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Original Article

Role of dendritic cells in consistency between upper and lower airway inflammatory responses: animal experimental studies

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Abstract: In recent years, studies on the consistency between upper and lower airway inflammation have been receiving more attention; however, the function and mechanism of dendritic cells (DCs) in this context are still not clear. In the present research, we studied the function and mechanism of DCs in the consistency between the upper and lower airway inflammatory responses. CD80, CD86, interferon gamma (IFN-γ), and interleukin 4 (IL-4) expression levels in nasal mucosa and lung tissues in a rat model of allergic rhinitis (AR) and asthma (AS) were detected to analyze the relationship between CD80 and CD86 expression levels and upper and lower airway inflammation and IL-4 and IFN-γ expression. The numbers of CD80, CD86, and IL-4-positive cells in the nasal mucosa and lung tissues in the AR and AS experimental groups were significantly higher; however, the number of IFN-γ-positive cells was significantly lower. CD80 and CD86 expression levels in the nasal mucosa positively correlated with their expression in lung tissues. CD80 and CD86 in the nasal mucosa and lung tissues positively correlated with IL-4 and negatively correlated with IFN-γ. DCs participated in the development of upper and lower airway inflammation. Then, DCs and the upper and lower airway inflammatory responses were consistent. The mechanism underlying of DCs in the consistency between the upper and lower airway inflammatory responses might be associated with its induction of the helper T (Th)2 cytokine-dominant expression, thus breaking the original expression balance between Th1 and Th2 cytokines.

Keywords: Allergic rhinitis, asthma, dendritic cells, interferon-gamma, interleukin-4

Introduction

Allergic rhinitis (AR) is an inflammatory disease of airway hyperresponsiveness caused by seasonal or perennial reactions to specific allergens mediated by immunoglobulin E (IgE) [1]. Its clinical symptoms include nasal itching, sneezing, runny nose, watery eyes, nasal congestion, and rhinostegnosis [2]. AR can also induce systemic inflammation and a variety of comorbidities, such as asthma (AS), nasal polyps, sinusitis, serous otitis media, and sleep disorders [3]. Studies have shown that approximately 20%-30% of AR patients also have AS and that approximately 50% AS patients also have AR [4]. Therefore, to accurately understand and treat inflammatory responses in the upper and lower airways, Simons suggested that AR and AS should be regarded as a complete disease entity called allergic rhinobronchitis [5]. In addition, according to the "one airway, one disease" hypothesis, the upper and lower airways might have a common basis of susceptibility to allergic reactions [6].

Clinically, the occurrence of AR symptoms in patients usually proceeds AS; however, the development of these two disorders might result from similar mechanisms. The connection between the upper and lower airways is achieved by mucosa, whose surface is covered with ciliary epithelium; the basement membrane in mucosa is continuous. After being inhaled by allergic individuals, sensitizing allergens first induce the activation of antigen-presenting cells (APCs) and T lymphocytes in the

local nasal cavity. These activated cells then migrate to regional lymph nodes and colonize the mucosa in the nasal cavity and the bronchi through efferent lymphatic vessels, thus causing similar sensitization statuses and common inflammatory statuses in the upper and lower airway mucosa [7, 8].

Allergic disease is a type of immunological disease with an imbalance in the helper T (Th)1/Th2 ratio, which indicates that the immune cytokines presenting Th1/Th2 phenotypes will undergo changes to cause the reduction of Th1 cytokines such as interferon gamma (IFN-γ) and interleukin 2 (IL-2), the increase of cytokines produced by Th2 such as IL-4 and IL-5, the penetration of specific IgE, and the activation of eosinophils (EOS). B7 costimulatory molecules can regulate the Th1/Th2 balance. The B7-1 (CD80) and B7-2 (CD86) costimulatory molecules are expressed in specific APCs, including activated B cells, monocytes, macrophages, dendritic cells (DCs) [9], Langerhans' cells, keratinocytes, and EOS. DCs are important APCs in this process and play very important roles. They have extraordinary capacities to induce immune responses. More and more evidence has indicated that DCs assist and guide the differentiation of naïve $CD4^+$ T cells into Th1 or Th2 effector/memory cells to produce cytokines such as IFN-γ, IL-4, IL-5, and IL-13 [10].

In recent years, studies on the consistency between upper and lower airway inflammation have been receiving more attention; however, the function and mechanism of DCs in this context are still not clear. This study aimed to detect the expression levels of CD80, CD86, IL-4, and IFN-γ in nasal mucosa and lung tissues in a rat model of AR and AS to study DC expression profiles in the development of upper and lower airway inflammation. Thus, whether there was consistency between upper and lower airway inflammation can be determined from the perspective of DCs. In addition, the function and the possible mechanism of the involvement of DCs in the consistency between upper and lower airway inflammation were further studied to provide effective targets and theoretical bases for the prevention and treatment of allergic diseases.

