*Original Article*

# Inhibition of lincRNA-Cox2 alleviates apoptosis and inflammatory injury of lipopolysaccharide-stimulated human bronchial epithelial cells via the Nrf2/HO-1 axis

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**This study mainly explored the role and mechanism of lincRNA-Cox2 in inflammatory injury of human bronchial epithelial cells. BEAS-2B cells were stimulated with lipopolysaccharide to establish an *in vitro* inflammatory injury model. Real-time polymerase chain reaction was used to detect lincRNA-Cox2 expression in LPS-stimulated BEAS-2B. Cell viability and apoptosis of cells were assessed using CCK-8 and Annexin V-PI double staining. The contents of inflammatory factors were determined by enzyme-linked immunosorbent assay kits. The protein levels of nuclear factor erythrocyte 2-related factor 2 and haem oxygenase 1 protein levels were measured by Western blot. The results showed that lincRNA-Cox2 was upregulated in LPS-stimulated BEAS-2B cells. lincRNA-Cox2 knockdown inhibited apoptosis and the release of tumour necrosis factor alpha, interleukin 1beta (IL-1β), IL-4, IL-5, and IL-13 in BEAS-2B cells. lincRNA-Cox2 overexpression had the opposite effect. lincRNA-Cox2 knockdown also inhibited LPS-induced oxidative damage in BEAS-2B cells. Further mechanistic studies showed that inhibition of lincRNA-Cox2 upregulated the levels of Nrf2 and HO-1, and si-Nrf2 reversed the effects of si-lincRNA-Cox2. In conclusion, lincRNA-Cox2 knockdown inhibited BEAS-2B apoptosis and the level of inflammatory factors by activating the Nrf2/HO-1 pathway.**

***Key Words*: lincRNA-Cox2, Nrf2/HO-1 pathway, BEAS-2B, airway inflammation, asthma**

Asthma is a heterogeneous disease involving chronic airway inflammation, typically characterised by recurrent changes in respiratory symptoms and reversible airflow limitation.[1] Chronic respiratory symptoms of asthma are particularly common in children.[2] In children with severe asthma, three phenotypes of airway inflammation have been described, including eosinophilic inflammation, paucigranulocytic inflammation and neutrophilic inflammation.[3] Airway inflammation is considered to be the most fundamental pathological change in the pathogenesis of asthma.[4] Inflammation of the airways disrupts the integrity of the epithelial barrier, thereby inducing and exacerbating asthma.[5] All levels of asthma are accompanied by varying degrees of airway inflammation.[6] Moreover, oxidative stress is also one of the pathogenesis of bronchial asthma.[7] Therefore, controlling airway inflammation and oxidative stress is a new direction in the treatment of asthma.

lincRNA-Cox2 is a newly observed non-coding RNA of 200 base pairs (bp) in length.[8] The role of lincRNA-Cox2 in immunity and inflammation is gaining increasing attention. lincRNA-Cox2 is localised in the cytoplasmic and nuclear compartments of macrophages.[9] It can promote the occurrence of inflammation by regulating the transcription of late inflammatory genes in macrophages.[10] lincRNA-Cox2 also affects IκBα degradation and is identified as a novel regulator of the nuclear factor kappa B (NF-κB) pathway.[11] Previous studies have found that lincRNA-Cox2 promotes uric acid-induced inflammatory damage in renal epithelial cell line by regulating the miR-150-5p/STAT1 axis.[12] In osteoarthritis, lincRNA-Cox2 knockout promotes chondrocyte proliferation and inhibits apoptosis.[13] These changes further underline the role of LincRNA-Cox2 in inflammation. Furthermore, lincRNA-Cox2 knockdown promotes Bacille Calmette-Guerin (BCG)-induced apoptosis in macrophages by promoting endoplasmic reticulum stress.[14] However, the role and mechanism of LincRNA-Cox2 in asthma remain unclear.

Nuclear factor erythrocyte 2-related factor 2 (Nrf2) is a major factor regulating redox homeostasis.[15] Nrf2 participate in asthma via regulation of oxidative stress in immune cells.[16] Clinical investigations show that the incidence of childhood bronchial asthma is related to the level of Nrf2.[17] Moreover, up-regulation of Nrf2 expression alleviates ovalbumin (OVA)-induced asthma in mice.[18] Nrf2 is a key factor involved in asthma attacks. Haem oxygenase 1 (HO-1) is an immunomodulatory molecule that reduces airway inflammation by reducing Th2- and Th17-mediated immune responses.[19] In addition, HO-1 is also a target gene of Nrf2; together, they regulate oxidative damage, inflammation, apoptosis and angiogenesis.[20] Activation of the Nrf2/HO-1 pathway can suppress oxidative stress and airway inflammation, and alleviate OVA-induced asthma.[21] Targeting the Nrf2/HO-1 pathway is also beneficial in mitigating reactive oxygen species (ROS)-mediated airway remodelling.[22] Therefore, Nrf2/HO-1 signalling may be crucial in the development of asthma.

In this study, lipopolysaccharide (LPS)-stimulated BEAS-2B were used as an *in vitro* model of airway inflammation. The study involved investigating the role of lincRNA-Cox2 in LPS-induced apoptosis and inflammatory injury in BEAS-2B cells and the mechanisms involved in the above processes.

## Materials and Methods

**Cell culture.** The human bronchial epithelial cell line (BEAS-2B) was purchased from the American Type Culture Collection

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(ATCC, Manassas, VA). Cells were incubated in Dulbecco's Modified Eagle Medium (DMEM, Thermo Fisher Scientific, Waltham, MA) containing 10% foetal bovine serum (Gibco, Carlsbad, CA). Culture conditions were set at 37°C and 5% $CO_2$.

**Cell transfection.** siRNA-lincRNA-Cox2, siRNA-Nrf2, siRNA (si-NC) and ov-lincRNA-Cox2 were synthesised by Hanbio (Shanghai, China). Lipofectamine 3000 (Invitrogen, Carlsbad, CA) was used for plasmid transfection.

