

The expression and significance of immunoglobulin free light chain in the patients with allergic rhinitis and nonallergic rhinitis

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ABSTRACT

Background: Inflammation has been shown to be an integral component of allergic rhinitis (AR). However, there is no noteworthy debate regarding this fact in nonallergic rhinitis (NAR). Some studies have suggested that exclusion of inflammation is indicative of NAR and other studies have indicated that most of the NAR patients have some degree of inflammation. Recently, it has been shown that the level of immunoglobulin free light chains (IgFLCs) in serum is increased in some autoimmune diseases and airway inflammation. This study was designed to show whether IgFLC is associated with non-IgE-mediated rhinitis to reveal the relationship between the expression of IgFLC and activation of mast cells and eosinophils.

Methods: Thirty patients with IgE-mediated AR and 30 patients with NAR and 30 healthy persons as control were involved this study. The total IgE, IgFLC, eosinophil cationic protein (ECP) and mast cell tryptase (MCT) in serum, and nasal secretions were assayed, respectively. For identifying the expression cells of IgFLC in nasal mucosa, the immunohistochemical (IHC) staining for kappa-FLC, gamma-FLC, ECP, and MCT were performed on 30 specimens. Meanwhile, the mRNA expression of kappa-FLC, gamma-FLC, and MCT was determined by real-time quantitative polymerase chain reaction.

Results: IgFLCs (kappa/lambda) levels in serum and nasal secretion were significantly increased in AR patients and NAR patients. The ECP and MCT levels in serum and nasal secretion were significantly enhanced in AR and NAR patients when compared with healthy control subjects ($p < 0.01$). There was a positive correlation between IgFLC (kappa/lambda) and MCT in nasal secretion of patients with NAR, but only IgFLC (kappa-FLC) was associated with MCT in AR. There was no correlation between IgFLC and ECP in nasal secretion. In serum expression level, there was a positive correlation between IgFLC (kappa) and ECP in AR or IgFLCs (lambda) and ECP in NAR. IHC staining showed that FLC⁺ cells were significantly increased in AR and NAR mucosa, kappa-FLC was mainly expressed in epithelial cells, and lambda-FLC was mainly expressed in subepithelial cells. Double immunofluorescence staining showed that the expression of lambda-FLC was mainly localized in mast cells in NAR nasal mucosa (45%).

Conclusion: These findings suggest strongly that IgFLC may play an important role in inducing local nasal mucosa inflammation especially those in AR and NAR.

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Rhinitis is a global health problem that causes major illness and disability worldwide. Patients from every country, all ethnic groups, and all ages suffer from rhinitis.¹ According to revised nomenclature of the European Academy of Allergology and Clinical Immunology² and the World Allergy Organization,³ rhinitis with nasal hyperactivity is often referred to as nasal hypersensitivity. Nasal hypersensitivity may be induced by immunologic or nonimmunologic mechanisms.^{4–7} Rhinitis induced by immunologic mechanism is called allergic rhinitis (AR) that is further classified as IgE mediated or non-IgE mediated. IgE-mediated AR is the most common clinical form. Non-IgE-mediated hypersensitive rhinitis induced by immune mechanism as a clinical entity is, however, lacking enough evidence. However, some recent studies propose that thymus stromal lymphopoietin–derived airway epithelial cells may be a contributor to patients with mugwort pollen–sensitive seasonal AR⁸ through the effect of thymus stromal lymphopoietin on dendritic cells resulting in Th2 immune response.

Immunoglobulin free light chains (IgFLCs) are produced in excess amounts during antibody formation. Some limited studies have identified several biological functions,^{9,10} such as complement activation and angiogenesis capabilities. Often, abnormal increase in path-

ological conditions, such as multiple sclerosis, rheumatoid arthritis, etc.,^{11–14} may be related to the progress and severity of the immunologic diseases.^{15,16} Redegeld¹⁷ was first to show that the specific IgFLCs may induce an immediate hypersensitive-like response, depending on the mast cells. Later, Redegeld and his research team proved sequentially that IgFLCs may elicit allergic asthma and proposed that IgFLCs may be a novel target in the therapy of chronic inflammatory diseases. Some later studies indicate that FLC plays a key role in numerous airway autoimmune diseases such as idiopathic pulmonary fibrosis, chronic hypersensitivity pneumonitis,¹⁸ asthma,¹⁹ AR, and nonallergic AR (NAR) with eosinophilia syndrome.²⁰ IgFLCs may provide an additional non-IgE immune pathway to augment or replace IgE-mediated hypersensitivity in chronic mucosal inflammatory disease.

