

Dairy lipids and *L. fermentum* incorporation in infant formula has long-term effects on intestinal permeability and immunity but no effect on metabolic dysfunction induced by an obesogenic diet in a minipig model

Marion Lemaire * , Gaëlle Boudry , Stéphanie Ferret-Bernard , Isabelle Nogret , Laurence Le Normand , Gwénaëlle Randuineau , Michèle Formal , Sylvie Guérin , Armelle Cahu , Pascale Le Ruyet , Isabelle Cuinet , Charlotte Baudry , Sophie Blat *

¹, Isabelle Le Hüerou-Luron *

¹ INRA, unité Adaptation Digestives, Nerveuses et Comportementales (ADNC) – Institut national de la recherche agronomique (INRA) : UR1341 – INRA, UR 1341 ADNC Domaine de la Prise 35590 St Gilles, France

The composition of human milk is better mimicked in infant formulas (IF) that include dairy lipids (DL) with benefits concerning digestion, gut physiology and microbiota demonstrated in a porcine model. Based on the DOHaD concept, perinatal nutrition may have sustained metabolic and physiologic impacts in adulthood. The objective of the present study was to investigate the long-term impact of the consumption of IF containing DL and a probiotic (*Lactobacillus fermentum* CECT 5716, Lf) on growth, intestinal barrier function, metabolic and immunologic status of adult Yucatan minipigs submitted to an obesogenic diet.

Twenty-six two-day-old piglets received a formula containing either: only plant lipids (PL), a half-half mixture of PL and DL (DL), a half-half mixture of PL and DL supplemented with Lf (DL+Lf) until weaning at the age of 28 days. Piglets were then fed a standard diet for 1 month and an obesogenic (high-fat, high-sucrose) diet for 3 months. Basal plasma lipid and glucose concentrations were measured and glucose tolerance assessed by intravenous glucose tolerance test (IVGTT). Five-month-old minipigs were then slaughtered and tissues collected to perform digestive functional investigations. Paracellular and transcellular permeability of intestinal segments were measured *ex vivo* in Ussing chambers. Ileal immune response was evaluated *in vitro* using explants stimulated with the mitogen Concanavalin A (ConA) or with a bacterial proinflammatory ligand, lipopolysaccharide (LPS).

The obesogenic diet led to lipid and glucose metabolism dysfunctions (dyslipidemia, adiposity and insulin resistance), which were not different according to the IF received in the young age. Neither were the growth and the feed intake between groups. However, the intestinal permeability of 5-month-old minipigs was modified by DL or DL+Lf incorporation. DL decreased LPS passage in jejunum and increased ileum transcellular permeability compared to PL pigs. These effects were strengthened by Lf supplementation and associated with an increased ileum

*Intervenant

conductance compared to PL pigs. DL+Lf intake during early life also improved the immune balance by increasing the anti-inflammatory (IL-10) and decreasing the pro-inflammatory (TNF- α and IL-8) responses of ileal explants compared to the PL group.

This study shows that early consumption of IF with DL and a probiotic (Lf) has no long-term effects on growth, body composition, plasma lipid profile and glucose metabolism of 5 month-old minipigs. However, it highlights a long-term effect of DL and Lf early consumption on intestinal barrier and immune orientation. Since the intestinal response to IF may be influenced by early-life microbiota colonization, changes in microbiota composition and consequences on the intestinal endocrine function are under investigation.