HARVARD CATALYST

THE HARVARD CLINICAL AND TRANSLATIONAL SCIENCE CENTER

Human Oral Microbiome: Collaboration Opportunity

Funded Projects

This initiative of the Harvard Catalyst Reactor Program, which was a follow up to the ReSourcing Big Data Symposium, also offered by Harvard Catalyst's Reactor Program, offered pilot funding for research proposals that utilize accessible data from the Human Oral Microbiome Database (HOMD). Funding of up to $50,000 was available to qualified investigators for proposals completed using the complete HOMD data set and tools developed by HOMD for comparison and analysis. The goal of this opportunity is to support collaborations leading to insights about the human oral microbiome and 1) changes in systemic health status; 2) metagenome, transcriptome, and proteome studies of microorganisms present in the human oral cavity; 3) comparison with curated 16S rRNA data bases for human nose, vagina, gut, and skin microbiomes, 4) phylogenetic comparison and analysis; and 5) oral ecological and biogeographical studies. However, this opportunity was not limited to these areas of collaboration.

This funding opportunity was only open to investigators who attended a training/educational event or met with Harvard Catalyst personnel.

Two pilot grants were awarded in amounts of up to $50,000 for each one-year project.

Funding decisions for the Human Oral Microbiome: Collaboration Opportunity pilot grants were announced in December 2015.

Combined Oligotyping and Metagenomic Approaches for a High-Resolution View of the Tongue Microbiome

Principal Investigator: Colleen Cavanaugh, PhD, Harvard University Faculty of Arts and Sciences

Co-Investigators: Gary Borisy, PhD, Forsyth Institute
Jorge Frias-Lopez, PhD, Forsyth Institute
Daniel Utter, BS, Harvard University Faculty of Arts and Sciences

Studies of the oral microbiome, collectively those microbes that live within our mouths, have revealed their critical importance in oral health as they provide a range of services for the host. However, many oral bacteria cannot be grown, thus culture-independent approaches, such as sequencing regions of the 16S rRNA gene, are used to study community composition. However, current methods of analysis are not very sensitive for bacterial identification. Oligotyping, a new method for 16S sequence analysis, has revolutionized our ability to detect fine scale genetic structure of microbial communities. Oligotyping results are difficult to compare between studies as no suitable reference databases exist. Here we aim to create an Oligotype Database to complement and expand the Forsyth Institute's Human Oral Microbiome Database (HOMD). Oligotype analysis of tongue biofilms will be conducted, and oligotypes will be incorporated into the HOMD. Second, we aim to associate oligotypes to functional genetic information. Using the same samples as for oligotyping, community genomic (metagenomic) sequences will be obtained, partitioned into operational genomes, and associations with a subject's oligotypes determined. Finally, we will demonstrate this coupled approach by characterizing tongue bacterial communities involved in a putative symbiosis that processes dietary nitrate for the host. Expanding the HOMD to include oligotypes, and associating them with functional gene content, facilitates future comparative studies of oral microbiota measured between laboratories and human populations across the world, including the future use of 16S sequence analyses in detection of disease organisms, developing methods for early diagnoses and preventive intervention.

Expanding the HOMD to Include Nasal- and Skin-associated Bacteria

Principal Investigator: Katherine Lemon, MD, PhD, Forsyth Institute

Co-Investigator: Isabel Fernandez Escapa, PhD, Forsyth Institute

Chronic rhinosinusitis (CRS) affects >5% of Americans and is almost universal in post-pubertal cystic fibrosis (CF) patients; however, the composition and genetic diversity of the bacterial communities (microbiome) in CRS remain understudied. The human nose and sinuses naturally harbor both harmless bacteria (commensals) and bacteria that can cause infections (pathogens), with these often belonging to the same group (genus). Therefore, to achieve clinically relevant results, microbiome studies based on DNA sequencing must distinguish between closely related bacteria inhabiting the same body site. The Human Oral Microbiome Database (HOMD) is an outstanding resource for identification and classification of species of bacteria present in the mouth. We propose to expand HOMD to include bacteria from adult and pediatric sinonasal and skin microbiomes in health and disease. We will use the expanded HOMD, in conjunction with new bioinformatic approaches, to reanalyze at a higher resolution published sinonasal microbiome studies from healthy vs. CRS subjects and to compare the sinus microbiome in CF vs. non-CF CRS. Doing this, we will determine whether there are harmless bacteria that have a negative, or positive, relationship with pathogens in these types of

CRS. We hypothesize that some of these harmless bacteria are in fact beneficial to humans (mutualists) and can block pathogen colonization or shift pathogen behavior towards living peacefully with the human host. This work will provide medical researchers with a useful tool for future sinonasal and skin microbiome studies and could help to develop novel strategies to control pathogen colonization and prevent/treat infections, e.g., CRS.