The pathogenesis of NAR with nasal hyperactivity is not clear and, therefore, results in the confusion of treatment. The aim of this study was to prove the hypothesis that IgFLCs may play an important role in the development of NAR through observing the expression level of IgFLC, mast cell tryptase (MCT; biomarker of mast cells), eosinophil cationic protein (ECP; biomarker of eosinophils) in nasal mucosa, nasal secretion, and serum from patients with negative results in allergen skin tests and determination of serum level of allergen-specific IgE.

MATERIALS AND METHODS

Patients

The Department of Otorhinolaryngology, Head and Neck Surgery, of China–Japan Union Hospital of Jilin University in China tested 60 patients with nasal hypersensitivity who had a chronic

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history of sneezing, rhinorrhea, and nasal obstruction for a period of at least 6 months. General inclusion criteria for this study were rhinitis subjects with no evidence of other immunologic disease or respiratory infection for 4 weeks and no treatment with systemic or nasal corticosteroids for 2 weeks. The 60 patients were divided into two groups—30 patients with AR (16 men and 14 women; mean age, 30.8 ± 8.1 years) and 30 patients with NAR (12 men and 18 women; mean age, 36.8 ± 13.2 years), according to the results of allergen skin-prick tests (SPTs; ALK, Horsholm, Denmark)—and 30 healthy volunteers (15 men and 15 women; mean age, 32.4 ± 5.6 years) as normal control.

The serum and nasal secretion from 60 patients with AR or NAR were collected to assay the levels of soluble FLC, MCT, ECP, and total IgE in serum and nasal secretions (Mediawiss Analytic GmbH, Moers, Germany).^{21–23} The inferior turbinate from 30 patients, which included 10 AR patients, 10 NAR patients, and 10 patients with deviation of nasal septum as control, respectively. The 30 inferior turbinates were removed and tested for histopathological observations and immunohistochemical (IHC) staining for κ FLC, λ FLC, ECP, and MCT. The specimens were divided into two groups. One group was fixed in 4% paraform solution and later embedded in paraffin for hematoxylin–eosin, toluidine blue, and IHC staining. The other group was immediately frozen in liquid nitrogen for future real-time quantitative polymerase chain reaction (PCR). This study had been approved by the Human Research Ethic Committee of China–Japan Union Hospital of Jilin University, and all the patients signed consent forms.

Allergen SPTs

SPTs were performed with the commercial standard inhalant allergen (ALK) containing 10 allergens, including *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, mugwort, common ragweed, *Blattella germanica*, mold mix, grass mix, trees mix, cat dander, and dog dander.²⁴ The patients took no antihistamines or other drugs that have antihistaminic effect at least 1 week before the test. SPT was performed on the patient's forearm. Positive and negative controls included histamine (10 mg/mL) and saline solution, respectively. The test results were read at 20 minutes and the skin index (SI) was calculated, which equals the wheal diameter ratio of allergen and histamine diameter. The SPT results were then divided into four categories: class 1+, SI < 0.5; class 2+, $0.5 \leq \text{SI} < 1.0$; class 3+, $1.0 \leq \text{SI} < 2.0$, and class 4+, SI ≥ 2.0 . A wheal diameter of at least 3 mm was considered positive.

Measurement of FLC, total IgE, MCT, and ECP

FLC levels in serum and nasal secretions were assayed *via* commercially available ELISA kit (R & D Systems, Minneapolis, MN) for human κ FLC (mg/L) and λ FLC (mg/L). The levels of MCT (ng/mL; marker of mast cell activation), ECP (ng/mL; marker of tissue eosinophil activation), and total IgE (U/mL) in nasal secretion and serum were determined by ELISA (UNICAP; Pharmacia Diagnostics, Uppsala, Sweden).

