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## **Imprinting power: early-life supplementation with prebiotic impacts immune system and energy metabolism in pigs subjected to challenge**

Cindy Le Bourgot, Stéphanie Ferret-Bernard, Sophie Blat, Laurence Le Normand, Michèle Formal, Frédérique Respondek, Emmanuelle Apper, Isabelle Le Huërou-Luron

Early microbiota colonization is crucial for development of immune and metabolic functions in a sustainable way, with consequences on the susceptibility to develop diseases. Both early colonization and diversity of the microbiota represent key factors of such nutritional programming. Our study aimed at evaluating effects of perinatal short-chain fructooligosaccharides (scFOS) consumption on intestinal functionality. Furthermore, we investigated whether perinatal scFOS supplementation impacts adult metabolic responses to a high-fat (HF) diet.

In the two studies, sows received a diet supplemented with scFOS (Profeed<sup>®</sup>) or maltodextrins (CTRL) for the last third of gestation and the entire lactation. In the first study, at postnatal day (PND) 28, pigs of each litter were weaned and divided into two groups receiving CTRL or scFOS until PND56. Short-chain fatty acids (SCFA) production was analysed at PND21 and PND56. Intestinal functionality was assessed at PND56. An oral vaccine challenge against *Lawsonia intracellularis* was performed and serum and ileal specific IgA measured at PND56.

In the second study, once weaned, pigs received scFOS or maltodextrin according to maternal diet for one month. Then, pigs were reared until 6 months of age under standard diet and received a HF diet providing 22.6% energy from lipids for 12 weeks. Faecal SCFA production was determined 3 and 9 weeks after the beginning of the HF diet. The entero-pancreatic axis, endocrine pancreas and glucose metabolism were measured at the end of the experiment.

In the first study, faecal contents of suckling pigs from scFOS mothers displayed a higher level of total SCFA ( $P < 0.001$ ), indicating a maternal diet-induced change in offspring gut microbiota. The number of goblet cells per crypt was increased in pigs from scFOS mothers ( $P = 0.06$ ) together with ileal concentrations of IFN $\gamma$  ( $P = 0.05$ ) and IL-4 ( $P = 0.07$ ) known to play a role in the regulation of mucin synthesis. Furthermore, ileal and serum specific IgA concentration was increased in pigs from scFOS mothers ( $P = 0.08$  and  $0.004$  respectively).

In the second study, early scFOS supplementation increased faecal SCFA production after 3 weeks of HF diet ( $P = 0.02$ ), revealing a transient modulation of fermentative activity. Ongoing taxonomic analysis will give more insights on microbiota changes. The number of caecal GLP-1-secreting L-cells ( $P = 0.03$ ) and the basal plasma concentration of GLP-1 ( $P = 0.10$ ) increased in scFOS group and were positively correlated ( $P = 0.003$ ;  $R = 0.59$ ), indicating an increased capacity to secrete GLP-1. scFOS animals tended to secrete more insulin ( $P = 0.09$ ) in response to a glucose stimulus without glucose profile modification.

Our results highlight the key role of perinatal nutrition on later adaptations to diverse challenges, involving the microbiota which, in turn, modify immune system and energy metabolism.