Technologies for engineering the microbiome

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Understanding the role of the gut microbiome in modulating host health and disease will require technologies for localized and long-term monitoring of microbiome and gut functions *in vivo*. Furthermore, new strategies are needed for precise modulation of microbiomes to enable new diagnostics and therapeutics, since existing approaches for modulating the microbiome can have significant off-target effects. Synthetic biology can provide new tools for studying and manipulating complex microbial communities.

We have created strategies for engineering commensal gut bacteria, such as *Bacteroides thetaiotaomicron*, a major and stable member of the human gut microbiome with synthetic gene circuits and we demonstrated that they are still functional in mice stably colonized with the engineered bacterium. This work provides a resource for *Bacteroides* genetic engineering towards future applications as non-invasive diagnostics and therapeutics in the gut microbiome. Furthermore, we have created technologies for the specific knockdown of bacteria living in mixed microbial communities. For example, we engineered CRISPR-Cas antimicrobials that kill bacteria based on their genetic signatures. In addition, we have built a technology platform for engineering phage host range, which enables the creation of well-defined phage cocktails that can kill specific subpopulations of bacteria within mixed microbial consortia.

We anticipate that these strategies will be useful for the targeted knockdown of bacteria in complex microbiomes to understand the functional role of these bacteria or achieve therapeutic effects.