Newly Identified Regulatory Roles for Vitamin B_{12} Suggest Coordination of Community Metabolism

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Project Goals: The goal of the Metabolic and Spatial Interactions in Communities (MOSAIC) Foundational Scientific Focus Area is to understand the fundamental mechanisms by which microbial metabolic interactions and spatial organization impact carbon, nitrogen, and energy dynamics in microbial communities. Our studies focus on the coupling of carbon and nitrogen cycles in microbial communities, the role of environmental variables in governing the rates of these cycles, and the impact of environmental perturbations on microbial community dynamics. We employ tractable model consortia whose member genome sequences have been defined, advanced omics measurements, functional imaging, taxonomic profiling, and modeling to elucidate interaction mechanisms within complex microbial communities. Our research supports the DOE goals to achieve a predictive understanding of Earth's integrated biogeochemical processes.

Individual members of complex microbial communities can interact by exchanging metabolites and signaling compounds. Using genome-informed approaches coupled to proteomics, chemical probing, and other molecular biology studies, we have predicted and tested B vitamin dependencies in a model autotroph-heterotroph community. In particular, our findings suggest requirements for vitamin B_{12} exchange to support community growth and to regulate microbial metabolism.

Vitamin B_{12} encompasses a group of closely related corrinoid compounds best known for their role as cofactors of enzymes, and also for playing regulatory roles by binding to riboswitches. Recent studies have also revealed that vitamin B_{12} is a cofactor of transcriptional regulators. A portion of vitamin B_{12} is photolabile, thereby when bound to these proteins it provides light-dependent regulation of transcription, controlling processes such as biosynthesis of carotenoids, tetrapyrroles, and photosystems. To identify new roles for B_{12}, we developed a chemical probe that mimics the natural vitamin, in fact to such an extent as to support microbial growth, transcription, and translation. This probe was deployed in individual bacterial isolates, and within a photoautotroph-heterotroph community. Coupling the probe to proteomics analyses, we identified more than 50 B_{12}-binding proteins including enzymes known to use it as a cofactor, a transcriptional regulator, enzymes in the one carbon pool by folate pathway, and enzymes involved in ubiquinone biosynthesis. Importantly, we also identify a B_{12}-dependent role for MetE (methionine synthase) in the photoautotroph when the organism limits vitamin salvage. The unexpected discovery of B_{12} involvement in these processes suggests a pivotal role in the control

of cell growth, potentially leading to coordination of cell behavior in complex multicellular systems. We predict that these roles for B_{12} may be generalizable in myriad communities, a possibility that we are now exploring.

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