

Letter to the Editor



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Disclosure

Kyung Hee Park reports a research grant from the National Research Foundation of Korea (NRF). Jung-Won Park reports being an unpaid chief technology officer for Prolagen Ltd. Kyoung Yong Jeong reports being a technical advisor of Prolagen Ltd. The authors

Allergenic Characterization of Parvalbumin, Tric l 1, From Atlantic cutlassfish, *Trichiurus lepturus*

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To the Editor,

The allergic sensitization pattern reflects cultural differences, including dietary habits, cooking methods, and regional fauna and flora. Current management of fish allergy typically involves avoiding all fish species.¹ However, such dietary restrictions can negatively impact nutrition and growth, particularly in children. Therefore, it is clinically important to differentiate between tolerated and allergenic fish species.

In a recent study, cutlassfish parvalbumin (PV) demonstrated strong immunoglobulin E (IgE) reactivity, underscoring its role as a major allergen and highlighting the need for region-specific diagnostics in Korea.² Another Korean pediatric study identified cutlassfish (28.7%) and yellow croaker (30.6%) as two of the most common causes of whitefish allergy based on clinical history.³ Yellow croaker was also the most common cause of anaphylaxis among whitefish allergy cases. These findings align with fish consumption patterns in Korea, emphasizing the need for region-specific allergen characterization.

This study characterized the PV derived from Atlantic cutlassfish, a commonly consumed species in Korea, and demonstrated its potential role in cross-reactivity among various fish species (**Supplementary Material S1**). One contig, Tl_Uni_05565, was selected and designated as Tric l 1 according to the nomenclature,⁴ as it showed the highest homology with allergenic PVs among the 8 homologous contigs. Its open reading frame encoded a protein of 109 amino acids with a molecular mass of 11.478 kDa and an isoelectric point of 4.608. It shares 64.6 to 83.5% sequence identity with allergenic PVs (**Supplementary Fig. S1**).

Both purified recombinant and natural Tric l 1 (**Figure A**) were recognized by the IgE reactivity in 100% (9/9) of the serum samples from fish-allergic patients (**Figure B, Supplementary Table S1**). The correlation of IgE reactivity between natural and recombinant Tric l 1 was statistically significant ($P < 0.001$) (correlation coefficient, $\rho = 0.986$). However, recombinant and natural Tric l 1 were able to inhibit a maximum of 29.5% and 58.8% of IgE reactivity to the cutlassfish extract, while 92.7% of self-inhibition was obtained (**Figure C**). In general, conformational epitopes play a major role in respiratory allergy, and linear epitopes dominate IgE reactivity in food allergy due to the denaturation of the allergen during cooking. However, conformational epitopes may also be relevant in raw fish allergy, as observed in the case of troponin C, where calcium binding induced structural changes that enhance IgE binding.⁵ In contrast, the addition of calcium did not significantly influence IgE reactivity to PV (**Figure D**) ($\rho = 0.972$ for natural and 0.977 for recombinant PV). Multiple IgE-reactive

Cutlassfish Parvalbumin

(Kyung Hee Park, Jung-Won Park, and Kyoung Yong Jeong) own stocks in Prolagen Ltd. At the same time, Kyoung Yong Jeong and Jung-Won Park also hold shares in Protia Ltd. The reported conflict of interest did not influence academic integrity in analyzing data and writing a paper.