Pathological and IHC Staining

Paraffin sections (4 mm) were stained with hematoxylin–eosin and (toluidine blue). The stained sections were observed by two independent pathologists who were blind to the clinical data. The number of glands in the lamina propria was counted at magnification power ($\times 200$), and 10 fields were randomly selected and analyzed. The results were expressed as number of glands per field of lamina propria. The number of eosinophils and mast cells were counted at high power (HP) magnification ($\times 400$), and 10 HP fields were randomly selected and analyzed. Results were expressed as cells percentage per HP field.

Paraffin sections were stained with mouse anti-human monoclonal antibody for κ FLC and λ FLC (Abnova, Inc., Taipei City, Tai-

wan) and rabbit anti-human polyclonal antibody for ECP and MCT (Santa Cruz Biotech, Inc., Santa Cruz, CA), respectively. The streptavidin peroxidase method was performed according to the manufacturer's instructions. The negative controls used phosphate-buffered saline solution instead of primary antibody. The number of positive cells were counted at HP magnification ($\times 400$), and 10 HP fields were randomly selected and scored by two independent observers who were blind to the diagnosis and clinical data. The HP-field-positive cell mean was regarded as the expression rate of positive cells.

Double Immunofluorescence Staining

The paraffin sections were initially stained with anti-human antibody for λ FLC and MCT or λ FLC and ECP (as mentioned previously). Next, these sections were stained with fluorescein isothiocyanate (goat anti-mouse IgG, green), and TRITC (goat anti-rabbit IgG, red). Use DAPI dyeing nuclear (blue). The color of double expression cells was yellow.

Real-Time Quantitative PCR

Total RNA was extracted from the specimens of nasal mucosa by Trizol reagent (Sangon Biotechnology, Shanghai, China). Complementary DNA (cDNA) was synthesized from μg of total RNA using the Quant cDNA synthesis kit (Tiangen Biotechnology, Beijing, China) according to the manufacturer's instructions. Levels of the FLC and MCT were determined by using the SYBR Green Real-Time PCR Detection System using specific primer sequences (κ FLC, 5'-3' left AGCCTGGGTACCTGCGAGCC, right AGTAGGCGTGCATGTGGGGG; λ FLC, 5'-3' left TGTCATTTGGATGGGAGACA, right GCGTCTAACCATGTCCAGT; MCT, 5'-3' left CTGTGCTGAGC-CAGGCTAAG, right GCCACCAGAATCACCTGAC). PCR reactions contained 40 ng of cDNA (total RNA equivalent), 250 nmol/L of primer pairs, 1X SYBR Green Real Master mix at 11.25 μL (Tiangen Biotechnology) in a final volume of 25 μL . PCR protocol consisted of 1 cycle at 94°C for 2 minutes followed by 40 cycles at 94°C for 15 seconds and at 55°C for 30 seconds, and at 68°C for 40 seconds. Relative gene expression was calculated with the comparative computed tomography method. Glyceraldehydes-3-phosphate dehydrogenase was used as a housekeeping gene for normalization and no template sample was used as a negative control.

Statistical Analysis

The data were analyzed by SPSS (Version 17.0; SPSS, Inc., Chicago, IL), and ELISA data were expressed as mean $\pm$ SD. FLC, ECP, MCT, and total IgE level in serum and nasal secretions were compared using one-way ANOVA. Relationships between FLC and MCT, ECP in serum, or nasal secretions were investigated by using the Spearman test. Cell count results were reported as median and interquartile ranges. The Wilcoxon-Mann-Whitney *U* test was used for between-group comparisons. A value of $p \leq 0.05$ was considered significant. A two-tailed value of $p < 0.05$ indicated statistical significance.