**Cell Counting Kit-8 (CCK-8).** The CCK-8 assay (ab228554; abcam, Cambridge, UK) was used to detect the cell viability of BEAS-2B. Cells were incubated with 10 µl of CCK-8 solution for 2 h. Next, the absorbance was measured at 460 nm using a microplate reader.

**Enzyme-linked immunosorbent assay (ELISA).** The levels of inflammatory factors tumour necrosis factor alpha (TNF-α), interleukin 1beta (IL-1β), IL-4, IL-5, and IL-13 in medium were determined by ELISA kit. The levels of ROS, ATP, catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase (GPx) in cells were also measured by ELISA kits. The kit details are as follows: Human TNF-α ELISA Kit (E-EL-H0109c; Elabscience, Wuhan, China), Human IL-1β ELISA Kit (E-EL-H0149c; Elabscience), Human IL-4 ELISA Kit (ml058093; mlbio, Beijing, China), Human IL-5 ELISA Kit (ml058095; mlbio), Human IL-13 ELISA Kit (ml063719; mlbio), Reactive Oxygen Species detection Reagent kit (S0033M; Beyotime, Beijing, China), ATP Detection Kit (S0026; Beyotime), Human Catalase ELISA Kit (EH0643; Wuhan Fine Biotech, Wuhan, China), Total SOD Activity Detection Kit (S0101S; Beyotime), and Glutathione Peroxidase Detection Kit (S0056; Beyotime). All procedures were carried out in accordance with the manufacturers' instructions. Each experiment was repeated with at least three independent experiments.

**Apoptosis.** The collected cells were washed with cold phosphate-buffered saline (PBS), centrifuged and resuspended in binding buffer, and 5 µl of Annexin V-FITC (Solarbio, Beijing, China) was added per $1 \times 10^5$ cells. The solution was incubated at room temperature in the dark for 10 min. Then, 5 µl of PI was added and the solution was incubated for 5 min. The rate of apoptosis was assessed by flow cytometry (Beckman Coulter, Bria, CA).

**Reverse transcription–quantitative polymerase chain reaction (RT-qPCR).** Total RNA of BEAS-2B cells was extracted with the RNA Simple Total RNA Kit (DP419; Tiangen, Beijing, China). Complementary DNA (cDNA) was synthesised by reverse transcription using the First Strand cDNA Synthesis Kit (VWR International, Viese, Belgium). Rt-qPCR was performed using the DNA Engine Opticon™ Real-Time PCR System (MJ Research, New Haven, CT). The data were analysed using the $2^{-\Delta\Delta CT}$ method. The primer sequences were as follows:
lincRNA-Cox2: forward: 5'-TCCTTTCCCCCTCAA TTCTT-3';
reverse: 5'-TTTTCCCAATCTGCTTTGGT-3'.
GAPDH: forward: 5'-ACCCAGAAGACTGTGGATGG-3',
reverse: 5'-TCTAGACGGCAGGTCAGGTC-3'.

**Western blotting.** Protein samples were extracted with radioimmunoprecipitation assay (RIPA) lysis buffer, and the protein content in the supernatant was quantified with the BCA kit. Protein was separated on 10% acrylamide gels with sodium dodecyl sulphate–polyacrylamide gel electrophoresis and transferred to polyvinylidene difluoride (PVDF) membranes. After incubating in 5% non-fat milk for 2 h to block nonspecific protein binding, the membranes were incubated with anti-GAPDH (1:1,000), anti-Nrf2 (1:1,000) or anti-HO-1 (1:1,000) antibody overnight at 4°C. Then, the membrane was washed four times with Tris-buffered saline with Tween 20 (TBST).

