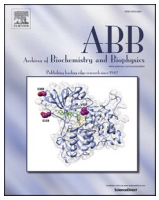
Archives of Biochemistry and Biophysics 773 (2025) 110603

Contents lists available at ScienceDirect

Archives of Biochemistry and Biophysics

journal homepage: www.elsevier.com/locate/yabbi



# MALAT1 elevates the secretion of Th2 cytokines via miR-422a/NUP155 axis in allergic rhinitis mice

Xu Zhang [1], Rui Yang [1], Daoming Bai, Mengyuan Liu, Xinyu Huang, Wei Wan, Chunping Yang [*]

*Department of Otorhinolaryngology Head and Neck Surgery, The Second Affiliated Hospital, Jiangxi Medical College, Nanchang University, Nanchang, Jiangxi, 330006, China*

ARTICLE INFO

*Keywords:*
MALAT1
Th2 cytokines
Allergic rhinitis
miR-422a
NUP155

ABSTRACT

MALAT1 is one of the most well-studied lncRNAs in various diseases. This work attempted to investigate whether long non-coding RNA MALAT1 participate in the development of allergic rhinitis (AR). In this work, nasal mucosal tissues were obtained from AR patients. The mouse AR model was established by sensitization and challenge with ovalbumin. MALAT1, GATA3 and NUP155 were up-regulated, miR-422a was down-regulated in AR patients and mice. The sneezing number, rubbing number and rhinorrhea were increased in AR mice as compared with normal mice. The levels of IL-4, IL-5, IL-9 and IL-13 were elevated in nasal lavage fluid of AR mice. MALAT1 deficiency repressed the secretion of Th2 cytokines in ILC2 cells, which was abrogated by NUP155 overexpression. NUP155 knockdown reversed the promotion of MALAT1 overexpression on the secretion of Th2 cytokines. Moreover, MALAT1 elevated NUP155 expression by sponging miR-422a. *In vivo*, MALAT1 silencing reduced the sneezing number, rubbing number and rhinorrhea, ameliorated damage of nasal mucosal tissues in AR mice. Similarly, NUP155 knockdown also significantly alleviated AR clinical symptoms, improved nasal mucosal pathology, and suppressed the secretion of Th2 cytokines *in vivo*. In conclusion, this work demonstrated that MALAT1 elevated the secretion of Th2 cytokines in ILC2 cells by regulating miR-422a/NUP155 axis, which contributed to AR progression. Thus, MALAT1 may be a potential target for AR treatment.

## 1. Introduction

Allergic rhinitis (AR) is a common allergic inflammatory disease of nasal mucosa caused by allergen exposure. It is characterized by elevated serum-specific IgE and increased type 2 cytokines in the nasal mucosa [1]. The global prevalence of AR is about 10–25 %. The age of onset is mainly between 20 and 40 years old [2,3]. The symptoms of AR usually include nasal congestion, increased nasal secretions, nasal itching, sneezing, conjunctival congestion, and often accompanied by asthma, sinusitis, conjunctivitis [3,4]. It seriously reduces the quality of life of patients. At present, the conventional treatment of AR includes avoiding allergen contact, washing nasal cavity with normal saline, oral antihistamine, nasal spray hormone, nasal spray hormone combined with antihistamine nasal spray, leukotriene receptor antagonist and allergen immunotherapy [5]. However, these treatments primarily offer symptomatic relief and their long-term clinical application is often limited by inevitable side effects. Therefore, there is an urgent need to develop novel therapeutic agents that specifically target the underlying pathogenesis of AR.

Group 2 innate lymphoid cells (ILC2s) are newly identified innate immune cells that functionally resemble T helper 2 (Th2) cells [6]. Upon allergen exposure, ILC2s are activated by epithelial cell-derived cytokines, such as IL-33 and IL-25, subsequently releasing type 2 cytokines including IL-4, IL-5, and IL-13 to regulate immune responses [7,8]. ILC2s differentiate from common lymphoid progenitor cells, and its differentiation and activation are regulated by the transcription factor GATA3 [9]. Previous studies have confirmed a significant increase in the proportion of ILC2s in the nasal mucosa and peripheral blood of AR patients, implicating their involvement in AR progression [10]. At present, the mechanism of ILC2 in AR has not been fully clarified.

Long non-coding RNAs (lncRNAs) are a new class of non-coding RNA molecules typically longer than 200 nucleotides that lack protein-coding capacity. It can be used as competitive endogenous RNAs (ceRNAs) to bind to specific miRNA, thus acting as a "sponge" of miRNAs to protect target mRNAs from inhibition [11]. LncRNA MALAT1 is first identified in lung cancer cells, which is widely involved in various cancers

* Corresponding author. Minde road, Nanchang, Jiangxi, China.
*E-mail address:* ndefy09036@ncu.edu.cn (C. Yang).
[1] Xu Zhang and Rui Yang contributed equally to this work and should be considered co-first authors.

https://doi.org/10.1016/j.abb.2025.110603
Received 22 May 2025; Received in revised form 19 August 2025; Accepted 25 August 2025
Available online 28 August 2025

[12–14]. It is extensively implicated in epigenetic regulation and closely related to biological characteristics such as tumor growth, invasion and metastasis [12,15]. A previous study has confirmed that MALAT1 is up-regulated in AR patients [16]. However, the precise mechanism of MALAT1 in AR still needs further investigation.

Bioinformatics analysis have showed that there were binding sites between MALAT1 and miR-422a. The downstream target gene of miR-422a is NUP155. This work speculated that MALAT1 may increase the expression of NUP155 by inhibiting miR-422a, thereby promoting the expression of GATA3 and the secretion of Th2 cytokines by ILC2 cells, and thus participating in the progression of AR.

## 2. Materials and methods

### 2.1. Participants

Nasal mucosa tissues were obtained from 18 AR patients and 18 age-matched non-allergic rhinitis (NAR) patients who underwent endoscopic sinus surgery at the Second Affiliated Hospital of Nanchang University. These patients were diagnosed following the Clinical Practice guidelines [17]. None of them used nasal spray hormone, oral glucocorticoid, antihistamines and antibiotics within 2 weeks before operation. All participants were informed and signed an informed consent. The study was conducted in compliance with the Declaration of Helsinki.

Methods of clinical sample extraction: 1) The nasal swab was inserted into the subject 's nasal cavity for sampling, and then the sampled nasal swab was placed in the tissue preservation solution and stored at a certain temperature. 2) The tissues on the preserved sampled nasal swabs were collected, mixed with DTT solution, shocked at 37 °C, and filtered by 100 μm filter to obtain cell filtrate. After centrifugation, the cell precipitate was retained. 3) The cells were resuspended in BEGM culture medium and incubated at 37 °C, and then the first adherent fibroblasts were removed by differential adhesion method, finally the nasal mucosal epithelial cells were collected.

### 2.2. Sorting and culture of ILC2 cells

Peripheral blood mononuclear cells (PBMCs) were isolated from peripheral blood of 18 AR patients by Ficoll-hypaque density gradient centrifugation as previous study described [18]. PBMCs were cultured in RPMI 1640 medium (Gibco, Grand Island, NY, USA) supplemented with 5 % fetal bovine serum (FBS; Gibco) at 37 °C and 5 % $CO_2$. ILC2 cells were freshly isolated from human peripheral blood. Activated ILC2 cells were obtained by culturing ILC2 cells in Yssels medium containing 1 % human serum for 7 days, with the addition of IL-2, IL-1β, IL-23, and TGF-β [19]. ILC2 cells were sorted from PBMCs applying Human ILC2 Isolation Kit (Miltenyi Biotec, Bergisch Gladbach, Germany). PBMCs ($1 \times 10^{-7}$ cells) were treated with Biotin-antibody cocktail at 4 °C for 10 min. Cells were incubated with anti-biotin microbeads at 4 °C for 15 min, and then sorted by LS separation column. The collected cell suspension was mixed with FcR blocking reagent and incubated with anti-CD294-PE (#12-2949-42; Thermo Fisher Scientific, San Jose, CA, USA), followed by incubation of *anti*-PE microbeads. Using a MS separation column, Lineage$^{-}$CD294$^{+}$ (ILC2) cells were obtained. ILC2 cells were cultured in RPMI 1640 medium and 10 % FBS at 37 °C and 5 % $CO_2$. The medium was contained 50 ng/mL IL-33, 50 ng/mL IL-25, 20 ng/mL IL-2 and 1 % penicillin/streptomycin (all from Solarbio, Beijing, China).

### 2.3. Flow cytometry

PBMCs and ILC2 cells were collected and incubated with Fc receptor blocking solution in darkness for 15 min. After washing repeatedly with FACs buffer for several times, cells were stained with anti-lineage-FITC (#22-7778-72; Thermo Fisher Scientific) and anti-CD294-PE (#12-2949-42; Thermo Fisher Scientific) in darkness for 15 min. Cells were stained with anti-lineage-FITC or anti-CD294-PE as control. After that, the proportion of Lineage$^{-}$CD294$^{+}$ cells was analyzed by FACSCalibur Flow Cytometer (Becton Dickinson, San Diego, CA, USA).

