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## *Invited Commentary*

# Maternal fatty acids and offspring development: extending beyond the cardiovascular and endocrine systems

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The developmental origins of health and disease or 'developmental programming' hypothesis has largely focused on the detrimental effects of a suboptimal early environment on the risk of developing metabolic diseases such as CVD, insulin resistance or type 2 diabetes. In particular, the detrimental effects of maternal undernutrition[1] or maternal overnutrition[2] on offspring metabolic health are widely recognised. Far less attention has been directed towards the potential consequences of exposure to suboptimal nutrition during fetal life on the risk of health outcomes beyond the cardiovascular or endocrine systems. However, there is growing evidence that the risk of developing diseases not typically considered 'metabolic' such as osteoporosis, schizophrenia and immune disorders could also have their origins in fetal life. This is further emphasised by a study by Niinistö *et al.*[3] reported in this edition of the *British Journal of Nutrition* that investigated the effects of changes in maternal dietary fatty acid composition on the risk of developing type 1 diabetes (T1D), an autoimmune disease.

In brief, the study by Niinistö *et al.*[3] utilised datasets available from the Finnish Type 1 Diabetes Prediction and Prevention Study (DIPP) to investigate the potential associations between the type of food consumed by the mother during pregnancy and the incidence of T1D in her children. Pregnant women completed a FFQ during the 8th month of pregnancy, so data have to be interpreted cautiously in relation to implications for diet throughout pregnancy. However, associations were identified between the maternal consumption of some food types, their fatty acid content (particularly saturated palmitic acid and monounsaturated palmitoleic acid) and the incidence of T1D during the reported follow-up period. While the associations were relatively weak, this paper serves as an important further step towards understanding the role that maternal diet during pregnancy plays in the development of offspring beyond the womb in relation to T1D and autoimmune-related conditions in general.

There is some evidence in the literature to suggest that the maternal environment influences the risk of development of immune-mediated conditions in the offspring. Previous work published on the DIPP cohort[4,5] as well as the work by Dunstan *et al.*[6] provide strong evidence for an effect of maternal diet on the risk development of asthma and specific allergies in the offspring. The direct mechanisms by which maternal diet may elicit an alteration in the immune development of the offspring are unknown. However, current hypotheses include the suggestion that increased exposure to *n*-6 long-chain PUFA *in utero* causes increased production of pro-inflammatory two-series PG and four-series leukotrienes in the offspring. This may result in the detrimental functioning of antigen-presenting cells, subsequent poor programming of T-cell function and the resulting development of a clinical phenotype[7]. Although during the early stages of pregnancy, the maternal serum fatty acid profile may change independently of dietary intake[8], this hypothesis is of immediate concern in light of recent studies that have highlighted a global change in the dietary intake of fats in recent decades. Epidemiological studies have demonstrated a shift away from diets high in *n*-3 polyunsaturated fats to diets high in the pro-inflammatory *n*-6 polyunsaturated fats over the past 20 years. To combat this potential detrimental dietary change, some studies have investigated the effect of increasing *n*-3 polyunsaturated fat intake through fish oil supplementation during pregnancy on offspring body composition[9] and allergen-specific immune responses[6]. The latter of which reported positive beneficial outcomes of maternal fish oil supplementation on the offspring.

More relevant to the current study by Niinistö *et al.*[3] is the role that maternal fatty acid profile may play in the development of T1D. The potential for the maternal environment to influence the incidence of T1D has previously been reported in a number of studies. Maternal age at delivery (>30 years old), a birth weight greater than 4 kg and delivery by caesarean section have all been associated with increased incidence of T1D[10]. Studies investigating the associations between the maternal intake of fatty acids and the offspring's risk of T1D have been more variable in their findings. For example, some studies in which the maternal fatty acid environment is identified by self-report FFQ found associations between the maternal intake of fat and the incidence of T1D. Stene *et al.*[11] reported an increased incidence of T1D with a low intake of cod-liver oil during pregnancy, and the current study by Niinistö *et al.*[3] reports that the incidence of T1D is reduced with an increased consumption of long-chain MUFA. However, in a large human population study in Norway, in which the maternal serum fatty acid profile was measured directly during late gestation, there was no association between the long-chain *n*-3 PUFA profile and the offspring's incidence of T1D[12]. These differences in findings may reflect limitations in using self-reported maternal questionnaires at a single time point during pregnancy. A further limitation also often not addressed is the potential

effects of offspring dietary intakes. Stene *et al.*[13] reported that offspring cod-liver oil intake during the first year of life exhibited protective effects against the development of T1D independently of maternal cod-liver oil intake. A US cohort study also identified strong protective associations between offspring *n*-3 PUFA consumption and β-cell autoimmunity[14]. Hence, while the current Niinistö study inspires some reflection on the role that maternal fatty acid intake may have on the offspring's incidence of T1D, it is important to note that this may be independent of offspring dietary effects, and hence future studies should ensure to collect both datasets and supplement this with direct measures of maternal serum fatty acid profiles. It may be of further interest to note that in the examples presented here of an association between maternal dietary fat intake and immune system diseases in the offspring, the focus has been on specific fat types. This is potentially in contrast to the evidence that observes the development of cardiovascular or endocrine disorders in the offspring that are more commonly associated with maternal 'total' dietary fat intake[15], although this is a hypothesis that would benefit from further prospective studies.

The current Niinistö study represents another growing area of interest that investigates the potential for gene–environment interactions to be significant in the development of immune-related disorders. Current evidence suggests that prospective investigations on the maternal intake of specific fat types in concert with observations of offspring diet may therefore provide beneficial gains in our understanding, treatment and potential prevention of common immune-related diseases.

## Conflicts of interest

The authors have no conflicts of interest to declare.

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