Materials and methods

Experimental animals and materials

A total of 40 6- to 8-week-old Sprague-Dawley (SD) rats with body weights between 160 g and 200 g were provided by Tengxin Biotechnology Co., Ltd. (Chongqing, China). All experiments were performed in accordance with the appropriate institution or the National Research Council Guide for the care and use of laboratory animals and approved by the Affiliated Hospital of Southwest Medical University. Rabbit anti-rat polyclonal antibodies against CD80, CD86, IL-4, IFN-γ, and ovalbumin (OVA) were all purchased from Beijing Biosynthesis Biotechnology Co., Ltd. (Beijing, China). Concentrated streptavidin-biotin complex (SABC) and 3,3'-diaminobenzidine (DAB) developing reagents were purchased from Wuhan Boster Biological Technology, Ltd. (Wuhan, China). Aluminum hydroxide was purchased from KeLong Chemical (Chengdu, China).

Model establishment

Rats were divided into the AR group, the AS group, the AR control group, and the AS control group using the random number table method, with 10 animals in each group. Animals were strictly raised in an SPF grade laboratory. The AR group was administered 20 mg of OVA dissolved in 1 ml of normal saline. Intraperitoneal injection was performed using 30 mg of aluminum hydroxide as the adjuvant. The injection was performed every other day continuously 8 times (15 d). Starting from day 16, 100 μl of 5% OVA solution in normal saline (50 mg of OVA and 50 mg of aluminum hydroxide were mixed evenly in 1 ml of normal saline to prepare a 5% OVA solution) was dropped intranasally every time, with 50 μl/side continuously for 10 d. Rats in the control group received an intraperitoneal injection of 30 mg of aluminum hydroxide in 1 ml of normal saline and intranasal dropping of normal saline; the time course was the same as that in the AR group. Nasal scratching actions, sneezing, nasal discharge, and the feeding behavior of animals were observed after each nasal provocation.

The 10 rats in the AS group received an intraperitoneal injection of 1 ml of 5% OVA solution

