



Microbiota diversity during neonatal colonization impacts gut physiology in a pig model

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Reduced gut microbiota diversity is suspected to be detrimental in a variety of diseases, including inflammatory bowel diseases⁽¹⁾. Variation in microbiota composition during gut colonization is known to influence neonatal mortality and may be a risk factor for various non-infectious diseases such as allergy, metabolic disorders and obesity later in life⁽²⁾. How neonatal microbiota diversity can modulate gut barrier function and defense systems is poorly understood. Therefore, the aim of the present study was to test the hypothesis that a complex microbiota is more suitable neonatally than a simplified microbiota for homeostatic development of gut function.

This hypothesis was tested in a neonatal pig model (Lelystad ethics protocol No. 2011097). Piglets were delivered by Caesarean section and were kept in SPF facilities. They were then administered orally at day 2 and 3 a simple microbiota (SM, $n=6$) alone or with a faecal bacterial suspension from an unrelated sow at day 4 (CM, $n=6$). The three bacterial genera and strains of the SM mixture ('Bristol mix') were recently shown to reliably colonize the gut of germfree pigs⁽³⁾. The piglets were slaughtered at 16 days of age. Segments of proximal jejunum, distal ileum and proximal colon and plasma were collected. Gut samples were analysed for villus-crypt morphology, enzyme activities (intestinal alkaline phosphatase, IAP; dipeptidyl-peptidase IV; sucrase), inducible heat shock proteins, soluble protein and IAP in digesta. Four plasma markers of inflammation (C-reactive protein, haptoglobin, TNF- α and α -acid glycoprotein) were analysed. Treatment effects were analysed by T-test.

At day 16, body weights and diversity of intestinal microbiota did not differ between the groups. However, an aberrant composition was observed in the jejunum and ileum of SM pigs [lower abundance of several presumed beneficial microbial groups (lactobacilli, butyrogenic species) and increase in a number of potential pathogens]. Jejunal crypts were deeper ($P<0.05$), ileal surface area tended to be larger ($P=0.080$) and colon crypts tended to be narrower ($P=0.056$) in CM pigs. Sucrase activity in the jejunal mucosa was lower in CM pigs ($P<0.05$) (other enzymes in jejunal and ileal tissue unaffected). Soluble protein and IAP activity were lower in ileal ($P<0.05$, both) and colonic ($P<0.05$ and $P<0.01$, respectively) digesta of CM pigs. Finally HSP70 relative concentration tended ($P=0.096$) to be lower in jejunal tissue. HSP27 tended to be lower in the ileum ($P=0.064$) but was higher in the colon ($P<0.05$) of CM pigs. Systemic inflammation did not differ between treatments.

Neonatal microbiota complexity profoundly affected various aspects of gut tissue and digesta characteristics, according to distinct regional patterns in pigs. CM reduced jejunal maturity, tended to reduce bacterial-induced stress on the intestine but increased it on the colon⁽⁴⁾. Finally, gut luminal degradation potential was higher in CM pigs.

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