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## Pu-erh tea and theabrownin ameliorate metabolic syndrome in mice via potential microbiota-gut-liver-brain interactions

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Metabolic Syndrome (MS) is a common metabolic disorder characterized by obesity, insulin resistance, cardiovascular disease and gut microbiota dysbiosis. Pu-erh tea and its ingredient theabrownin have known functions on the reduction of body weight gain and fat accumulation. However, few studies systematically analyze the different contributions and mechanisms of their anti-metabolic syndrome functions through multi-omics combination analysis. We used meta-genomics, transcriptomics and metabolomics technology to investigate the anti-metabolic syndrome mechanism of Pu-erh tea and theabrownin in MS mice. Our results suggested that Pu-erh tea and theabrownin interventions could improve the physiological functions of liver, jejunum and adipose tissues in MS mice. Hepatic transcriptome revealed that both interventions could regulate the circadian rhythm pathway. Glycerophospholipid and linoleic acid

metabolism were also modulated by both interventions through serum and brain metabolome analysis. Faecal metagenome demonstrated that both interventions could increase the relative abundance of *Clostridiales bacterium 42\_27*, *Blautia coccoides* and *Firmicutes bacterium ASF500*, but decrease the relative abundance of *Brevundimonas vesicularis*. Otherwise, compared with Pu-erh tea, theabrownin markedly upregulated the levels of hepatic antioxidants (i.e., SOD, GSH), prominently down-regulated hepatic inflammatory factors (i.e., IL-1, IL-6, TNF- $\alpha$ ) and malondialdehyde oxidant, but modestly reduced obesity associated short-chain fatty acids in faeces in MS mice. Taken together, our data provided insights into the homogeneous and heterogeneous natural biological functions of theabrownin and Pu-erh tea in the treatment of metabolic syndrome.

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