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Title: Metabolite-mediated Sex-specific Associations between Microbiome and Fat Distribution

Summary:
We hypothesize that there are different sex-specific microbial signatures linked to regional adiposity in men and women. Such differences could be largely attributable to the biological functions of sex hormones and fatty acids. Sex hormones have been shown to be associated with both regional adiposity and gut microbiota. Fatty acids from the lipid pathways have shown pronounced effect in the mechanism of determining the adiposity site, whereas amino acids were shown to play catalyst roles in this process. To examine the above hypothesis, our current study has two aims. First, identify the sex-specific microbial compositions that associate with fat distribution in men and women. Second, identify the metabolites that could be potential mediators to the association between the microbial signature and fat distribution. To achieve these two aims, we conducted the following analyses separately in women and men. First, we univariately screened the metabolites that are associated with fat distribution by sex. Second, we explored the sex-specific microbial signatures using the Wald test. Third, we implemented sparse partial least square discriminant analysis to synthesize the joint distribution across microbiome, metabolites, and fat distribution. Fourth, we conducted mediation analysis to identify the metabolic mediators for the association between microbiome and fat distribution.

Questions:
1. Confounding issues
2. Multivariate mediation analysis
3. Causal modeling
4. Microbial/host metabolites discrimination
5. Potential Bayesian framework

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