

Letter to the Editor

Inhibition of cytokine production in Gastro-allergic Anisakiasis and *Anisakis simplex* sensitization-associated chronic urticaria

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We read with interest the article “Different Th1/Th2 responses to *Anisakis simplex* (*A.s.*) are related to distinct clinical manifestations in sensitized patients”(1). The authors analyse cytokine production with crude extract (CE) and thermostable extract in patients with specific IgE against *A.s.* By finding a similar cellular response to both extracts, they come to the conclusion of the possibility of risk when these patients eat cooked or frozen fish: To our understanding, this statement is not based on allergological concepts, where neither the detection of specific IgE nor the cellular response to different allergens is equivalent to overt allergic symptoms. Further, in the special case of Gastro-allergic Anisakiasis, it has been shown that not only excretory secretory products are responsible for the allergic reaction, but also these have to be delivered by the live larva of *A.s.* when penetrating the gastric mucosa (2,3).

On the other side, we analysed with interest their table 2 about the values of different cytokines when stimulated with mitogen versus *A.s.* crude extract (CE). In a similar evaluation of 23 patients with *A.s.* sensitization-associated urticaria (10 patients with Gastro-allergic urticaria and 13 with *A.s.* sensitization-associated chronic urticaria), we compared the induction of cytokines by *A.s.*CE as well as Concanavalin A (ConA)-stimulated peripheral blood mononuclear cells (PBMC) by the same cytometric bead array kit (CBA; BD Biosciences, Madrid, Spain). We observed lower levels of IL6, IL-10, IL-17, TNF and IFN in CE than in ConA-stimulated PBMC (all $p < 0.01$). On the other side, IL-2, a cytokine important for growth and survival of Th1 and Th2 subsets showed by far higher values when stimulated with CE ($p = 0.02$), underlining the

potency of the used extract and proving the specific stimulation of patient cells which guaranties the induction of immunological responses. Thus, the lower values for the other cytokines can be interpreted as inhibition.

Even if differences in the extract preparation, the concentrations or mitogen used make difficult a direct comparison, similar results seem to be present in the study by González-Muñoz *et al.* as shown in their table 2, but no interpretation of these has been performed. Differential cytokine production is one of the many mechanisms proposed to play a role in modulating the host response by helminth parasites (4). Here, the results demonstrate that a past *A.s.* infection is able to modulate not only Th1- and Th2-related cytokines, but also the pro-inflammatory IL-6, IL17 cytokines and the release of IL-10, as shown by stimulation with *A.s.*CE. We are currently analysing whether TGF- β could be responsible for the *A.s.*- induced cytokine inhibition.

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