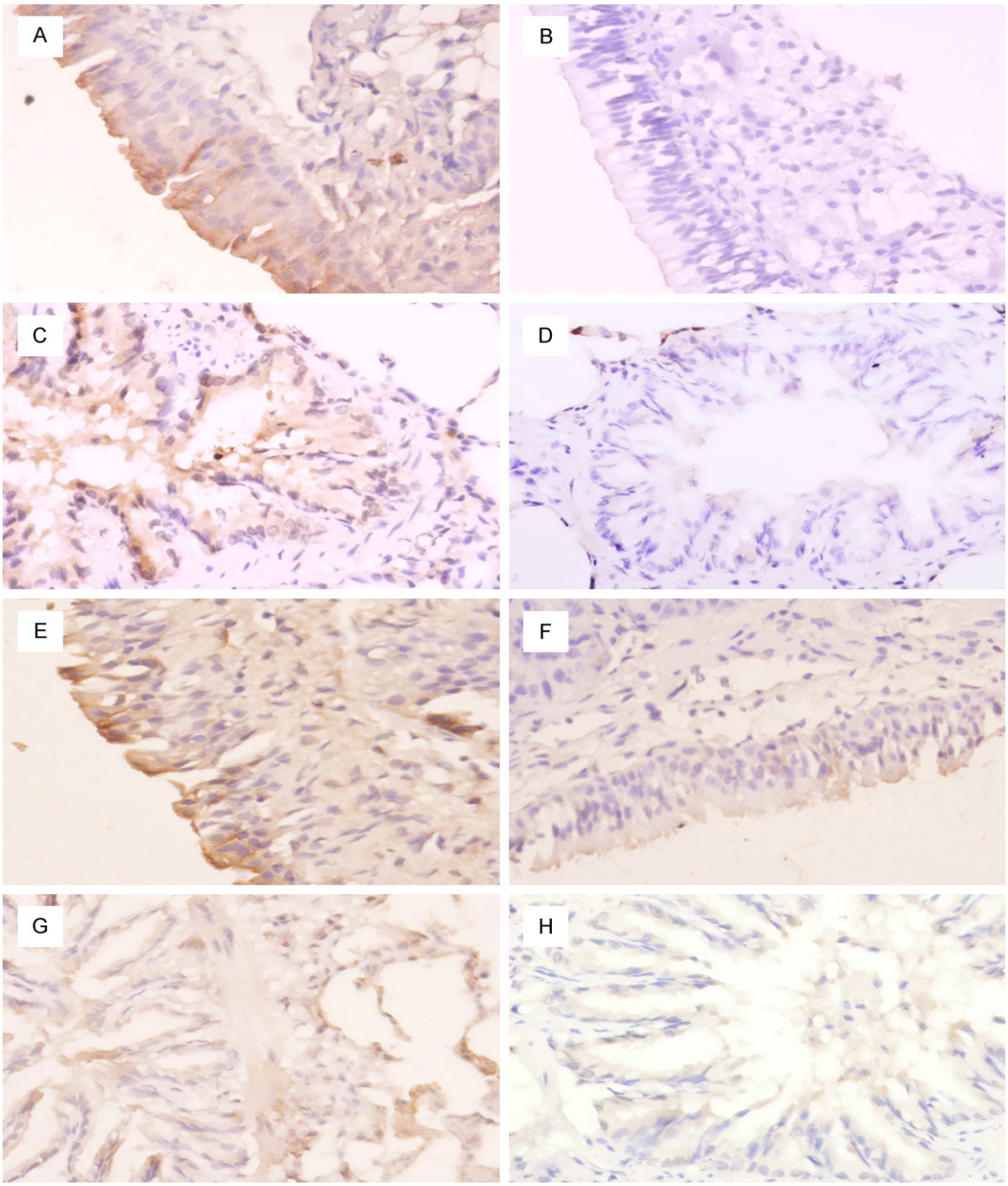

Figure 1. Immunostaining of CD80 positive cells in the nasal mucosa and lung tissues in the the AR and AS experimental and control groups. A, B, E and F: CD80 positive cells were mainly located in the epithelial layer and the lamina propria of the nasal mucosa. A small proportion of these cells were found surrounding glands and blood vessels. Immunohistochemistry detection produced light yellow or brown-yellow staining in cytoplasms and cell membranes (400×). C, D, G and H: CD80 positive cells were mainly located in the alveolar epithelial cells and bronchial mucosa epithelial cells. A small proportion of these cells were also found surrounding glands and blood vessels. Cytoplasms and cell membranes had light yellow or yellow-brown staining (400×). A-D: Refer to the AR groups; E-H: Refer to the AS groups.

on days 1, 8, and 15. On day 16, rats in the experimental group received 30 min of atomization inhalation of vaporized 1% OVA solution (10 mg of OVA and aluminum hydroxide each

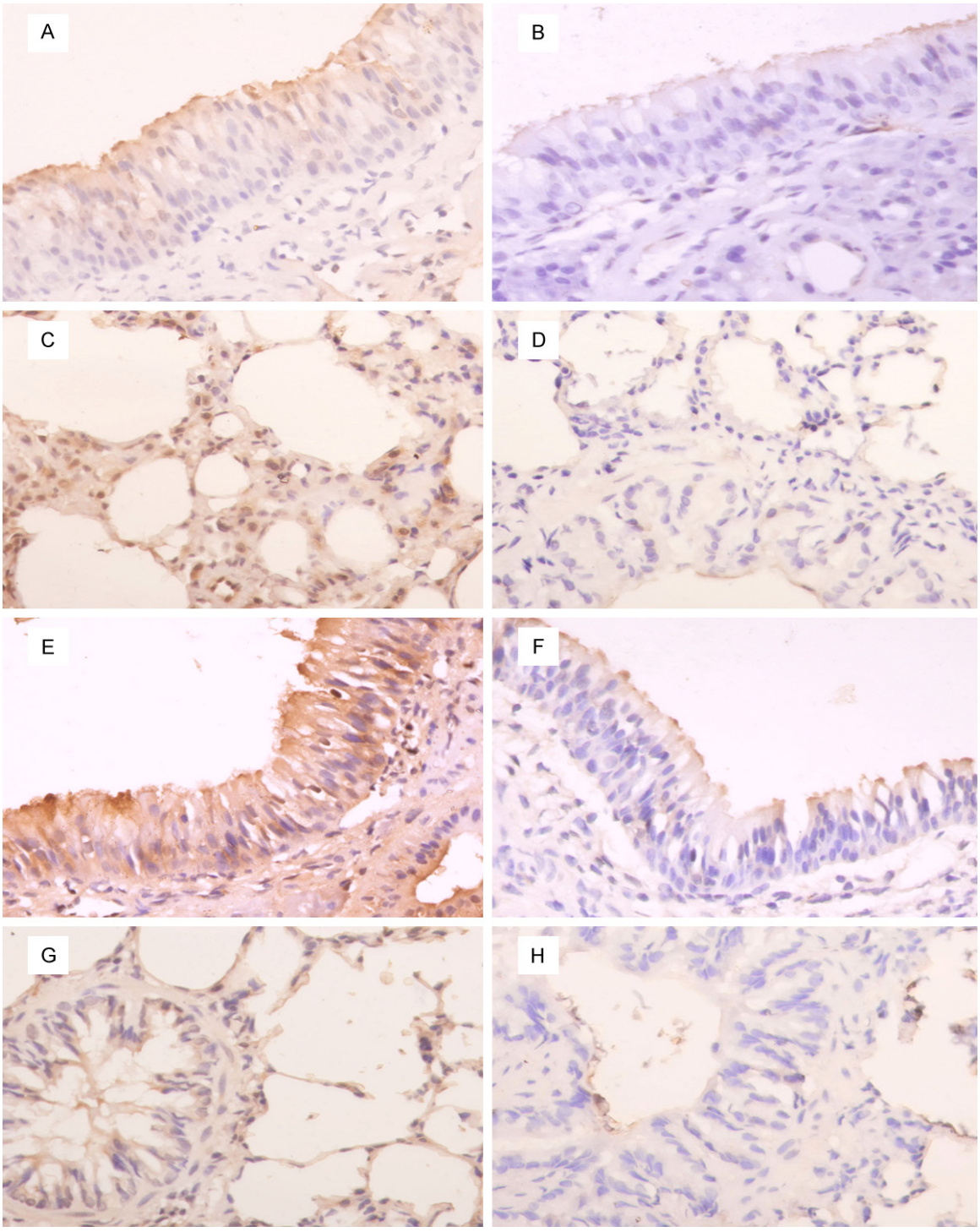

Figure 2. Immunostaining of CD86 positive cells in the nasal mucosa and lung tissues in the AR and AS experimental and control groups. A, B, E and F: In the nasal mucosa, CD86 positive cells were mainly located in the epithelial layer and the lamina propria with light yellow or yellow-brown staining in cytoplasms and cell membranes (400×). C, D, G and H: In the lung tissues, CD86 positive cells were mainly located in the alveolar epithelial and bronchial mucosa epithelial. The stainings were similar to the former (400×). A-D: Refer to the AR groups; E-H: Refer to the AS groups.

