PI5P4Kβ

PI5P4Kβ (Phosphatidylinositol-5-Phosphate 4-Kinase beta) is a protein-coding gene that plays a role in the metabolism of phosphoinositides, which are important signaling molecules in cells. Specifically, PI5P4Kβ is a member of the PI5P4K family of kinases, which catalyze the conversion of phosphatidylinositol 5-phosphate (PI5P) to phosphatidylinositol 4,5-bisphosphate (PI(4,5)P2) in a process called phosphorylation.

PI(4,5)P2 is an important regulator of cellular signaling pathways, and its levels are tightly controlled. PI5P4Kβ is involved in this regulation by controlling the levels of PI(4,5)P2 in the cell. Mutations in the PI5P4Kβ gene have been associated with a range of diseases, including cancer and neurodegenerative diseases. Therefore, understanding the function and regulation of PI5P4Kβ is important for understanding cellular signaling and disease processes.

Phosphatidylinositol 5-phosphate 4-kinase β (PI5P4Kβ) evolved into a GTP sensor from ATP-utilizing kinase. Mechanistically, PI5P4Kβ has acquired the guanine efficient association (GEA) motif by mutating its nucleotide base recognition sequence, enabling the evolutionary transition from an ATP-dependent kinase to a distinct GTP/ATP dual kinase with its KM for GTP falling into physiological GTP concentrations-the genesis of GTP sensing activity. Importantly, the GTP sensing activity of PI5P4Kβ is critical for the manifestation of cellular metabolism and tumorigenic activity in the multicellular organism. The combination of structural, biochemical, and biophysical analyses used in our study provides a novel framework for analyzing how a protein can evolutionarily acquire a novel activity, which potentially introduces a critical function to the cell [1)].

1)
Takeuchi K, Senda M, Ikeda Y, Okuwaki K, Fukuzawa K, Nakagawa S, Sasaki M, Sasaki AT, Senda T. Functional molecular evolution of a GTP sensing kinase: PI5P4Kβ. FEBS J. 2023 Mar 1. doi: 10.1111/febs.16763. Epub ahead of print. PMID: 36856076.