

Popular summary

The aim of the project is finding if there is a link between composition of commensal bacteria community (termed microbiome) thriving in mother's milk and child's skin as well as gut, and clinical course of food allergy (FA) in children. Moreover, we plan on determining if the microbiomes under study influence regulation of expression of genes whose products are important for regulation of immune response (cytokines and Foxp3).

We plan to recruit up to 150 0-6 months old infants with FA and/or atopic dermatitis (AD) (up to 50 children in each group: FA, FA+AD, AD). Control group will involve up to 150 healthy infants. All subjects will be fully assessed allergologically, we will also determine composition of their skin (based on swab analysis) and gut microbiomes (based on stool analysis). Moreover, their mothers' milk microbiomes will be assessed as well. Methylation level of selected genes will be determined based on blood samples.

Subjects will be treated in a standard way, then observed for a year during regular visits (every three months) in an Outpatients Clinic. After 12 months their allergological status will be determined again, together with determination of the level of tolerance to previously sensitizing food. Skin and gut microbiomes will also be assessed again.

Basing on the results, a hypothesis of the influence of the way of feeding and mother's milk microbiome on not only child's gut but also skin microbiome and epigenetic gene expression regulation will be proved or disproved. Moreover, we will determine if acquirement of tolerance to food allergens is connected with microbiome at early infancy and its changes over time, as well as with changes in gene methylation level during the course of the study.

Food allergy (FA) affects 4-10% of children. It is more frequently encountered in AD children, around 15-30% of their population being affected by FA as well AD, the most frequent chronic disease in children (15-20% of children affected worldwide) is in turn more frequent in FA children than in the general population. FA and AD are frequent, but their incidence displays increasing trend. In light of published studies, involvement of skin in pathogenesis of FA seems to be plausible. Until now, bases of relation between AD and FA are unknown. It was impossible to determine what are determinants of different types of reaction to food allergens: skin reaction, gut reaction, reaction from both organs or no reaction at all. Some studies support a concept whereby the skin and gut are linked via modulation of the immune environment via microbiome. Currently it is not clear whether modulation of the gut microbiome can impact upon the skin microbiome and vice versa.

New methods of studying microbiome based on marker genes such as 16S rRNA gene were devised recently. A few studies report that gut microbiome is altered in FA children compared to healthy ones. It is thought that microbiome at early infancy may determine both development of FA and its clinical course and acquirement of tolerance to food allergens. In parallel, skin microbiome is altered in AD children. Certain studies point at a possibility that skin microbiome at early infancy may determine AD development until the end of the first year of life.

A connection of breastfeeding with diversity of child's gut microbiome was demonstrated. There is no data showing link between mother's milk microbiome and child's skin microbiome development.

Changes in gene expression regulation at the epigenetic level are implied in development of both FA and tolerance. Such a regulation is a quick means of adaptation to environmental changes. It was shown that changes in methylation level positively influencing tolerance were more frequently found in patients receiving probiotics. However, there is no studies unequivocally stating such a link.

Finding if mother's milk microbiome influences child's gut and skin microbiome, as well as determination of differences in this respect between FA children of varying clinical course and healthy ones together with demonstration of influence of epigenetics on the course of allergy might contribute to elucidation of pathogenesis mechanisms in FA. It may also constitute basis for follow-up studies aimed at design of improved diagnostic tools. Moreover, conclusions emerging from our project might be useful in setting up novel models of food allergy treatment as well as prophylaxy.