The RIM101 pathway regulates endosomal lipid traffic and metabolism

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S. cerevisae has been successfully and extensively used as a model to study lipid metabolism. Yet, our knowledge of lipid import mechanisms in yeast is rather limited. Sterol uptake, which only occurs under hypoxic conditions, is regulated through the action of the plasma membrane-localized ABC transporters Pdr11 and Aus1[1]. Fatty acid uptake is facilitated by the plasmamembrane fatty acid transporter Fat1 but alternative mechanisms must exist as FAT1 deletion alone does not completely abrogate fatty acid import[2]. Thus, a second mode of fatty acid import has been described which depends on the yeast protein kinase 1 (Ypk1) and on functional endocytosis[3].

Here we use 1,2-dioctanoyl-*sn*-glycerol (DOG) to trigger and track lipid uptake and distribution inside the cell. The RIM101 pathway is known to sense pH changes and lipid alterations at the plasmamebrane triggering a transcriptional response. Here we reveal that the RIM101 pathway, which includes the Rim21-based sensor complex, is crucial for endosomal DOG transport to the ER, lipid droplet, vacuole and redistribution to the plasmamembrane. This endosomal traffic can be interpreted as receptor recycling, but importantly it regulates the cellular availability of externally supplied lipids. We suggest that in addition to established lipid uptake mechanisms in yeast, lipids can alternatively be incorporated by endocytosis and distributed in a RIM101-dependent fashion.

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