RESULTS

FLC, ECP, MCT, and IgE

Compared with that in normal control, the FLC levels in serum were significantly increased in AR patients (κ , 14.20 ± 11.69 and $p = 0.000$; λ , 3.11 ± 1.83 and $p = 0.002$) and NAR patients (κ , 13.30 ± 10.83 and $p = 0.000$; λ , 5.05 ± 6.04 and $p = 0.006$). Similarly, levels of nasal FLCs were also significantly increased in AR (κ , 10.26 ± 5.60 and $p = 0.000$; λ , 3.63 ± 1.88 and $p = 0.003$) and NAR (κ , 8.35 ± 5.45 and $p = 0.001$; λ , 4.16 ± 2.63 and $p = 0.002$) but not in controls. It is worth noting that there was no significant difference of FLC levels of serum and nasal secretions between AR and NAR ($p > 0.05$). The ECP and

Table 1 Compare κ FLC, λ FLC, ECP, MCT, IgE concentrations in serum, and nasal secretions from AR, NAR patients, and control ($\bar{x} \pm s$)

Group	κ FLC	λ FLC	Total IgE	ECP	MCT
Serum					
AR	14.20 $\pm$ 11.69	3.11 $\pm$ 1.83	205.13 $\pm$ 140.43	15.48 $\pm$ 12.89	20.73 $\pm$ 24.16
NAR	13.30 $\pm$ 10.83	5.05 $\pm$ 6.04	103.9 $\pm$ 83.9	14.43 $\pm$ 14.03	32.98 $\pm$ 31.91
Control	4.50 $\pm$ 3.92	1.72 $\pm$ 1.41	83.44 $\pm$ 43.45	5.12 $\pm$ 3.52	6.80 $\pm$ 7.95
F	9.601	6.019	16.307	7.790	3.832
P*	0.715	0.057	0.000	0.718	0.201
P#	0.000	0.045	0.000	0.001	0.043
P\$	0.001	0.001	0.150	0.002	0.007
Nasal secretions					
AR	10.26 $\pm$ 5.60	3.63 $\pm$ 1.88	197.2 $\pm$ 148.4	17.27 $\pm$ 11.79	32.29 $\pm$ 24.75
NAR	8.35 $\pm$ 5.45	4.16 $\pm$ 2.63	98.34 $\pm$ 58.92	11.34 $\pm$ 7.38	36.71 $\pm$ 54.50
Control	4.04 $\pm$ 3.32	2.39 $\pm$ 1.18	62.94 $\pm$ 34.90	4.85 $\pm$ 3.84	4.01 $\pm$ 4.78
F	12.690	6.285	13.334	16.669	7.857
P*	0.134	0.305	0.000	0.007	0.623
P#	0.000	0.018	0.000	0.000	0.002
P\$	0.001	0.001	0.049	0.003	0.000

Data are expressed as mean $\pm$ SD ($\bar{x} \pm s$). Multiple samples were compared by the single factor analysis of variance ANOVA.

*AR and NAR.

#AR and control.

\$NAR and control.

IgFLC = immunoglobulin free light chains; MCT = mast cell tryptase; ECP = eosinophil cationic protein; AR = allergic rhinitis; NAR = nonallergic rhinitis.

Table 2 Compared the relationship between FLC and MCT/ECP in AR and NAR

	Serum				Nasal Sections			
	κ FLC vs ECP	κ FLC vs MCT	λ FLC vs ECP	λ FLC vs MCT	κ FLC vs ECP	κ FLC vs MCT	λ FLC vs ECP	λ FLC vs MCT
AR								
R	0.450	0.187	0.20	0.040	0.111	0.616	0.198	0.321
P	0.013	0.323	0.289	0.835	0.561	0.000	0.295	0.084
NAR								
R	0.004	0.038	0.361	0.027	0.009	0.455	0.182	0.498
p	0.982	0.842	0.050	0.888	0.962	0.012	0.336	0.005

Correlation analysis using the linear correlation analysis, inspection level of $\alpha = 0.05$ ($p \leq 0.05$).

MCT = mast cell tryptase; ECP = eosinophil cationic protein; IgFLC = immunoglobulin free light chains.

