DESTINI : A Novel Enzyme for Comprehensive Spatial Profiling of Metabolites and Proteins within Cellular Compartments

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The spatial distribution of biomolecules, such as metabolites, plays a critical role in understanding biological systems. However, conventional purification methods have limitations in providing a comprehensive map of these important biological components. To overcome this limitation, we have firstly developed a novel enzyme called DESTINI (desthiobiotin ligase) that enables the labeling of proximal proteins and metabolites with desthiobiotin (DTB; a sulfur-free biotin analog). Using DESTINI, we can effectively label nearby proteins and metabolites, and successfully detect DTB-labeled metabolites using mass spectrometry. This approach allows us to target DESTINI to different subcellular compartments, including the mitochondrial matrix, nucleus, cytosol, and ER, enabling us to obtain compartment-specific information about metabolites in living cells. Overall, DESTINI opens up new opportunities for identifying the spatial distribution of metabolomes as well as proteomes within the same cellular compartment using a single enzymatic labeling tool.