### 2.4. Animal model of AR

Female BALB/C mice (8 weeks old) were purchased from Shanghai SLAC Laboratory Animal Co., Ltd (China) and housed under SPF conditions. Upon arrival at the laboratory, mice underwent a 1-week acclimatization period. Subsequently, to induce drug sensitization and establish an AR model, starting from the end of the first week of acclimatization, mice began the sensitization protocol. The sensitization drug was prepared by adding 10 μg ovalbumin (OVA; Sigma-Aldrich, St. Louis, MO, USA) and 200 μL aluminum hydroxide adjuvant (Biodragon, KX0210054) to 200 μL PBS. Mice received intraperitoneal injections of the sensitizing drug twice a week for two weeks, completing a total of 4 injections. Following the sensitization phase, starting from the end of the third week, mice underwent intranasal challenge to stimulate drug effect and induce AR symptoms. The challenge drug consisted of 20 μL normal saline containing 200 μg OVA, administered once daily for one week, totaling 7 intranasal administrations. Throughout the sensitization and challenge process, control group mice received an equivalent volume of 0.9 % normal saline, without OVA or adjuvant. After the successful establishment of the OVA-induced AR model (i.e., upon completion of the 4-week sensitization and challenge process), OVA-induced AR mice were randomly grouped and injected via the tail vein with lentivirus-mediated sh-MALAT1 (experimental group) or sh-NC (negative control group). Specifically targeting MALAT1, shRNA (sh-MALAT1) and scrambled shRNA (sh-NC) were synthesized and packaged into lentivirus particles by Genepharm (Shanghai, China) for *in vivo* silencing of MALAT1. After the experimental intervention, the general state of the mice was observed daily, including the frequency of sneezing, rubbing behavior, and the amount of rhinorrhea. [20]. Finally, at the end of the experimental observation period, nasal lavage fluid was collected as previously described, and nasal mucosal tissues were obtained for further analysis. All protocols were authorized by the Ethics Committee of the Second Affiliated Hospital of Nanchang University.

### 2.5. Hematoxylin and eosin (H&E) staining

Nasal mucosal tissues were fixed with paraformaldehyde and embedded with paraffin. Paraffin sections with 5 μm were stained with hematoxylin for 5 min, and then stained with eosin for 1 min. Finally, the sections were observed under optical microscope.

### 2.6. Immunohistochemistry (IHC)

Paraffin sections of nasal mucosal tissues were incubated with EDTA Antigen Retrieval Solution (Beyotime, Shanghai, China) and then blocked with bovine serum albumin (MedChemExpress, Monmouth Junction, NJ, USA). Sections were incubated with *anti*-NUP155 (#66359-1-Ig; Proteintech, Wuhan, China, 1:200) and *anti*-GATA3 antibody (#66400-1-Ig; SanYing, Wuhan, China, 1:100), followed by staining with goat anti-mouse IgG (#SA00004-1; Proteintech). After that, sections were stained with DAB, and then counterstained with hematoxylin. The sections were observed under optical microscope.

### 2.7. Cell transfection

The pcDNA3.1 vector carrying full length of MALAT1 or NUP155 was used for overexpression of MALAT1 or NUP155. SiRNA specially targeting MALAT1 or NUP155 (si-MALAT1, si-NUP155) were used for knockdown of MALAT1 or NUP155. MiR-422a mimic was synthesized for miR-422a overexpression. The empty pcDNA3.1 vector, scrambled siRNA (si-NC) and mimic NC served as control. All these vectors or

oligonucleotides were obtained from Genepharm. Cells were transfected with vectors or oligonucleotides applying Lipofectamin 2000 reagent (Invitrogen, Carlsbad, CA, USA).

### 2.8. Bioinformatic analysis

The GSE124926 dataset (microarray data) was obtained from the Gene Expression Omnibus database. Based on this dataset, three Type3 samples were used as the treatment group and three Baseline samples as the control group. Differentially expressed genes (DEGs) were identified using the limma package in R, with a logFC absolute value greater than 1 and a p-value less than 0.05 as the criteria. Correlation heatmaps and principal component analysis (PCA) were used to assess the intra-group reproducibility levels between the treatment and control groups. After differential analysis, we intersected the DEGs with the predicted target genes of miR-422 from the StarBase (https://www.starbase.sysu.edu.cn/) and TargetScan (https://www.targetscan.org/vert_80/) databases, resulting in four intersecting genes: NUP155, MAPK1, ANKRD52, and ZFP36L2.

### 2.9. Quantitative real-time PCR (qRT-PCR)

Total RNA and small RNA were extracted from ILC2 cells, activated ILC2 cells, and nasal mucosal tissues applying TRIzol Reagent or PureLink™ miRNA (Invitrogen, USA). Total RNA and small RNA were reversely transcribed into cDNA using High Capacity cDNA RT kit or TaqMan™ MicroRNA RT kit (Applied Biosystem, Foster City, CA, USA). PCR reaction was carried out to examine the expression of mRNA and miRNA applying TB Green® Premix Ex Taq™ II (Takara, Dalian, China). The expression of mRNA and miRNA was normalized to GAPDH or U6, and calculated using the $2^{-\triangle\triangle CT}$ method.

### 2.10. Western blotting

Total proteins and nuclear proteins were extracted from ILC2 cells and nasal mucosal tissues utilizing ProteoPrep Total Protein Extraction Kit (Merck Millipore, Billerica, MA, USA) and Nuclear Protein Extraction Kit (Solarbio). Proteins were separated by 10 % SDS-PAGE gel electrophoresis and blotted on nitrocellulose membranes. The membranes were incubated with primary antibodies at 4 °C overnight and then treated with secondary antibody at room temperature for 2 h. TATA-box binding protein (TBP) and GAPDH served as loading control. All antibodies, *anti*-GATA3 (#PA5-20892; 1:1000), *anti*-IL-4 (#PA5-25165; 1:1000), *anti*-IL-5 (#PA5-99397; 1:1000), *anti*-IL-9 (#PA5-86781; 1:1000), *anti*-IL-13 (#PA5-96053; 1:1000), *anti*-NUP155 (#PA5-20564; 1:1000), *anti*-TBP (#PA5-116,009; 1:1000), *anti*-GAPDH (#PA1-988; 1:2000) and goat anti-rabbit IgG (#31460; 1:10,000), were obtained from Thermo Fisher Scientific. The bands were developed by ECL reagent and then analyzed by ImageJ software.

### 2.11. Enzyme-linked immunosorbent assay (ELISA)

The levels of IL-4, IL-5, IL-9 and IL-13 in nasal lavage fluid of mice and cell supernatant were evaluated by ELISA Kits. Mouse ELISA kits and Human ELISA Kits were obtained from Beyotime, expect for Human IL-9 ELISA Kit (FineTest, Wuhan, China).

### 2.12. Dual-luciferase assay

The potential binding sites of miR-422a with MALAT1 and NUP155 were predicted using the starBase database. Based on these predictions, we designed wild-type (WT) and mutant-type (MUT) sequences, which were then inserted into the pmirGLO reporter plasmid. The plasmids were constructed by Qingke Biotechnology (Nanjing, China). The resulting reporter plasmids were co-transfected with miR-422a mimic or negative control mimic (mimic NC) into ILC2 cells using Lipo 8000™ Transfection Reagent (Beyotime). After 48 h of transfection, the luciferase activities of firefly and Renilla were measured using the Dual-Luciferase Reporter Assay System (Beyotime), with Renilla luciferase activity used for normalization. All experiments were performed in triplicate.

### 2.13. RNA pull down

Using Pierce Magnetic RNA-Protein Pull-Down Kit (Thermo Fisher Scientific), the relationship among MALAT1, miR-422a and NUP155 was verified. The miR-422a mimic sequence was 5′-ACUGGACUUAGGGUCAGAAGGC-3′. The mimic control (miR-NC) sequence was 5′-UUCUCCGAACGUGUCACGUTT-3′. First, miR-422a was labeled with biotinylation applying Pierce RNA 3' End Desthiobiotinylation Kit (Thermo Fisher Scientific). Cell lysates were treated with RNAase-free DNAase I, and then incubated with biotinylation-labeled miR-422a (Bio-miR-422a) in the presence of streptavidin magnetic beads. After that, the RNA potentially targeting miR-422a was captured by the beads and RNA was eluted from the RNA-miR-422a complex. Then a biotin-based RNA pull-down assay was performed to detect the expression of MALAT1 and NUP155, and normalized to a biotinylated mimic control (Bio-NC) by qRT-PCR.

### 2.14. Statistical analysis

Each assay was performed for 3 times. Data were analyzed by SPSS 22.0 statistical software (IBM, Armonk, NY, USA) and expressed as mean ± standard deviation. Two-tailed Student's *t*-test and one-way ANOVA were used to analyze the statistical difference. $P < 0.05$ was considered as a significant difference.

## 3. Results

### 3.1. MALAT1 and GATA3 were up-regulated, miR-422a was down-regulated in AR patients and mice

To investigate the potential role of MALAT1 in AR, we collected the nasal mucosal tissues from AR and NAR patients and examined the expression of MALAT1, miR-422a and GATA3 in nasal mucosal tissues. Compared with NAR patients, increased expression of MALAT1 and GATA3, decreased expression of miR-422a were observed in nasal mucosal tissues of AR patients (Fig. 1a–c). MALAT1 expression was negatively correlated with miR-422a expression (Fig. 1d). Results obtained from western blotting revealed that the levels of GATA3, IL-4, IL-5, IL-9 and IL-13 were significantly increased in nasal mucosal tissues of AR patients (Fig. 1e). Additionally, we constructed a murine AR model to mimic AR conditions *in vivo*. The experimental timeline (Fig. 1f) outlined the key stages of adaptive feeding, sensitization injections, and nasal drug stimulation, providing a clear time framework for this study. Compared normal mice, AR mice exhibited general symptoms of AR including frequent sneezing and rubbing, and increased rhinorrhea (Fig. 1g–i). Moreover, the general morphology of nasal mucosal tissues was examined by H&E staining. As shown in Fig. 1j, we observed a large amount of inflammatory cell infiltration in nasal mucosal tissues of AR mice, accompanied by increased of mucosa thickness. The levels of IL-4, IL-5, IL-9 and IL-13 were elevated in nasal lavage fluid of AR mice (Fig. 1k). Up-regulation of MALAT1 and down-regulation of miR-422a were observed in AR mice (Fig. 1l and m). Additionally, we sorted ILC2 cells from PBMCs of AR patients. Compared with PBMCs, the proportion of ILC2 cells was notably increased after cell sorting (Fig. 1n). Further qRT-PCR analysis showed that the expression of miR-422a in activated ILC2 cells was significantly lower than in non-activated ILC2 cells (Fig. 1o). Overall, these comprehensive findings demonstrate the consistent dysregulation of MALAT1 and miR-422a in both human AR patients and AR mouse models, alongside their association with AR pathology and ILC2 activation.

