

Editorial

Explaining the link between maternal lipid profiles and food allergy in offspring

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Food allergy is widely believed to have increased in prevalence in recent decades. These increases have been attributed to factors associated with the modern westernized lifestyle, a hypothesis supported by a greater food allergy prevalence in more developed and Western countries and in urban compared with rural areas.¹ Despite recent progress in understanding risk factors for food allergy, reasons for the increase in food allergy and between-country differences remain largely unknown.

The report by Hong et al² in this issue of the *Journal* investigates a novel prenatal risk factor for food allergy. The authors use a lipidomics approach that uses mass spectrometry to identify individual lipids present in plasma to measure lipid metabolites (including cholesterol esters, diacylglycerols, lysophosphatidylcholine, lysophosphatidylethanolamines, phosphatidylcholine, phosphatidylethanolamines, and triacylglycerols [TAGs]) in maternal plasma 1 to 3 days after delivery. Lipidomics is a growing area of research recognized as a powerful hypothesis-generating platform, and this is the first study to use this approach in patients with food allergy.³

In this urban, low-income, minority birth cohort (n = 1068 mother-child dyads) the authors identified several maternal plasma TAG metabolites associated with an altered risk of food allergy, which was defined as a positive specific IgE level with symptoms consistent with IgE-mediated food allergy. Six TAG metabolites of a possible 216 maternal metabolites evaluated were significantly associated with the risk of food allergy. In general, TAGs associated with a decreased risk of food allergy had longer acyl chains and more double bonds, whereas TAGs with shorter acyl chain carbons and fewer bonds were associated with an increased risk of food allergy. By using a weighted TAG score, each SD increment was associated with a 1.9-fold (95% CI, 1.4- to 2.6-fold) increased risk of food allergy in the offspring.

Investigating risk factors for food allergy in a low-income minority cohort is commendable because this is an understudied group in food allergy research. However, it also raises

questions about the generalizability of these findings to other populations and settings that will need to be addressed in future studies.

This article contributes to a body of evidence suggesting that factors present before birth might set the scene for later development of food allergy. There is some evidence of immune differences at birth between children who go on to have food allergy and those who do not.⁴ However, it is also clear that post-natal interventions, such as timely introduction of allergenic foods, can prevent the development of food allergy among those at high risk.⁵ Interestingly, Hong et al² found that the association between maternal TAG score and food allergy was less pronounced, although still present, among those with timely solid-food introduction (before 7 months of age). Although the current study did not measure timing of allergenic food introduction, it is likely that those with delayed solid-food introduction would also have delayed introduction of allergenic foods, which might drive this interaction.

The TAGs associated with a reduced risk of food allergy in this study, those with longer acyl chains and more double bonds, are predominantly composed of polyunsaturated fatty acids (PUFAs). PUFAs, especially n-3 PUFAs, have long been associated with inhibiting proinflammatory cytokines and modulating immune responses, offering a plausible pathway for protecting against allergy. Although animal models suggest a role for dietary fatty acids in the development of allergy, the evidence in human subjects is less clear, as summarized in a recent European Academy of Allergy and Clinical Immunology position paper.⁶ Few existing studies have investigated food allergy as an outcome, although several studies have investigated food sensitization, with some of these suggesting that high maternal n-3 PUFA intake can reduce allergic sensitization in offspring. Randomized controlled trials of supplementation with n-3 PUFAs, such as fish oil, during pregnancy and breastfeeding for allergy prevention have shown conflicting results; benefits from supplementation were potentially related to pre-trial maternal and infant n-3 PUFA levels. In the present study the TAG associations were only apparent for food allergy outcomes, and no association was observed for food sensitization in the absence of clinical food allergy. It is possible that the TAGs identified in this study influence conversion from food sensitization to food allergy rather than production of IgE antibodies, although this finding requires validation in future studies.

Maternal TAGs of shorter acyl carbon chains and fewer bonds, which were associated with an increased food allergy risk in offspring in the present study, are predominantly composed of saturated and monounsaturated fatty acids. Although some *in vitro* and animal studies suggest that some saturated fatty acids can induce proinflammatory signaling, there is limited evidence that maternal intake of saturated fats during pregnancy is associated with food sensitization and allergy.⁶

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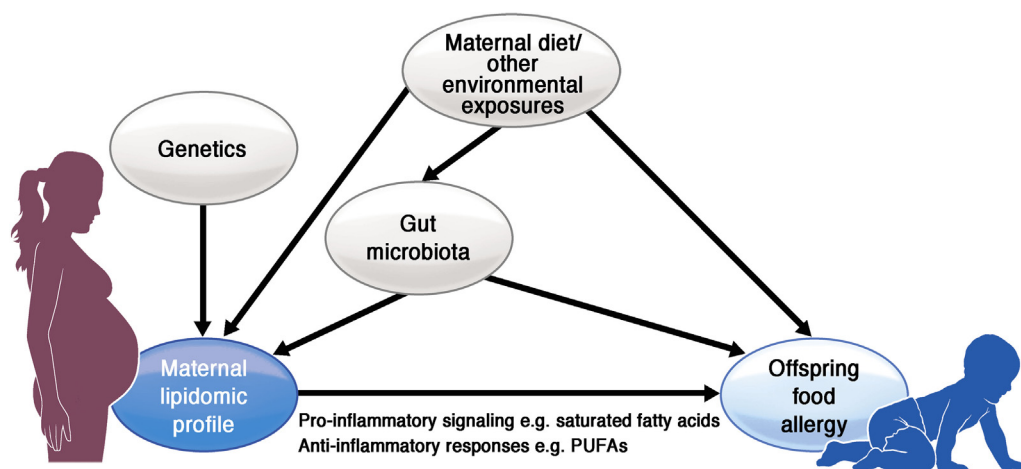


FIG 1. Potential explanations for a link between maternal lipidomic profiles and food allergy risk in offspring.

There are also several other potential explanations for the observed association between maternal lipid profiles and food allergy in offspring. Perhaps the most likely of these is the existence of a common cause, such as genetic polymorphisms, maternal diet, or other environmental exposures, shared by maternal TAG levels and food allergy development in offspring (Fig 1). Lipid metabolism and lipid levels are influenced by a number of genetic polymorphisms, as well as by diet.⁷ There is a complex interplay between diet, gut microbiota, lipid metabolism, and immunity. While diet, including intake of dietary fats and fiber, influences the composition of the gut microbiota,⁸ microbes in the gut in turn affect lipid metabolism.⁹ Multiple studies have linked the composition of the gut microbiota with immune functioning and allergic disease, although the exact relationship between the gut microbiome and food allergy remains unclear.¹⁰

The use of novel approaches and advances in technology, such as lipidomics, to enable exploration of complex maternal-fetal environments has the potential to further our understanding of food allergy development. Validation of these findings in independent prospective cohorts will be required, and future mechanistic studies might be helpful to untangle the biological explanation for the observed associations.

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