Lipidomics Reveals Triacylglycerol Accumulation Due to Impaired Fatty Acid Flux in Opa1-Disrupted Fibroblasts

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Mots-clés	dominant optic atrophy [14], fatty acid oxidation [15], lipid droplets [16], membrane/fusion [17], mitochondria [18], Optic neuropathy [19]
Résumé en anglais	OPA1 is a dynamin GTPase implicated in mitochondrial membrane fusion. Despite its involvement in lipid remodeling, the function of OPA1 has never been analyzed by whole-cell lipidomics. We used a nontargeted, reversed-phase lipidomics approach, validated for cell cultures, to investigate OPA1-inactivated mouse embryonic fibroblasts (Opa1 MEFs). This led to the identification of a wide range of 14 different lipid subclasses comprising 212 accurately detected lipids. Multivariate and univariate statistical analyses were then carried out to assess the differences between the Opa1 and Opa1 genotypes. Of the 212 lipids identified, 69 were found to discriminate between Opa1 MEFs and Opa1 MEFs. Among these lipids, 34 were triglycerides, all of which were at higher levels in Opa1 MEFs with fold changes ranging from 3.60 to 17.93. Cell imaging with labeled fatty acids revealed a sharp alteration of the fatty acid flux with a reduced mitochondrial uptake. The other 35 discriminating lipids included phosphatidylcholines, lysophosphatidylcholines, phosphatidylethanolamine, and sphingomyelins, mainly involved in membrane remodeling, and ceramides, gangliosides, and phosphatidylinositols, mainly involved in apoptotic cell signaling. Our results show that the inactivation of OPA1 severely affects the mitochondrial uptake of fatty acids and lipids through membrane remodeling and apoptotic cell signaling.
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