

The gut microbiota consists of the majority of cells (100 trillion, versus 10 trillion human cells) and genes (8 million, versus 30,000 human genes) associated with our bodies. Recent advances in DNA sequencing technologies, coupled with advances in bioinformatics, now allow us to understand the critical roles our microbial symbionts play in nutrition. In this seminar, I describe some of the tools my laboratory has developed for analysis of high-throughput microbial community data and their application to the problems of obesity and malnutrition. Remarkably, different mouse models of obesity, such as ob/ob and TLR5 knockout mice, become obese in different ways (energy harvest versus behavioral effects), and traits related to adiposity can be transplanted from humans to mice via the gut microbiota. Specific mechanisms affecting nutrition can then be identified through metabolite and transcript profiling, and hypotheses about key taxa can be tested by using microculture to produce defined microbial communities that can be transplanted into mice, which recapture the phenotype of the stool transplant and can be designed to protect otherwise germ-free mice from acquiring obesity when co-housed with mice with increased adiposity due to transmission of the microbial community from an obese human donor. The prospects for developing these techniques into a type of personalized medicine based not on the human genome, in which we are all 99.9% identical, but on the human microbiota, in which we can be 90% different, are exciting.