were mixed evenly in 1 ml of normal saline) once per day continuously for 10 d. Rats in the control group received vaporized normal saline instead of OVA solution; intraperitoneal injection and atomization inhalation were performed using the same method with equal amounts

Table 1. The numbers of CD80 and CD86 positive cells in the nasal mucosa and lung tissues in the AR and AS experimental and control groups

Groups	Number (n)	CD80		CD86	
		Nasal mucosa	Lung tissue	Nasal mucosa	Lung tissue
AR experimental group	10	23.94±4.90	25.62±4.02	24.42±4.67	22.94±4.34
AR control group	10	2.24±0.45	2.38±0.58	2.06±0.53	2.04±0.73
AS experimental group	10	21.90±3.05	25.02±3.48	22.42±3.70	25.10±4.58
AS control group	10	2.16±0.87	2.54±0.86	1.90±0.54	2.14±0.35
t value[a]		13.943[c]	18.075[c]	15.049[c]	15.004[c]
t value[b]		19.661[c]	19.846[c]	17.377[c]	15.808[c]

Abbreviations: AR, allergic rhinitis; AS, asthma. t value[a]: AR group compared with control group; t value[b]: AS group compared with control group; all [c]$P < 0.05$.

and the same time course. After each atomization inhalation, face-scratching actions, breathing, and the feeding behaviors of animals were observed.

Observation of animal behaviors

Criteria for evaluation of the AR model: after the last nasal sensitization, nasal scratching actions, sneezing, nasal discharge, and the feeding behaviors of animals were observed immediately and after 30 min. The above indicators were scored using the quantitative scoring method of totaling itemized scores: a total score of more than 5 points indicated that the model was established successfully. The scoring methods were as follows: ① nasal scratching action (nasal itching) -no nasal scratching, light nasal scratching for 1-2 times, and severe scratching around the nose were ranked as 0, 1, and 2 points, respectively; ② sneezing-no sneezing, sneezing 1-3 times, 4-10 times, and more than 11 times were ranked as 0, 1, 2, and 3 points, respectively; ③ nasal discharge (clear nasal mucus) -no nasal secretions, secretion to the nostrils, secretion past the front nostrils, and nasal mucus all over the face were ranked 0, 1, 2 and 3 points, respectively; and ④ feeding behavior-free movement, quiet and low motility, slow motion and proneness and motionlessness were ranked as 0, 1, 2, and 3 points, respectively.

Criteria for evaluation of the AS model: after the last provocation, nasal scratching actions, sneezing, nasal discharge, and the feeding behaviors of animals were observed. The above indicators were scored using the quantitative scoring method of totaling itemized scores; a total score of more than 5 points indicated that the model was established successfully. The scoring methods were as follows: ① head and face scratching action-no head and face scratching, light head and face scratching 1-2 times, and severe head and face scratching were ranked as 0, 1, and 2 points, respectively; ② breathing-stable breath, shortness of breath, difficulties in breathing, difficulties in breathing combined with wheezing sounds or mucus secretion, and irregular breathing or sudden death were ranked as 0, 1, 2, 3, and 4 points, respectively; and ③ feeding behavior-free movement, quiet and low motility, slow motion and proneness and motionlessness were ranked as 0, 1, 2, and 3 points, respectively.

Specimen collection and immunohistochemical staining

Rats in the AR group and its control group were sacrificed 30 min after the last provocation, while rats in the AS group and its control group were sacrificed 2 h after atomization inhalation. After the rats were anesthetized using 2% sodium pentobarbital and decapitated, nasal mucosa and lung tissues were collected, embedded in paraffin, and sectioned. The SABC method was used for immunohistochemistry according to the specific steps in the instructions included with the reagent kit. In each batch of section staining, the primary antibody was replaced with phosphate-buffered saline (PBS) to be used as the negative control.

Cell counting method and statistical analysis

The results were obtained by two doctors individually without knowing either the conditions