MCT levels in serum and nasal secretion were significantly enhanced in AR and NAR patients compared with those in healthy control subjects ($p < 0.01$). ECP concentrations in secretions was, however, increased in AR patients (17.270 $\pm$ 11.80) compared with those in NAR (11.34 $\pm$ 7.38; $p < 0.05$; Table 1).

Total IgE levels were measured in serum and nasal secretions. Significantly increased IgE concentrations in serum were found in AR (205.13 $\pm$ 140.43 U/mL) patients but not in patients with NAR (103.9 $\pm$ 83.9 U/mL; $p = 0.24$), when compared with healthy controls (83.44 $\pm$ 43.45 U/mL; $p < 0.01$). In nasal secretions, total IgE concentrations were increased in AR (197.2 $\pm$ 148.4 U/mL) patients when compared with NAR (98.34 $\pm$ 58.92 U/mL) patients ($p < 0.01$) and, interestingly, was higher than normal controls (62.94 $\pm$ 34.90 U/mL) in NAR patients ($p < 0.01$; Table 1).

In the AR and NAR groups, we investigated the correlation between FLC and ECP/MCT in serum and nasal secretions ($n = 30$). In nasal secretion, the FLC levels revealed a significantly positive correlation with MCT in the NAR group (κ FLC versus MCT, $r = 0.455$ and $p < 0.05$; λ FLC versus MCT, $r = 0.498$ and $p < 0.05$), but in the AR group, the positive correlation was only found in κ FLC and MCT (κ FLC versus MCT, $r = 0.616$ and $p < 0.05$). In serum κ FLC there was a significantly positive correlation with ECP in the AR group ($r = 0.450$; $p < 0.05$) and λ FLC revealed a

significantly positive correlation with ECP in the NAR group ($r = 0.361$; $p < 0.05$; Table 2).

Histopathological and IHC Staining

Table 3 shows the median percentage and interquartile ranges of eosinophils, plasma cells, and mast cells in nasal mucosa from patients with AR, NAR, and controls. There were significant differences in all inflammatory cell percentages among patients with rhinitis and controls. Histopathological examination showed that the percentage of eosinophils was higher in AR mucosa than in NAR and controls ($p < 0.01$), and the percentage of mast cells was higher in AR and NAR mucosa than that in controls ($p < 0.01$; Table 3; Fig. 1).

IHC staining of nasal mucosa showed that FLC expression cells were significantly increased in AR and NAR mucosa but not in controls. Interestingly, κ FLC was mainly expressed in epithelial cells and λ FLC was mainly expressed in some subepithelial cells.

Double Immunofluorescence Staining

Because κ FLC is mainly expressed in epithelial cells, we only examined λ FLC to identify expressional cells. FLC stained with green and ECP/MCT was stained with red; the nucleus was dyed with blue. The color of coexpression positive cells was yellow. Double

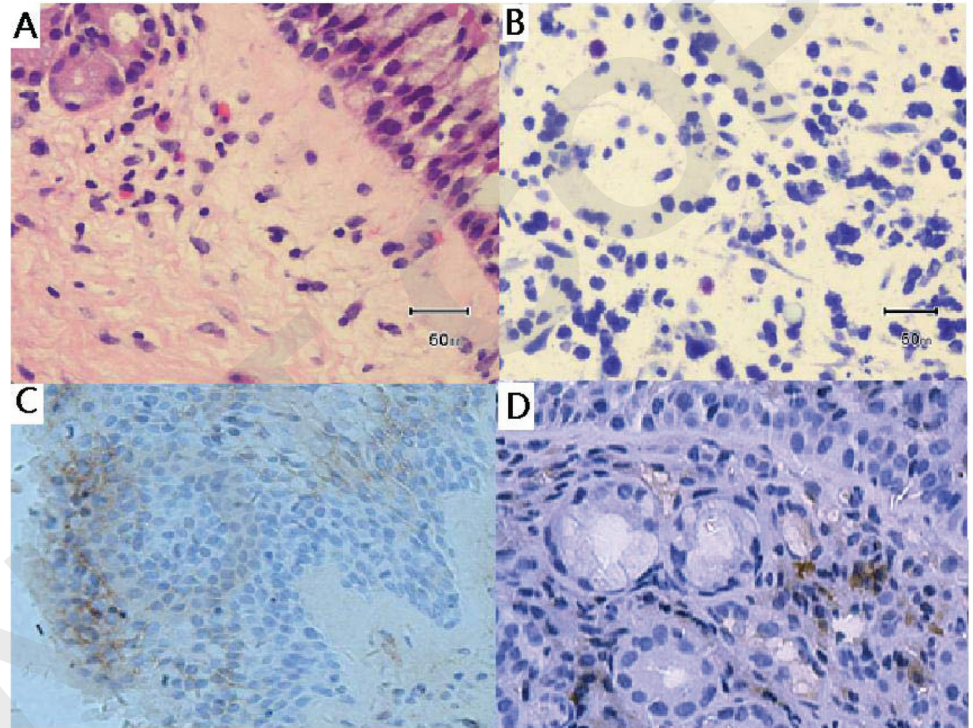
Table 3 Histopathological observations and IHC staining results in three groups

