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P0613 Effect of lyso-Gb3 on the intestinal microbiota may contribute to gastrointestinal symptoms in Fabry's disease patients

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Background: Fabry's disease is an X-linked, lysosomal storage disorder due to α-galactosidase A deficiency, characterized by the lysosomal accumulation of glycosphingolipids, mainly globotriaosylceramide (Gb3) and its deacetylated form as globotriaosylsphingosine (lyso-Gb3). Some of the disease symptoms affect the gastrointestinal tract, causing nausea, vomiting, diarrhea, constipation and difficulty in gaining weight. Certain colonic alterations such as polyps and cancer are frequent in these patients.

Lyso-Gb3 accumulates in different organs, including liver and intestines, and plasma. We hypothesized that bile secretion may result in Lyso-Gb3 intestinal concentration exceeding that in plasma (500 nM), which could alter the intestinal microbiota composition and the development of gastrointestinal symptoms.

In this study, we describe the effect of lyso-Gb3 on the growth of human intestinal microbiota.

Materials/methods: Microbiota from pooled faeces of healthy individuals was stabilized in a dynamic simulator of the gastrointestinal tract (LWT-*Food Sci Technol*, 2015, 61:283) and incubated in presence or not (control) of 500 nM of lyso-Gb3. After incubation under strict anaerobic conditions for 24 h at 37 ºC, the bacterial concentration (log copy number/mL) was estimated through quantitative real time polymerase chain reaction (qPCR) using specific primers for bacterial groups representative of the human gut microbiota. Data were analyzed by *t*-Student test. Values are tabulated as mean and standard deviation.

Results: Lyso-Gb3 significantly modified the growth of different bacterial groups of the human intestinal microbiota (Table).

Table 1. Bacterial changes (log copy number/mL) in presence of lyso-GB3.

	Control	Control	500 nM lyso-Gb3
Bacterial group	0 h	24 h	24 h
Akkermansia	6.74$$0.06	6.22$$0.10	5.91$$0.10
Bacteroides	6.50$$0.22	7.62$$0.13	6.73$$0.10
B. fragilis	3.78$$0.02	1.55$$0.35	5.09$$0.18
Bifidobacterium	4.40$$0.06	4.09$$0.05	3.92$$0.10
Bilophila	6.75$$0.04	7.94$$0.09	7.96$$0.07
Clostridium leptum	5.26$$0.05	5.20$$0.16	4.85$$0.05
Blautia coccoides	6.80$$0.06	7.07$$0.02	6.81$$0.12
Sulfate-reducing bacteria (DSR)	6.21$$0.07	7.48$$0.10	7.52$$0.07
Enterobacteriaceae	6.76$$0.07	8.70$$0.08	8.95$$0.14
Enterococcus	6.19$$0.05	7.74$$0.17	8.06$$0.07
Faecalibacterium	7.88$$0.10	7.48$$0.06	7.53$$0.16
Lactobacillus	5.42$$0.10	4.18$$0.05	3.91$$0.06
Prevotella	2.79$$0.28	3.70$$0.09	4.34$$0.32
Roseburia	3.72$$0.15	3.11$$0.08	3.33$$0.16
Ruminococcus	3.98$$0.07	3.09$$0.14	2.94$$0.18

Conclusions: Lyso-Gb3 affects the intestinal microbiota composition. In particular, it favours the growth of *Bacteroides fragilis* that may be responsible of colonic alterations such as colon polyps and cancer.