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Fish Oil Intake During Gestation and Lactation Attenuated STZ-Induced Diabetes in Male Offspring via Activation of Brown Fat and Modulating Oxylipin Profile

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Objectives: Fish oil (FO) has been demonstrated to activate brown thermogenesis and attenuate inflammation in the brown adipose tissue (BAT). Previously, we have reported that maternal FO supplementation promotes BAT activity of the weaned mice pups. However, whether maternal FO intake could confer sustainable metabolic benefits to offspring remains uncovered. Therefore, this study aimed to determine the differential impact of maternal FO during pregnancy versus lactation on BAT transcriptome and evaluate the role of bioactive lipid metabolites derived from maternal FO supplementation on the extended metabolic benefits of older pups in the context of type 1 diabetes (T1D).

Methods: BAT samples were collected for RNA sequencing at birth and weaning in the pups with or without maternal FO supplementation. Transcriptomic data were analyzed for profiling of differential expression genes (DEGs) and pathway enrichment analysis. The separate set of 8-week-old male pups with or without maternal FO were injected with streptozotocin (STZ) to induce type 1 diabetes (T1D). In these animals, glucose tolerance, insulin secretion, and plasma levels of oxylipins were assessed. The expression levels of thermogenesis-related genes, inflammatory markers, and mitochondrial respiratory chain complexes were measured in the BATs.

Results: The RNA-seq analysis revealed that FO intake throughout pregnancy and lactation, but not gestation only, significantly altered BAT transcriptome by upregulating glucose and lipid metabolism pathways and downregulating apoptosis-related pathways. The n-6/n-3 ratio maintained lowered in the 8-week-old pups with maternal fish oil. Consequently, the pups with maternal FO 1) provided the resistance to STZ-induced T1D, 2) promoted thermogenesis-related gene expression and mitochondrial respiratory protein complex in the BAT, 3) reduced proinflammatory oxylipin production compared with the control mice.

Conclusions: Our results suggested that maternal FO intake in pregnancy and lactation, at least partly, protects against the risk of T1D of the offspring through augmented BAT function and anti-inflammatory oxylipin production.

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