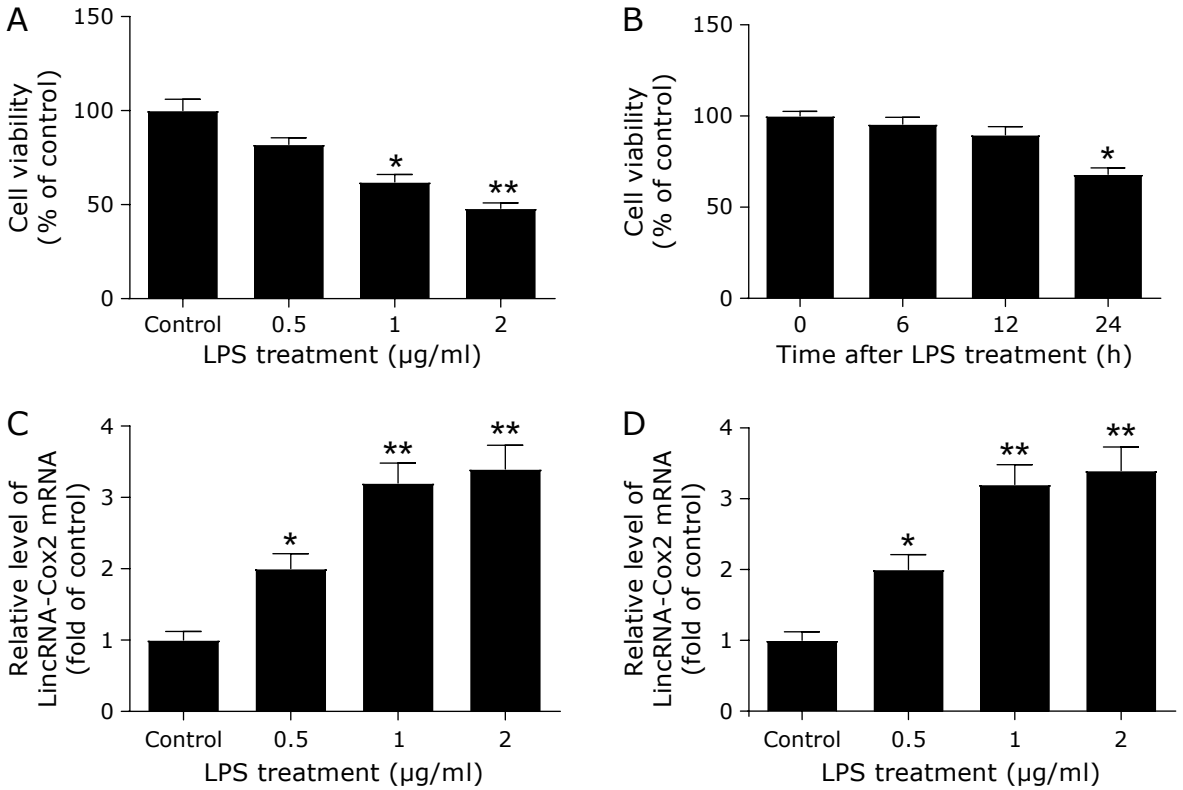


**Fig. 1.** Expression levels of LincRNA-Cox2 in LPS-stimulated BEAS-2B. BEAS-2B cells were treated with different concentrations of LPS (0.5, 1, 2 µg/ml) and different durations (0 h, 6 h, 12 h, 24 h). (A, B) Cell viability was assessed with the CCK-8 kit. (C, D). The expression level of LincRNA-Cox2 was detected by qPCR. *$p$<0.05, **$p$<0.01 compared to control group.

The membrane was incubated with horseradish peroxidase–conjugated secondary antibody (1:5,000) at room temperature. The membrane was incubated with highly sensitive chemiluminescent reagents (abcam) to visualise protein bands.

**Statistical analysis.** The data are presented as the mean of three independent biological replicates. Differences between two groups were analysed with an unpaired *t* test, and differences between more than two groups were analysed by one-way analysis of variance (ANOVA) combined with Tukey's test. $p<0.05$ was considered statistically significant.

## Results

**lincRNA-Cox2 was upregulated in LPS-stimulated BEAS-2B cells.** First, cells were stimulated with LPS to construct a model of bronchial epithelial cell injury. The viability of cells was significantly reduced after treatment with different concentrations and durations of LPS (Fig. 1A and B). The lincRNA-Cox2 level in BEAS-2B cells was significantly increased in a concentration- and time-dependent manner after LPS treatment (Fig. 1C and D). In the subsequent experiments, 1 μg/ml LPS was used to treat BEAS-2B cells for 12 h to establish an effective model of bronchial cell inflammation.

**lincRNA-Cox2 knockdown inhibited apoptosis and inflammatory cytokine release in BEAS-2B cells.** To evaluate the role of lincRNA-Cox2, its expression was silenced with siRNA. Silencing was confirmed RT-qPCR (Fig. 2A). Compared with the control group, LPS stimulation reduced the viability of BEAS-2B cells and promoted apoptosis (Fig. 2B and C). Low expression of lincRNA-Cox2 enhanced the viability of LPS-treated BEAS-2B cells and decreased apoptosis. In addition, LPS treatment significantly promoted the secretion of TNF-α, IL-1β, IL-4, IL-5, and IL-13 (Fig. 2D and E, $p<0.05$). However, lincRNA-Cox2 knockdown reversed these effects, effectively inhibiting the release of inflammatory cytokines.

**lincRNA-Cox2 overexpression promoted apoptosis and inflammatory cytokine release in BEAS-2B cells.** Next, lincRNA-Cox2 was overexpressed in BEAS-2B cells. RT-qPCR results showed that ov-lincRNA-Cox2 transfection elevated lincRNA-Cox2 expression more than 6-fold compared with the control group (Fig. 3A). lincRNA-Cox2 overexpression significantly reduced the viability of LPS-stimulated BEAS-2B cells (Fig. 3B). LPS treatment obviously increased the apoptotic ratio, and lincRNA-Cox2 overexpression further increased the apoptotic ratio (Fig. 3C). Furthermore, LPS stimulated BEAS-2B cells secreted more IL-1β, TNF-α, IL-4, IL-5, and IL-13. lincRNA-Cox2 overexpression exacerbated this stimulation and effectively increased the secretion of these cytokines (Fig. 3D and E, $p<0.05$).

**lincRNA-Cox2 knockdown inhibited LPS-induced oxidative damage in BEAS-2B cells.** Next, the levels of oxidative stress-related indicators were examined to determine the role of lincRNA-Cox2 in redox homeostasis. LPS-stimulated BEAS-2B cells produced more ROS, while lincRNA-Cox2 knockdown

