ICoLA 2019
The 8th International Congress on Lipid &Atherosclerosis(ICoLA)
The 58th Conference of the Korean Society of Lipid & Atherosclerosis
September 5(Thu.) ~ 7(Sat.), 2019, Conrad Hotel Seoul, Republic of Korea

The role of phospholipase D1/phosphatidic acid in amino acid-sensing mTORC1 signaling

Mee-Sup Yoon*

Department of Molecular Medicine, School of Medicine, Gachon University, Republic of Korea

msyoon@gachon.ac.kr

Abstract

Phospholipase D1 catalyzes the hydrolysis of phosphatidylcholine (PC) to phosphatidic acid (PA), which serves as a second messenger to regulate a range of signaling proteins. PLD1-produced PA binds with high affinity to the FKBP12 rapamycin binding domain (FRB) domain of the mammalian target of rapamycin (mTOR), a master regulator of cell growth. We identified a role for PLD1 in amino acid sensing pathway. Amino acid availability activates signaling by mTORC1. The class III PI-3-kinase Vps34 mediates amino acid signaling to mTORC1 by regulating lysosomal translocation and activation of the phospholipase PLD1. In addition, leucyl-tRNA synthetase (LRS) as a leucine sensor for the activation of Vps34-PLD1 upstream of mTORC1. LRS physically interacts with Vps34 in amino acid-stimulatable non-autophagic complexes. The UNE-L domain of LRS c-terminal is required for the non-canonical function of LRS in activating Vps34-PLD-mTORC1 signaling. Collectively, our findings provide compelling evidence that PLD/PA plays a in amino acid activation of mTORC1 via a non-canonical mechanism of LRS.

Keywords

Phosphatidic acid, Phospholipase D1, mTOR, amino acids