

The Gut Microbiota Modulates Energy Metabolism in the Hibernating Brown Bear *Ursus arctos*

Graphical Abstract



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In Brief

Sommer et al. show that the microbiota and serum metabolites in brown bears differ seasonally between hibernation and active phase. Colonization of mice with a bear microbiota promoted increased adiposity. These findings suggest that seasonal microbiota variation may contribute to metabolism of the hibernating brown bear.

Highlights

- Bear microbiota composition differs seasonally between hibernation and active phase
- Blood metabolites differ seasonally in the brown bear
- The bear gut microbiota promote energy storage during summer



The Gut Microbiota Modulates Energy Metabolism in the Hibernating Brown Bear *Ursus arctos*

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SUMMARY

Hibernation is an adaptation that helps many animals to conserve energy during food shortage in winter. Brown bears double their fat depots during summer and use these stored lipids during hibernation. Although bears seasonally become obese, they remain metabolically healthy. We analyzed the microbiota of free-ranging brown bears during their active phase and hibernation. Compared to the active phase, hibernation microbiota had reduced diversity, reduced levels of Firmicutes and Actinobacteria, and increased levels of Bacteroidetes. Several metabolites involved in lipid metabolism, including triglycerides, cholesterol, and bile acids, were also affected by hibernation. Transplantation of the bear microbiota from summer and winter to germ-free mice transferred some of the seasonal metabolic features and demonstrated that the summer microbiota promoted adiposity without impairing glucose tolerance, suggesting that seasonal variation in the microbiota may contribute to host energy metabolism in the hibernating brown bear.

INTRODUCTION

Free-ranging brown bears (*Ursus arctos*) undergo cycles of intense eating and weight gain during the summer followed by prolonged dormant hypometabolic fasting for up to 6 months during the winter (Evans et al., 2012; Tøien et al., 2011). Despite the large fat accumulation before hibernation, bears remain metabolically healthy (Arinell et al., 2012; Nelson, 1973; Stenvinkel et al., 2013), which contrasts with the strong association between obesity and insulin resistance in humans. Thus, the brown bear may constitute a model for healthy obesity and studying hibernation might be a promising approach to develop novel

therapies for obesity. The intestines of mammals harbor diverse microbial ecosystems that have profound effects on host physiology (Sommer and Bäckhed, 2013). The gut microbiota contributes to energy harvest from the diet (Bäckhed et al., 2004, 2007; Sommer and Bäckhed, 2013; Sommer et al., 2015) and is altered in obesity and type 2 diabetes (Khan et al., 2014). Furthermore, diet, which is seasonally variable in bears (Persson et al., 2001; Stenvinkel et al., 2013; Stofik et al., 2013), strongly affects the gut microbiota (Ley et al., 2008; Zoetendal and de Vos, 2014) and both fasting and hibernation alter the gut microbiota composition (Carey et al., 2013; Crawford et al., 2009; Dill-McFarland et al., 2014; Sonoyama et al., 2009).

Here, we investigated how hibernation in free-ranging brown bears affects the gut microbiota and plasma metabolites, and whether a seasonally altered microbiota contributes to the healthy obesity phenotype during summer. We used 16S rRNA profiling and next-generation sequencing to comprehensively analyze the fecal microbiota of free-ranging brown bears captured during hibernation (February) and during the active period (June) of the same year (Figure 1A). We showed that the winter microbiota comprised fewer bacterial taxa (Figure S1A) and was more homogenous than the summer microbiota (Figure S1B), which may reflect the varied diet among bears during the summer.

RESULTS AND DISCUSSION

Principal coordinate analysis of the overall composition of the bear fecal microbiota samples using unweighted UniFrac revealed a clear separation depending on the seasonal origin (Figures 1B and S2). We identified 24 bacterial phyla in the bear fecal microbiota (Table S1). The dominating bacterial phyla in the summer microbiota were Proteobacteria, Firmicutes, and Actinobacteria (Figure 1C). In the winter microbiota, Bacteroidetes increased in abundance, whereas Firmicutes and Actinobacteria were less abundant (Figure 1D). A number of low abundant phyla were only present in the summer microbiota (Figure S3A). At the species level, 199 of the 4,447 detected operational taxonomic units (OTUs) were significantly altered ($q < 0.05$; $q = \text{FDR}$

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