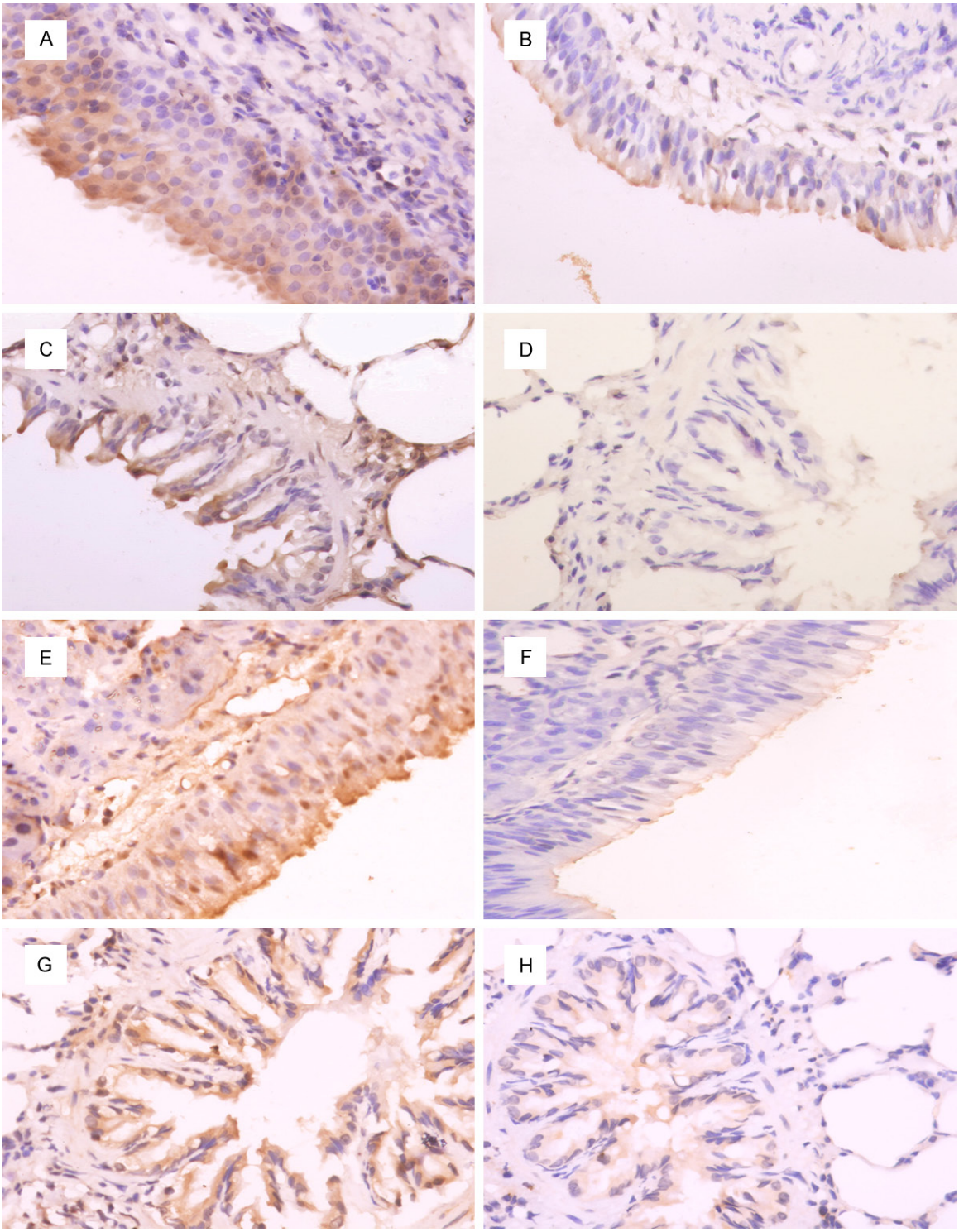

Figure 3. Immunostaining of IL-4 positive cells in the nasal mucosa and lung tissues in the AR and AS experimental and control groups. A, B, E and F: Immunostaining of IL-4 positive cells (light yellow or yellow-brown cytoplasms and cell membranes) were expressed in the epithelial layer and the lamina propria of the nasal mucosa (400×). C, D, G and H: Positive IL-4 expression was detected in the alveolar epithelial cells and bronchial mucosa epithelial cells, with yellow-brown or yellow staining (400×). A-D: Refer to the AR groups; E-H: Refer to the AS groups.

of the pathological sections or the experimental information. Five regions were randomly selected under a low-power field (10×). The counting grid was installed onto the objective

Table 2. The numbers of IL-4 and IFN-γ positive cells in the nasal mucosa and lung tissues in the AR and AS experimental and control groups

Groups	Number (n)	IL-4		IFN-γ	
		Nasal mucosa	Lung tissue	Nasal mucosa	Lung tissue
AR experimental group	10	141.1±10.73	138.46±12.31	2.96±0.34	2.78±0.33
AR control group	10	34.96±4.80	36.86±5.18	32.62±4.33	35.46±5.59
AS experimental group	10	139.60±10.50	139.24±10.45	2.58±0.52	2.66±0.42
AS control group	10	34.38±5.13	34.10±4.73	35.24±4.02	37.54±4.33
t value[a]		28.570[c]	24.065[c]	21.585[c]	18.440[c]
t value[b]		28.468[c]	28.980[c]	25.474[c]	25.354[c]

Abbreviations: AR, allergic rhinitis; AS, asthma; IL-4, Interleukin-4; IFN-γ, Interferon-gamma. t value[a]: AR group compared with control group; t value[b]: AS group compared with control group; all [c]$P < 0.05$.

lens, and cell counting was performed under a high-power field (40×). The mean value was calculated, and the results were presented as means ± standard deviations ($\bar{x} \pm s$). Statistical analyses were performed using SPSS19.0 statistical software. Comparisons of mean values of measurement data between two groups were performed using the independent-samples *t*-test. Statistical analysis of correlations was performed using the linear correlation method. The significance level α equals to 0.05; $P < 0.05$ indicates statistical significance.

