Regulation of Cell Size and Membrane Turnover by a Novel Phosphoinositide Kinase

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Phosphatidylinositol 3-phosphate (PI3P) and Phosphatidylinositol 5-phosphate (PI5P) are low abundant phosphoinositides crucial for key cellular events such as endosomal trafficking and autophagy. Phosphatidylinositol 5-phosphate 4-kinase (PIP4K) is an enzyme that regulates PI5P in vivo but can act on both PI5P and PI3P, in vitro. In this study, we report a novel role for PIP4K in regulating PI3P levels in Drosophila tissues. Loss-of-function mutants of the only PIP4K gene in Drosophila (dPIP4K29) show reduced cell size in larval salivary glands. We find that PI3P levels are elevated in dPIP4K29 tissues and that reverting PI3P levels back towards wild type, without changes in PI5P levels, can also rescue the reduced cell size phenotype. dPIP4K29 mutants also show an upregulation in autophagy and the reduced cell size can be reverted by decreasing Atg8a, that is required for autophagosome maturation. Lastly, increasing PI3P levels in wild type salivary glands can phenocopy the reduction in cell size and associated upregulation of autophagy seen in dPIP4K29. Thus, our study reports for the first time, a role for a PIP4K-regulated PI3P pool in the control of autophagy and cell size regulation that may explain the reported role of PIP4K in regulating neurodegeneration and tumour growth.