Metabolic Landscape of the Mammalian Digestive Tract

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The mammalian gut microbiota has been linked to host metabolism, development of the immune system, and a range of diseases.
Sequencing data tells us which microbes thrive where in the gut, but we know little about the nutritional conditions and microbial metabolism in different gut regions.
Here we characterize the intestinal metabolism of mice colonized with microbiota of different composition using metabolomics and 16S rRNA sequencing by systematically sampling intestinal content and mucus at 15 gut sites. Major metabolome differences exist between small and large intestine as well as mucus and content.
As a consequence of the predominantly anaerobic community in the large intestine, we observed accumulation of fermentation products. Amino acids and carbon sources were found in higher concentrations in content than mucus samples.
To separate the microbial contribution to intestinal metabolism from nutritional factors and environmental conditions, colonized mice were compared to germ-free mice. In colonized mice, the complex microbiota secreted products of bacterial fermentation, evokes an increased host production of primary bile acids and modifies secondary bile acids. In mice colonized with a medium complexity microbiota consisting of 12 bacteria, primary bile acid production was increased compared to germ-free animals, but without conversion to secondary bile acids. By combining high-throughput metabolomics with 16S rRNA sequencing, we are able to identify significant associations between location-specific metabolomes and microbiota compositions to derive hypotheses about niche-specific metabolism of individual species.

Karin H.U. Meier

I received a BSc from the University of Heidelberg and a MSc in Biotechnology from ETH. Presently, I am a systems biology graduate student in Uwe Sauer's Metabolomics lab at ETH, working in close collaboration with gut microbiome labs at the Inselspital in Bern and the University of Oklahoma. In different projects we investigate the effects of community composition, localization within the gut and pathogenic infections on metabolism. Ultimately, we attempt to lay a foundation for understanding intestinal metabolism. The high complexity of intestinal samples poses an analytical challenge which I addressed by establishing and continuously improving LC-MS methods.

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