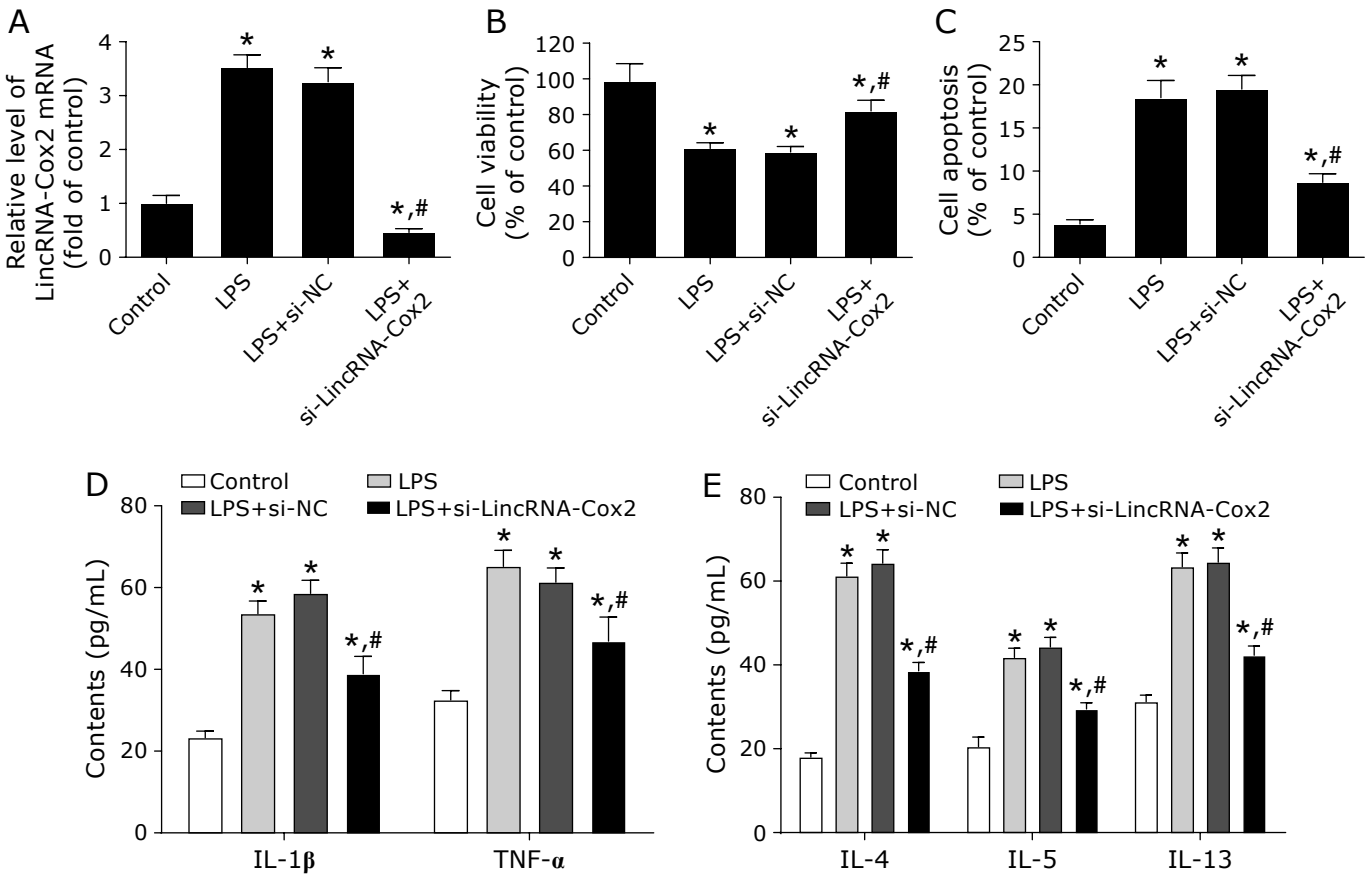


**Fig. 2.** Knockdown of LincRNA-Cox2 inhibited BEAS-2B cell apoptosis and inflammatory cytokine release. BEAS-2B cells were transfected with si-LincRNA-Cox2 for 24 h and then treated with LPS (1 μg/ml) for 12 h. (A) The transfection efficiency of si-LincRNA-Cox2 was detected by qPCR. (B) Cell viability was measured by CCK-8 kit. (C) Apoptosis ratio was detected by flow cytometry. (D) The content of TNF-α and IL-1β was determined by ELISA. (E) The content of IL-4, IL-5, and IL-13 was measured using ELISA. *$p<0.05$, compared with the control group; #$p<0.05$, compared with the LPS + si-NC group.


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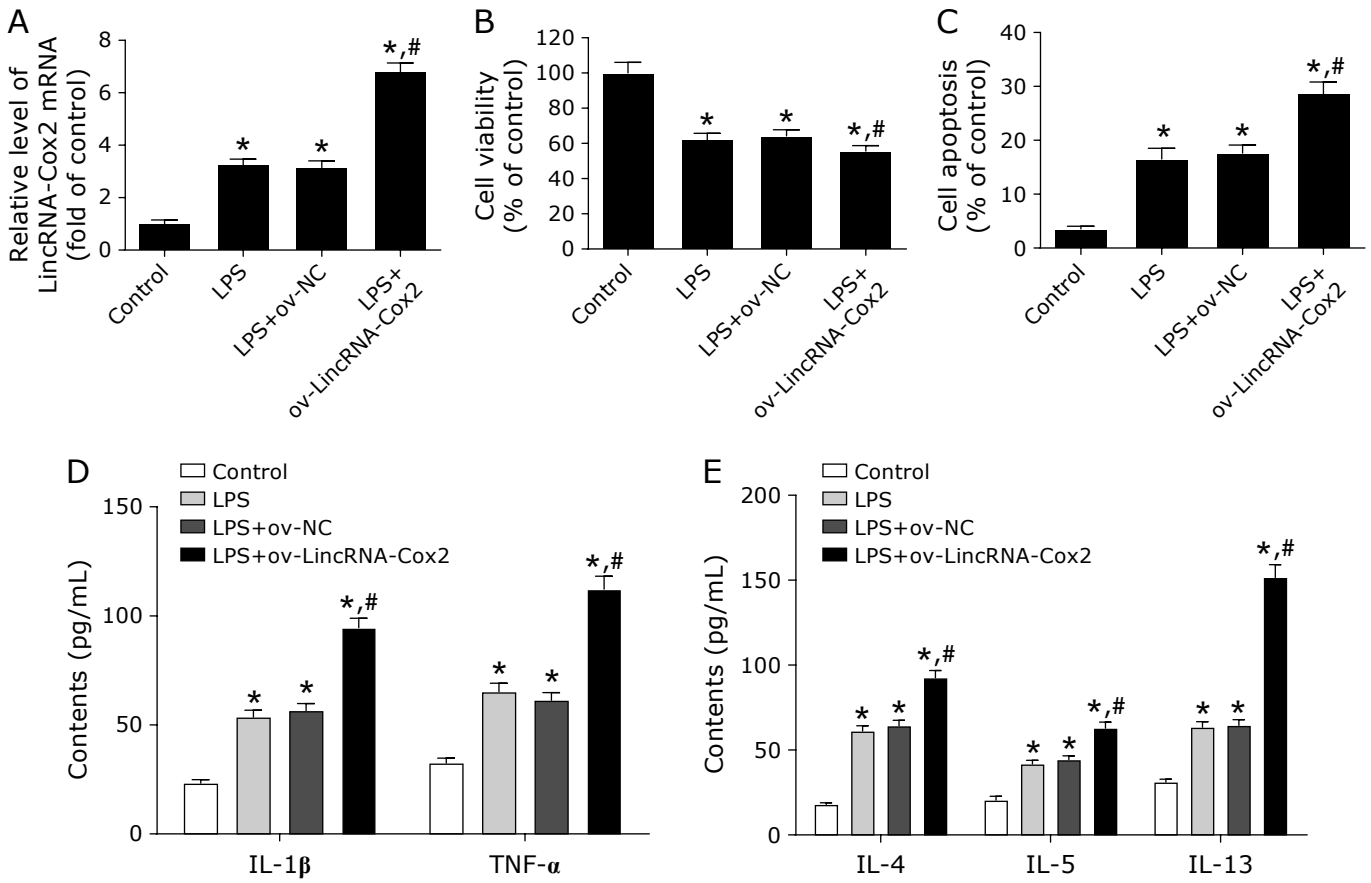


