Proteomics and Pan-omics Measurements for Comprehensive Systems Characterization of Biological Systems

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Project Goals: This project is implementing and applying advanced capabilities for comprehensive molecular characterization of biological systems, including the extension of proteomics to cover post-translational protein modifications and the implementation of broad metabolomics, lipidomic and glycomic measurements, together with more widely available genomics and transcriptomics capabilities. Applications to microbes, plants and microbial communities enhance scientific understanding by elucidating phenotypic relationships between environmentally important microorganisms and higher organisms, as well as metabolic activities within microbial communities.

The goal of BER's Genome Science Program (GSP) is to achieve a predictive systems level understanding of plants, microbes and biological communities via the integration of fundamental science and technology developments to enable biological solutions to challenges in energy, environment and climate. Achieving this goal requires comprehensive proteomics, metabolomics, lipidomics, and glycomics, i.e. pan-omics measurement capabilities, and the integration of data generated by these approaches. We are facilitating understandings of biological systems by applying pan-omics molecular measurement capabilities in biology-driven collaborative projects led by investigators actively engaged in developing systems biology approaches in support of BER's research agenda. Our strategy benefits from advances in high resolution nano-liquid chromatography (LC) separations combined with high mass accuracy mass spectrometry (MS) measurements and other developments that afford large gains in measurement quality and throughput. These efforts also include the automation of key steps in proteomics sample processing; fractionation of protein samples based on surface membrane protein enrichment and subcellular fractionation methods using differential gradient centrifugation; and implementation of novel methods for protein extraction from environmental (e.g., soil) samples. Additional advancements involve the implementation of targeted proteomics methods (e.g., activity-based protein profiling and multiple reaction monitoring) and approaches for elucidating protein isoforms (e.g., integrated top-down and bottom-up proteomics) and post-translational modifications (e.g. ,phosphoproteomics and characterization of protein glycosites).

The application to studies of fungus-growing ant–microbe symbiosis as a paradigmatic example of organic complexity generated through symbiotic association illustrates integration of these capabilities . Over the last decade, it has become a model system for studying symbiosis. We have demonstrated in-depth profiling of the fungal garden complete with bacteria (fungus alone, isolated bacteria, and fungal garden intact) to understand the relationship between the fungus and the bacterial protectors. Proteomics and metabolomic studies of the secreted proteins from the bacteria have been characterized in an effort to understand the relationship between the ants and the fungus. These studies demonstrate the ability to use pan-omics measurements on an ecosystem level, spanning bacteria to multi-cellular organisms.

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