ABSTRACT

The main goal in reversing the allergy epidemic is the development of effective prophylactic strategies. Early life events, such as exposures to microbes, have a major influence on the development of balanced immune responses. Due to their ability to interact with host immune system and to modulate host immune responses probiotics, mainly bifidobacteria and lactobacilli have been used with some success in prevention of allergic disease.

In order to be referred to as probiotic, bacterial strain has to undergo rigorous testing. We have selected three new *Lactobacillus* (*L.*) strains out of 24 human isolates according to their antagonistic activity against pathogenic bacteria, resistance to low pH and milieu of bile salts. Safety of these strains was proven upon intragastric administration to mice; moreover, we have shown their ability to shift cytokine Th1 - Th2 balance towards non-allergic Th1 response in isolated splenic cells.

Allergen specific prophylaxis using probiotics as vehicles for mucosal delivery of recombinant allergen is an attractive concept for development of well-tolerated and effective allergy vaccines. We have shown that neonatal mono-colonization of germ-free mice with the *L. plantarum* NCIMB8826 strain producing the major birch pollen allergen Bet v 1 attenuates the development of birch pollen allergy later in life. The mechanisms involve a shift towards a non-allergic Th1 phenotype accompanied by increased regulatory responses, which were antigen-specific as colonization by a wild type strain exerted no such effects.

Intrinsic immunomodulatory properties of the probiotic strain play a key role in its ability to interact with the immune system of the host. We have further shown that neonatal mother-to-offspring mono-colonization with *Bifidobacterium longum* CCDM367, a human isolate with Treg rather than Th1 immunomodulatory properties, was able to reduce allergic sensitization by activating regulatory responses via TLR2 and MyD88 signaling pathways.

Understanding what makes ‘allergen an allergen’ is a key in allergy prophylaxis or treatment. We have shown in a mouse model of food allergy that even minor irreversible changes in OVA secondary structure caused by thermal processing alter both its digestion and antigenic epitopes formation. This leads to activation of different T cell subpopulations, induces shift towards Th1 response and ultimately reduces its allergenicity.

Taken together, understanding the immunomodulatory potential of bacteria in the early host development can pave a new way for probiotic use in early nonspecific prevention of type I allergy. Combining the probiotics with relevant allergen can make this approach even allergen-specific.