**Fig. 3.** Overexpression of LincRNA-Cox2 promoted apoptosis and inflammatory cytokine release in BEAS-2B cells. BEAS-2B cells were transfected with pcDNA3.1-LincRNA-Cox2 for 24 h and then treated with LPS (1 μg/ml) for 12 h. (A) qPCR was used to discover the transfection efficiency of ov-LincRNA-Cox2. (B) Cell viability was measured by CCK-8 kit. (C) Flow cytometry was used to detect the ratio of apoptosis. (D, E) The content of TNF-α, IL-1β, IL-4, IL-5, and IL-13 was determined by ELISA. *$p$<0.05, compared with the control group; $^{\#}p$<0.05, compared with the LPS + ov-NC group.

reduced the level of ROS (Fig. 4A). Furthermore, LPS treatment elevated ATP, CAT, SOD, and GPx in cells. Silencing lincRNA-Cox2 markedly raised the levels of these molecules (Fig. 4B–E). However, there was no significant difference in LincRNA-Cox2 expression between BEAS-2B cells treated with ROS scavengers (NAC) (Supplemental Fig. 1A and B*).

**lincRNA-Cox2 knockdown inhibited apoptosis and inflammatory factor levels in BEAS-2B cells by activating the Nrf2/HO-1 pathway.** Next, the mechanism of lincRNA-Cox2 in BEAS-2B cells was explored. si-lincRNA-Cox2 effectively enhanced the protein levels of Nrf2 and HO-1 in LPS-stimulated BEAS-2B (Fig. 5A–C). After co-treatment of cells with si-lincRNA-Cox2 and si-Nrf2, the levels of Nrf2 and HO-1 were increased. Moreover, si-Nrf2 reversed the effects of si-lincRNA-Cox2. Compared with the LPS + si-LincRNA-Cox2 group, co-treatment with si-lincRNA-Cox2 and si-Nrf2 markedly reduced cell viability and increased the ratio of apoptosis (Fig. 5D and E). Furthermore, lincRNA-Cox2 knockdown decreased the levels of IL-1β and TNF-α in LPS-stimulated cells, and si-Nrf2 reversed the decrease in inflammatory factor levels caused by si-lincRNA-Cox2 (Fig. 5F). The above results indicate that the Nrf2/HO-1 axis is involved in the regulation of lincRNA-Cox2 on BEAS-2B cells.

**Knockdown of LincRNA-Cox2 inhibited BEAS-2B cell oxidative damage by activating the Nrf2/HO-1 pathway.** Next, we explored the role of Nrf2/HO-1 in BEAS-2B cell oxidative damage. si-LincRNA-Cox2 effectively inhibited the ROS levels in LPS-stimulated BEAS-2B, and si-Nrf2 enhanced the levels of ROS (Fig. 6A). After co-treatment of cells with si-LincRNA-Cox2 and si-Nrf2, the levels of ATP were decreased, as well as si-Nrf2 reversed the effects of si-LincRNA-Cox2 (Fig. 6B). Furthermore, knockdown of LincRNA-Cox2 increased the levels of CAT, SOD, and GPx in LPS-stimulated cells, as well as si-Nrf2 reversed the effect of si-LincRNA-Cox2 (Fig. 6C–E). The above results indicated that the Nrf2/HO-1 axis was involved in the regulation of LincRNA-Cox2 on BEAS-2B cells.

## Discussion

Numerous studies have shown that reducing inflammation and oxidative stress in lung and airway epithelial cells is an effective strategy for improving asthma.[23] In asthma, inflammation and oxidative stress do not exist independently; rather, they coexist and interact.[4] Previous studies found that reducing airway inflammation and oxidative stress in the lungs can reduce symptoms of chronic asthma in mice.[24,25] Bronchial epithelial cells are important cells in inflammatory response. In addition to regulating defense homeostasis, bronchial epithelial cells also regulate airway inflammation by secreting a variety of defense proteins, such as mucin, cytokines and chemokines.[26] In this study, lincRNA-Cox2 was upregulated in LPS-stimulated BEAS-2B cells.

It has been gradually reported that lncRNAs affect asthma events by acting on immune response, inflammatory response and cytokine expression.[27] RNA-seq and loss-of-function

