglandins & Other Lipid Mediators*, vol. 147, article 106378, 2020.

[96] B. B. Li, Y. L. Chen, and F. Pang, "MicroRNA-30a targets ATG5 and attenuates airway fibrosis in asthma by suppressing autophagy," *Inflammation*, vol. 43, no. 1, pp. 44–53, 2020.

[97] H. B. Qin, B. Xu, J. J. Mei et al., "Inhibition of miRNA-221 suppresses the airway inflammation in asthma," *Inflammation*, vol. 35, no. 4, pp. 1595–1599, 2012.

[98] S. Bartel, G. Carraro, F. Alessandrini, S. Krauss-Etschmann, F. L. M. Ricciardolo, and S. Bellusci, "miR-142-3p is associated with aberrant WNT signaling during airway remodeling in asthma," *American Journal of Physiology-Lung Cellular and Molecular Physiology*, vol. 315, no. 2, pp. L328–L333, 2018.

[99] E. Alharris, H. Alghetaa, R. Seth et al., "Resveratrol attenuates allergic asthma and associated inflammation in the lungs through regulation of miRNA-34a that targets FoxP3 in mice," *Frontiers in Immunology*, vol. 9, 2018.

[100] R. Jin, S. Hu, X. Liu, R. Guan, L. Lu, and R. Lin, "Intranasal instillation of miR410 targeting IL4/IL13 attenuates airway

inflammation in OVA induced asthmatic mice," *Molecular Medicine Reports*, vol. 19, no. 2, pp. 895–900, 2019.

[101] Y. Liang, Y. Feng, W. Wu et al., "MicroRNA-218-5p plays a protective role in eosinophilic airway inflammation via targeting delta-catenin, a novel catenin in asthma," *Clinical and Experimental Allergy*, vol. 50, no. 1, pp. 29–40, 2020.

[102] D. Zhang, Y. Wu, and G. Sun, "miR-192 suppresses T follicular helper cell differentiation by targeting CXCR5 in childhood asthma," *Scandinavian Journal of Clinical and Laboratory Investigation*, vol. 78, no. 3, pp. 236–242, 2018.

[103] J. Wang, H. Y. Li, H. S. Wang, and Z. B. Su, "MicroRNA-485 modulates the TGF-/ Smads signaling pathway in chronic asthmatic mice by targeting Smurf2," *Cellular Physiology and Biochemistry*, vol. 51, no. 2, pp. 692–710, 2018.

[104] L. Xia, X. Wang, L. Liu et al., "Lnc-BAZ2B promotes M2 macrophage activation and inflammation in children with asthma through stabilizing BAZ2B pre-mRNA," *Journal of Allergy and Clinical Immunology*, vol. 147, no. 3, pp. 921–932, 2021.

[105] Y. J. Zhu, D. Mao, W. Gao, G. Han, and H. Hu, "Analysis of lncRNA expression in patients with eosinophilic and neutrophilic asthma focusing on LNC_000127," *Frontiers in Genetics*, vol. 10, 2019.

[106] M. Y. Fan, J. Xu, Q. Xiao, F. Chen, and X. Han, "Long noncoding RNA TCF7 contributes to the growth and migration of airway smooth muscle cells in asthma through targeting TIMMDC1/Akt axis," *Biochemical and Biophysical Research Communications*, vol. 508, no. 3, pp. 749–755, 2019.

[107] L. Ma, Q. Zhang, J. Hao, J. Wang, and C. Wang, "LncRNA PVT1 exacerbates the inflammation and cell-barrier injury during asthma by regulating miR-149," *Journal of Biochemical and Molecular Toxicology*, vol. 34, no. 11, article e22563, 2020.

[108] Y. Wei, B. Han, W. Dai et al., "Exposure to ozone impacted Th1/Th2 imbalance of CD(4+) T cells and apoptosis of ASMCs underlying asthmatic progression by activating lncRNA PVT1-miR-15a-5p/miR-29c-3p signaling," *Aging (Albany NY)*, vol. 12, no. 24, pp. 25229–25255, 2020.

