ALLERGY, GENETICS

IL33, ALLERGY AND HELMINTHS: SHOT IN THE LEG?

10.04.2019

Ever since our NEJM paper in 2010 that showed an IL33/ST2 association there are new studies on IL33.

Grotenboer 2013 did a functional annotation of the gene and it's receptor in humans while there is no more doubt about the involvement of IL33 in human allergy. Right now IL33 suppression is already used as an experimental screening test for allergic reactivity with ongoing phase II studies of anti-IL33 or anti ST2. Good IL33 reviews can be found for example in frontiers in immunology by Tataori et al. or in nature immunology by Smith.

These reviews do not tell you so much about the regulation while regulation has recently elucidated by Gour et al. who describe a tropomyosin–dectin-1 interaction of the human host. Why is tropomyosin such a frequent target of human IgE?

> Muscle protein tropomyosin is an important IgE target in a number of nematode infections; Onchocerca volvulus ; Ascaris lumbricoides; Anisakis simplex; and tropomyosin from the blood fluke Schistosoma mansoni is also a human IgE antigen. Tropomyosin is highly conserved across many invertebrates and is responsible for much of the IgE cross-reactivity between Ascaris and dust-mites.

I haven't found any good answer to this question. As tropomyosin affects contractility – this seems like "shooting into the leg" of worms whenever they attempt to invade.

Maybe Gour et al. did not know the earlier dissertation from Berlin that already showed a reduced inflammation in the OVA mouse model by administration of recombinant tropomyosin.

> The broad cross reactivity to tropomyosin gives rise to the question if helminth tropomyosin could induce allergic reactions to itself and/or tropomyosin of different organisms. Considering the fact that filarial nematodes express tropomyosin on their surface […] and that the continuing turnover of microfilariae confronts the host with relevant amounts of tropomyosin makes this question even more appropriate.

Worms seems to be attacked by anti-worm-surface-tropomyosin IgE whenever the worm tries to invade the epithelium during an acute infection. During invasion extracellular IL33 is cleaved into a shorter form with enhanced activity attracting more immune cells. During chronic infestation nothing happens as long as the worm does not invade and doesn't trigger any IL33 alarmin. As there is continuous tropomyosin antigen antigen contact, the host is slowly desensitzed, clearing IgE in favor of IgG4.

Is this also a model that explains allergy? We don't know the details but maybe this antigen recognition / response system is being disturbed where allergens like Der p1 mimicking a worm infection by tropomyosin can trigger the allergic reaction in particular as Der p1 a cysteine protease also mimicks an invasion signal.

23.12.2019 Addendum

Parasite tropomyosin ist detected in in 55%-62% of patients (cockroach tropomyosin rPer a 7, Ascaris tropomyosin rAsc l 3).