Critical Role of Phosphatidylcholine in Intracellular Transport Dynamics

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Cellular physiological functions rely on intricate interactions among biomolecules. While extensive research has been focused on exploring protein-protein and protein-DNA interactions, studies on specific interactions between transmembrane proteins and lipids residing in the same membrane have been profoundly challenging. In this study, we developed a methodology to decipher the precise membrane protein-phosphatidylcholine (PC) interactome within living cells solely. Given the established correlation between dysregulated cellular PC levels and the onset and progression of various human diseases, including cancer and neurodegenerative disorders, understanding these interactions holds profound significance. By external addition to cells of an alkyne-modified choline head group together with a diazirine-modified fatty acid, cells metabolically incorporated these analogs into phosphatidylcholine lipids generating bifunctional lipids that enable identifying and visualizing the full spectrum of PC-protein interacting partners. Endogenous PC molecular species level downregulation significantly affects Endoplasmatic Reticulum (ER) protein exit and intracellular transport. Thus, our results highlight the pivotal role of PC molecular species as coordinators of intracellular protein trafficking through the Early Secretory Pathway.