Tissue	AR	AR vs NAR	NAR	NAR vs Control	Control	AR vs Control
Eosinophil cell (hematoxylin-eosin), %	9.3 (7.8–13.5)	$p < 0.05$	5.6 (4.03–7.48)	$p < 0.05$	3.55 (2.5–4.55)	$p < 0.05$
Plasma cell (hematoxylin-eosin), %	11.45 (8.55–12.65)	$p < 0.05$	8.35 (6.8–10.2)		5.6 (4.73–8.8)	$p < 0.05$
Mast cell (toluidine blue), %	6.85 (5.6–7.98)		6.75 (5.58–9.18)	$p < 0.05$	3.15 (2.43–4.3)	$p < 0.05$
κ FLC (IHC), %	7.5 (6.43–9.35)		9.1 (7.4–10.58)	$p < 0.05$	4 (2.58–5.6)	$p < 0.05$
λ FLC (IHC), %	11.75 (9.48–13.68)		12.03 (8.26–14.6)	$p < 0.05$	2.15 (1.15–3.75)	$p < 0.05$

Data are expressed as median and interquartile ranges. The Wilcoxon-Mann-Whitney U test was used for between-group comparisons.

IgFLC = immunoglobulin free light chains; AR = allergic rhinitis; NAR = nonallergic rhinitis; IHC = immunohistochemical.

Figure 1. Histopathological and immuno-histochemical (IHC) staining results (A) Hematoxylin-eosin staining for nasal mucosa in nonallergic rhinitis (NAR; original magnification, $\times 200$). The eosinophils were stained with red. (B) Toluidine blue stained with nasal mucosa in NAR (original magnification, $\times 200$). The mast cells were stained with dark blue (IHC staining). (C and D) In NAR (original magnification, $\times 200$). (C) κ -free light chain (κ FLC⁺); (D) λ FLC⁺. The positive cells were stained with dark brown. κ FLC is mainly expressed in epithelial cells. λ FLC is mainly expressed in subepithelial cells.



immunofluorescence staining showed that the expression of λ FLC was mainly localized in mast cells in NAR nasal mucosa (45%), but a few was found in eosinophils (15%). It was also shown that expression of λ FLC was localized in mast cells in AR nasal mucosa (25%) and slightly localized in eosinophils in NAR mucosa (17%; Fig. 2).

Real-Time Quantitative PCR

The levels of FLC mRNA was increased in AR and NAR nasal mucosa but not in controls ($p < 0.05$). In addition, there was no statistical significance between AR and NAR ($p > 0.05$). The correlation analysis showed a positive correlation between λ FLC mRNA and MCT mRNA in NAR ($R = 0.697$; $p < 0.05$; Table 4; Fig. 3).

