

Letters

UNCOVERED REACTIVITY TO LUPINE IN LENTIL-ALLERGIC PATIENTS

Lupine (*Lupinus albus*, Leguminosae) is well documented as causing food allergy.¹ Cross-reactivity among lupine, peanut, and other Leguminosae has been reported.¹⁻⁵ Cross-reactive allergens to almond have been described in lupine-allergic patients' sera.⁶ Herein, we describe the immunologic and clinical findings of lupine reactivity in 6 lentil-allergic adults.

A 20-year-old woman (patient 1) allergic to lentil and peanut reported itchy mouth, difficulty swallowing, tongue swelling, disseminated urticaria, asthma, and abdominal pain on lupine seed ingestion. Skin prick-prick testing (SPPT) with lupine seeds elicited a positive result (9.5-mm wheal). Specific IgE to lupine (CAP-FEIA) was 7.61 kUA/L. The severity of the reaction precluded further oral challenges. These clinical findings prompted us to evaluate a possible cross-reactivity between lupine and lentil.

Five consecutive lentil-allergic adults (4 women; median age, 48 years; age range, 18-54 years; double-blind, placebo-controlled food challenge (DBPCFC)—positive or a convincing severe reaction) were recruited during a 5-year period. They had not ingested lupine previously. Results of SPPT to lentil were positive in all patients. Median specific IgE to lentil was 6.13 kUA/L (range, 0-30.7 kUA/L). All the patients signed an informed consent form for evaluation of lupine allergy. Patient 2, a 49-year-old man, and patient 3, a 27-year-old woman, both nonallergic to peanut, showed positive SPPT and specific IgE to lupine (11- and 7.5-mm wheals and >100 and 1.42 kUA/L,

respectively). Both patients underwent DBPCFC with lupine flour.⁷ Patient 2 showed intense oropharyngeal pruritus, difficulty swallowing, and dyspnea with a 0.6-g cumulative dose. Patient 3 showed oropharyngeal pruritus, nausea, and intense abdominal pain with a 10-g cumulative dose.

Patient 4 showed a positive SPPT reaction (4-mm wheal) and specific IgE (2.87 kUA/L) to lupine. Results of SPPT and specific IgE to lupine were negative in patients 5 and 6. Open oral challenges with lupine seeds (25-g cumulative dose) elicited a negative result in these 3 patients. Results of lentil and lupine reactivity are summarized in Table 1.

Lentil and lupine extracts were separated by sodium dodecyl sulfate–polyacrylamide gel electrophoresis in 4% to 20% Tris hydrochloride linear gradient precast gel. IgE immunoblot with sera from the 3 lentil- and lupine-allergic patients (patients 1, 2, and 3) (1:10 dilution) were performed as described elsewhere.⁸ All sera reacted to 49-, 36-, 18-, and 16-kDa proteins in lentil immunoblot. IgE immunoblot to lupine showed IgE binding to a 72- to 73-kDa protein in all sera. Two of 3 sera recognized a 36-kDa protein. To evaluate cross-reactivity between lentil and lupine, immunoblot inhibitions were performed with sera from patients 2 and 3, both DBPCFC positive to lupine. Serum from patient 2 showed dose-dependent, almost complete inhibition by lupine of all bands in the lentil immunoblot. No inhibition of the lupine immunoblots by lentil was obtained. Serum from patient 3 showed complete inhibition of lupine by lentil in all concentrations used. No inhibition of reactive IgE bands was observed in lentil immunoblot with lupine as inhibitor. Results are shown in Figure 1.

These findings show lupine sensitization in 4 of 6 lentil-allergic adults and clinical reactivity to lupine in 3 of 6. To our knowledge, only an isolated case of lupine-induced anaphylaxis in a patient reporting symptoms with lentil had been described.³ Immunoblot inhibition in the 2 DBPCFC-positive patients showed opposite re-

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Table 1. Immunologic and Clinical Reactivity to Lentil and Lupine in 6 Lentil-Allergic Patients

Patient No.	Lentil					Lupine				
	SPPT, mm	CAP-FEIA, kU/L	Symptoms	Diagnostic challenge	Allergy	SPPT, mm	CAP-FEIA, kU/L	Symptoms	Diagnostic challenge	Allergy
1	8.5	20.2	U, AE, P, E, OAS, T, DS, A, G	^a	Yes	9.5	7.61	U, AE, P, E, OAS, DS, T, GI, A, G	^a	Yes
2	5.0	6.1	P, DY, A	^a	Yes	11.0	>100	Not consumed	DBPCFC	Yes
3	16.5	30.7	U, P, OAS, R, O, A	^a	Yes	7.5	1.42	Not consumed	DBPCFC	Yes
4	12.0	7.8	OAS, DS, T, GI, A, G	^a	Yes	4.0	2.87	Not consumed	OFC	No
5	5.0	0	U, AE, P, E, A	DBPCFC	Yes	0	0	Not consumed	OFC	No
6	9.0	0	U, AE, P, E, GI, A	^a	Yes	0	0	Not consumed	OFC	No

Abbreviations: AE, angioedema; A, asthma; DBPCFC, double-blind, placebo-controlled food challenge; DS, difficulty swallowing; DY, dysphonia; E, erythema; G, general malaise; GI, gastrointestinal; OAS, oral allergy syndrome; O, ocular; OFC, open food challenge; P, pruritus; R, rhinitis; SPPT, skin prick-prick testing; T, tongue swelling; U, urticaria.

