Scientists develop new approach for sampling gut bacteria

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Scientists at Forsyth, Massachusetts General Hospital and the Harvard School of Public Health have developed a new protocol for collecting saliva and stool samples for genomic and transcriptomic analyses. This method eliminates the need for specialized personnel and facilities while keeping the sample intact. It also provides critical insight into the genetic makeup of the microbiome of the digestive tract and the bacteria associated with celiac disease, oral cancer, perodontitis and obesity.

This study, "Relating the metatranscriptome and metagenome of the human gut," will be published in the *Proceedings of the National Academy of Sciences* and available online the week of May 19th. By removing some of the burden for the study subjects, this technique will enable both longitudinal studies and large collection studies that are not limited by geography.

In recent years, the Human Microbiome Project has helped define the normal bacterial makeup of the human body. Scientists have conducted large-scale studies to analyze the microbial (bacterial) organisms living in and on the human body. Studying human-bacteria interactions could lead to new ways to monitor human health status and to new methods for preventing or treating oral and systemic human diseases. However, such studies typically require subjects to report to clinics for sample collection—a complicated practice that is impractical for large studies. To address these issues, the team of scientists developed a protocol that allows subjects to collect microbiome samples at home and ship them to laboratories for multiple types of molecular analysis. The microbial

species, gene, and gene transcript composition were consistent in all samples despite the diverse sampling methods. Subsequent analysis of these samples revealed interesting similarities and differences between the measured functional potential and activity of the human microbiome.

Dr. Jacques Izard, Associate Member of Staff at The Forsyth Institute designed the choice of the fixatives and the sampling protocol in collaboration with Dr. Curtis Huttenhower, Harvard School of Public Health; and Dr. Andrew Chan, Massachusetts General Hospital.

"It was rewarding to confirm the findings of the human microbiome project by showing that genetic diversity is lower than the bacterial diversity present in a sample," said Dr. Izard. "Furthermore, we are excited about the opportunities this protocol presents for future large-scale studies. As the sensitivity of the sequencing technologies and the computing tools are improving, minute change can be detected. Our collaborative group demonstrated that we can analyze samples self-collected and shipped, in confidence for future biological marker discovery".

"Several longitudinal Harvard cohort studies – including the Nurses' Health Study and the Health Professionals Follow-up Study – follow over 200,000 individuals that reside across the U.S. Participants have provided us a wealth of prospective information on diet, lifestyle and diagnoses of several diseases over the last 30 years. In this work, we demonstrate the feasibility of having individuals within these cohorts self-collect their samples at home. Scaling up this collection to the larger cohort represents a great opportunity to study the microbiome as a risk factor for multiple chronic diseases," said Dr. Chan.

Overview of Study

Although the composition of the human microbiome is now well-

studied, there is little known about the more than the eight million genes in the microbiota, and their regulation remain largely uncharacterized. This knowledge gap is in part because of the difficulty of acquiring large numbers of samples amenable to functional studies of the microbiota. This project demonstrates the representativeness of self-collected, self-shipped, saliva and stool samples in metagenomic and metatranscriptomic assays of the microbiome.

This is one of the first human microbiome studies in a well-phenotyped prospective cohort incorporating taxonomic, metagenomic, and metatranscriptomic profiling at multiple body sites using self-collected samples. Stool and saliva were provided by eight healthy subjects, with the former preserved by three different methods (freezing, ethanol, and RNAlater) to validate self-collection. Within-subject microbial species, gene, and transcript abundances were highly concordant across sampling methods, with only a small fraction of transcripts (