



Perinatal exposure to GOS/inulin prebiotics prevent food allergy by promoting tolerance and protecting intestine

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Allergy 1

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Local remodeling, mast cell activation and sphingosine-1-phosphate elevation precede atopic dermatitis

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Atopic dermatitis (AD) is an inflammatory skin disease whose pathogenic mechanisms remain unclear. Chronic lesions have been extensively characterized however few studies have investigated the initial phases of AD, including early skin alterations prior to any visible lesion. We recently reported a novel method of computer-assisted image analysis for *in situ* measurement of mouse skin mast cells (MC) activation. We applied similar morphometric approaches to quantify local MC activation status and skin remodeling after a single epicutaneous exposure to antigen/ovalbumin (OVA), compared to saline controls in a human AD-like preclinical model. Remarkably, epidermal and dermal thickening was substantiated after a single OVA application, also resulting in early cellular infiltration in the vascularized hypodermis layer of the skin. Furthermore, skin remodeling correlated with augmented local chemokine production, MC activation, and increased levels of a potent sphingolipid metabolite sphingosine-1-phosphate (S1P) that we have shown could activate MC-derived chemokine production. Importantly, cell infiltration was severely mitigated in mice genetically ablated for sphingosine kinase 1, predominant enzyme isoform producing S1P, and in MC-deficient *Kit^{W-sh/W-sh}* mice. We conclude that MC and S1P could initiate the development of AD by driving early inflammatory infiltration and skin remodeling through their contribution to local chemokine production, offering perhaps new prophylactic approaches for this disease whose treatment management still remains a clinical challenge.

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Perinatal exposure to GOS/inulin prebiotics prevent food allergy by promoting tolerance and protecting intestine

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Aims: Food allergies (FA) are increasing and prevention strategies are nonexistent. They are linked to imbalance of microbiota and immune system. Fibers as prebiotics have been proposed to restore this balance and seem to be one alternative to prevent or reduce allergies, particularly during infancy. In this context, we evaluated early nutritional intervention with prebiotics, via the mother during pregnancy and lactation (perinatal), to prevent food allergic risk in mice.

Method: Pregnant and lactating mice were exposed or not to GOS/Inulin prebiotics. Then, pups were intraperitoneally sensitized and then orally exposed to wheat allergen to mimic FA. Phenotypic and blood markers of allergy, immune cells and microbiota were analyzed.

Results: In mice exposed to GOS/Inulin prebiotics *via* their mothers, we observed a decrease of FA symptoms associated with a fall of allergic markers (IgE), a rise of tolerance markers (IgA) and a protection from the alteration of intestinal permeability and epithelium. Immunity was also modified by prebiotics as shown by the decrease of IL-4 and IL-5 productions and the increase of IFN- γ and TGF- β secretions associated with a rise of T regulatory cells in gut lymphoid organs. Prebiotics also induced a strong modification of mother mice intestinal microbiota especially for *Lactobacillus* that was the only one being transferred to pups.

Conclusion: Prebiotics supplemented diet during perinatal period protects pups against FA by decreasing levels of allergic markers, clinical symptoms and intestinal permeability. Moreover, prebiotics also modulate immune reaction during allergy toward tolerance and modify intestinal microbiota.