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## **Addition of dairy lipids and probiotic in infant formulas modulates gut microbiota and intestinal physiology with long-term consequences; a preclinical study in a minipig model**

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Whereas breast milk is the gold standard, most infants are at least partly formula-fed. The aim of the present study was to investigate the short- and long-term effects of the addition of dairy lipids (DL) in infant formulas as an alternative to plant lipid-based infant formula, on gut microbiota composition and activity, and on intestinal immune and barrier functions, and of a probiotic, *Lactobacillus fermentum* (Lf), on the same parameters.

Piglets received from postnatal day (PND) 2 to 28 a balanced formula containing either: only plant lipids (PL), a half-half mixture of PL and DL (DL), or a half-half mixture of PL and DL supplemented with Lf (DL+Lf). Pigs were subsequently fed a standard diet for 1 month and then challenged with a high-fat, high-sucrose diet for 3 months until PND140. Dietary-induced changes in gut microbiota composition were observed at both PND28 and PND140, mainly within Firmicutes (*Lachnospiraceae*, *Ruminococcaceae* and *Lactobacillaceae* families) and Bacteroidetes (*Prevotellaceae*, *Bacteroidaceae* and *Bacteroidales* S24-7 group families) phyla. At PND28, twenty fecal metabolites (such as valerate, butyrate, amino acids, glucose) discriminated the three groups. DL and DL+Lf reinforced tight junction protein expressions in colon, with moderate changes in epithelial barrier permeability. At PND140, DL+Lf decreased the inflammation risk through decreased ileal pro-inflammatory cytokine secretion and increased ileal expression of genes encoding tight junction proteins. A slight but persisting and coherent effect of probiotic Lf on gut microbiota composition was observed between PND28 and PND140, even after discontinuation of its intake. Correlations between gut microbiota composition and intestinal physiology confirmed the involvement of gut microbiota in such processes.

In conclusion, the addition of DL in infant formula changed the microbial signature and gut physiology in infants. The addition of Lf enhanced the beneficial effects observed in the long term. The addition of DL±Lf appears to be safe.

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