[109] W. L. Wang, X. M. Luo, Q. Zhang, H. Q. Zhu, G. Q. Chen, and Q. Zhou, "The lncRNA PVT1/miR-590-5p/FSTL1 axis modulates the proliferation and migration of airway smooth muscle cells in asthma," *Autoimmunity*, vol. 54, no. 3, pp. 138–147, 2021.

[110] L. Lin, Q. Li, W. Hao, Y. Zhang, L. Zhao, and W. Han, "Upregulation of LncRNA Malat1 induced proliferation and migration of airway smooth muscle cells via miR-150-eIF4E/Akt signaling," *Frontiers in Physiology*, vol. 10, p. 1337, 2019.

[111] X. Y. Li, S. L. Ye, and Y. Lu, "Long non-coding RNA NEAT1 overexpression associates with increased exacerbation risk, severity, and inflammation, as well as decreased lung function through the interaction with microRNA-124 in asthma," *Journal of Clinical Laboratory Analysis*, vol. 34, no. 1, 2020.

[112] S. N. Sun, M. Yao, L. Yuan, and J. Qiao, "Long-chain noncoding RNA n337374 relieves symptoms of respiratory syncytial virus-induced asthma by inhibiting dendritic cell maturation via the CD86 and the ERK pathway," *Allergologia et Immunopathologia*, vol. 49, no. 3, pp. 100–107, 2021.

[113] X. Y. Zhang, L. X. Zhang, C. J. Tian et al., "LncRNAs BCYRN1 promoted the proliferation and migration of rat airway smooth muscle cells in asthma via upregulating the expression of transient receptor potential 1," *American Journal of Translational Research*, vol. 8, no. 8, pp. 3409–3418, 2016.

[114] W. F. Huang, C. Yu, S. Liang et al., "Long non-coding RNA TUG1 promotes airway remodeling and mucus production in asthmatic mice through the microRNA-181b/HMGB1 axis," *International Immunopharmacology*, vol. 94, article 107488, 2021.

[115] D. Devadoss, G. Daly, M. Manevski et al., "A long noncoding RNA antisense to ICAM-1 is involved in allergic asthma associated hyperreactive response of airway epithelial cells," *Mucosal Immunology*, vol. 14, no. 3, pp. 630–639, 2021.

[116] X. Chen, J. Yang, H. Shen et al., "Muc5ac production inhibited by decreased lncRNA H19 via PI3K/Akt/NF-kB in asthma," *Journal of Asthma and Allergy*, vol. 14, pp. 1033–1043, 2021.

[117] H. Yu, N. Qi, and Q. Zhou, "LncRNA H19 inhibits proliferation and migration of airway smooth muscle cells induced by PDGF-BB through miR-21/PTEN/Akt Axis," *Journal of Asthma and Allergy*, vol. 14, pp. 71–80, 2021.

[118] J. Zhang, Y. Zhou, H. Gu et al., "LncRNA-AK149641 associated with airway inflammation in an OVA-induced asthma mouse model," *Journal of Bioenergetics and Biomembranes*, vol. 52, no. 5, pp. 355–365, 2020.

[119] W. Pei, Y. Zhang, X. Li et al., "LncRNA AK085865 depletion ameliorates asthmatic airway inflammation by modulating macrophage polarization," *International Immunopharmacology*, vol. 83, article 106450, 2020.

[120] P. Gao, Y. Ding, B. Yin, and H. Gu, "Long non-coding RNA LINC-PINT retards the abnormal growth of airway smooth muscle cells via regulating the microRNA-26a-5p/PTEN axis in asthma," *International Immunopharmacology*, vol. 99, article 107997, 2021.

