Fecal microbiota composition and activity of patients with propionic acidemia

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Propionic acidaemia (PA) is an inherited metabolic disorder of propionate metabolism, where the gut microbiota could play a role in pathophysiology and therefore represent a relevant therapeutic target. Yet, little is known about gut microbiota composition and activity in patients with PA. Although clinical practice varies between metabolic centres, management of PA requires combined dietary and pharmaceutical treatments, both known to affect the microbiota. The aim of this study was to characterize the gut microbiota and its metabolites in faecal samples of patients with PA compared with healthy controls from the same household. Eight patients (aged 3-14y) and eight controls (4-31y) were recruited from centre 1 (UK) and seven patients (11-33y) and six controls (15-54y) from centre 2 (Austria). Stool samples were collected four times over a 3-month period, alongside data on dietary intake and drug/antibiotic use. Several microbial taxa differed between patients with PA and healthy controls, e.g., Proteobacteria levels were increased, whereas butyrate producing genera such as Roseburia and Faecalibacterium were decreased. Most measured microbial metabolites were lower in patients with PA. Butyrate was depleted in patients from centre 1, and the microbiota profile of these patients showed the lowest diversity and stability in the 3-month period. As the first study to map the gut microbiota of patients with PA, this work represents an important step forward for developing new therapeutic strategies to further improve PA clinical status. Given our findings, new dietary strategies should not only consider microbial propionate production but also butyrate production and microbiota stability.