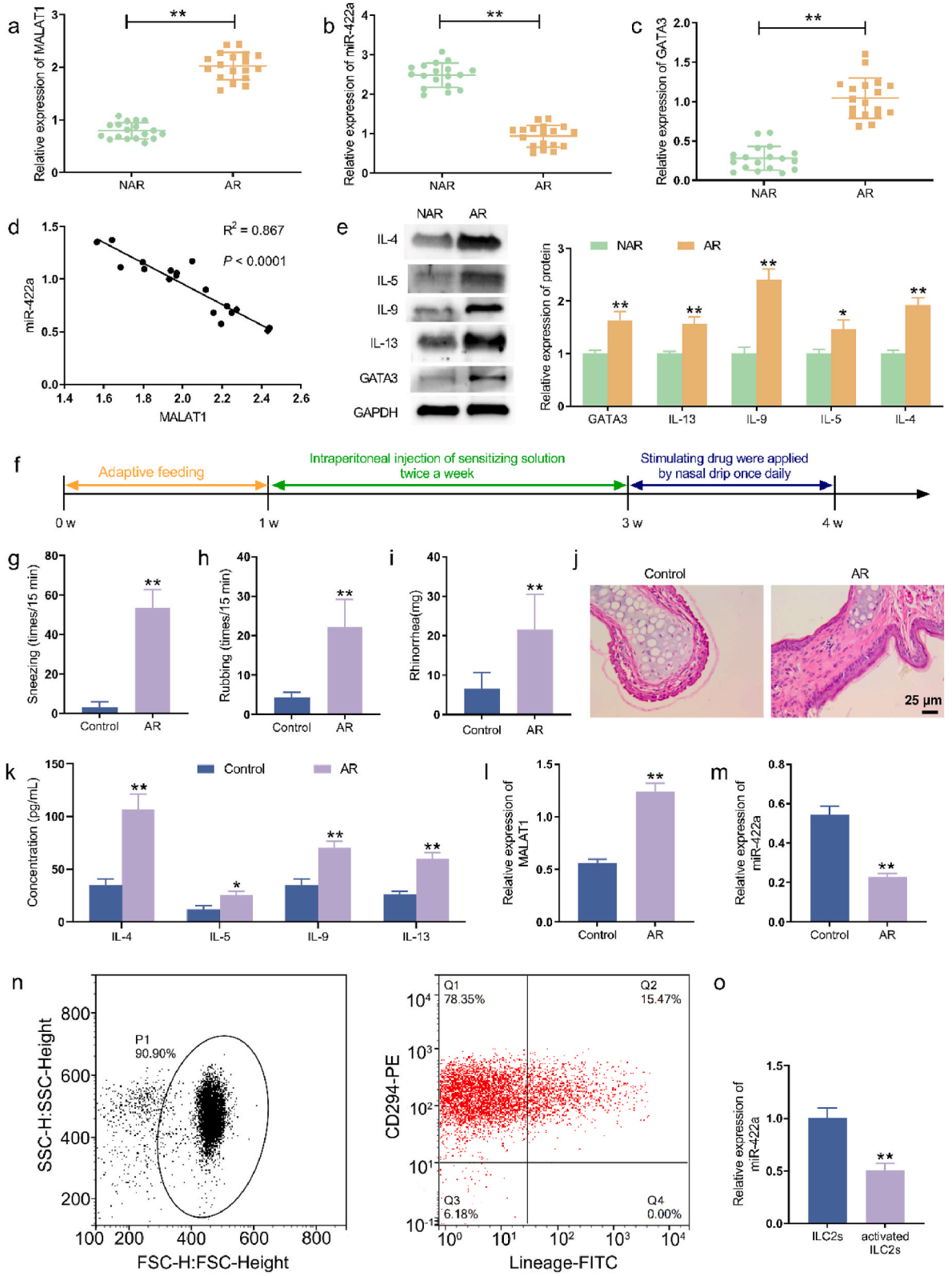



**Fig. 1. The expression of MALAT1, miR-422a and GATA3 in AR patients and mice.** (a–c) qRT-PCR examined the expression of MALAT1 (a), miR-422a (b) and GATA3 (c) in nasal mucosal tissues of AR and NAR patients. (d) Pearson's correlation coefficient was detected the correlation between MALAT1 and miR-422a. (e) Western blotting assessed the expression of GATA3, IL-4, IL-5, IL-9 and IL-13 in nasal mucosal tissues of AR and NAR patients. (f) Timeline for AR mouse modeling. (g–i) The sneezing number (g), rubbing number (h) and rhinorrhea (i) of AR and normal mice. (j) H&E staining examined the pathological changes of nasal mucosal tissues. (k) ELISA detected the levels of IL-4, IL-5, IL-9 and IL-13 in nasal lavage fluid of AR and normal mice. (*l*–m) qRT-PCR examined the expression of MALAT1 (l) and miR-422a (m) in nasal mucosal tissues of AR and normal mice. (n) Flow cytometry analyzed the proportion of ILC2 cells. (o) qRT-PCR examined the expression of miR-422a. $^{*}P < 0.05$, $^{**}P < 0.01$ vs NAR/Control/ILC2s group.

### 3.2. MALAT1 regulated the secretion of Th2 cytokines in ILC2 cells

To further reveal the role of MALAT1 in AR, MALAT1 was silenced in ILC2 cells by transfection of si-MALAT1. MALAT1 expression was decreased in ILC2 cells in the presence of si-MALAT1 (Fig. 2a). This reduction was accompanied by up-regulation of miR-422a in ILC2 cells, as determined by qRT-PCR (Fig. 2b). Results of qRT-PCR and western blotting revealed that GATA3 expression was decreased in ILC2 cells following transfection of si-MALAT1 (Fig. 2c–e). The levels of IL-4, IL-5, IL-9 and IL-13 were reduced in si-MALAT1-expressing ILC2 cells as compared with si-NC (Fig. 2f–i). Additionally, MALAT1 was overexpressed in ILC2 cells. MALAT1 overexpression caused a boost of MALAT1 and GATA3 expression and a down-regulation of miR-422a in ILC2 cells (Supplementary Fig. 1a–e). Likewise, the levels of IL-4, IL-5, IL-9 and IL-13 were elevated in ILC2 cells when MALAT1 was overexpressed (Supplementary Fig. 1f–i). Collectively, these findings demonstrate that MALAT1 expression levels are associated with the modulation of miR-422a, GATA3, and Th2 cytokine secretion in ILC2 cells.

### 3.3. MALAT1 elevated NUP155 expression by sponging miR-422a

To identify differentially expressed genes associated with AR, we first performed gene expression profiling. The cluster heatmap (Fig. 3a) showed a clear separation and good intra-group reproducibility between Type3 group (simulated AR state) and Baseline group (control) samples, indicating significant differences in gene expression patterns between the two groups. The volcano plot (Fig. 3b) further revealed differentially expressed genes in the Type3 group relative to the Baseline group, with some genes being significantly upregulated (red dots) or downregulated (blue dots). By combining prediction results from different databases (BEG, Starflane, TargetScan), a Venn diagram (Fig. 3c) identified NUP155, ZFP36L2, MAPK1, and ANKRD52 as common potential target genes. Violin plots (Fig. 3d) validated that NUP155, MAPK1, and ANKRD52 were significantly upregulated, while ZFP36L2 was significantly downregulated in the AR group. To investigate the regulatory role of miR-422a on these potential target genes, miR-422a mimic transfection experiments (Fig. 3e) showed that it significantly reduced NUP155 expression and upregulated MAPK1 expression, while having no significant effect on the expression of ZFP36L2 and ANKRD52, suggesting that NUP155 might be a direct target gene of miR-422a. *In vivo* experiments, including qRT-PCR (Fig. 3f), IHC (Fig. 3g), and Western blotting (Fig. 3h), consistently demonstrated significantly elevated NUP155 expression in the nasal mucosa tissues of OVA-induced AR mice.

Moreover, to further investigate the regulatory relationship among MALAT1, miR-422a, and NUP155, we silenced MALAT1 expression using siRNA technology. The results showed that both mRNA and protein levels of NUP155 were significantly reduced in si-MALAT1 treated cells (Fig. 4a and b). Dual-luciferase reporter assays (Fig. 4c) confirmed that miR-422a could directly target and inhibit the luciferase activity of both wild-type MALAT1 and NUP155. RNA pull-down assays (Fig. 4d) further confirmed that biotin-labeled miR-422a significantly enriched MALAT1 and NUP155, corroborating their direct binding relationship with miR-422a.

Taken together, these results suggest that MALAT1 might upregulate NUP155 expression by competitively binding miR-422a (acting as a sponge for miR-422a), thereby forming a MALAT1/miR-422a/NUP155 regulatory axis.