[121] Y. Jiang, X. Guo, and J. Qin, "Silencing of circHIPK3 hampers platelet-derived growth factor-induced proliferation and migration in airway smooth muscle cells through the miR-375/MMP-16 axis," *Cytotechnology*, vol. 73, no. 4, pp. 629–642, 2021.

[122] X. Wang, C. Xu, Y. Cai et al., "CircZNF652 promotes the goblet cell metaplasia by targeting the miR-452-5p/JAK2 signaling pathway in allergic airway epithelia," *The Journal of Allergy and Clinical Immunology*, vol. 150, no. 1, pp. 192–203, 2022.

[123] J. Q. Huang, F. Wang, L. T. Wang, Y. M. Li, J. L. Lu, and J. Y. Chen, "Circular RNA ERBB2 contributes to proliferation and migration of airway smooth muscle cells via miR-98-5p/IGF1R signaling in asthma," *Journal of Asthma and Allergy*, vol. 14, pp. 1197–1207, 2021.

[124] J. C. Wang, Y. Huang, R. X. Zhang et al., "miR-338-3p inhibits autophagy in a rat model of allergic rhinitis after PM2.5 exposure through AKT/mTOR signaling by targeting UBE2Q1," *Biochemical and Biophysical Research Communications*, vol. 554, pp. 1–6, 2021.

[125] Y. Huang, Z. Q. Guo, R. X. Zhang et al., "Effect of PM2.5 on MicroRNA expression and function in nasal mucosa of rats with allergic rhinitis," *American Journal of Rhinology & Allergy*, vol. 34, no. 4, pp. 543–553, 2020.

[126] K. Specjalski and E. Jassem, "MicroRNAs: potential biomarkers and targets of therapy in allergic diseases?," *Archivum Immunologiae et Therapiae Experimentalis (Warsz)*, vol. 67, no. 4, pp. 213–223, 2019.

[127] L. Li, S. Zhang, X. Jiang, Y. Liu, K. Liu, and C. Yang, "MicroRNA-let-7e regulates the progression and development of allergic rhinitis by targeting suppressor of cytokine signaling 4 and activating janus kinase 1/signal transducer and activator of transcription 3 pathway," *Experimental and Therapeutic Medicine*, vol. 15, no. 4, pp. 3523–3529, 2018.

[128] Y. Gao and Z. Yu, "MicroRNA16 inhibits interleukin13induced inflammatory cytokine secretion and mucus production in nasal epithelial cells by suppressing the IkappaB kinase beta/nuclear factorkappaB pathway," *Molecular Medicine Reports*, vol. 18, no. 4, pp. 4042–4050, 2018.

[129] R. P. Panganiban, K. A. Lambert, M. H. Hsu, Z. Laryea, and F. T. Ishmael, "Isolation and profiling of plasma microRNAs: biomarkers for asthma and allergic rhinitis," *Methods*, vol. 152, pp. 48–54, 2019.

[130] G. X. Ruan, X. L. Wen, and Z. W. Yuan, "Correlation between miR-223 and IL-35 and their regulatory effect in children with allergic rhinitis," *Clinical Immunology*, vol. 214, article 108383, 2020.

[131] T. X. Lu, E. J. Lim, J. A. Besse et al., "miR-223 deficiency increases eosinophil progenitor proliferation," *Journal of Immunology*, vol. 190, no. 4, pp. 1576–1582, 2013.

[132] K. Specjalski, A. Maciejewska, J. Romantowski, R. Pawłowski, E. Jassem, and M. Niedoszytko, "miRNA profiles change during grass pollen immunotherapy irrespective of clinical outcome," *Immunotherapy*, vol. 14, no. 6, pp. 433–444, 2022.

[133] Z. J. Yu, L. Zeng, X. Q. Luo et al., "Vitamin D3 inhibits micro RNA-17-92 to promote specific immunotherapy in allergic rhinitis," *Scientific Reports*, vol. 7, no. 1, p. 546, 2017.

