Food Allergy: From Diagnosis to Prevention Through Integrative Omics

Lynn Vanhaecke

ABSTRACT:
IgE-mediated cow's milk allergy (IgE-CMA) is among the earliest food allergies to develop in childhood and is primarily triggered by the milk proteins β-lactoglobulin (BLG) and casein. Elucidating the mechanisms underlying IgE-CMA (and other food allergies) is essential for identifying new biomarkers and designing effective strategies for treatment and prevention. We established a longitudinal *in vivo* murine model in which two mouse strains (BALB/c and C57Bl/6) were sensitized to BLG using either cholera toxin or an oil emulsion. Following sensitization, mice underwent oral challenge, with clinical symptoms assessed alongside measurements of antibody (IgE, IgG1) and cytokine (IL-4, IFN-γ) levels, as well as metabolomic/lipidomic fingerprinting of fecal samples. Findings from these models were integrated with fecal microbiome–metabolome data from children with IgE-CMA and healthy controls enrolled in a clinical trial (NCT04249973). Analyses included polar metabolomics, lipidomics, and 16S rRNA sequencing, complemented by *in vitro* gastrointestinal digestions to confirm microbial contributions to observed metabolic changes. In mice, sensitization was accompanied by distinct microbial-derived metabolic alterations—most notably in bile acid, energy, and tryptophan pathways—that preceded allergic inflammation. These alterations were recapitulated in the patient cohort, where gut dysbiosis and associated metabolic changes coincided with markers of low-grade inflammation. Collectively, our findings indicate that gut dysbiosis precedes allergic inflammation and fosters chronic low-grade inflammation in children on elimination diets, highlighting promising avenues for preventive and therapeutic interventions.