Results

Model evaluation

Rats in the AR group presented the following typical AR symptoms on days 4 and 5 after provocation: frequent sneezing (> 10/p/min), nasal scratching, a large amount of clear mucus, and reduced feeding. Symptoms were gradually relieved after 2 h, and the total itemized scores were all larger than 5 points. Rats in the AR control group had only mild sneezing and nasal scratching actions. After 5-7 min of atomization inhalation, rats in the AS group had head and face scratching followed by presentations of increased and deepened breathing, nodding breathing, quiet and low motility, arched back, and forelimb retraction. For severe cases, mouth and lip cyanosis, delayed motion, proneness or motionlessness, and wheezing sounds were observed until the end of the provocation period. The total itemized scores after the last atomization inhalation were all larger than 5 points. Rats in the AS control group only had symptoms of mild nasal and face scratching and increased breathing. There was no mortality for any of the animals.

CD80 and CD86 expression in the AR and AS experimental and control groups

CD80- and CD86-positive cells were mainly located in the epithelial layer and the lamina propria of the nasal mucosa and in the alveolar epithelial cells and bronchial mucosa epithelial cells. Cytoplasm and cell membranes had light yellow or yellow-brown staining. The CD80 and CD86 expression levels in the nasal mucosa and lung tissues between the AR and AS experimental and control groups were significantly different (all $P < 0.05$) (**Figures 1**, **2**; **Table 1**).

IL-4 and IFN-γ expression in the AR and AS experimental and control groups

Positive IL-4 expression was detected in numerous cell types, including inflammatory cells, nasal epithelial cell, alveolar epithelial cells, bronchial mucosa epithelial cells, fibroblasts, glands and endothelial cells, which had yellow-brown or yellow staining. The numbers of IL-4-positive cells in the AR and AS experimental groups were significantly higher than those in the corresponding AR and AS control groups ($P < 0.05$) (**Figure 3**; **Table 2**). Positive IFN-γ expression was also detected in the same place, with yellow-brown or yellow staining. In the nasal mucosa and lung tissues in the AR and AS experimental groups, IFN-γ either did not exhibit significant expression or was not expressed; in contrast, IFN-γ was expressed in the control groups (all $P < 0.05$) (**Figure 4**; **Table 2**).

Correlation of positive CD80 and CD 86 expression between the nasal mucosa and lung tissues in the AR and AS experimental groups

Correlation analysis results showed that CD80 and CD86 expression levels in the nasal mucosa in the AR and AS experimental groups were

