DETECTION AND MONITORING OF INTRACELLULAR SITES OF TRIGLYCERIDES AND CHOLESTERYL ESTERS FORMATION AND STORAGE THROUGH A POLARITY-DRIVEN PIXEL CLASSIFICATION

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All living systems are maintained by a constant flux of metabolic energy, characterized by a series of complex reactions, regulating several biological processes, from the maintenance of intracellular energetic homeostasis to the intercellular signaling pathways [1]. Among the different metabolic pathways, the process of lipids storage and lipolysis, consisting in an ensemble of chemical reactions that regulate the conversion of fatty acids (FA) into triglycerides (TAG) and cholesterol into cholesteryl esters (CE), and their subsequent storage in the form of lipid droplets (LD), is of fundamental importance [2]. Any impairment in this metabolic cycle can be directly involved in the onset of several metabolic diseases, such as type II diabetes and atherosclerosis [3], but it can also result in oxidative stress, that is one of the main promoters of neurodegeneration [4]. A complete spatial mapping of the intracellular sites of TAG and CE formation and storage is, therefore, crucial to highlight any potential metabolic imbalance, thus predicting and counteracting its progression. Here, we present a machine learning assisted, polarity-driven segmentation which enables to localize and quantify triglycerides and cholesteryl esters biosynthesis sites in all intracellular organelles, thus allowing to monitor in real-time the overall process of the turnover of these non-polar lipids in living cells. This technique is then applied to normal and differentiated PC12 cells to test how the level of activation of biosynthetic pathways changes in response to the differentiation process.

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