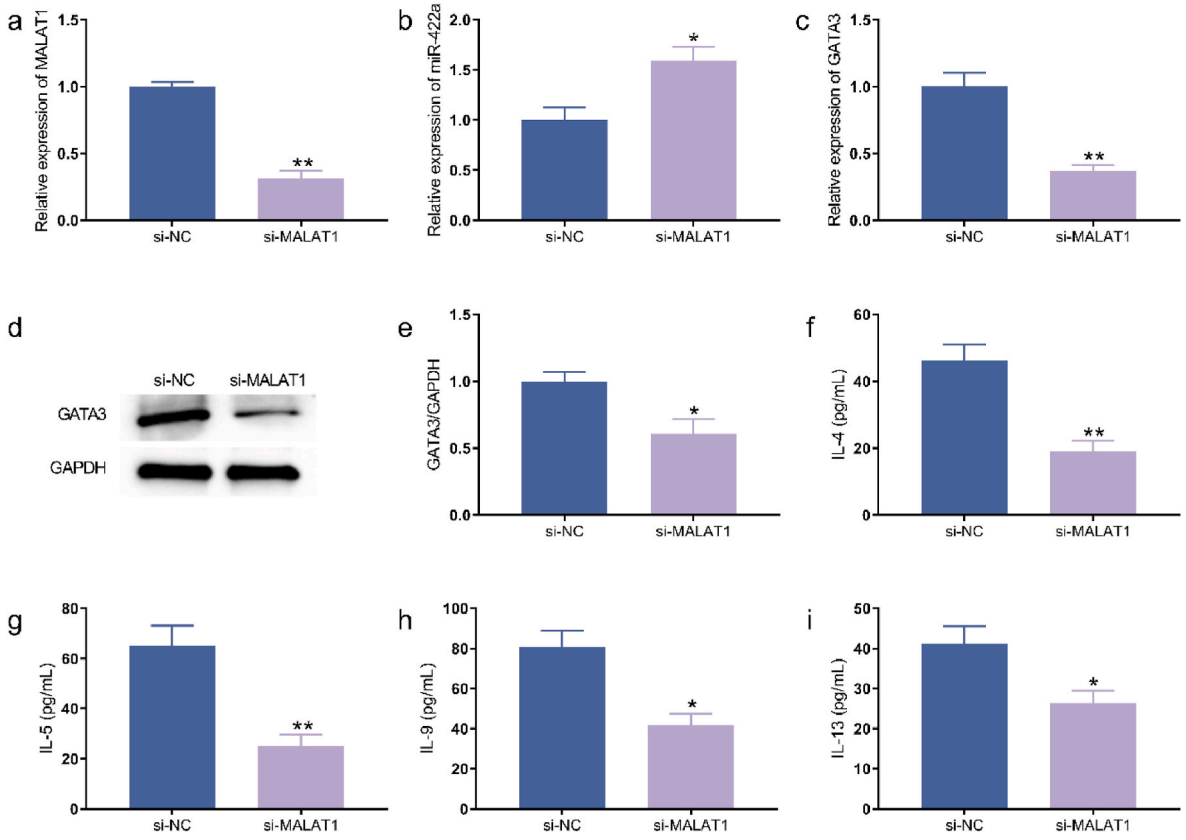



**Fig. 2. MALAT1 deficiency reduced the secretion of Th2 cytokines.** ILC2 cells were transfected with si-MALAT1 or si-NC. (a–c) qRT-PCR examined the expression of MALAT1 (a), miR-422a (b) and GATA3 (c) in ILC2 cells. (*d*–e) Western blotting detected the expression of GATA3 in ILC2 cells. (f–i) ELISA examined the levels of IL-4 (f), IL-5 (g), IL-9 (h) and IL-13 (i) in ILC2 cells. *$P < 0.05$, **$P < 0.01$ vs si-NC group.

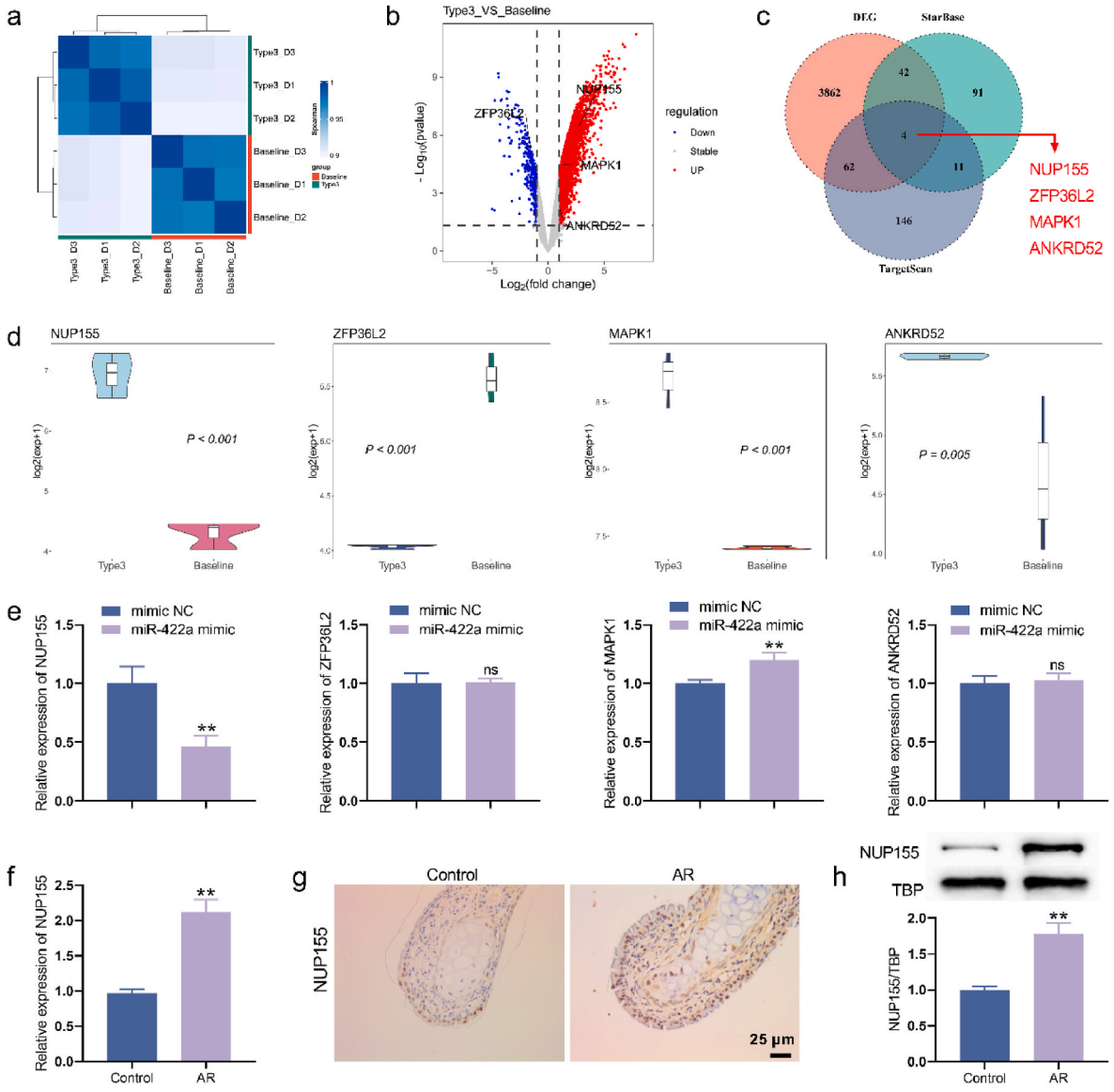



**Fig. 3. NUP155 was a target of miR-422a.** Dataset GSE124926 was downloaded from the GEO database. Differential expression analysis was performed using the R package limma, comparing three Type3 samples as the treated group with three Baseline samples as the control group, applying a threshold of $|\log FC| > 1$ and p-value $<0.05$. (a) The correlation heatmap demonstrated the within-group reproducibility of the Type3 and Baseline samples in this dataset. (b) Volcano plots showed the DEGs between ILC2 cells and activated ILC2 cells in GSE124926 dataset. (c) Venn diagram displayed the target genes of miR-422a based on TargetScan, starBase and GSE124926 dataset. (d) Expression levels of the screened candidate DEGs. (e) qRT-PCR detected the expression of NUP155, ZFP36L2, MAPK1, and ANKRD52 in ILC2 cells following transfection of miR-422a mimic or mimic NC. (f–h) qRT-PCR (f), IHC (g) and western blotting (h) assessed the expression of NUP155 in nasal mucosal tissues of AR and normal mice. $^{**}P < 0.01$ vs mimic NC/Control group; ns, no significant difference vs mimic NC group.

### *3.4. Silencing NUP155 alleviated AR symptoms and suppressed inflammation*

To further investigate the role of NUP155 in AR and its feasibility as a potential therapeutic target, we conducted NUP155 gene silencing experiments in an OVA-induced AR mouse model. First, we validated the efficiency of lentiviral-mediated knockdown (Fig. 5a and b). All subsequent experiments utilized sh-NUP155-1 for knockdown. The experimental design was as shown in Fig. 5c; during the sensitization phase (Week 1), mice were injected via the tail vein with lentiviral vectors encoding sh-NUP155 or sh-NC, and then subjected to OVA sensitization and challenge according to the established protocol to establish the AR model. Subsequently, we evaluated the effect of NUP155 silencing on the clinical symptoms of AR mice. The results showed that sh-NUP155 treatment significantly reduced the number of sneezes (Fig. 5d), nose rubs (Fig. 5e), and rhinorrhea (Fig. 5f) in mice, suggesting that NUP155 silencing effectively alleviated AR clinical symptoms. H&E staining results (Fig. 5g) showed obvious inflammatory cell infiltration and mucosal edema in the nasal mucosa of AR model group mice. In contrast, the degree of inflammatory cell infiltration and mucosal edema was significantly reduced in the nasal mucosa of sh-NUP155-treated mice, and the structure approached normal, indicating that NUP155 silencing helped inhibit AR-induced tissue damage and inflammatory responses. Finally, ELISA results (Fig. 5h) showed that sh-NUP155 treatment significantly reduced the levels of Th2 cytokines such as IL-4, IL-5, IL-9, and IL-13 in the nasal lavage fluid of AR mice, further supporting the crucial role of NUP155 in AR inflammation. In summary, these results indicated that NUP155 played an important role in the OVA-induced AR mouse model, and its gene silencing effectively alleviated AR symptoms, improved nasal mucosal pathological changes, and suppressed Th2 cytokine secretion, suggesting NUP155 as a potential therapeutic target for allergic rhinitis.

