Study details

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Journal

Journal of the American Chemical Society

https://doi.org/10.1021/jacs.5c03851

Abstract

Most eukaryotic membranes comprise phospholipids bearing two hydrophobic tails, but N-acylphosphatidylethanolamine (NAPE) stands out as a long-known but poorly understood phospholipid with three hydrophobic groups. What little attention NAPE has received has been devoted to understanding its metabolic functions as a precursor to N-acylethanolamine (NAE), a bioactive lipid that acts as an endocannabinoid. Yet, levels of NAPE increase during myocardial infarction and ischemia, suggesting potential signaling roles for this lipid. Here, we exploit photoaffinity labeling (PAL) to identify NAPE-interacting proteins and elucidate signaling functions of NAPE. By positioning diazirine and alkyne groups in metabolically distinct regions of the NAPE molecule, we ensured that our PAL probe reported on interactions of NAPE and not NAE. Our studies identified several NAPE interactors, including two single-pass transmembrane proteins, CD147/Basigin and CD44, both of which serve as chaperones for monocarboxylate transporters (MCTs) from the SLC16A family that mediate lactate flux across the plasma membrane. Functional studies revealed that NAPE stimulates lactate efflux by MCTs dependent upon CD147 and CD44, establishing NAPE as a bona fide signaling lipid and pointing to potential physiological roles in metabolic and energy homeostasis that may be pathologically relevant in ischemia.

Lipid probes utilized

Bifunctional NAPE

Cell line analyzed

HeLa

Uncaging & Crosslinking timeline

Lipid Probe	Uptake time	Interaction time	Crosslinking time
LEI-401	30 min	60 min	30 min

Mass spectrometry quantification method

SILAC

Additional sample preparation ?

None

Lipid interactomics data analysis

Data as submitted by the original authors was not normalized. To make these results more similar to the other datasets presented here, we performed median normalization to center the distribution around a logFC value of 0 (see the R file below for wrangling). We also needed to do an Ensemble query to find the gene names for the accession numbers of proteins identified in this dataset.

Data wrangling

Use the download button below to download the R script used to wrangle the authors' original submission into the data visualization tools on the Lipid Interactome:

Use the download button below to download the original data file prior to wrangling: