

Commentary

***Anisakis simplex* and cross-reacting antigens**

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The immune response to infectious organisms is made up of humoral and cellular components. The humoral immune response involves the generation of immunoglobulins (Igs) that recognize epitopes on the surface of proteins and other antigens in the infectious organism. The cellular immune response is generated by the uptake of these proteins by antigen-presenting cells. These antigenic proteins undergo intracellular processing, and their digested peptides are presented on the surface of antigen-presenting cells in the context of the major histocompatibility antigens (human leukocyte antigens, HLAs). The combination of peptide with the major histocompatibility complex is presented to the T-cell receptor for T-cell stimulation. Stimulation occurs after T-cell receptor–major histocompatibility complex interaction and when additional components on the surface of T cells bind to their counterparts on the surface of antigen-presenting cells. The T-cell receptor recognizes certain motifs of the processed antigenic peptides. *Anisakis simplex* is a nematode that is known to generate both humoral¹ and cellular^{1,2} immune responses.

Antigenic cross-reactivity is an integral part of the immune response. In simple terms, it means that the immune response specific to one antigen (A) can redundantly recognize a second antigen (B) that shares part of the antigenic epitopes with the first antigen (A). This antigenic cross-reactivity occurs when parts of the sequence of antigen A are similar to parts of the sequence of antigen B, or when the three-dimensional structure of antigen A has surface epitopes that are similar to those of antigen B.

Antigenic cross-reactivity is a well-defined phenomenon in the allergy field, in which the generated IgE response can recognize similar antigens/allergens.³ A number of allergens (antigens) have a known set of cross-reacting allergens. One of the most famous cross-reactivities is the latex–fruit allergy

syndrome.⁴ Patients with the latex–fruit allergy syndrome, who are allergic to latex, develop symptoms of oral allergy when they ingest certain fruits, such as banana, avocado, chestnut, potato, and kiwi, among others. This cross-reactivity is felt to be secondary to homologous allergens in latex and these fruits. One such example is Hev b 7 in latex and patatin in potatoes.^{5,6} An additional example of antigenic cross-reactivity is the adverse reaction to celery in patients who are allergic to birch and mugwort.⁷ This antigenic cross-reactivity is believed to be secondary to the homology between the allergens Epi g 1 in celery and Bet v 1 in birch.⁸

In this issue of the *International Journal of Dermatology*, Guarneri *et al.* demonstrate yet another type of antigenic mimicry. The two major antigens in the nematode *Anisakis simplex* (Ani s 2, a paramyosin, and Ani s 3, a tropomyosin) were found to be homologous to paramyosins and tropomyosins of other species. This homology is probably the cause of cross-reactivity in IgE binding to proteins from *Anisakis*, German cockroach, chironomids,^{9,10} and dust mite.¹⁰ In addition to the known homology to IgE binding, however, the authors describe a sequence homology between the processed antigenic peptides that bind to the major histocompatibility molecules between *A. simplex* and other species. In other words, the peptides produced as a result of processing the *A. simplex* antigens are similar in sequence to the peptides produced after processing antigens from other species. These species include cockroach, dust mites, and crustaceans. What this means is that, in addition to the humoral allergenic cross-reactivity related to IgE binding, there is also cross-reactivity in the cellular immune response initiated by antigen processing into peptides and presentation to the T-cell receptor in the context of the major histocompatibility antigens (HLAs).

In clinical practice, infestation with *A. simplex* causes gastrointestinal distress and acute urticaria. In one report,

A. simplex was felt to be related to chronic urticaria in endemic areas suggestive of type 1 hypersensitivity mediated via IgE.¹¹ In another report, a patient with *A. simplex* presented with an eczematous eruption and had positive patch testing to *A. simplex* suggestive of type 4 hypersensitivity mediated by a cellular immune response.¹² The homologies in the humoral and cellular immune responses will cause redundancies that will impact on the accuracy of skin testing. Prick skin testing to *A. simplex* is available in endemic areas.

Therefore, the clinical relevance of this homology is that skin prick testing to *A. simplex* may be false positive in patients who are allergic to dust mite, cockroach, or crustaceans. Furthermore, given the homology in the cellular immune response, patch testing to *A. simplex* may be false positive in patients with reactions to the homologous allergens. The other clinical implication of this is that patients allergic to dust mite, cockroach, or crustaceans may mount a more robust immune response when infected with *A. simplex*. Whether this translates into worse or milder clinical manifestations in patients who are allergic to dust mite, cockroach, or crustaceans remains to be seen.

References

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