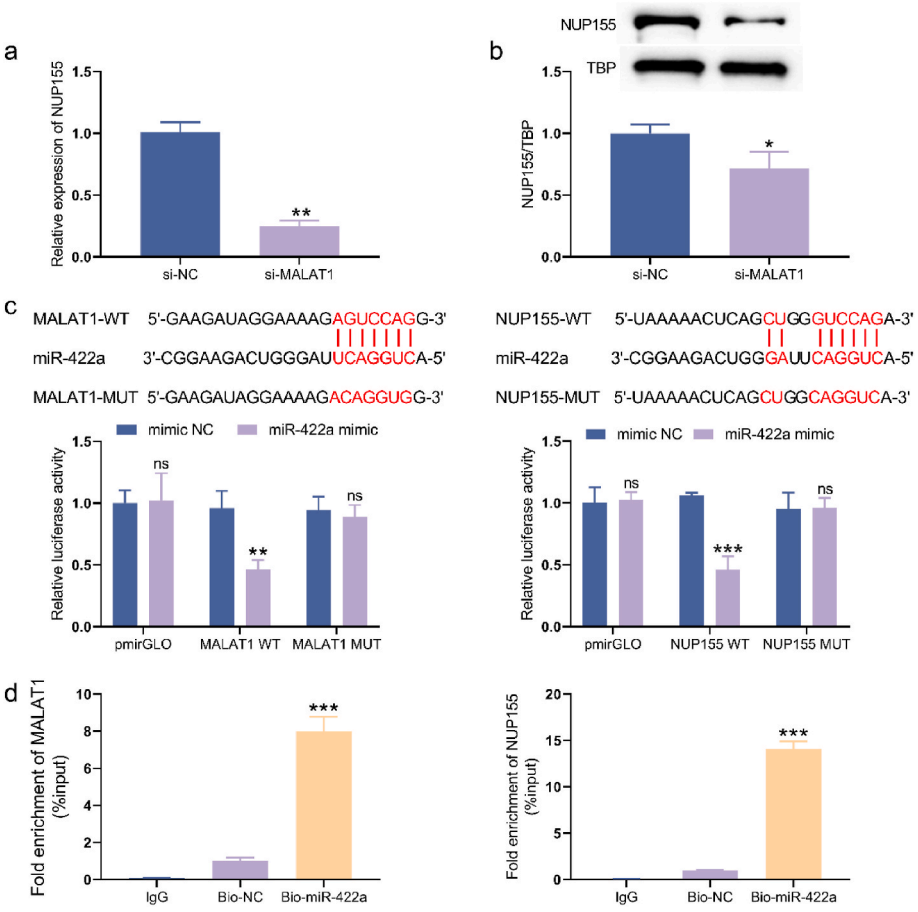



**Fig. 4. The relationship among MALAT1, miR-422a and NUP155.** (a–b) qRT-PCR (a) and western blotting (b) detected the expression of NUP155 in ILC2 cells following transfection of si-MALAT1 or si-NC. (c) Dual-luciferase reporter assay to detect the interactions of miR-422a with MALAT1 and NUP155 (Binding sites of miR-422a with MALAT1 and NUP155 were predicted using the starBase website, and mutation sites were designed accordingly). (d) RNA pull down verified the relationship among MALAT1, miR-422a and NUP155. $^{**}P < 0.01$, $^{***}P < 0.001$ vs si-NC/mimic NC/Bio-NC group; ns, no significant difference vs mimic NC group.

### *3.5. MALAT1 affected the secretion of Th2 cytokines in ILC2 cells by regulating NUP155*

NUP155 was silenced in ILC2 cells by transfection of si-NUP155 (Fig. 6a). The expression of GATA3, IL-4, IL-5, IL-9 and IL-13 was reduced in ILC2 cells in the presence of si-NUP155, as determined by qRT-PCR (Fig. 6b). This reduction accompanied by a decrease level of IL-4, IL-5, IL-9 and IL-13 in ILC2 cells following transfection of si-NUP155 (Fig. 6c). Moreover, MALAT1 deficiency reduced NUP155 expression in ILC2 cells, which was abrogated by NUP155 overexpression (Fig. 6d). Results of qRT-PCR and ELISA uncovered that NUP155 overexpression reversed MALAT1 silencing-mediated decrease level of GATA3, IL-4, IL-5, IL-9 and IL-13 in ILC2 cells (Fig. 6e and f). Additionally, MALAT1 overexpression-mediated up-regulation of NUP155 in ILC2 cells was reversed by si-NUP155 (Supplementary Fig. 2a). The expression of GATA3, IL-4, IL-5, IL-9 and IL-13 was elevated in ILC2 cells in the presence of MALAT1 overexpression vector, which was rescued by NUP155 deficiency, as determined by qRT-PCR (Supplementary Fig. 2b). NUP155 knockdown reversed MALAT1 up-regulation-mediated promotion of IL-4, IL-5, IL-9 and IL-13 levels in ILC2 cells (Supplementary Fig. 2c). Collectively, these data indicate that NUP155 mediates the effects of MALAT1 on GATA3 expression and Th2 cytokine secretion in ILC2 cells.

### *3.6. MALAT1 knockdown ameliorated AR in mice*

To verify the role of long non-coding RNA MALAT1 in AR and to explore its potential as a therapeutic target, we conducted MALAT1 silencing experiments in an OVA-induced AR mouse model. As depicted in the experimental design (Fig. 7a), after one week of acclimatization, mice received tail vein injections of lentiviral vector-mediated sh-MALAT1 or sh-NC during the sensitization phase (Week 1), followed by OVA sensitization and challenge according to the established protocol to establish the AR model. Results showed that MALAT1 deficiency significantly reduced the frequency of sneezing and nose rubbing, and decreased rhinorrhea in AR mice (Fig. 7b–d). H&E staining results indicated that the nasal mucosa tissues of AR mice exhibited obvious congestion, edema, and inflammatory cell infiltration. The nasal mucosa thickness was significantly increased in AR mice. In contrast, in the sh-MALAT1-treated group, the inflammatory cell infiltration and mucosal edema in the nasal mucosa were significantly reduced, and the structure approached normal (Fig. 7e). ELISA result found that the levels of IL-4, IL-5, IL-9, and IL-13 were significantly decreased in AR mice after sh-MALAT1 administration (Fig. 7f). Concurrently, we verified the molecular effects of sh-MALAT1 in the mouse nasal mucosa. qRT-PCR results (Fig. 7g) showed that MALAT1 mRNA expression was significantly reduced, while miR-422a expression was significantly elevated in the nasal mucosa of AR mice treated with sh-MALAT1. Finally, immunohistochemical staining results (Fig. 7h) indicated that, compared to the AR + sh-NC treated group, the protein expression of NUP155 and GATA3 was markedly decreased in the nasal mucosa of AR + sh-MALAT1 group mice, further confirming the effect of MALAT1 silencing on downstream molecular targets. In summary, these results demonstrated that MALAT1 played an important role in the OVA-induced AR