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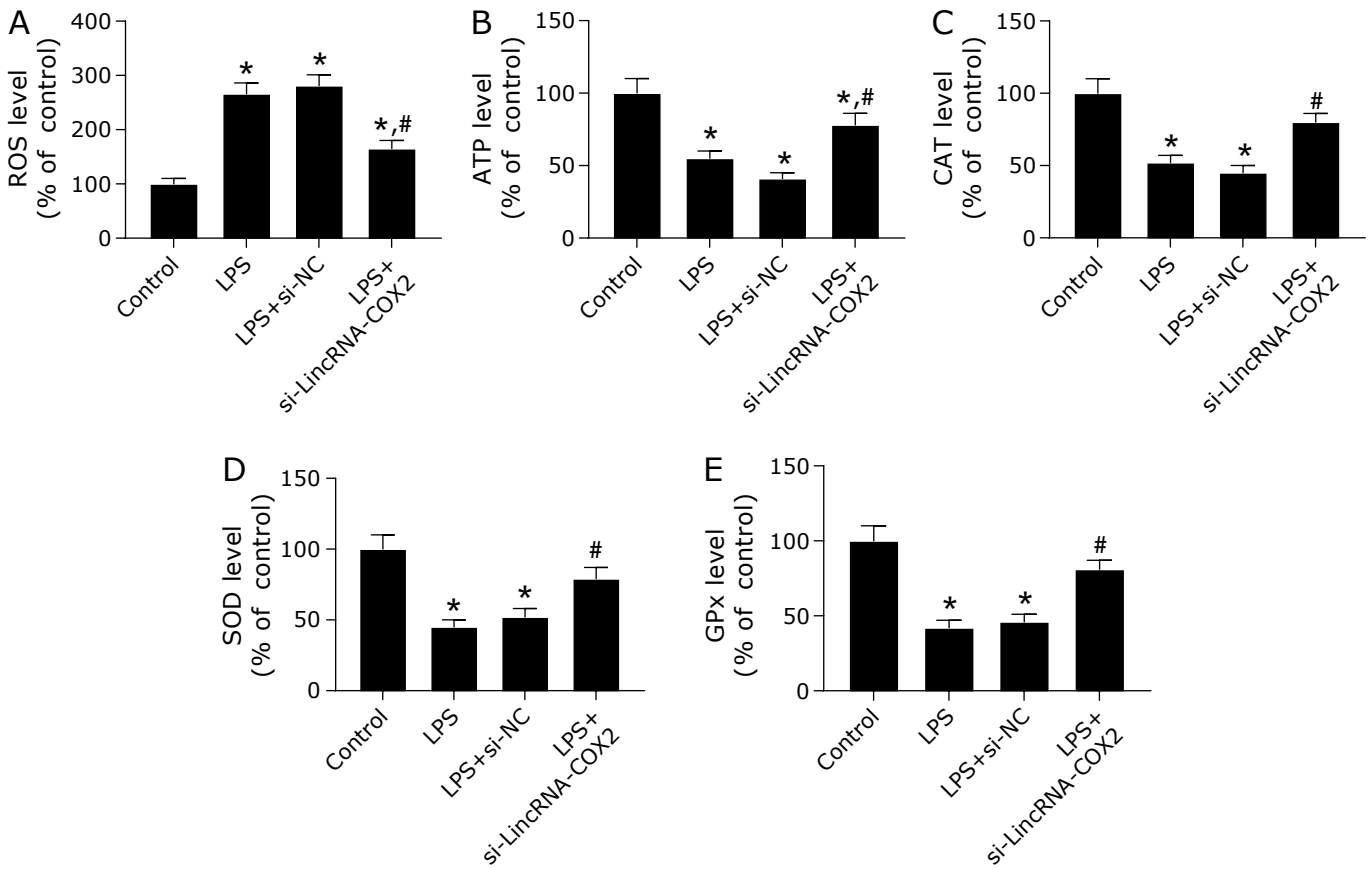


**Fig. 4.** Knockdown of LincRNA-Cox2 inhibited LPS-induced oxidative damage in BEAS-2B cells. BEAS-2B cells were transfected with si-LincRNA-Cox2 for 24 h and then treated with LPS (1 μg/ml) for 12 h. (A) The levels of ROS in BEAS-2B cells. (B) The levels of ATP in BEAS-2B cells. (C) The levels of CAT in BEAS-2B cells. (D) The levels of SOD in BEAS-2B cells. (E) The levels of GPx in BEAS-2B cells. *$p$<0.05, compared with the control group; #$p$<0.05, compared with the LPS + si-NC group.

analysis revealed that lincRNA-Cox2 has the ability to activate and repress different immune-related genes.[28] Genetic deletion of lincRNA-Cox2 alters the expression of immune-related genes in macrophages and mouse tissues.[29] It has been reported that lincRNA-Cox2 knockdown reduced the level and migration ability of proinflammatory cytokines by inhibiting the IL-6/JAK3/STAT3 signaling pathway. lincRNA-Cox2 knockdown also regulated nuclear translocation of nuclear factor NF-κB P65 and enhanced phagocytosis in RAW264.7 cells.[30] Thus, LincRNA-Cox2 can regulate the development of inflammation. Moreover, lincRNA-Cox2 knockdown alleviates macrophage and microglia inflammation by inhibiting NLRP3 inflammasome activation and by enhancing autophagy.[31] Intranasal delivery of extracellular vesicles of si-lincRNA-Cox2 reduces LPS-induced proliferation of mouse microglia.[32] This is critical for reducing neuroinflammation in the brain. A recent study showed the important role of lincRNA-Cox2 in the respiratory system. lincRNA-Cox2 is upregulated in LPS-induced alveolar macrophages and regulates the level of inflammation and lung homeostasis in the state of acute lung injury.[33] Therefore, lincRNA-Cox2 may play a role in airway inflammation. The findings from this study confirmed that lincRNA-Cox2 knockdown inhibits apoptosis and reduced inflammation and oxidative damage. On the other hand, lincRNA-Cox2 overexpression has the opposite effect.

