

## **Fatty Acid Lipotoxicity in the Yeast:**

### **To Store or not to Store, this is the Question.**

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In the yeast *Saccharomyces cerevisiae* neutral lipids accumulate in an organelle called lipid particle/droplet (LP) which was considered as a storage compartment but also plays a major role in protecting the cell from the lipotoxic effect of unsaturated free fatty acids (FFA). When yeast cells are grown on oleic acid supplemented media proliferation of peroxisomes is induced, and at the same time large amounts of FFA are incorporated into triacylglycerols (TAG) or steryl esters (SE) resulting in massive production of LP. The biosynthesis of this organelle was found to depend on the four acyltransferases responsible for TAG and SE synthesis, Dga1p, Lro1p and Are1p, and Are2p. Mutants with only one of these four enzymes active can still form LP when grown on glucose containing media, whereas a mutant with deletion of all four genes cannot. Previously, it has been argued that the quadruple mutant  $\Delta dga1\Delta lro1\Delta are1\Delta are2$  might not be able to grow on oleic acid supplemented media as the toxic substance cannot be channeled to neutral lipid depots. In recent studies, however, we found that the LP deficient yeast strain can recover from the oleic acid shock. Under these conditions, cells show enlarged ER membrane structures, altered lipid composition and accumulation of some second messenger molecules. We hypothesize that these cells reveal tolerance or resistance to the negative regulation caused by oleic acid and/or to apoptotic degradation. Our results suggest that oleic acid plays rather an important role in cell signaling than effecting membrane fluidity by incorporation into phospholipids. Furthermore, these results challenge the role of LP in the lipotoxic response.

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