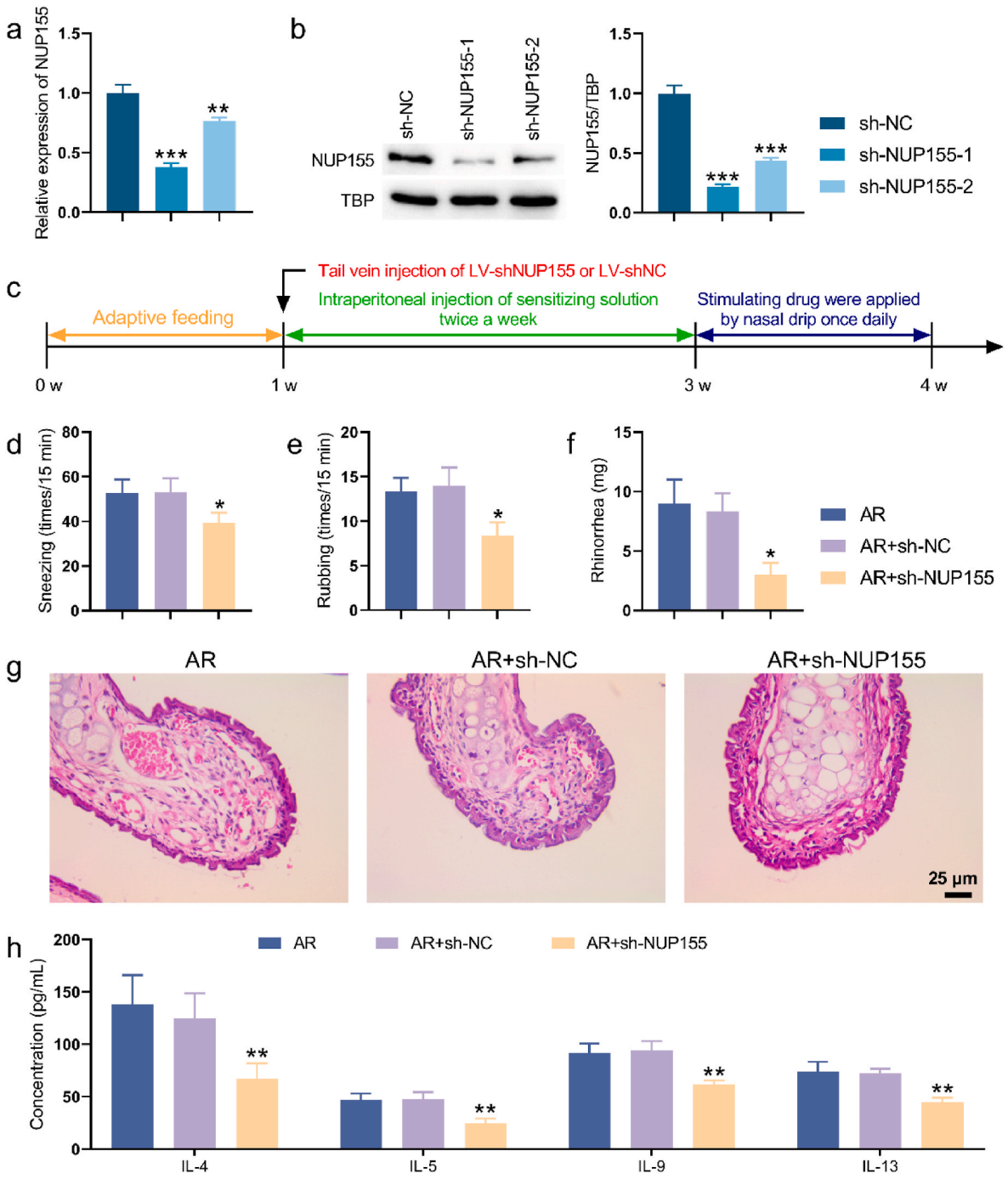



**Fig. 5.** Therapeutic effects of NUP155 gene silencing in an AR mouse model. (a–b) Validation of shNUP155 knockdown efficiency on NUP155 mRNA and protein expression. (c) Schematic timeline for AR mouse model establishment and lentivirus intervention. (*d*–f) Effect of sh-NUP155 on the number of sneezes (d), nose rubs (e), and amount of rhinorrhea (f) in AR mice. (g) H&E staining showed histological changes in nasal mucosa. (h) ELISA detected the levels of IL-4, IL-5, IL-9, and IL-13 in nasal lavage fluid. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$ vs sh-NC/AR + sh-NC group.

mouse model, and its gene silencing effectively alleviated AR symptoms, improved nasal mucosal pathological changes, and inhibited Th2 cytokine secretion, suggesting that MALAT1 could be a potential therapeutic target for allergic rhinitis.

## 4. Discussion

The accumulation and activation of ILC2 in airway mucosa is considered to be a key factor in the pathogenesis of AR and other type II airway inflammation [8]. In this work, we found that MALAT1 and GATA3 were up-regulated, miR-422a was down-regulated in AR patients and mice. MALAT1 deficiency repressed the secretion of Th2 cytokines in ILC2 cells, while MALAT1 overexpression enhanced the secretion of Th2 cytokines in ILC2 cells. Moreover, MALAT1 elevated NUP155 expression by sponging miR-422a. MALAT1 regulated the secretion of Th2 cytokines via miR-422a/NUP155 axis. *In vivo*, MALAT1 silencing ameliorated the progression of in AR mice.

Long non-coding RNA MALAT1 is one of the most well-studied lncRNAs in various diseases [21]. Recent computational studies have deeply elucidated the multifaceted roles of MALAT1 in cancer progression, particularly offering significant mechanistic insights into its regulation of ferroptosis and enhancement of drug resistance [22]. Given the

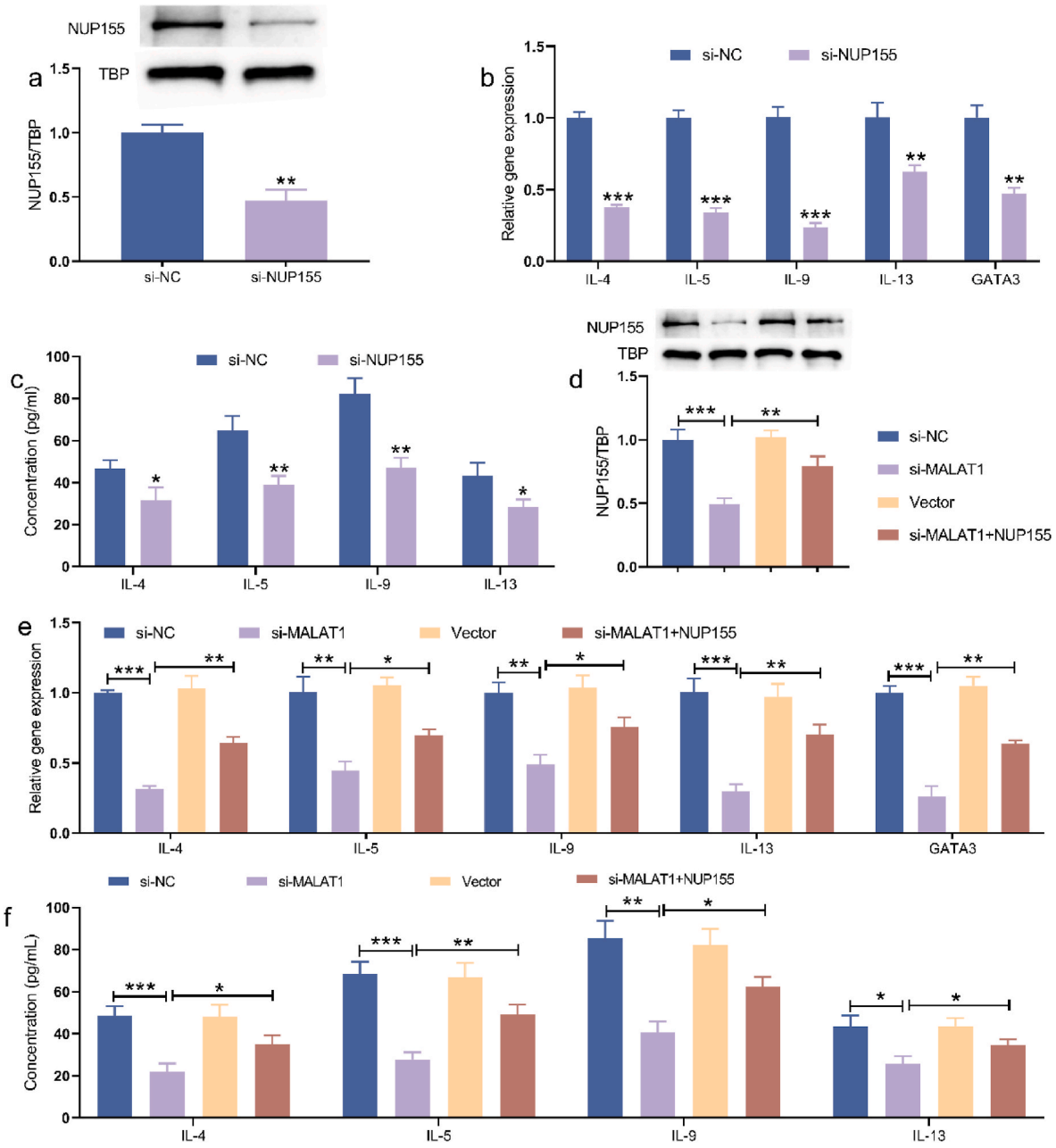



**Fig. 6. MALAT1 silencing reduced the secretion of Th2 cytokines by regulating NUP155.** ILC2 cells were transfected with si-NUP155 or si-NC. (a) Western blotting examined the expression of NUP155 in ILC2 cells. (b) qRT-PCR detected the expression of IL-4, IL-5, IL-9, IL-13 and GATA3 in ILC2 cells. (c) ELISA evaluated the levels of IL-4, IL-5, IL-9 and IL-13 in ILC2 cells. ILC2 cells were transfected with si-MALAT1/si-NC and NUP155/Vector. (d) Western blotting examined the expression of NUP155 in ILC2 cells. (e) qRT-PCR detected the expression of IL-4, IL-5, IL-9, IL-13 and GATA3 in ILC2 cells. (f) ELISA evaluated the levels of IL-4, IL-5, IL-9 and IL-13 in ILC2 cells. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$ vs si-NC/si-MALTA1 group.

diverse regulatory functions of MALAT1 across various diseases, we focused on its role in AR. The study of Wu et al. has confirmed that MALAT1 is up-regulated in AR patients. MALAT1 acts as ceRNA to up-regulate GATA3 expression by binding miR-135 b-5p, and then elevates Th2 differentiation of $CD4^{+}$ T cells in children with AR [16]. A previous study has revealed that the expression of miR-422a is decreased in AR patients [23]. In this work, we also found the up-regulation of MALAT1 and down-regulation of miR-422a in AR patients. To elucidate the core mechanisms by which MALAT1 regulates ILC2 cell function, we performed detailed bioinformatics and molecular biology experiments. Applying TargetScan and starBase databases, we analyzed the down-stream target of miR-422a. We then intersected these predicted target genes with the abnormally expressed genes identified from the GSE124926 microarray in activated ILC2 cells, revealing four potential miR-422a target genes: NUP155, ZFP36L2, MAPK1, and ANKRD52. Based on the differential expression patterns of these four genes, violin plots verified that NUP155, MAPK1, and ANKRD52 were significantly upregulated in the AR group, while ZFP36L2 was significantly down-regulated. Subsequent qRT-PCR results showed that miR-422a mimic inhibited NUP155 expression and upregulated MAPK1 expression, but had no significant effect on the expression of ZFP36L2 and ANKRD52, suggesting that NUP155 might be a direct target gene of miR-422a. More critically, we performed dual-luciferase reporter assays and RNA pull-down assays, which clearly confirmed that MALAT1 can directly bind to miR-422a, and miR-422a can also directly bind to NUP155. These results collectively established the molecular regulatory axis

