

2023 Annual Research Day – Oral session
April 19th, 2023, 2:00 p.m. – 4:30 p.m., PHAB 2A

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Cell Biology

Adipose tissue phosphatidylcholine remodeling modulates insulin signaling

Phosphatidylcholines (PCs) are major components of cell membranes. Previous studies indicated that membrane PC composition is regulated by lysophosphatidylcholine acyltransferase (LPCAT) and an alteration in cell membrane saturation has been implicated in a variety of metabolic disorders, including obesity, insulin resistance, and cardiovascular diseases. LPCAT3 is the major isoform of LPCAT in adipose tissues. To study the impact of LPCAT3 on adipose tissue lipid metabolism and its metabolic consequences, we prepared adipocyte-specific *Lpcat3* knockout (KO) mice. Based on the analysis of high-throughput transcriptome sequencing and plasma adipokine profile, we gained insights to investigate the role of LPCAT3 in regulating adipose tissue insulin signaling. We revealed that LPCAT3 deficiency significantly reduced polyunsaturated PCs in the plasma membrane of adipocytes, resulting in increased insulin sensitivity. Mechanistically, we demonstrated that inhibiting LPCAT3 in adipose tissue promoted insulin receptor and AKT activation by influencing membrane lipid rafts and attenuated diet-induced insulin resistance. Conversely, adipose tissues from *ob/ob*, *db/db*, and high-fat diet-fed mice had significantly higher LPCAT3 activity which blunts insulin signaling. Moreover, the treatment of polyunsaturated PCs on human or mouse mature adipocytes significantly worsened cellular insulin signaling. Our findings suggest that targeting LPCAT3 in adipose tissues to manipulate membrane phospholipid saturation would be a new strategy to treat insulin resistance.