

Zinc supplementation and allergy

Zinc is an essential trace element and an important factor of approximately 300 human enzymes.

It plays an important role in cellular growth, differentiation, and apoptosis. The immune system with its fast growing rates is especially dependent from available zinc since many studies have shown that insufficient levels of zinc increase the risk of developing infectious diseases, autoimmune disorders, and allergies. Especially the development, differentiation, and activation of antigen-specific T cells, part of the adaptive immune system, are zinc-dependent processes. The antigenic stimulation of T cells results in the differentiation of T helper (Th) cell subpopulations.

Th1 cells induce cellular responses against intracellular microbes and are interferon(IFN)-gamma-producing cells. Th2 cells mediate humoral immune responses against worms, and produce the cytokine interleukin (IL)-4, which triggers IgE antibody production. Regulatory T cells (Treg) suppress Th1 and Th2 mediated immune reactions by producing IL-10 and other cytokines, and control the peripheral tolerance. Treg highly express CD25 (IL-2 receptor alpha-chain), the transcription factor forkhead box p3 (Foxp3), and cytotoxic T-lymphocyte antigen (CTLA)-4. Even though T helper cells regulate and co-ordinate immune responses, they are also associated in the development of autoimmune diseases (Th1) as well as in the induction of allergies, which are Th-2 driven diseases.