DISCUSSION

Although inflammation has been shown to be an integral component of AR, there is a noteworthy debate regarding this fact in NAR. Nonallergic perennial rhinitis is a chronic non-IgE-mediated condition that is characterized by the symptoms that are similar to those seen in AR. Some studies have suggested that exclusion of inflammation is indicative of NAR and other studies have shown that most of the NAR patients have some degree of inflammation.²⁵ Antihistamines or nasal steroid positive treatment effects on AR and NAR suggest that possible common mechanisms in some stage of inflam-

mation may be involved in both diseases, despite the differences in pathogenesis.²⁶ Mast cells are abundant in the nasal mucosa of AR, consistent with their role in maintaining inflammation in allergic airway disease. Some patients with NAR were found to have increased numbers of mast cells in nasal mucosa. These results are similar to those of Comoqlu²⁷ and suggest local allergic inflammation in NAR nasal mucosa.

In the present study, the increased level of MCT in the serum and nasal secretion from the patients with AR and NAR shows the important role of mast cells in maintaining chronic inflammation of NAR. It has been shown that IgFLC can induce mast cell activation, resulting in immediate hypersensitivity-like responses.²⁸ Ultrastructural analysis of the light chain-activated skin mast cells reveals swollen and emptied mast cell granules and fusion of mast cell granules to form degranulation channels—typical signs of anaphylactic mast cell degranulation.²⁹

An increased IgFLC level in nasal secretion of patients with AR or NAR was established by Powe *et al.*²⁰ In this study, the level of IgFLC in nasal secretion was not only enhanced but also increased significantly in serum of AR and NAR patients, respectively. Through correlation analysis of expression levels of IgFLC (κ and λ), MCT, and ECP, the most valuable and interesting information was provided in this study.³⁰ Cheng's³¹ studies suggest that eosinophils and ECP take

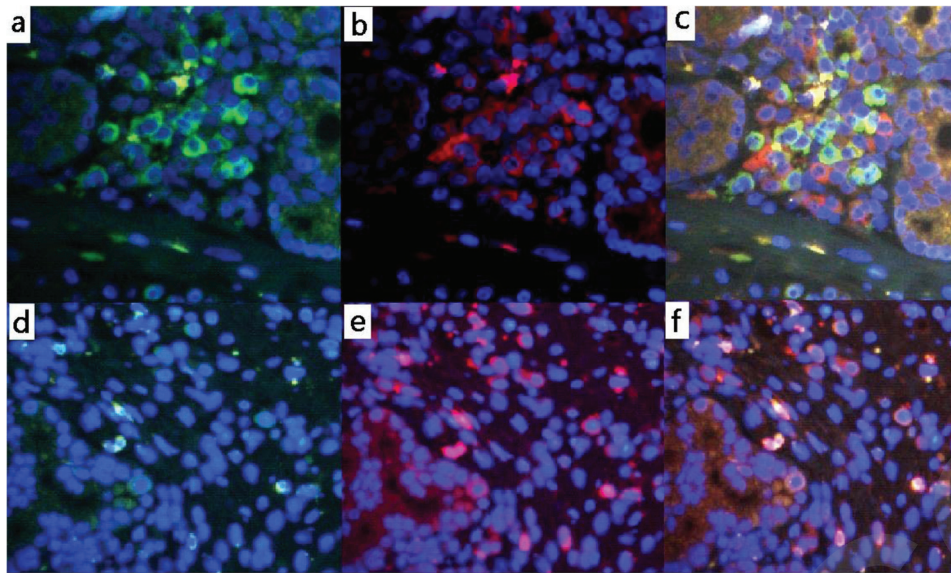


Figure 2. (A–C) Stained lambda-free light chain (λ FLC) and mast cell tryptase (MCT) in nonallergic rhinitis (NAR) nasal mucosa. (D–F) Stained λ FLC and eosinophil cationic protein (ECP) in NAR nasal mucosa (original magnification, $\times 400$). FLC stained with green and ECP/MCT stained with red; the nuclear dyed with blue. The color of coexpression positive cells was yellow.

