Fat-shaped microbiota affects microvesicular steatosis and lipid metabolism in malnourished mice

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Protein malnutrition is characterized by stunted growth, hepatic steatosis and a damaged gut mucosal architecture. Since high-fat shaped gut microbiota has an increased ability in providing nutrients and energy from food to the host, the aim of this study was to determine whether such a microbiota could beneficially impact on the consequences of malnutrition.

The cecal content of specific pathogen free C57Bl/6J mice fed a high-fat diet or a low-protein diet was transplanted in two groups of germ-free C57Bl/6J recipient mice, named HFM and LPM respectively, which were subsequently fed a low-protein diet for 8 weeks.

Body weight gain was comparable between the two groups of microbiota-recipient mice.

Plasma lipid levels were lower in HFM compared with LPM mice. In particular, total cholesterol levels were reduced by 12.28% ($p = 0.048$), high-density lipoprotein-cholesterol by 16.01% ($p = 0.018$) and triglycerides by 20.71% ($p = 0.032$).

Liver histology indicated an increased occurrence and severity of microvesicular steatosis in the HFM group. No signs of macrovesicular steatosis were noticed. In order to evaluate glycogen accumulation in livers, the PAS staining was performed and no differences were observed between the two groups. Similarly, the staining for the extracellular matrix with the Masson's trichrome did not show anomalous fibrosis in livers from both HFM and LPM mice.

The length of small and large intestine was comparable in the two experimental groups that received different microbiota. Villi in duodenum, jejunum, and ileum had a normal appearance and showed comparable length and width in both groups. Moreover, the ileal crypts showed the same depth in the two groups, whereas, in the large intestine, crypts of LPM mice were slightly deeper than those of HFM mice.

To evaluate if the two different microbiota had an impact on mucus production, the abundance of neutral and acid mucins produced by goblet cells in the ileum and large intestine was analyzed and no differences were observed. Nonetheless, the expression of antimicrobial genes promoting oxidative stress and immune response at the ileal epithelium (Duox2, Duoxa2, Saa1, Ang4, Defa5) was

increased.
In conclusion, the transplant of the caecal microbiota shaped by a high-fat diet in mice fed a low-protein diet represents a noxious stimulus for the ileal mucosa and impairs hepatic lipoprotein secretion, promoting the occurrence of hepatic microvesicular steatosis.

Key words

Steatosis; small intestine; malnutrition; gut microbiota.