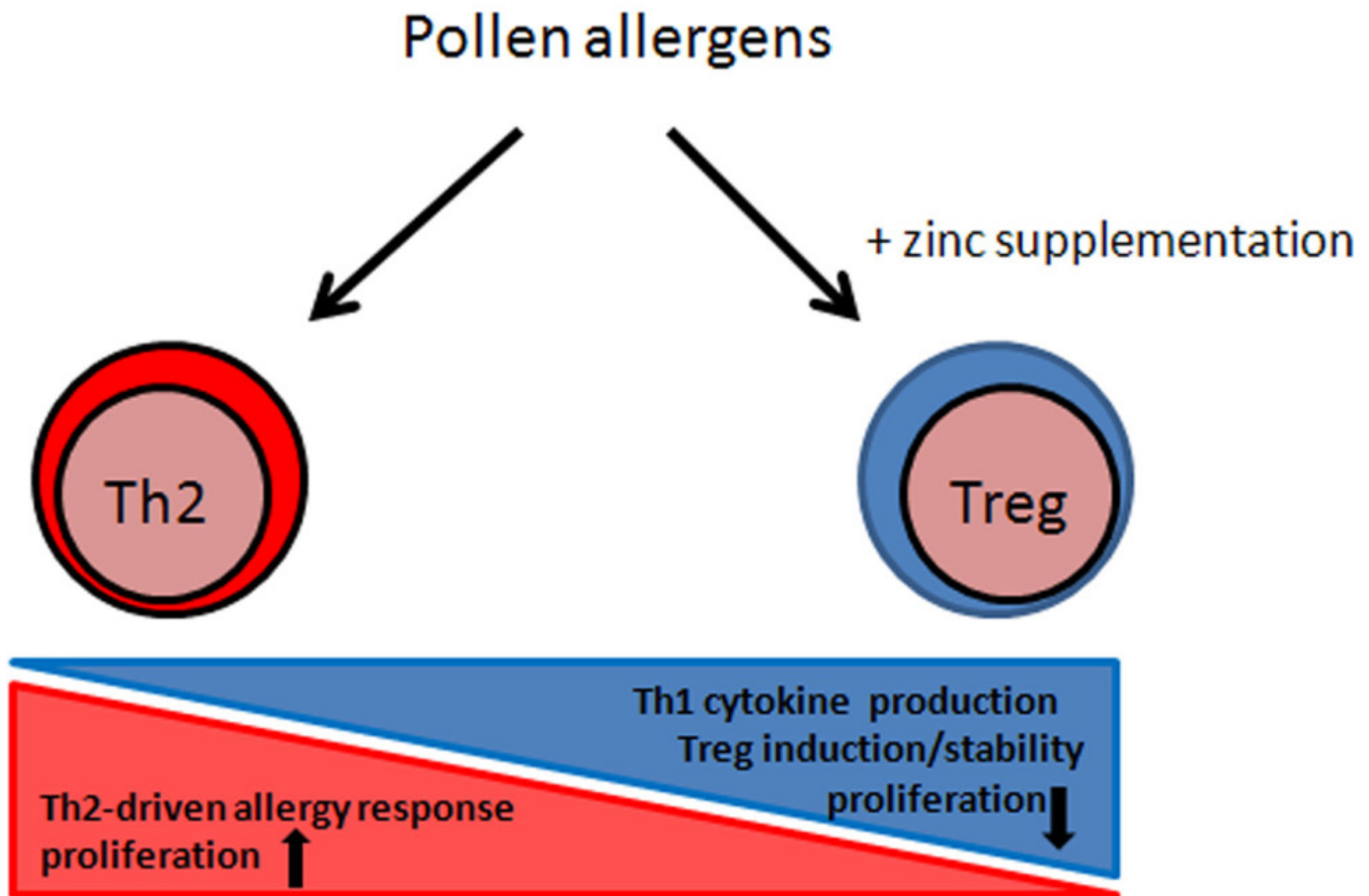


Fig. 1. The response to pollen allergens results in enhanced proliferation of T cells and increased Th2 cytokine releases. The presence of zinc plus allergen reduces T cell growth, induces Treg and switches the Th2-driven response into a Th1 cytokine milieu by releasing IFN-gamma, and TNF-alpha. Therefore, zinc supplementation may be a benefit for allergic patients.

Zinc deficiency and allergic hyperresponsive reactions are often accompanied. Treg are also affected by allergy, but some studies reveal that allergen immunotherapy in rhinitis and asthma is associated with the induction of Treg leading to clinical improvement. To investigate the influence of zinc on allergen reactions, allergen-induced cell growth, Treg cell numbers and cytokine expression in non-atopic and atopic subjects were compared. Peripheral blood mononuclear cells (PBMC) from non-atopic and atopic subjects were treated with timothy-grass (*Phleum pratense*)-derived allergen and pre-incubated with or without zinc. Exposure with timothy grass pollen is one of the major causes of allergic rhinitis in many parts of the world. The response to pollen allergens results in enhanced proliferation of T cells and increased Th2 cytokine releases. By using 50 μ M zinc sulfate in combination with allergen, a significant reduction of PBMC proliferation of atopic subjects was observed. 50 μ M zinc sulfate plus allergen enhanced Th1

cytokine responses shown by increased IFN-gamma / IL-10 ratios as well as increased tumor necrosis factor(TNF)-alpha release. Additionally, zinc supplementation and allergen increased Foxp3+ Treg, and upregulated the mRNA expression of Treg specific CTLA-4 mRNA in atopic subjects. Interestingly, 50 µM zinc sulfate alone led to an increase of CD25high+ Th cells in atopic and non-atopic subjects indicating a zinc-dependent effect on Treg growth, generally.

Taken together, the application of zinc and allergen leads to suppressed proliferation, the induction of regulatory T cells, and to a Th1 cytokine production (Fig. 1). Th 2-driven responses by timothy-grass (pollen) allergens can be altered by zinc supplementation. Therefore, zinc might be able to dampen allergic reactions by switching the Th cell response and decreasing proliferation. In addition, Treg may be therapeutic targets for zinc-induced modulation of the allergic immune reaction.

Lothar Rink

Institute of Immunology, RWTH University Aachen, Medical Faculty, Aachen, Germany

Publication

[Zinc enhances the number of regulatory T cells in allergen-stimulated cells from atopic subjects](#)

Rosenkranz E, Hilgers RD, Uciechowski P, Petersen A, Plümäkers B, Rink L.

Eur J Nutr. 2015 Nov 20