

Regulation of Lipid Droplet Generation in Huh-7 Cells through a Receptor-regulated Signaling Pathway.

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Increases in the availability of free fatty acids can promote amplification in the number and the size of lipid droplets (LD) in cells. It is unclear, however, what the mechanistic driver of this process is. Fatty acids are taken up into cells and this has been considered as a means of activating LD generation, however the increase in the number and size of LD formation is extremely rapid following oleate addition to starved cells which suggests a tightly regulated process. A range of cells possess cell surface G protein coupled receptors which have been shown to bind fatty acids, Huh-7 cells express GPR120.

We now show that oleate stimulates rapid (15 min) LD formation in starved Huh-7 cells. This stimulation is dependent upon and involves GPR120 activating, apparently through Gi, a PI-3-kinase-dependent phospholipase D signaling pathway that controls LD generation. In cells exposed to oleate for longer periods (~3 hours) the increase in LD formation is less dependent upon the GPR120-regulated pathway implying the presence of an additional mechanism. Many defects in lipid metabolism are increasingly being shown to be dependent upon the PI-3-kinase pathway. This data suggests a mechanism whereby increases in LD generation, in for example lipomas, may be regulated.

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