[134] Z. Ma, Y. Teng, X. Liu et al., "Identification and functional profiling of differentially expressed long noncoding RNAs in nasal mucosa with allergic rhinitis," *Tohoku Journal of Experimental Medicine*, vol. 242, no. 2, pp. 143–150, 2017.

[135] K. C. Wang and H. Y. Chang, "Molecular mechanisms of long noncoding RNAs," *Molecular Cell*, vol. 43, no. 6, pp. 904–914, 2011.

[136] J. Wang, M. Cui, F. Sun et al., "HDAC inhibitor sodium butyrate prevents allergic rhinitis and alters lncRNA and mRNA expression profiles in the nasal mucosa of mice," *International Journal of Molecular Medicine*, vol. 45, no. 4, pp. 1150–1162, 2020.

[137] X. Wei, M. Xu, C. Wang, S. Fang, Y. Zhang, and W. Wang, "Genome-wide analysis of long non-coding RNA expression profile in nasal mucosa with allergic rhinitis," *BMC Medical Genomics*, vol. 14, no. 1, p. 100, 2021.

[138] L. Yue, X. Yin, F. Hao et al., "Long non-coding RNA Linc00632 inhibits interleukin-13-induced inflammatory cytokine and mucus production in nasal epithelial cells," *Journal of Innate Immunity*, vol. 12, no. 1, pp. 116–128, 2020.

[139] H. Kiu and S. E. Nicholson, "Biology and significance of the JAK/STAT signalling pathways," *Growth Factors*, vol. 30, no. 2, pp. 88–106, 2012.

[140] J. M. Li, H. Zhang, and Y. J. Zuo, "MicroRNA-218 alleviates sepsis inflammation by negatively regulating VOPP1 via JAK/STAT pathway," *European Review for Medical and Pharmacological Sciences*, vol. 22, no. 17, pp. 5620–5626, 2018.

[141] B. Cai, J. P. Cai, Y. L. Luo, C. Chen, and S. Zhang, "The specific roles of JAK/STAT signaling pathway in sepsis," *Inflammation*, vol. 38, no. 4, pp. 1599–1608, 2015.

[142] R. Z. Paracha, J. Ahmad, A. Ali et al., "Formal modelling of toll like receptor 4 and JAK/STAT signalling pathways: insight into the roles of SOCS-1, interferon-$\beta$ and proinflammatory cytokines in sepsis," *Plus One*, vol. 9, no. 9, 2014.

[143] H. W. Liu, Z. L. Hu, H. Li, Q. F. Tan, J. Tong, and Y. Q. Zhang, "Knockdown of lncRNA ANRIL suppresses the production of inflammatory cytokines and mucin 5AC in nasal epithelial cells via the miR-15a-5p/JAK2 axis," *Molecular Medicine Reports*, vol. 23, no. 2, 2021.

[144] Y. Yang, Y. Zhang, Y. Yang et al., "Differential expression of long noncoding RNAs and their function-related mRNAs in the peripheral blood of allergic rhinitis patients," *American Journal of Rhinology & Allergy*, vol. 34, no. 4, pp. 508–518, 2020.

[145] Y. Zhou, X. Chen, Y. Zheng et al., "Long non-coding RNAs and mRNAs expression profiles of monocyte-derived dendritic cells from PBMCs in AR," *Frontiers in Cell and Development Biology*, vol. 9, article 636477, 2021.

[146] Y. Ma, L. Shi, and C. Zheng, "Microarray analysis of lncRNA and mRNA expression profiles in mice with allergic rhinitis," *International Journal of Pediatric Otorhinolaryngology*, vol. 104, pp. 58–65, 2018.

[147] Z. Gál, A. Gézsi, Á. F. Semsei et al., "Investigation of circulating lncRNAs as potential biomarkers in chronic respiratory diseases," *Journal of Translational Medicine*, vol. 18, no. 1, p. 422, 2020.

