

Badanie oddziaływania kwasu fosfatydowego z białkiem mTOR oraz wpływ cholesterolu na tę interakcję

Selectivity of mTOR-Phosphatidic Acid Interactions is Driven by Acyl Chain Structure and Cholesterol

ABSTRACT

The need to understand the molecular details of the specificity of peripheral membrane proteins towards phosphatidic acid (PA) is undeniable. The diversity of PA species, classified according to acyl chain length and saturation, results in a complex and puzzling network of functional effects that exert a critical influence on cellular physiology. As a result, a large number of studies have been carried out in recent years on the role of phosphatidic acid in human diseases. One of the key proteins in this context is mTOR, which is considered to be the most important cellular sensor of essential nutrients and at the same time regulates cell proliferation, and which also seems to require PA for the formation of stable and active complexes. Here, in the presence or absence of cholesterol in specific membranes, we investigated the specific recognition of three physiologically important PA species by the mTOR FRB domain. Using a wide range of methods based on model lipid membrane systems, we elucidated how the length and saturation of the PA acyl chains influence the specific binding of the mTOR FRB domain to the membrane. We also discovered that cholesterol exerts a strong modulatory effect on PA FRB recognition. Our data provide insight into the molecular details of some previously reported physiological effects and reveal novel mechanisms for fine-tuning PA-dependent signalling cascades.