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Microbiome Research: What's in the Pipeline?

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Advances in sequencing technologies have enhanced extensive efforts in characterizing the human microbiome. However, most of these high-throughput techniques only provide snapshots of microbial communities and bacterial diversity occurring at a single place at a given time while yielding little direct information about the functions of the bacteria and whether or not they are alive. More so, individual taxa within bacterial communities intermittently rise and fall in abundance due to selection, mutation, migration, and drift which influence their metabolic abilities. Meanwhile, the causes and significances of these alterations remain unclear. Therefore, future microbiome research would be geared towards understanding the principles that govern the microbiome's dynamics using a systems biology approach. Such a metagenomic systems biology approach would enhance a network based analysis of microbe-microbe and microbe-host cell interactions. In the coming years, models that enhance prediction of the gut microbial functions and dynamics under various conditions would enhance personalized interventions to dysbiosis.

Meanwhile as we continue to unravel the assembly, functions and dynamics of the microbiome using systems biology, our current strategies for correcting dysbiosis and its associated diseases are taking new turns. Indeed, the administration of probiotics and fecal replacement therapy for restoring gut microbial richness have been phenomenal over the years, yet efforts are being made to understand the mechanism by which these microbes influence health. This will enhance the identification and regulation of the activities of gut microbial biomolecules that impact health. Such molecules can then be synthesized and used as therapeutics to modulate microbe-microbe and microbe-host cell cross-talk. One such example is the demonstration that certain *Clostridial* species produce butyrate which binds to G protein coupled receptors (GPR41 and GPR43) to modulate the production of regulatory T cells [1]. Also, recent studies [2,3] have demonstrated that oral administration of nontoxigenic *C. difficile* spores and their purified extracts could prevent the recurrence of *C. difficile* infection and this opens a new window into the possibility of using purified bacteria products instead of the bulk of feces that are currently administered to treat *C. difficile* infection.

In future, a number of microbial therapeutic products capable of alleviating various diseases will be available on the market. Also, microbial replacement therapies may soon become standard practice as our knowledge about the challenges and implications of the microbiome increases.

Yet, for this to happen, there is the need to develop biome-specific annotation platforms which will improve interpretation of multi-omic data. Additional challenges that need to be met include improvement of methods for extracting biomolecules from complex ecosystems such as the human gut; developing more efficient and high-throughput methods for complete genomic assembly [4,5]; meeting the high computational memory (RAM) requirements for *de novo* assembly of large metagenomes and metatranscriptomes or by developing resources of modest memory requirements [6]; and developing mathematical and statistical models to integrate the data and provide meaningful biological information.

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