Mining the intestinal microbiome secretome for treatments of metabolic and inflammatory diseases

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Abstract
Changes in gut microbiota composition and activity are associated with a wide variety of disorders, including type 2 diabetes and inflammatory bowel diseases. However, specific gut bacteria-derived molecules which directly or indirectly regulate the physiological and pathological processes remain unknown. Second Genome has developed a unique microbiome discovery platform that associates human clinical phenotypes with key specific gut bacterial strains and secreted products. This approach was validated through comprehensive microbiome analysis using fecal samples from healthy subjects, individuals with type 2 diabetes and individuals with ulcerative colitis. Specific bacterial strains were identified as associated with these disorders. Administration of these strains, and importantly also their key secreted mediators, improved metabolic and intestinal barrier functions in high-fat diet (HFD)-induced obesity or in dextran sulphate sodium (DSS)-induced colitis mice models. These findings underscore the promise of Second Genome’s microbiome discovery platform in identifying bacteria secreted products with the therapeutic potential to treat type 2 diabetes and inflammatory bowel diseases.

Second Genome: Microbiome to Medicine™

1) Second Genome technology platform identifies bacterial strains which prevent increased adiposity in HFD-induced obese mice

2) Second Genome technology platform identifies bacterial strains which protect from lowered glucose tolerance on HFD-induced obese mice

3) Intestinal microbiome peptides inhibit gluconeogenesis in precision-cut liver slices from mice

4) Second Genome technology platform identifies bacterial strains which protect barrier function in a DSS-induced colitis mouse model

5) Second Genome technology platform identifies proteins which reduce barrier disruption, weight loss and disease pathology in a DSS-induced colitis mouse model

Figure 1. Probiotic treatment with bacterial strains identified from RyG8-treated patients shows protection against increased adiposity in HFD-induced obese mice. Female aortic obese (RyG8) mice were administered by oral gavage with clinical phenotypes

Conclusions
1) Second Genome technology platform can identify specific bacterial strains and bacterial-secreted products associated to human clinical phenotypes.
2) Second Genome demonstrates that the identified specific bacterial strains protect against adiposity and glucose intolerance in HFD-induced obese mice.
3) Specific peptides from identified bacterial strains associated to healthy metabolic clinical phenotypes inhibit gluconeogenesis in precision-cut liver slices from mice.
4) Second Genome demonstrates that the identified bacterial strains and specific secreted mediators reduce barrier disruption, weight loss and disease pathology in a DSS-induced colitis mouse model.