[148] T. Wang, W. Cai, Q. Wu, D. Chen, P. Wang, and Z. Xu, "Exosomal lncRNA nuclear paraspeckle assembly transcript 1 (NEAT1)contributes to the progression of allergic rhinitis via modulating microRNA-511/nuclear receptor subfamily 4 group a member 2 (NR4A2) axis," *Bioengineered*, vol. 12, no. 1, pp. 8067–8079, 2021.

[149] X. Wu, S. Zhao, W. Huang et al., "Aberrant expressions of circulating lncRNA NEAT1 and microRNA-125a are linked with Th2 cells and symptom severity in pediatric allergic rhinitis," *Journal of Clinical Laboratory Analysis*, vol. 36, no. 3, article e24235, 2022.

[150] H. Zhao, N. Cheng, Q. Wang et al., "Effects of honey-extracted polyphenols on serum antioxidant capacity and metabolic phenotype in rats," *Food & Function*, vol. 10, no. 5, pp. 2347–2358, 2019.

[151] Z. Xu, P. Li, L. Fan, and M. Wu, "The potential role of circRNA in tumor immunity regulation and immunotherapy," *Frontiers in Immunology*, vol. 9, p. 9, 2018.

[152] J. Chen, X. Xiao, S. He, Y. Qiao, and S. Ma, "Altered circular RNA expression profiles in an ovalbumin-induced murine model of allergic rhinitis," *Allergologia et Immunopathologia*, vol. 49, no. 2, pp. 94–103, 2021.

[153] C. Y. Qiu, X. Y. Cui, M. P. Lu et al., "CircRNA expression profiles and circRNA-miRNA-mRNA crosstalk in allergic rhinitis," *World Allergy Organization Journal*, vol. 14, no. 6, article 100548, 2021.

[154] K. I. Suehiro, A. Suto, K. Suga et al., "Sox12 enhances Fbw7-mediated ubiquitination and degradation of GATA3 in Th2 cells," *Cellular & Molecular Immunology*, vol. 18, no. 7, pp. 1729–1738, 2021.

[155] E. J. Davey, G. Greicius, J. Thyberg, and E. Severinson, "STAT6 is required for the regulation of IL-4-induced cytoskeletal events in B cells," *International Immunology*, vol. 12, no. 7, pp. 995–1003, 2000.

[156] W. P. Zheng and R. A. Flavell, "The transcription factor GATA-3 is necessary and sufficient for Th2 cytokine gene expression in CD4 T cells," *Journal of Immunology*, vol. 196, no. 11, pp. 4426–4435, 2016.

[157] W. E. Paul and J. F. Zhu, "How are T(H)2-type immune responses initiated and amplified?," *Nature Reviews Immunology*, vol. 10, no. 4, pp. 225–235, 2010.

[158] X. Y. Zhu, X. Wang, Y. Wang, and Y. Zhao, "The regulatory network among CircHIPK3, LncGAS5, and miR-495 promotes Th2 differentiation in allergic rhinitis," *Cell Death & Disease*, vol. 11, no. 4, p. 216, 2020.

[159] T. Wang, P. Wang, D. Chen, Z. Xu, and L. Yang, "circARRDC3 contributes to interleukin-13-induced inflammatory cytokine and mucus production in nasal epithelial cells via the miR-375/KLF4 axis," *Molecular Medicine Reports*, vol. 23, no. 2, 2021.

[160] Y. Q. Zhu, B. Liao, Y. H. Liu et al., "MicroRNA-155 plays critical effects on Th2 factors expression and allergic inflammatory response in type-2 innate lymphoid cells in allergic rhinitis," *European Review for Medical and Pharmacological Sciences*, vol. 23, no. 10, pp. 4097–4109, 2019.

[161] L. Wang, X. Liu, X. Song, L. Dong, and D. Liu, "MiR-202-5p promotes M2 polarization in allergic rhinitis by targeting MATN2," *International Archives of Allergy and Immunology*, vol. 178, no. 2, pp. 119–127, 2019.

