

Supplementary Information 5. Functional enrichment analysis of 162 PI(3,5)P<sub>2</sub>-specific binding proteins. Enriched biological processes of identified PI(3,5)P<sub>2</sub>-BPs in the yeast protein interaction network (PIN) were illustrated by GO trees (node = enriched GO terms; edge = relationships in GO). The PIN was retrieved from the Database of Interacting Proteins (DIP) and only the largest connected component, including 4,822 proteins and 25,176 interactions, was studied. Among the 162 PI(3,5)P<sub>2</sub>-BPs, 128 of them were covered by the PIN. Functional enrichment of the interacting network was assessed by the BiNGO, a Cytoscape plugin, with P-value  $\leq 0.001$  (Hypergeometric test). The P-value was adjusted by applying Benjamini and Hochberg multiple testing procedures to control the false discovery rate. Significant overrepresented GO terms (GO level  $\geq$  5) of the interacting network were predicted as the potential functional roles of PI(3,5)P<sub>2</sub>-BPs in biological networks. Red = protein sorting; green = cytoskeleton organization; yellow = protein phosphorylation; blue = macromolecular complex assembly; grey = other functions, such as signal transduction, protein metabolic process, and regulation of gene expression, to name a few.