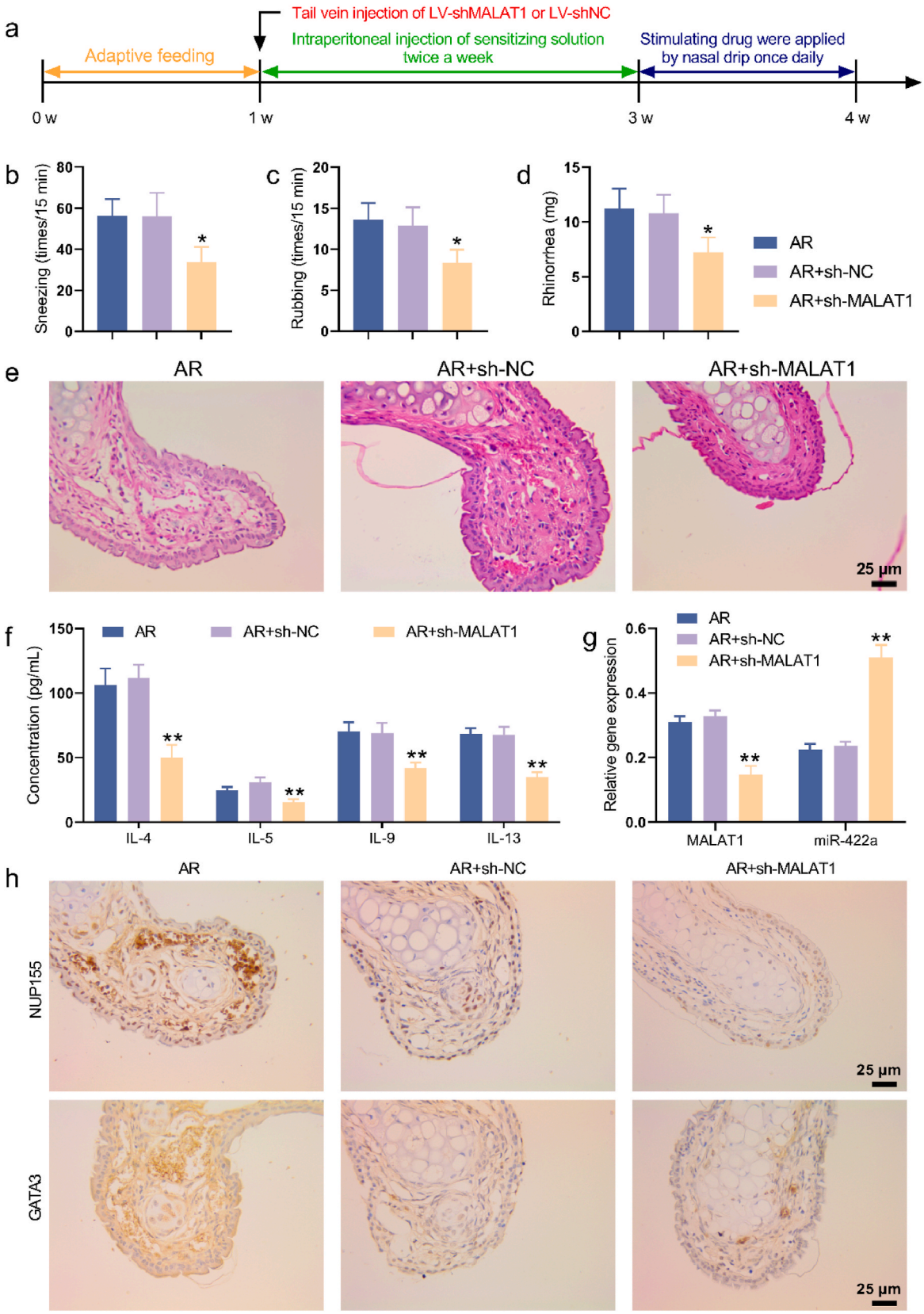



**Fig. 7. MALAT1 knockdown ameliorated AR in mice.** AR mice were injected with lentivirus-mediated sh-MALAT1 or sh-NC. (a) Schematic timeline of OVA-induced AR mouse model establishment and lentivirus intervention. (b–d) The sneezing number (b), rubbing number (c) and rhinorrhea (d) of mice. (e) H&E staining examined the pathological changes of nasal mucosal tissues. (f) ELISA detected the levels of IL-4, IL-5, IL-9 and IL-13 in nasal lavage fluid of mice. (g) qRT-PCR examined the expression of MALAT1 and miR-422a in nasal mucosal tissues of mice. (h) IHC detected the expression of NUP155 and GATA3 in nasal mucosa tissues. $^{*}P < 0.05$, $^{**}P < 0.01$ vs AR + sh-NC group.

where MALAT1 sponges miR-422a, thereby upregulating NUP155 expression.

NUP155 encodes a nucleoporin, which is one of the important components of the nuclear pore complex [24]. Its main function is to control the transport of genetic material from the nucleus to the cytoplasm for translation into proteins. Some minor changes in NUP155 may increase the possibility of common sporadic atrial fibrillation. In the process of atrial fibrillation, NUP155 regulates the transcription and translation of many genes, which seriously threatens the health of young people [25]. In bidirectional nucleocytoplasmic transport events, NUP155 acts as a p53 repression target to regulate the cancer-relevant signaling pathways in liver cancer development [26]. A study analyzed immune cell infiltration through the xCell database found that the expression of NUP155 is positively correlated with the infiltration levels of Treg cells and Th2 cells, indicating that NUP155 plays a crucial role in immunity [27]. However, there is currently no research on the potential role of NUP155 in atopy, whether in mice or humans. At the ILC2 cell level, we for the first time thoroughly explored the function of NUP155 within the context of allergic inflammation. We confirmed that MALAT1's regulation of Th2 cytokine secretion is NUP155-dependent: NUP155 overexpression reversed the inhibition of MALAT1 knockdown on the levels of GATA3, IL-4, IL-5, IL-9 and IL-13 in ILC2 cells. GATA3 is a transcription factor known to induce Th2 differentiation. ILC2 responds to IL-33 and IL-25 derived from epithelial cells, activates and releases IL-4, IL-5, IL-13 and other cytokines, which is the main pathway for ILC2 to mediate type II inflammation [6]. Our findings further showed that MALAT1 overexpression promoted Th2 cytokine secretion, and this effect could be abolished by NUP155 deficiency. These findings at the ILC2 cell level clearly outline the complete pathway by which MALAT1 regulates Th2 cytokine secretion in ILC2 cells via the miR-422a/NUP155 axis, thereby promoting AR progression.

Based on the aforementioned in vitro and molecular mechanistic findings, we further validated the roles of MALAT1 and NUP155 in the pathological process of AR *in vivo*. This study for the first time elucidated the precise role of NUP155 in AR progression, revealing its high expression in AR mice. Silencing NUP155 significantly ameliorated clinical symptoms such as sneezing and nose rubbing in AR mice, reduced nasal mucosal congestion, edema, and inflammatory cell infiltration, and significantly decreased local nasal GATA3 expression and levels of Th2 cytokines including IL-4, IL-5, IL-9, and IL-13. Concurrently, our research on MALAT1 silencing further confirmed its therapeutic potential in the AR mouse model. MALAT1 silencing also significantly alleviated clinical symptoms in AR mice, improved pathological damage to the nasal mucosa, and markedly inhibited local nasal Th2 cytokine levels. At the molecular level, MALAT1 silencing promoted miR-422a expression while inhibiting the expression of NUP155 and GATA3, as well as Th2 cytokine levels. These *in vivo* results strongly support the crucial roles of MALAT1 and NUP155 in AR pathogenesis and further confirm that MALAT1 influences AR progression by regulating the miR-422a/NUP155 axis, suggesting that targeting this axis may hold therapeutic potential.

This study for the first time established the role of the MALAT1/miR-422a/NUP155 regulatory axis in the pathological process of AR and demonstrated that targeting MALAT1 or NUP155 *in vivo* can effectively improve AR phenotypes. This provides potential new therapeutic targets for AR. Particularly for AR patients predominantly characterized by ILC2-mediated type II inflammation, precise intervention in this axis could have significant clinical implications. However, translating these basic research findings into clinical applications still faces challenges. Targeted therapies involving long non-coding RNAs and miRNAs require overcoming issues such as delivery efficiency, specificity, off-target effects, and long-term safety. For instance, safely and effectively delivering shMALAT1 or shNUP155 to the nasal mucosa while maintaining sufficient therapeutic concentrations and avoiding systemic side effects is a crucial area for future research. Furthermore, more extensive clinical sample validation and deeper mechanistic studies are needed to fully understand the complete regulatory network of this axis in human AR patients and to explore more stable, specific, and less toxic intervention strategies, such as developing small molecule inhibitors or antisense oligonucleotides.

In conclusion, this study revealed that MALAT1 promotes the secretion of Th2 cytokines in ILC2 cells by regulating the miR-422a/NUP155 axis, thereby driving AR progression. Therefore, MALAT1 and NUP155 may serve as potential therapeutic targets for AR, but their clinical translation warrants further exploration.

## CRediT authorship contribution statement

**Xu Zhang:** Writing – review & editing, Writing – original draft, Investigation, Formal analysis, Data curation, Conceptualization. **Rui Yang:** Writing – review & editing, Writing – original draft, Investigation, Formal analysis, Data curation, Conceptualization. **Daoming Bai:** Writing – review & editing, Writing – original draft, Methodology, Investigation. **Mengyuan Liu:** Writing – review & editing, Methodology, Investigation. **Xinyu Huang:** Writing – review & editing, Software. **Wei Wan:** Writing – review & editing, Validation. **Chunping Yang:** Writing – review & editing, Supervision, Resources, Project administration, Funding acquisition.

