Effects of Gut Microbially Produced Phenolic Acids on Host Metabolic Health

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Gut microbes play an important role in maintaining our health and disease susceptibility. Multiple diseases including type 2 diabetes (T2DM), obesity, and metabolic syndrome are associated with altered gut microbial structure and function. Phenylacetylglutamine (PAGln), a gut microbial metabolite derived from amino acid phenylalanine (Phe), is clinically and mechanistically linked to cardiovascular disease and positively associated with diabetes. Hippuric acid, an alternative gut microbial metabolite from Phe, is inversely associated with metabolic syndrome, diabetes, and blood pressure. My study aimed to test a hypothesis that dietary provision of phenylacetic acid (PAA), PAGln precursor, would worsen host metabolic health, while phenylpropionic acid (PPA), hippurate precursor, would improve host metabolic health. Prior to glucose tolerance testing, lab personnel put Black 6 mice on dietary provision of PAA, PPA, or neither (control). I performed LC-MS/MS analysis on fasted plasma to measure levels of circulating hippurate, PAGly, and free and acyl-carnitines. Dietary provision of PAA and PPA increased levels of PAGln/PAGly and hippurate, respectively, according to the metabolic pathways. The PPA group had higher glucose tolerance levels only in male mice, while the PAA group had significantly lower levels of circulating free and acyl-carnitines for both male and female mice. The results of this study will help further understand how gut microbes and their metabolites impact the host, as well as guide future therapeutic strategies that are more effective in preventing and reducing the progression of metabolic diseases.

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