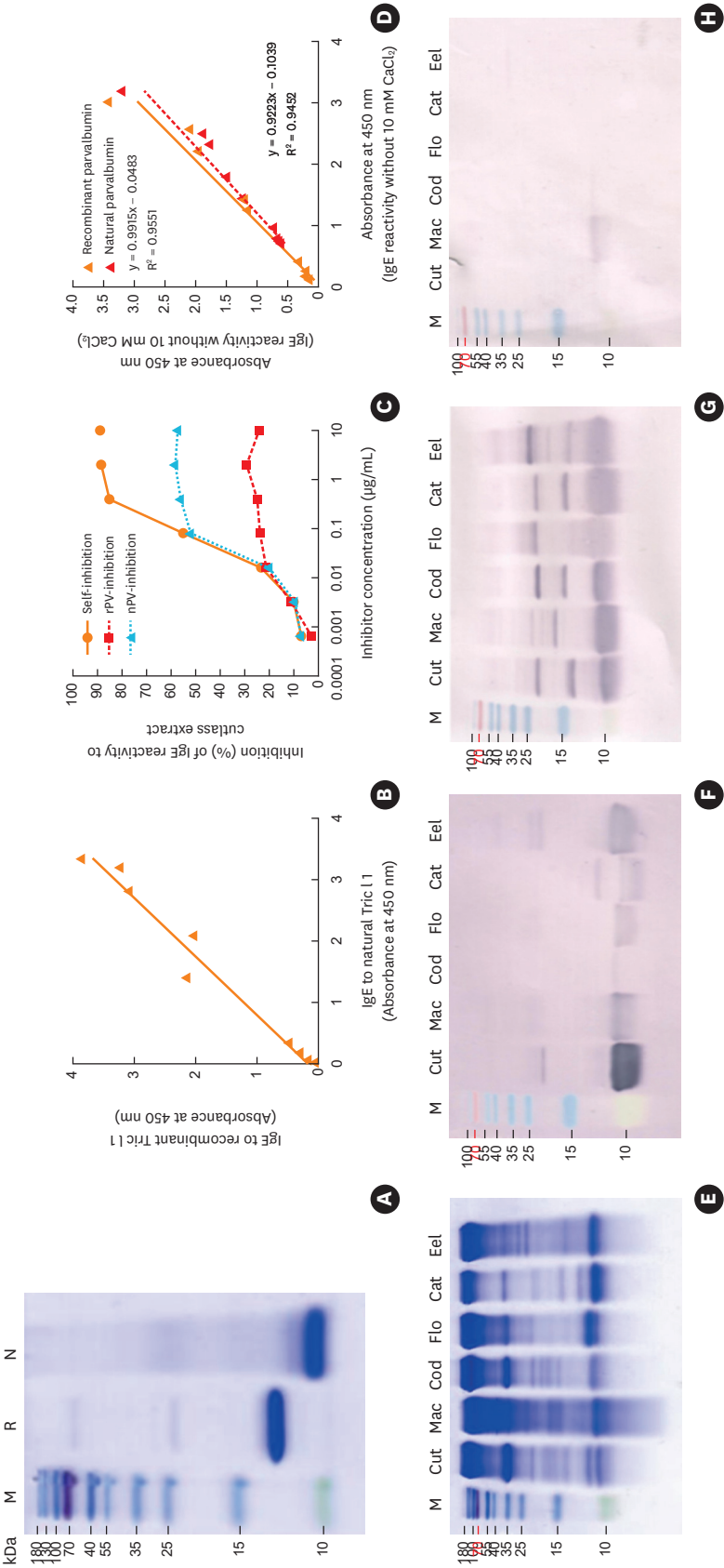


Figure. IgE reactivity of Tric l 1. SDS-PAGE of purified recombinant and natural Tric l 1 (A). Correlation of IgE reactivity between natural and recombinant Tric l 1 (B). Inhibition analysis of Tric l 1 (C) and effect of Ca on IgE reactivity (D). IgE reactive components in the extracts from commonly consumed fish in Korea. Protein profiles were analyzed by SDS-PAGE (E), parvalbumin detection by immunoblotting with anti-parvalbumin (F), IgE immunoblotting (G), and inhibition immunoblot analysis using recombinant Tric l 1 (H).

components, probably due to the nucleation or multimerization of β -PV, were detected by anti-frog PV monoclonal antibodies and IgE antibodies from patients' sera (**Figure E and F**). Inhibition immunoblotting demonstrated that recombinant Tric l 1 could substantially inhibit IgE binding to extracts from multiple fish species (**Figure G and H**). However, inhibition was incomplete for mackerel, indicating interspecies variability and the necessity of individualized clinical assessment for predicting cross-reactivity.

In conclusion, we identified and characterized Tric l 1, a novel PV allergen from Atlantic cutlassfish, as the most important allergen in this species. This molecule may serve as a valuable component in regionally tailored diagnostic strategies for fish allergy.⁶

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SUPPLEMENTARY MATERIALS

Supplementary Material S1

Material and methods

Supplementary Table S1

Clinical features of the enrolled patients

Supplementary Fig. S1

Amino acid sequence alignment of parvalbumin fish allergens. Tric l 1 (Largehead hairtail/ Atlantic cutlassfish, *Trichiurus lepturus*); Sco s 1 (Atlantic mackerel, *Scomber scombrus*, CAX32965); Ras k 1 (Indian mackerel, *Rastrelliger kanagurta*, ANW10058); Gad c 1 (Baltic cod, *Gadus callarias*, P02622); Gad m 1 (Atlantic cod, *Gadus morhua*, AAK63086); Cyp c 1 (Common carp, *Cyprinus carpio*, CAC83658); Cten i 1 (Grass carp, *Ctenopharyngodon idella*, QCY53440); Pan h 1 (Striped catfish, *Pangasianodon hypophthalmus*, XP_026772003); Thu a 1 (Yellowfin tuna, *Tunnus albacares*, CAQ72967); Sal s 1 (Atlantic salmon, *Salmo salar*, CAA66403).

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