High-fat feeding rather than obesity drives taxonomical and functional changes in the gut microbiota in mice

Background: It is well known that the microbiota of high-fat (HF) diet-induced obese mice differs from that of lean mice, but to what extent, this difference reflects the obese state or the diet is unclear. To dissociate changes in the gut microbiota associated with high HF feeding from those associated with obesity, we took advantage of the different susceptibility of C57BL/6J;BomTac (BL6) and 129S6/SvEvTac (Sv129) mice to diet-induced obesity and of their different responses to inhibition of cyclooxygenase (COX) activity, where inhibition of COX activity in BL6 mice prevents HF diet-induced obesity, but in Sv129 mice accentuates obesity.

Results: Using HiSeq-based whole genome sequencing, we identified taxonomic and functional differences in the gut microbiota of the two mouse strains fed regular low-fat or HF diets with or without supplementation with the COX-inhibitor, indomethacin. HF feeding rather than obesity development led to distinct changes in the gut microbiota. We observed a robust increase in alpha diversity, gene count, abundance of genera known to be butyrate producers, and abundance of genes involved in butyrate production in Sv129 mice compared to BL6 mice fed either a LF or a HF diet. Conversely, the abundance of genes involved in propionate metabolism, associated with increased energy harvest, was higher in BL6 mice than Sv129 mice.

Conclusions: The changes in the composition of the gut microbiota were predominantly driven by high-fat feeding rather than reflecting the obese state of the mice. Differences in the abundance of butyrate and propionate producing bacteria in the gut may at least in part contribute to the observed differences in obesity propensity in Sv129 and BL6 mice.