Table 4 Real-time quantitative PCR results in three groups

Tissue	AR	AR vs NAR	NAR	NAR vs Control	Control	AR vs Control
MCT (mRNA)	4.1 (3.2–5.6)	$p < 0.05$	4.2 (2.5–6.2)	$p < 0.01$	2.5 (1.3–3.5)	
κ FLC (mRNA)	8.9 (6.1–15.6)		9.3 (6.7–15.5)	$p < 0.05$	3.6 (3.0–5.8)	$p < 0.01$
λ FLC (mRNA)	1.2 (1.0–2.3)		2.6 (2.0–3.2)	$p < 0.01$	1.1 (0.8–1.5)	$p < 0.01$

Data are expressed as median and interquartile ranges. The Wilcoxon-Mann-Whitney U test was used for between-group comparisons. IgFLC = immunoglobulin free light chains; AR = allergic rhinitis; NAR = nonallergic rhinitis; PCR = polymerase chain reaction.

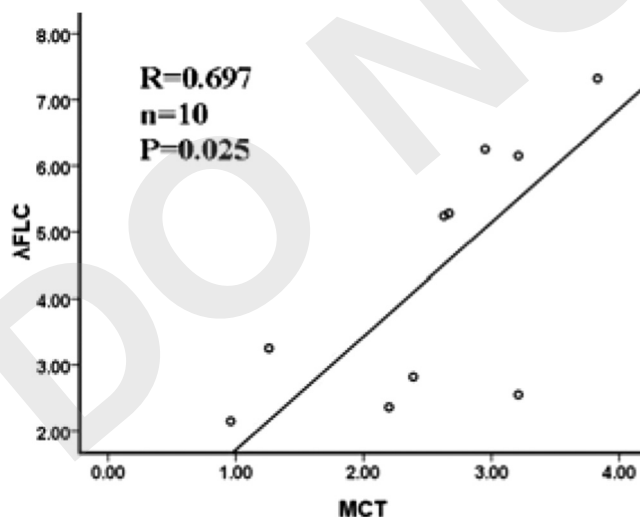


Figure 3. The correlation analysis shows a positive correlation between lambda-free light chain (λ FLC) and mast cell tryptase (MCT) mRNA in the nonallergic rhinitis (NAR) group.

part in the pathogenesis of NAR. In our study not only ECP but also MCT and IgFLC take part in the pathogenesis of AR and NAR. In nasal secretion, there was a significant positive relation between IgFLC (κ and λ) and MCT levels in NAR but not in AR; this correlation is only found between κ FLC and MCT. In serum, there was only association of MCP with IgFLC. The positive correlation between

κ FLC and MCP in AR and λ FLC and ECP in NAR was found. The real-time PCR for FLC and MCT shows that levels of FLC mRNA are increased in AR and NAR nasal mucosa. Positive correlation between λ FLC and MCT mRNA levels in NAR was found. These findings strongly suggest that the IgFLC with activated mast cells may play an important role in inducing local nasal mucosa inflammation, especially in NAR. Specifically, the increase in IgFLC mRNA in nasal mucosa suggests that there is a possibility of producing IgFLC in nasal mucosa. The subtype difference of IgFLC in correlation with ECP in AR and NAR may imply that κ FLC and λ FLC may belong to different immunoglobulins and exert different potential functions, suggesting effects of IgFLC on eosinophils still needs to be explored.

The positive relation between IgFLC and MCT implies that mast cells may be the active cells of IgFLC. Using double immunofluorescence staining in this study, we first showed that the expression of λ FLC was mainly localized in mast cells in NAR nasal mucosa (45%) but also a few were observed in the eosinophils (15%). The active mechanism of IgFLC is not completely clear. Recently, a little evidence suggests that IgFLC may change some component of cell membrane structure.²⁹

In conclusion, this study shows the positive correlation between IgFLC (κ and λ) and MCT in nasal secretions of NAR patients; however, there is only κ FLC associated with MCT in AR. The cause of this difference in NAR and AR remains unknown. Moreover, the positive association of ECP with a different subtype of IgFLC was the first to be found in this study. These findings suggest that possible common immunologic mechanisms mediated by IgFLC may be involved in both AR and NAR, despite the differences in pathogenesis. Future research should be performed to disclose whether the prevention of FLC-induced activation of immune cells could be of therapeutic value in the treatment of AR and NAR.

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