## Ethics statement

All participants were informed and signed an informed consent. The trial was conducted in compliance with the Declaration of Helsinki. This study has obtained approval from the Ethics Committee of The Second Affiliated Hospital, Jiangxi Medical College, Nanchang University.

## Funding

This research was supported by the National Natural Science Foundation of China (NO.82160211).

## Conflicts of interest

The authors declare that they have no conflicts of interest.

## Abbreviation

| | |
|---|---|
| AR | Allergic rhinitis |
| ceRNA | competitive endogenous RNA |
| DEGs | differentially expressed genes |
| ELISA | enzyme-linked immuno sorbent assay |
| FBS | foetal bovine serum |
| H&E | Hematoxylin and eosin |
| IHC | Immunohistochemistry |
| ILC2 | Group 2 innate lymphoid cells |
| lncRNA | Long non-coding RNA |
| NAR | non-allergic rhinitis |
| OVA | ovalbumin |
| PBMCs | Peripheral blood mononuclear cells |
| qRT-PCR | quantitative real-time PCR |
| Th2 | T helper 2 |

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.abb.2025.110603.

## Data availability

The data used to support the findings of this study are available within the article. The GSE124926 dataset analyzed during the current

study are available in the Gene Expression Omnibus database.

## References


[1] G. Ciprandi, G.L. Marseglia, R. Castagnoli, C. Valsecchi, C. Tagliacarne, S. Caimmi, et al., From IgE to clinical trials of allergic rhinitis, Expert Rev Clin Immunol. 11 (2015) 1321–1333, https://doi.org/10.1586/1744666x.2015.1086645.

[2] C.L. Ng, D.Y. Wang, Latest developments in allergic rhinitis in allergy for Clinicians and researchers, Allergy 70 (2015) 1521–1530, https://doi.org/10.1111/all.12782.

[3] Z.A. Siddiqui, A. Walker, M.M. Pirwani, M. Tahiri, I. Syed, Allergic rhinitis: diagnosis and management, Br. J. Hosp. Med. 83 (2022) 1–9, https://doi.org/10.12968/hmed.2021.0570.

[4] M.D. Seidman, R.K. Gurgel, S.Y. Lin, S.R. Schwartz, F.M. Baroody, J.R. Bonner, et al., Clinical practice guideline: allergic rhinitis, Otolaryngol. Head Neck Surg. 152 (2015) S1–S43, https://doi.org/10.1177/0194599814561600.

[5] D.I. Bernstein, G. Schwartz, J.A. Bernstein, Allergic rhinitis: mechanisms and treatment, Immunol. Allergy Clin. 36 (2016) 261–278, https://doi.org/10.1016/j.iac.2015.12.004.

[6] H. Kabata, K. Moro, S. Koyasu, The group 2 innate lymphoid cell (ILC2) regulatory network and its underlying mechanisms, Immunol. Rev. 286 (2018) 37–52, https://doi.org/10.1111/imr.12706.

[7] H. Hammad, B.N. Lambrecht, Barrier epithelial cells and the control of type 2 immunity, Immunity 43 (2015) 29–40, https://doi.org/10.1016/j.immuni.2015.07.007.

[8] A. Kato, Group 2 innate lymphoid cells in airway diseases, Chest 156 (2019) 141–149, https://doi.org/10.1016/j.chest.2019.04.101.

[9] D.N. Kasal, Z. Liang, M.K. Hollinger, C.Y. O'Leary, W. Lisicka, A.I. Sperling, et al., A Gata3 enhancer necessary for ILC2 development and function, Proc. Natl. Acad. Sci. U. S. A 118 (2021), https://doi.org/10.1073/pnas.2106311118.

[10] J. Dhariwal, A. Cameron, M.B. Trujillo-Torralbo, A. Del Rosario, E. Bakhsoliani, M. Paulsen, et al., Mucosal type 2 innate lymphoid cells are a key component of the allergic response to aeroallergens, Am. J. Respir. Crit. Care Med. 195 (2017) 1586–1596, https://doi.org/10.1164/rccm.201609-1846OC.

[11] R.S. Zhou, E.X. Zhang, Q.F. Sun, Z.J. Ye, J.W. Liu, D.H. Zhou, et al., Integrated analysis of lncRNA-miRNA-mRNA ceRNA network in squamous cell carcinoma of tongue, BMC Cancer 19 (2019) 779, https://doi.org/10.1186/s12885-019-5983-8.

[12] X. Zhang, M.H. Hamblin, K.J. Yin, The long noncoding RNA Malat1: its physiological and pathophysiological functions, RNA Biol. 14 (2017) 1705–1714, https://doi.org/10.1080/15476286.2017.1358347.

[13] B. Goyal, S.R.M. Yadav, N. Awasthee, S. Gupta, A.B. Kunnumakkara, S.C. Gupta, Diagnostic, prognostic, and therapeutic significance of long non-coding RNA MALAT1 in cancer, Biochim. Biophys. Acta Rev. Canc 1875 (2021) 188502, https://doi.org/10.1016/j.bbcan.2021.188502.

[14] J. Kim, H.L. Piao, B.J. Kim, F. Yao, Z. Han, Y. Wang, et al., Long noncoding RNA MALAT1 suppresses breast cancer metastasis, Nat. Genet. 50 (2018) 1705–1715, https://doi.org/10.1038/s41588-018-0252-3.

[15] T. Gutschner, M. Hämmerle, S. Diederichs, MALAT1 – a paradigm for long noncoding RNA function in cancer, J. Mol. Med. (Berl.) 91 (2013) 791–801, https://doi.org/10.1007/s00109-013-1028-y.

[16] X.H. Wu, S.J. Zhao, W.Q. Huang, L.H. Huang, X.Y. Luo, S.L. Long, Long non-coding RNA MALAT1 promotes Th2 differentiation by regulating microRNA-135b-5p/GATA-3 axis in children with allergic rhinitis, Kaohsiung J. Med. Sci. 38 (2022) 971–980, https://doi.org/10.1002/kjm2.12587.

[17] J. Bousquet, V.J. Lund, P. van Cauwenberge, C. Bremard-Oury, N. Mounedji, M. T. Stevens, et al., Implementation of guidelines for seasonal allergic rhinitis: a randomized controlled trial, Allergy 58 (2003) 733–741, https://doi.org/10.1034/j.1398-9995.2003.00076.x.

[18] A. Jerram, T.V. Guy, L. Beutler, B. Gunasegaran, R. Sluyter, B. Fazekas de St Groth, et al., Effects of storage time and temperature on highly multiparametric flow analysis of peripheral blood samples; implications for clinical trial samples, Biosci. Rep. 41 (2021), https://doi.org/10.1042/bsr20203827.

[19] K. Golebski, X.R. Ros, M. Nagasawa, S. van Tol, B.A. Heesters, H. Aglmous, et al., IL-1β, IL-23, and TGF-β drive plasticity of human ILC2s towards IL-17-producing ILCs in nasal inflammation, Nat. Commun. 10 (2019) 2162, https://doi.org/10.1038/s41467-019-09883-7.

[20] T. Van Nguyen, C.H. Piao, Y.J. Fan, D.U. Shin, S.Y. Kim, H.J. Song, et al., Anti-allergic rhinitis activity of α-lipoic acid via balancing Th17/Treg expression and enhancing Nrf 2/HO-1 pathway signaling, Sci. Rep. 10 (2020) 12528, https://doi.org/10.1038/s41598-020-69234-1.

[21] G. Arun, D. Aggarwal, D.L. Spector, MALAT1 long non-coding RNA: functional implications, Noncoding RNA 6 (2020), https://doi.org/10.3390/ncrna6020022.

[22] S. Gupta, D.A. Silveira, J.C. Mombach, R.F. Hashimoto, Targeting NSCLC drug resistance: systems biology insights into the MALAT1/miR-145-5p axis and Wip1 in regulating ferroptosis and apoptosis, J. R. Soc., Interface 22 (2025) 20240852, https://doi.org/10.1098/rsif.2024.0852.

[23] R.P. Panganiban, Y. Wang, J. Howrylak, V.M. Chinchilli, T.J. Craig, A. August, et al., Circulating microRNAs as biomarkers in patients with allergic rhinitis and asthma, J. Allergy Clin. Immunol. 137 (2016) 1423–1432, https://doi.org/10.1016/j.jaci.2016.01.029.

[24] C. Franz, P. Askjaer, W. Antonin, C.L. Iglesias, U. Haselmann, M. Schelder, et al., Nup155 regulates nuclear envelope and nuclear pore complex formation in nematodes and vertebrates, EMBO J. 24 (2005) 3519–3531, https://doi.org/10.1038/sj.emboj.7600825.

[25] X. Zhang, S. Chen, S. Yoo, S. Chakrabarti, T. Zhang, T. Ke, et al., Mutation in nuclear pore component NUP155 leads to atrial fibrillation and early sudden cardiac death, Cell 135 (2008) 1017–1027, https://doi.org/10.1016/j.cell.2008.10.022.

[26] K. Holzer, A. Ori, A. Cooke, D. Dauch, E. Drucker, P. Riemenschneider, et al., Nucleoporin Nup155 is part of the p53 network in liver cancer, Nat. Commun. 10 (2019) 2147, https://doi.org/10.1038/s41467-019-10133-z.

[27] Z.Q. Wang, Z.X. Wu, Z.P. Wang, J.X. Bao, H.D. Wu, D.Y. Xu, et al., Pan-cancer analysis of NUP155 and validation of its role in breast cancer cell proliferation, migration, and apoptosis, BMC Cancer 24 (2024) 353, https://doi.org/10.1186/s12885-024-12039-6.