

DEFINING FAM46C-DEPENDENT LIPID REMODELLING IN CELLULAR HOMEOSTASIS

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FAM46C is a multifunctional protein associated with cellular homeostasis and developmental processes. Multiple studies have linked FAM46C to erythroid, sperm-cell, plasma-cell and macrophage maturation, supporting a broad biological relevance across differentiating cell types.

Based on our previous work, we propose that FAM46C acts at the endoplasmic reticulum through interaction with FND-C3A and contributes to the coordination of intracellular trafficking dynamics, secretory routes and stress responses. To further explore the functional networks in which FAM46C is embedded, we applied a network-based data-mining strategy to identify protein modules and pathways associated with FAM46C. This analysis confirmed FAM46C within proteosta-

sis and trafficking axes but also highlighted an unexpected lipid metabolism component, with PRDX6 emerging as the most relevant associated hub. Preliminary lipidomic analyses suggested that FAM46C expression triggered changes in oxidized phospholipid species and ceramides, supporting a possible role in lipid remodelling. In parallel, pharmacological inhibition of sphingosine kinases suggested a selective vulnerability in FAM46C-expressing models, indicating that FAM46C-dependent alterations in lipid homeostasis may reveal biologically relevant dependencies. Overall, these findings provide an initial framework for envisaging FAM46C as a regulator of intracellular lipid remodelling and identify the PRDX6-linked lipid stress pathway as a promising candidate for further mechanistic investigation.