The co-involvement of multiple immune cells and cytokines during an asthma attack makes asthma highly heterogeneous.[34] The inflammatory response of asthma is very complex, and the Th1/Th2 imbalance is an important in asthma pathogenesis.[35] IL-4, IL-5, and IL-13 are Th2 cytokines, and elevated Th2 cytokines can exacerbate airway inflammation and lead to asthma attacks.[36] Anti-cytokine therapy can inhibit the inflammatory response from the source, and the inhibition of cytokines IL-4, IL-5, and IL-13 is expected to become a new therapeutic target for asthma. For example, overexpression of miR-200a and miR-200b suppressed the expression of IL-4, IL-5, and IL-13, thereby inhibiting the progression of asthmatic inflammation.[37] Furthermore, monoclonal antibody biologics that target and inhibit the Th2 cytokines IL-4, IL-5, and IL-13 have considerable potential in the treatment of severe asthma.[38] In the present study, lincRNA-Cox2 knockdown inhibited the release of TNF-α, IL-1β, IL-4, IL-5, and IL-13 in LPS-stimulated BEAS-2B cells, and lincRNA-Cox2 overexpression promoted the release of these inflammatory factors. Taken together, inhibition of lincRNA-Cox2 seems to attenuate cellular inflammation in BEAS-2B by regulating the secretion of TNF-α, IL-1β, IL-4, IL-5, and IL-13.

Nrf2/HO-1 signalling is an important pathway involved in respiratory diseases, especially allergic asthma. The mechanisms by which multiple compounds alleviate asthma are related to Nrf2/HO-1 signalling. 18β-Glycyrrhetinic acid suppresses OVA-induced allergic airway inflammation by enhancing the Nrf2/HO-1 pathway.[39] Curcumin down-regulates the level of TNF-α, IL-1β, and IL-6 through the Nrf2/HO-1 pathway, and alleviated airway inflammation in asthmatic mice.[40] These events provide powerful directions for the treatment of asthma. Airway inflam-


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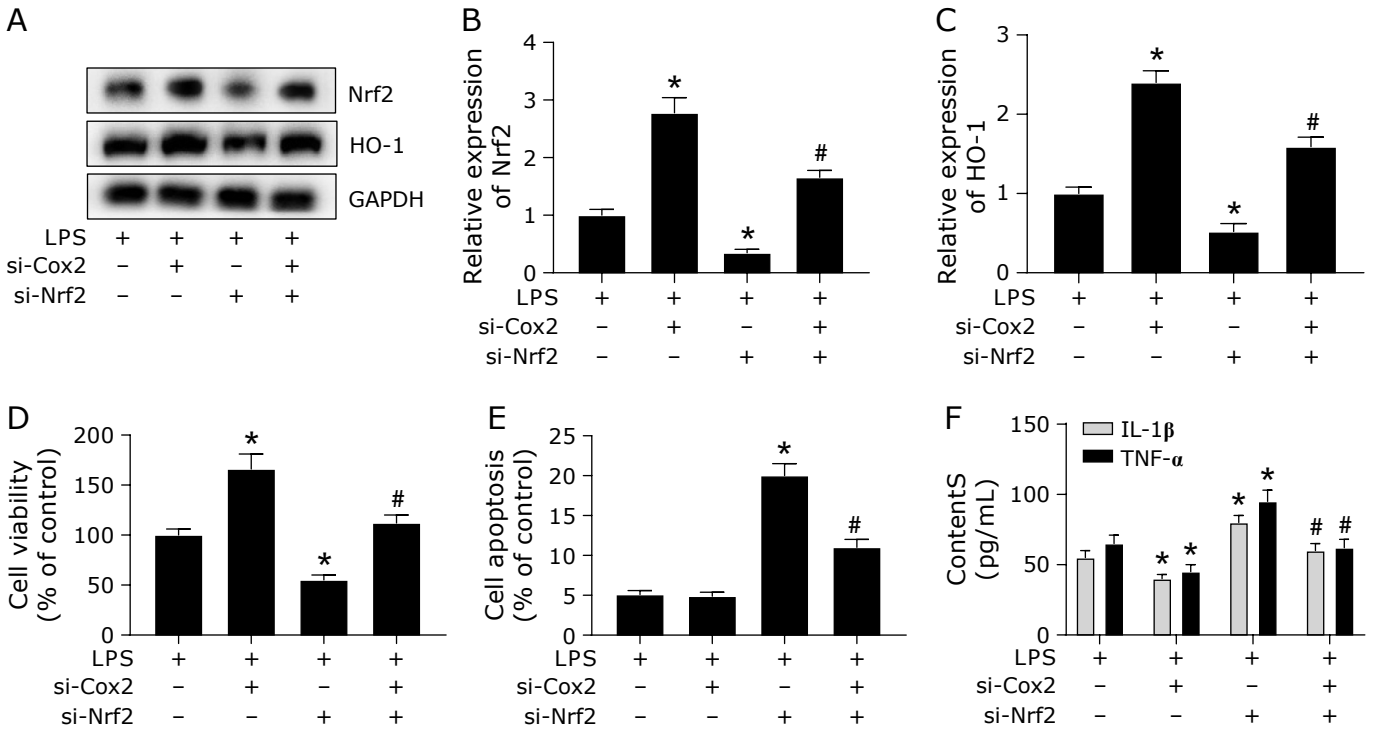


**Fig. 5.** Knockdown of LincRNA-Cox2 inhibited BEAS-2B cell apoptosis and the levels of inflammatory factors by activating the Nrf2/HO-1 pathway. BEAS-2B cells were transfected with si-LincRNA-Cox2 or si-Nrf2 for 24 h and then treated with LPS (1 μg/ml) for 12 h. (A–C) Protein expression levels of Nrf2 and HO-1. (D) Cell viability was measured using the CCK-8 kit. (E) Apoptosis ratio was detected by flow cytometry. (F) The levels of IL-1β and TNF-α in medium. *$p$<0.05, compared with the control group; $^{\#}p$<0.05, compared with the LPS + si-LincRNA-Cox2 or LPS + si-Nrf2 group.

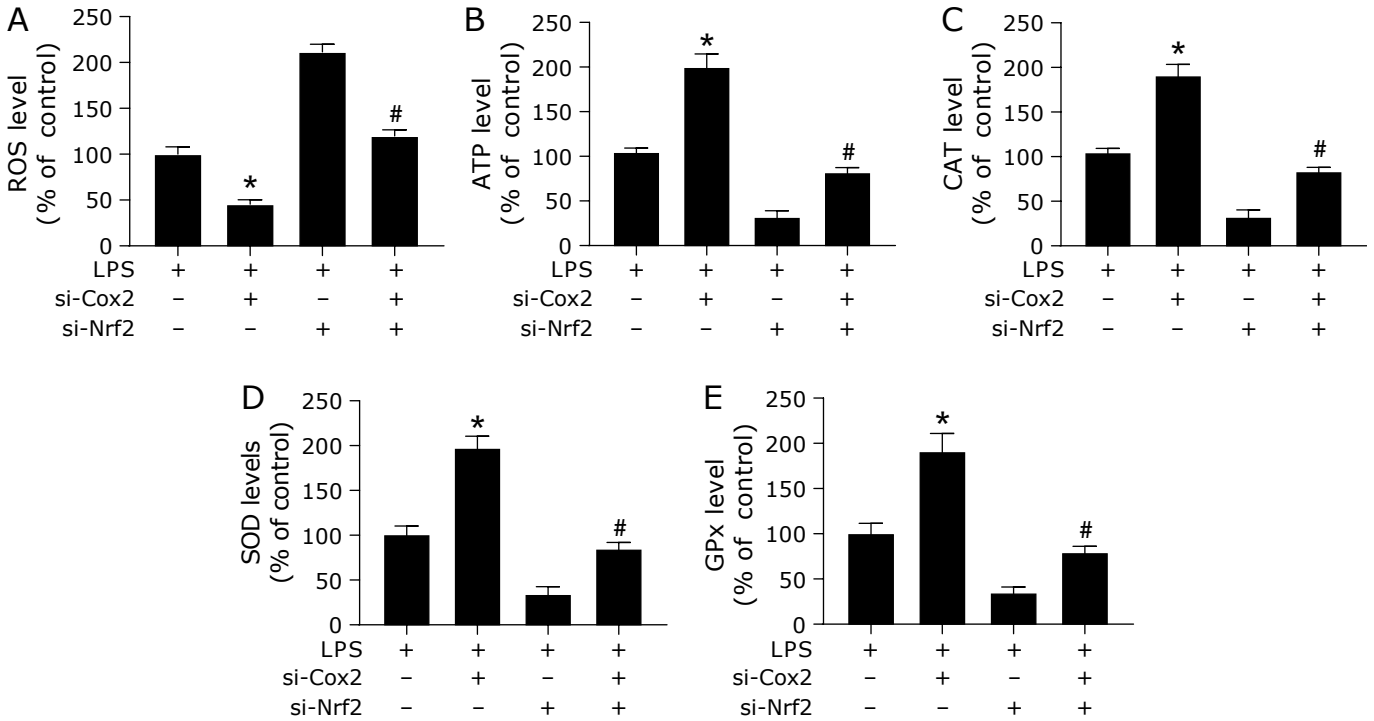


**Fig. 6.** Knockdown of LincRNA-Cox2 inhibited BEAS-2B cell oxidative damage by activating the Nrf2/HO-1 pathway. BEAS-2B cells were transfected with si-LincRNA-Cox2 or si-Nrf2 for 24 h and then treated with LPS (1 μg/ml) for 12 h. (A) The levels of ROS in BEAS-2B cells. (B) The levels of ATP in BEAS-2B cells. (C) The levels of CAT in BEAS-2B cells. (D) The levels of SOD in BEAS-2B cells. (E) The levels of GPx in BEAS-2B cells. *$p$<0.05, compared with the control group; $^{\#}p$<0.05, compared with the LPS + si-LincRNA-Cox2 or LPS + si-Nrf2 group.

mation and hyperresponsiveness are important triggers of asthma attacks. Studies have shown that Nrf2$^{-/-}$ and HO-1$^{-/-}$ mice present airway hyperresponsiveness, and airway hyperresponsiveness is closely related to oxidative stress.[41] Formononetin has been reported to inhibit airway inflammation and oxidative stress in asthma model mice, and the underlying mechanism is activation of the Nrf2/HO-1 pathway.[42] Thus, upregulating the Nrf2/HO-1 antioxidant signalling pathway seems to be a feasible strategy for asthma relief.

To gain a deeper understanding of the underlying mechanisms underlying the anti-inflammatory and antioxidant effects of lincRNA-Cox2 in asthma, the relationship between lincRNA-Cox2 and Nrf2/HO-1 signalling was examined. Inhibition of lincRNA-Cox2 increased the levels of Nrf2 and HO-1, while si-Nrf2 reversed the effects of si-lincRNA-Cox2. Compared with the si-lincRNA-Cox2 group, co-treatment with si-lincRNA-Cox2 and si-Nrf2 significantly decreased cell viability and increased the ratio of apoptosis. Furthermore, lincRNA-Cox2 knockdown reduced the levels of IL-1β and TNF-α in LPS-stimulated cells, and si-Nrf2 reversed the reduction in inflammatory factor levels caused by si-lincRNA-Cox2. These data suggest that lincRNA-Cox2 knockdown suppresses inflammatory factor levels in BEAS-2B cells by activating the Nrf2/HO-1 pathway.

In conclusion, lincRNA-Cox2 was upregulated in LPS-stimulated BEAS-2B cells. lincRNA-Cox2 knockdown inhibited apoptosis and decreased the levels of inflammatory factors and oxidative damage. It is possible that low expression of lincRNA-Cox2 inhibits BEAS-2B apoptosis and inflammatory factor release by activating the Nrf2/HO-1 pathway. lincRNA-Cox2 may be a potential target for the treatment of asthma. Although we actively explored the role of lincRNA-Cox2 in BEAS-2B cells, there are still shortcomings in this study. To verify the precise relationship between lincRNA-Cox2 and asthmatic airway inflammation, further evidence from animal experiments and clinical data are needed.

## Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by XL, LY, and YZ. The first draft of the manuscript was written by HY and JL and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.


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## Availability of Data and Materials

All data generated or analyzed during this study are included in this published article.

## Ethics Approval and Consent to Participate

Not applicable.

## Conflict of Interest

No potential conflicts of interest were disclosed.

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