[162] L. Wang, X. Yang, W. Li, X. Song, and S. Kang, "MiR-202-5p/MATN2 are associated with regulatory T-cells differentiation and function in allergic rhinitis," *Human Cell*, vol. 32, no. 4, pp. 411–417, 2019.

[163] X. Liu, Y. Ren, X. Sun, H. Huang, and X. Liu, "Bioinformatics-based approaches predict that MIR-17-5P functions in the pathogenesis of seasonal allergic rhinitis through regulating ABCA1 and CD69," *American Journal of Rhinology & Allergy*, vol. 33, no. 3, pp. 269–276, 2019.

[164] T. Wang, D. Chen, P. Wang, Z. Xu, and Y. Li, "miR-375 prevents nasal mucosa cells from apoptosis and ameliorates allergic rhinitis via inhibiting JAK2/STAT3 pathway," *Biomedicine & Pharmacotherapy*, vol. 103, pp. 621–627, 2018.

[165] Y. Zhou, T. Zhang, Y. Yan et al., "MicroRNA-223-3p regulates allergic inflammation by targeting INPP4A," *Brazilian Journal of Otorhinolaryngology*, vol. 87, no. 5, pp. 591–600, 2021.

[166] H. Yu, H. Sun, Z. Wang, and Y. Liu, "MicroRNA let-7a upregulates OPN expression in a mouse model of allergic rhinitis," *Journal of Laryngology and Otology*, vol. 131, no. 11, pp. 955–960, 2017.

[167] Y. Quan-Jun, Z. Jian-Ping, Z. Jian-Hua et al., "Distinct metabolic profile of inhaled budesonide and salbutamol in asthmatic children during acute exacerbation," *Basic & Clinical Pharmacology & Toxicology*, vol. 120, no. 3, pp. 303–311, 2017.

[168] L. Wang, Q. Lv, X. Song, K. Jiang, and J. Zhang, "ADRB2 suppresses IL-13-induced allergic rhinitis inflammatory cytokine regulated by miR-15a-5p," *Human Cell*, vol. 32, no. 3, pp. 306–315, 2019.

[169] Q. Zeng, W. Liu, R. Luo, and G. Lu, "MicroRNA-181a and microRNA-155 are involved in the regulation of the differentiation and function of regulatory T cells in allergic rhinitis children," *Pediatric Allergy and Immunology*, vol. 30, no. 4, pp. 434–442, 2019.

[170] J. Wang, Z. Cui, L. Liu et al., "MiR-146a mimic attenuates murine allergic rhinitis by downregulating TLR4/TRAF6/NF-kappaB pathway," *Immunotherapy*, vol. 11, no. 13, pp. 1095–1105, 2019.

[171] Z. Chen, Y. Q. Deng, F. Li, B. K. Xiao, X. H. Zhou, and Z. Z. Tao, "MicroRNA-466a-3p attenuates allergic nasal inflammation in mice by targeting GATA3," *Clinical and Experimental Immunology*, vol. 197, no. 3, pp. 366–375, 2019.

[172] J. Liu, Y. Jiang, M. Han et al., "MicroRNA-345-5p acts as an anti-inflammatory regulator in experimental allergic rhinitis via the TLR4/NF- $\kappa$B pathway," *International Immunopharmacology*, vol. 86, article 106522, 2020.

[173] J. Wang, J. Yin, H. Peng, and A. Liu, "MicroRNA-29 mediates anti-inflammatory effects and alleviation of allergic responses and symptoms in mice with allergic rhinitis," *Allergy Asthma and Clinical Immunology*, vol. 17, no. 1, 2021.

[174] L. F. Xiao, L. Jiang, Q. Hu, and Y. Li, "MicroRNA-133b ameliorates allergic inflammation and symptom in murine model of allergic rhinitis by targeting Nlrp3," *Cellular Physiology and Biochemistry*, vol. 42, no. 3, pp. 901–912, 2017.

