High-throughput Screen to Discover Secreted Activators of Microbial Metabolites

Soil bacteria live in complex communities that include bacteria, fungi, and plants, collectively referred to as the soil microbiome. Bacterial survival and behavior depend on the local microenvironments of each cell within the microbiome. For example, neighboring cells of two different bacterial species can communicate via the production and sensing of secreted compounds. Many such interactions are poorly understood. Here, I explored the molecular identity of secreted bacterial signaling compounds that elicit changes in secreted metabolite production. I first constructed luminescent transcriptional reporters for the production of several characterized secreted compounds, using *Bacillus subtilis* as a model organism. A liquid-based, 96-well-plate format was used to test the response of these reporters to a large collection of cell-free conditioned media generated from monocultures of environmental bacteria. Each luminescent reporter had different expression kinetics, which led to challenges when choosing a control for comparative purposes. After assay optimization and hit identification, conditioned media that elicited metabolite production will be fractionated to isolate and identify the compound(s) responsible. This work thus establishes an approach to study the roles of key metabolites with potential signaling roles within microbial communities. Understanding these complex interactions has implications not only for the soil microbiome, and thus agriculture, but also for the microbiomes of the intestine and other organs crucial for human health.