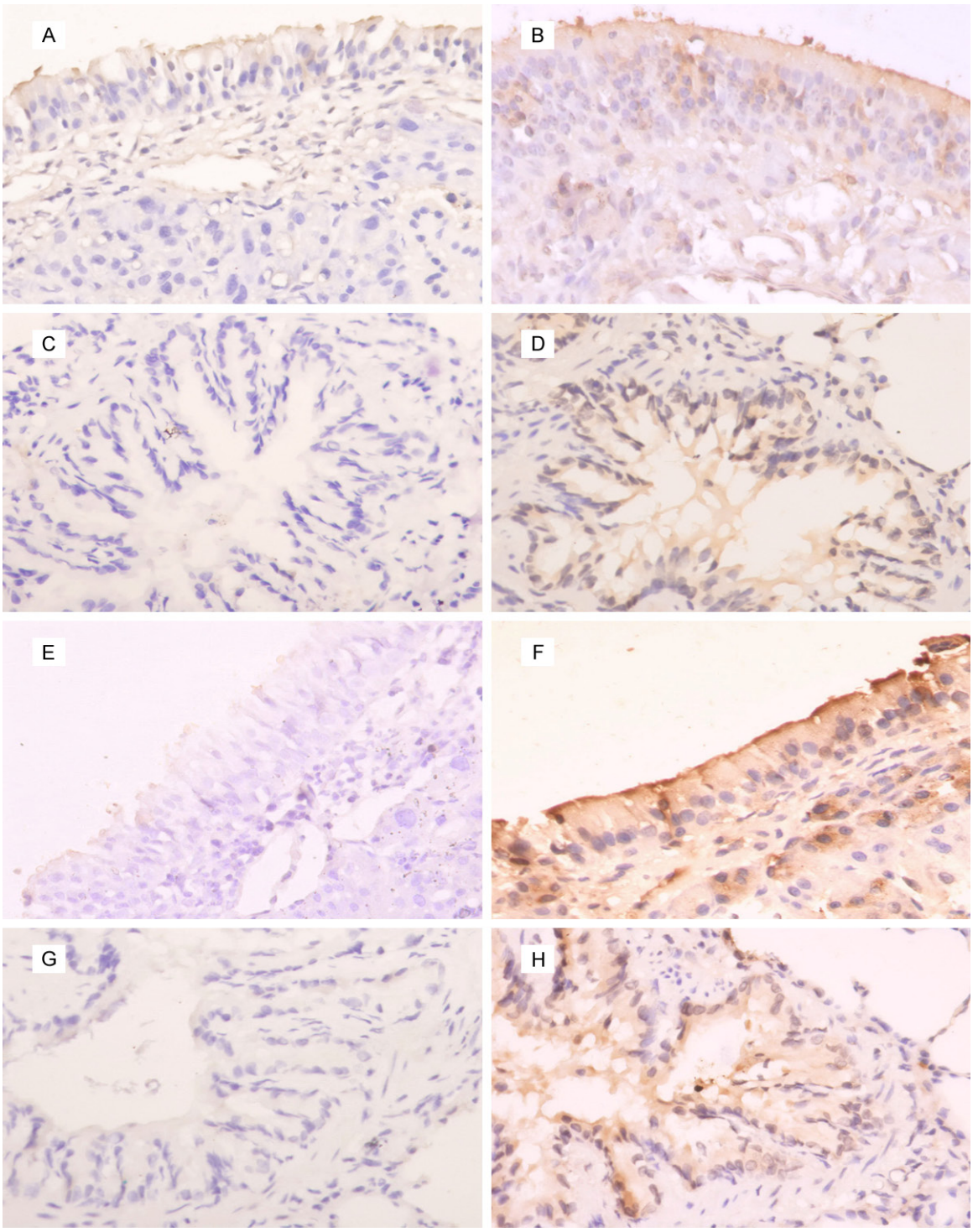

Figure 4. Immunostaining of IFN-γ positive cells in the nasal mucosa and lung tissues in the AR and AS experimental and control groups. A, B, E and F: The distribution and numbers of IFN-γ positive cells (light yellow or yellow-brown cytoplasms and cell membranes) were dominantly located in the epithelial layer and the lamina propria of the nasal mucosa (400×). C, D, G and H: Alveolar epithelial cells and bronchial mucosa epithelial cells in the lung tissues were positively stained (400×). In the nasal mucosa and lung tissues in the AR and AS experimental groups, IFN-γ either did not exhibit significant expression or was not expressed; in contrast, IFN-γ was expressed in the control groups. A-D: Refer to the AR groups; E-H: Refer to the AS groups.

Table 3. Correlation of positive CD80 and CD 86 expression between the nasal mucosa and lung tissues in the AR and AS experimental groups (r value)

Groups	Number (n)	r value	
		CD80	CD86
AR experimental group	10	0.709	0.870
AS experimental group	10	0.639	0.795

Abbreviations: AR, allergic rhinitis; AS, asthma. All $P < 0.05$.

Table 4. Correlation between positive CD80 and CD86 expression and positive IL-4 and IFN-γ expression in the nasal mucosa and lung tissues in the AR and AS groups (r value)

Groups	Number (n)	IL-4	IFN-γ
Nasal mucosa in the AR experimental group			
CD80	10	0.755	-0.832
CD86	10	0.887	-0.804
Lung tissues in the AR experimental group			
CD80	10	0.840	-0.893
CD86	10	0.673	-0.656
Nasal mucosa in the AS experimental group			
CD80	10	0.849	-0.765
CD86	10	0.652	-0.816
Lung tissues in the AS experimental group			
CD80	10	0.859	-0.734
CD86	10	0.729	-0.790

Abbreviations: AR, allergic rhinitis; AS, asthma; IL-4, Interleukin-4; IFN-γ, Interferon-gamma. All $P < 0.05$.

positively correlated with CD80 and CD86 expression levels in the lung tissues of their corresponding groups (all $P < 0.05$) (**Table 3**).

Correlation between positive CD80 and CD86 expression and positive IL-4 and IFN-γ expression in the nasal mucosa and lung tissues in the AR and AS experimental groups

Correlation analysis results showed that CD80 and CD86 expression levels in the nasal mucosa and lung tissues in the AR and AS experimental groups positively correlated with IL-4 expression levels and negatively correlated with IFN-γ expression levels in the nasal mucosa and lung tissues in the AR and AS experimental groups (all $P < 0.05$) (**Table 4**).

Discussion

Function of DCs in AR and AS

It is well known that AR and AS onset are influenced by both genetic and environmental factors. Although the locations of onset and the presentation of symptoms of these two diseases are different, the consistency between them has obtained extensive recognition as upper and lower airway inflammatory responses [11]. In recent years, the proposed "Th2 allergic reaction hypothesis" has correlated these two diseases together with DCs that are specifically responsible for APCs in the body. Studies have shown that Th2 cell recruitment, differentiation, and activation play critical roles in the developmental process of allergic diseases. The polarization process is controlled by APCs that provide support for the differentiation of naive T cells into Th2 cells. DCs play a very important role in this process. For example, they can promote the inhibitory activities of specific regulatory cells of allergens [12]. In addition, studies in humans and mice have also confirmed that DCs in the nose play critical roles in the process of Th2 effector activation; under conditions of DCs depletion or presence, the production status of allergic reaction products can be reduced or increased [13].

DCs not only can play a major role in the initiation and development processes of the immune responses but also can regulate the properties of immune events. Therefore, DCs are considered to be the key mediators of immune tolerance and Th1/Th2 polarization [14]. The characteristics of the phenotype of mature DCs include the expression of immune stimulatory molecules, including major histocompatibility (MHC)-I molecules, MHC-II molecules, CD80, CD86, CD40, Etc. As costimulatory molecules, CD80 and CD86 collaborate with the T cell receptor signaling pathway to enhance transcription factor activation to achieve T cell proliferation and differentiation. Their overexpression is closely associated with the development of allergic diseases [12, 15]. The functions of CD80 and CD86, which are involved in the allergic response, may be different; however, they both provide costimulatory signals for T cell proliferation and cytokine production and participate in the activation of immune reactions [16-19]. Therefore, as costimulatory molecules

on DC surfaces and as determinants of the mature DC phenotype, CD80 and CD86 can be used to detect and determine the expression conditions and functions of DCs and to reflect the severity of inflammation.