^a Not challenged because of a convincing history of severe anaphylaxis.

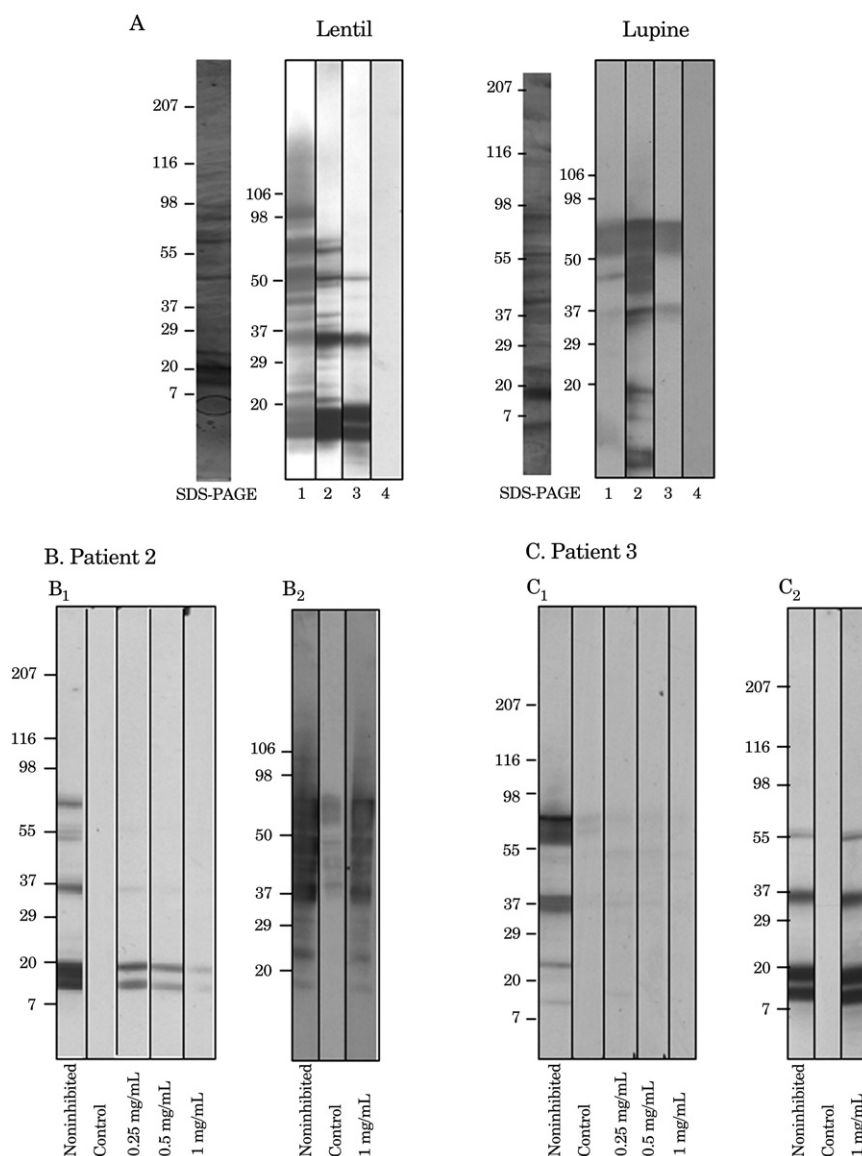


Figure 1. A, Sodium dodecyl sulfate–polyacrylamide gel electrophoresis (SDS-PAGE) and immunoblot of lentil and lupine extracts with sera from 3 patients allergic to lentil and lupine (1-3 indicate patients; 4, negative control). B, Inhibition experiments with serum from patient 2. B₁ shows inhibition of lentil immunoblot by lupine extract (0.25-1 mg/mL; control: inhibition of lentil by lentil). B₂ shows inhibition of lupine immunoblot by lentil extract (1 mg/mL; control: inhibition of lupine by lupine). C, Inhibition experiments with serum from patient 3. C₁ shows inhibition of lupine immunoblot by lentil extract (0.25-1 mg/mL; control: inhibition of lupine by lupine). C₂ shows inhibition of lentil immunoblot by lupine extract (1 mg/mL; control: inhibition of lentil by lentil.).

sults. Lupine seems to be the primary sensitizer in patient 2, with onset of lentil allergy at 47 years of age. Given the frequent use of lupine as an ingredient in other foods,^{1,4,9} he could have become sensitized through previous lupine inadvertent ingestion. In contrast, lentil seems to be the primary sensitizer in patient 3, with onset of lentil allergy at 5 years of age and a recent anaphylactic reaction. Lupine (patient 2) and lentil (patient 3) could contain most relevant IgE epitopes leading to poor inhibition by a secondary sensitizer; however, when the primary sensitizer is used as inhibitor, almost complete inhibition is achieved

in a dose-dependent manner. Lentil- and lupine-allergic patients should be questioned about lupine and lentil reactivity, respectively. If there is no evidence of recent tolerance on ingestion, oral challenges should be performed.

