Table S1: Cellular regulators that impact LNP trafficking and their known endocytic function.

Cellular Effectors	Influence on intracellular trafficking	References
Calcium Homeostasis	Acts as a signaling molecule to mediate exocytosis, calcium homeostasis in lysosomes necessary to maintain function, deregulation of such a homeostasis augments lysosomal storage disorders.	1–3
Arachidonic Acid Metabolism	Present as fatty acid in phospholipids of cell membrane is generated by activity of phospholipase A-2 and regulates signaling mediators like phospholipase C (PLC). Both regulate membrane fusion and tubule formation in the endolysosomal system. Arachidonic acid is a key inflammatory intermediary.	4–6
V_o-ATPase	Maintains acidic pH of endocytic vesicles Submembranous pH regulates micropinosome formation.	7,8
Cathepsins	Proteases in endocytic compartments (especially lysosomes) that degrade proteins or lipids. Involved in endosomal escape of viruses.	9–11
JNK1/MAPK8	Signaling molecule activated by growth factors known to induce macropinocytosis, Associated with cytoskeleton and endocytic vesicles	12,13
p38	Subset of MAPK pathway, signaling molecule that regulates formation of early endosomes.	14
PKC	PKC is involved in membrane ruffling and micropinosome formation.	12
NFkB	Main function in inflammation and cancer little known about impact to cellular trafficking.	15
mTOR	Late endosomes form an active site form mTOR mediated cell signaling and mTOR in turn regulates lysosomal biogenesis.	16,17
Chloride Homeostasis	Defects in chloride channels linked to defective endocytosis in renal tubules and also implicated in lysosomal neurodegenerative disorders.	18,19

Abbreviations: JNK1-c-Jun N-Terminal Kinase, MAPK8- Mitogen-activated protein kinase 8, PKC- Protein Kinase C, NFkB- Nuclear factor kappa B, mTOR- mammalian target of rapamycin.

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