Quantitative Omics Strategies for Investigating the Oral Microbiome in Dental and Systemic Diseases

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Microbes play an integral role in many human biochemical and metabolic processes. Distinct groups of microorganisms exist in different niches of the human body, where, during healthy states, they are generally in homeostasis with their immediate environment. These microbial populations, and their potential role in human disease, are rapidly becoming an area of focus. Perturbations of the normal microbial community have been linked to deleterious health outcomes, such as metabolic disease and hypertension. The oral microbiome is of particular interest, as the oral cavity is a primary point of entry into the body. A change in the oral microbiome can lead to infectious disease of the mouth, such as cavities and periodontal disease. There is additional evidence that systemic diseases, such as diabetes, are connected via inflammatory pathways to periodontal disease, potentially linking the oral microbiome with overall health.

Genetic sequencing technologies have rapidly advanced our understanding of the various populations of microbes harbored throughout the human body. There is significant effort underway to sequence and characterize the oral microbiome, which will hopefully shed light on how perturbations to population composition affect oral and systemic disease. However, the direct chemical actors in biological systems are generally proteins. Furthermore, many proteins catalyze important enzymatic reactions, resulting in a diverse pool of small molecule products. These metabolites are the molecular markers most closely related to phenotype in the flow of genetic information: (genotype) genes → transcripts → proteins → metabolites (phenotype). The switch from a positive/symbiotic host-oral microbiome relationship to a negative/pathogenic disease state (*e.g.*, periodontal disease, systemic disease) is likely mediated, if not outright controlled, by a collection of proteins and/or small molecules. Yet, to date, large-scale surveys of the proteome and metabolome of oral microbiota, and the connection of these to disease states, have been lacking. Quantitative, mass spectrometry-based technologies have rapidly advanced in the last decade or so, making large-scale

proteomic and metabolomics investigations feasible tasks. We present here a beginning analysis of the oral microbiome proteome and metabolome isolated from dental plaque samples collected in collaboration with the Marshfield Clinic Research Foundation.

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