This study used the above features of DCs to detect CD80 and CD86 to determine DC expression. CD80 and CD86 expression levels in the nasal mucosa and lung tissues in the AR and AS experimental groups were significantly higher than those in the corresponding control groups, indicating that DCs participated in the onset of upper and lower airway inflammation. In addition, correlation analysis results showed that CD80 and CD86 expression levels in the nasal mucosa in the AR and AS experimental groups positively correlated with their expression levels in lung tissues. These results confirmed that there was consistency between the upper and lower airway inflammatory responses from the perspective of DCs. In addition, some studies showed that CD86 expression in the nasal mucosa of perennial AR caused by dust mites was higher than that in the nasal mucosa of healthy individuals [13]. The level of DCs in the circulating blood of AS patients was also higher than that in the circulating blood of normal individuals [20]. These results are similar to our results. Furthermore, DCs play a core role in the initial startup process of Th2 responses in allergic reactions; in addition, DCs are necessary for the maintenance of many basic features of AS through the local reactions of allergen-specific Th2 cells in airways [21]. Therefore, during AR and AS occurrence and development, DCs exhibited a consistently increasing trend in the nasal cavity and lung tissues, indicating the consistency in DC participation in the onset of upper and lower airway inflammatory diseases.

Relationship between DCs and Th1/Th2 type cells

After $CD4^+$ T cells are activated by DCs, they can differentiate into different subsets of cells, including Th1 and Th2 cells, based on differences in cytokine microenvironments, surface molecules on cell membranes, types and doses of antigens, APCs, and other cellular regulatory factors. Th1 cells secrete IFN-γ, tumor necrosis factor alpha (TNF-α), IL-2, IL-12, and IL-18, while Th2 cells secrete IL-4, IL-5, IL-9 and IL-13 [22]. A previous study demonstrated that IL-4 mRNA expression was significantly up-regulated at the early provocation stage in AR mouse models and that the IL-4 level in bronchoalveolar lavage fluid was also significantly increased compared to that in the control group [23]. During AS onset, the levels of some cytokines (such as IL-4 and IL-5) in patient sera increased, and the levels of other factors (such as IFN-γ and IL-2) decreased [24, 25]. The expression profiles of Th1- and Th2-type cytokines in AR and AS have been previously reported; however, the relationship between DCs and Th1- and Th2-type cytokines in AR and AS and their functions and mechanisms are rarely reported.

To further investigate the mechanism of DCs in the consistency between upper and lower airway inflammatory responses and their association with Th1- and Th2-type cytokines in AR and AS, this study assessed IL-4 and IFN-γ expression levels in the nasal mucosa and lung tissues in AR and AS rats. The IL-4 expression levels in the nasal mucosa and lung tissues in the AR and AS experimental groups were significantly higher than those in the control groups; in contrast, the IFN-γ expression levels in the nasal mucosa and lung tissues in the AR and AS control groups were significantly higher than those in the experimental groups. Correlation analyses between the CD80 and CD86 expression levels and the IL-4 and IFN-γ expression levels in the nasal mucosa and lung tissues in the AR and AS experimental groups showed that CD80 and CD86 expression levels positively correlated with the IL-4 expression level and negatively correlated with the IFN-γ expression level. Therefore, we speculated that DCs might participate in the deviation process of immune reactions in AR and AS because they induced dominant expression of Th2 cells to break the original expression balance between Th1/Th2 cytokines, thus resulting in the increased expression of cytokines, such as IL-4, and the decreased expression of other cytokines, such as IFN-γ, in Th1-type cell reactions. Therefore, the inhibition of Th2 cytokines through the increase of Th1 cytokines may have therapeutic functions on both AR and AS. Studies have shown that under the conditions of IFN-γ depletion or pretreatment with IFN-γ polyclonal antibodies, DCs could decrease the development of the AS reaction and present IFN-γ-dependent regulatory mechanisms [26].

Some studies also confirmed that treating sensitized mice with the Th1-related cytokines IL-12 or IFN-γ before provocation tests could reduce the IL-4 and IL-5 expression levels in bronchoalveolar lavage fluid and could inhibit antigen-induced eosinophilic inflammation and airway hyperresponsiveness [27]. In addition, IFN-γ could also influence the function of IL-13 in the AS disease development process, such as goblet cell hyperplasia and eosinophil production in airways [28]. Therefore, treatment of allergic diseases by blocking or regulating DCs and/or cytokines is very promising.

In summary, the results of this study confirmed that there was consistency between upper and lower airway inflammation from the perspective of DCs, which participated in the onset of upper and lower airway inflammation. This functional mechanism might be associated with the induction of the dominant Th2 cells expression by DCs, thus breaking the original expression balance between Th1/Th2 cytokines. The results of this study will provide theoretical bases for treatments specifically targeting DCs and related cytokines in the future.

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Disclosure of conflict of interest

None.

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