[175] H. Tang, H. Jiang, J. Zheng et al., "MicroRNA-106b regulates pro-allergic properties of dendritic cells and Th2 polarisation by targeting early growth response-2 in vitro," *International Immunopharmacology*, vol. 28, no. 2, pp. 866–874, 2015.

[176] Y. Teng, R. Zhang, C. Liu et al., "miR-143 inhibits interleukin-13-induced inflammatory cytokine and mucus production in nasal epithelial cells from allergic rhinitis patients by targeting IL13R alpha 1," *Biochemical and Biophysical Research Communications*, vol. 457, no. 1, pp. 58–64, 2015.

[177] C. Y. Zhao, W. Wang, H. C. Yao, and X. Wang, "SOCS3 is upregulated and targeted by miR30a-5p in allergic rhinitis," *International Archives of Allergy and Immunology*, vol. 175, no. 4, pp. 209–219, 2018.

[178] H. C. Liu, Y. Liao, and C. Q. Liu, "miR-487b mitigates allergic rhinitis through inhibition of the IL-33/ST2 signaling pathway," *European Review for Medical and Pharmacological Sciences*, vol. 22, no. 23, pp. 8076–8083, 2018.

[179] H. Li, F. Quan, P. Zhang, and Y. Shao, "Long non-coding RNA SNHG16, binding with miR-106b-5p, promoted cell apoptosis and inflammation in allergic rhinitis by upregulating leukemia inhibitory factor to activate the JAK1/STAT3 signaling pathway," *Human & Experimental Toxicology*, vol. 40, 12_Supplement, pp. S233–S245, 2021.

[180] R. Wang, S. Xue, Y. Liu, M. Peng, and B. Guo, "The correlation of long non-coding RNA NEAT1 and its targets microRNA (miR)-21, miR-124, and miR-125a with disease risk, severity, and inflammation of allergic rhinitis," *Medicine (Baltimore)*, vol. 100, no. 4, article e22946, 2021.

[181] X. Zhu, X. Wang, Y. Wang, and Y. Zhao, "Exosomal long non-coding RNA GAS5 suppresses Th1 differentiation and promotes Th2 differentiation via downregulating EZH2 and T-bet in allergic rhinitis," *Molecular Immunology*, vol. 118, pp. 30–39, 2020.

[182] J. Song, T. Wang, Y. Chen, and R. Cen, "Long non-coding RNA growth arrest-specific 5 and its targets, microRNA-21 and microRNA-140, are potential biomarkers of allergic rhinitis," *Journal of Clinical Laboratory Analysis*, vol. 35, no. 10, 2021.

[183] Y. Meng, C. Wang, and L. Zhang, "Advances and novel developments in allergic rhinitis," *Allergy*, vol. 75, no. 12, pp. 3069–3076, 2020.

[184] H. Huang, Y. Ren, H. Liang et al., "Mechanism of TCONS_00147848 regulating apoptosis of nasal mucosa cells and alleviating allergic rhinitis through FOSL2-mediated JAK/STAT3 signaling pathway," *Scientific Reports*, vol. 11, no. 1, article 15991, 2021.

[185] T. Wang, P. Wang, D. Chen, Z. Xu, and L. Yang, "circARRDC3 contributes to interleukin13induced inflammatory cytokine and mucus production in nasal epithelial cells via the miR375/KLF4 axis," *Molecular Medicine Reports*, vol. 23, no. 2, 2021.

[186] X. Yu, M. Wang, H. Zhao, and Z. Cao, "Targeting a novel hsa circ 0000520/miR-556-5p/NLRP3 pathway-mediated cell pyroptosis and inflammation attenuates ovalbumin (OVA)-induced allergic rhinitis (AR) in mice models," *Inflammation Research*, vol. 70, no. 6, pp. 719–729, 2021.