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THE GENETIC ASSOCIATION OF THE *FPRL1* PROMOTER POLYMORPHISM WITH CHRONIC URTICARIA IN A KOREAN POPULATION

Chronic urticaria (CU) is a common immunologic disorder in the general population, but its pathogenic mechanisms are not fully understood. In general, mast cell activation has been considered to play a central role in CU.¹ A recent study² of urticaria suggested that neutrophil infiltration has a key role in its pathogenesis. Increased numbers of neutrophils were found in skin tissue from patients with chronic idiopathic urticaria.³ Moreover, the role of neutrophils has been suggested for other types of urticaria, including cholinergic⁴ and aspirin-intolerant urticaria.⁵

Formyl peptide receptor-like 1 (*FPRL1*) is a chemoattractant receptor and is mainly expressed on neutrophils, monocytes, and dendritic cells. *FPRL1* plays an important role in the regulation of immune responses by the increasing migration of neutrophils and monocytes with the generation of reactive oxygen species.⁶ However, there have been no published reports, to our knowledge, regarding the relation between the *FPRL1* and CU. We hypothesized that the functional variability according to *FPRL1* gene polymorphisms may be associated with CU.

To investigate the genetic association of the *FPRL1* promoter polymorphism with CU, 193 patients with CU and 231 controls were enrolled from Ajou University Hospital, Suwon, Korea; they pro-

vided informed consent, and the study protocol was approved by the institutional review board of Ajou University Hospital. All the patients and controls belonged to the same ethnic group. Patients with CU were defined as having daily itchy wheals for more than 6 weeks. Controls with no personal or family history of allergic disease were recruited. Atopy was defined as 1 or more positive skin prick test reactions to 55 common aeroallergens (Bencard Co, West Sussex, United Kingdom). The total serum IgE level was measured using the UniCAP system (Pharmacia Diagnostics, Uppsala, Sweden). Genomic DNA was extracted using the Puregene DNA Purification Kit (Gentra, Minneapolis, Minnesota). Three single nucleotide polymorphisms of the *FPRL1* gene (-6138C>T, -6136G>T, and -5840G>T) were genotyped using the SNaPshot Primer Extension kit (Applied Biosystems, Foster City, California). The sequences of the amplifying and extension primers were as follows: for *FPRL1*-61318C>T: forward, 5'-CAGGAAACAGCTATGACC-3'; reverse,

Table 1. Genotype and Haplotype Frequencies of *FPRL1* Genetic Polymorphisms^a

	Patients With Chronic Urticaria (n=193)	Controls (n=231)	P value
-6138C>T			
CC	142 (73.6)	155 (67.1)	.19
CT	48 (24.9)	69 (29.9)	.46
TT	3 (1.6)	7 (3.0)	.22
-6136G>T			
GG	89 (46.1)	126 (54.5)	.02 ^b
GT	73 (37.8)	89 (38.5)	.008 ^b
TT	31 (16.1)	16 (6.9)	.13
-5840G>T			
GG	68 (35.2)	65 (28.1)	.21
GT	92 (47.7)	117 (50.6)	.46
TT	33 (17.1)	49 (21.2)	.20
ht1[CGT]			
ht1/ht1	11 (5.7)	18 (7.8)	.35
ht1/-	96 (49.7)	121 (52.4)	.48
-/-	86 (44.6)	92 (39.8)	.39
ht2[CGG]			
ht2/ht2	16 (8.3)	15 (6.5)	.61
ht2/-	62 (32.1)	72 (31.2)	.60
-/-	115 (59.6)	144 (62.3)	.80
ht3[CTG]			
ht3/ht3	15 (7.8)	16 (6.9)	.19
ht3/-	87 (45.1)	86 (37.2)	.11
-/-	91 (47.2)	129 (55.8)	.88
ht4[TGT]			
ht4/ht4	3 (1.6)	6 (2.6)	.02 ^b
ht4/-	17 (8.8)	43 (18.6)	.01 ^b
-/-	173 (89.6)	182 (78.8)	.63
ht5[TGG]			
ht5/ht5			.28
ht5/-	16 (8.3)	27 (11.7)	.28
-/-	177 (91.7)	204 (88.3)	NA

Abbreviation: NA, not applicable.

^a Logistic regression analysis was used to analyze the single nucleotide polymorphisms and haplotypes controlling for age and sex as covariates with 3 alternative models, including codominant, dominant, and recessive model.

^b Statistically significant.

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