Figure SI-1: **Binding of recombinant GST-tagged PH domain of Phospholipase C delta 1 (PI(4,5)P2 binding) and GRP1 (PI(3,4,5) binding)**

PC/PE, PC/PE/PI(4,5)P2 and PC/PE//PI(3,4,5)P3 liposomes were immobilized onto a L1 chip by injecting 100 μL liposomes at 10 μL/min over the sensor chip surface. After washing with 30 μL of 20 mM NaOH, stable immobilization levels of approximately 6600RU and 7000RU and 6800RU were obtained respectively for PC/PE, PC/PE//PI(4,5)P2 and PC/PE//PI(3,4,5)P3. Various concentrations of GST-PLCδ1PH and GST-DYN1PH were injected over immobilized liposomes. The sensorgrams shown have been subtracted with the corresponding signal obtained when the sample was passed over immobilized PC/PS liposomes. No binding was observed when various concentrations of GST (4 μM to 125 nM) were injected over the immobilized liposomes (not shown).

A: Injection of GST-PLCδ1PH (3.5 μM, 1.75 μM, 875 nM, 437 nM, 218 nM, 109 nM) over immobilized PC/PE/PI(4,5)P2 liposomes.

B: Injection of GST-PLCδ1PH (3.5 μM, 1.75 μM, 875 nM, 437 nM, 218 nM, 109 nM) over immobilized PC/PE/PI(3,4,5)P3 liposomes.

C: Injection of GST-GRP1PH (3 μM, 1.5 μM, 750 nM, 375 nM, 188 nM, 94 nM) were injected over immobilized PC/PE//PI(4,5)P2 liposomes.

D: Injection of GST-GRP1PH (3 μM, 1.5 μM, 750 nM, 375 nM, 188 nM, 94 nM) were injected over immobilized PC/PE//PI(3,4,5)P3 liposomes.

Figure SI-2: PI(3,4,5)P3 protein interaction network. Proteins purified using PI(3,4,5)P3 targets were organized via direct interactions and molecular function using the Search Tool for the Retrieval of Interacting Genes/Proteins database (String http://string.embl.de/). Proteins involved in transport and trafficking are outlined in yellow, small GTPases and GTPase regulators are outlined in blue, kinases and phosphatases are outlined in red and cystoskeletal proteins are outlined in black. Proteins able to interact directly with phosphoinositides and phospholipids are noted with a star. Proteins identified specifically with PI(3,4,5)P3 and not previously reported to interact with PI(3,5)P2 and PI(4,5)P2 are represented with shaded boxes.

Table SI-1: Specific proteins purified using PI(3,4,5)P3 target. Proteins identified using PI(3,4,5)P3 are shown (shaded according to their purification using liposomes, beads or both liposomes and beads substrates). Proteins previously identified using PI(3,5)P2 and PI(4,5)P2 are also indicated.
Protein accession number, ID and name are as in UniprotKB.

Table SI-2: Potential lipid associated proteins
Potential Lipid associated proteins were identified using LIPIDMAPS database

(http://www.lipidmaps.org/) and SwissProt database (http://beta.uniprot.org/uniprot/). The databases were interrogated by both protein keywords and lipid class association to identify lipid interacting proteins and lipid-associated protein sequences.

Table SI-3: Biological processes classification for PI(3,4,5)P3 purified proteins. Proteins were classified according to their biological processes using the IProClass Integrated Protein Informatics Resource for Genomic & Proteomic Research (http://pir.georgetown.edu).