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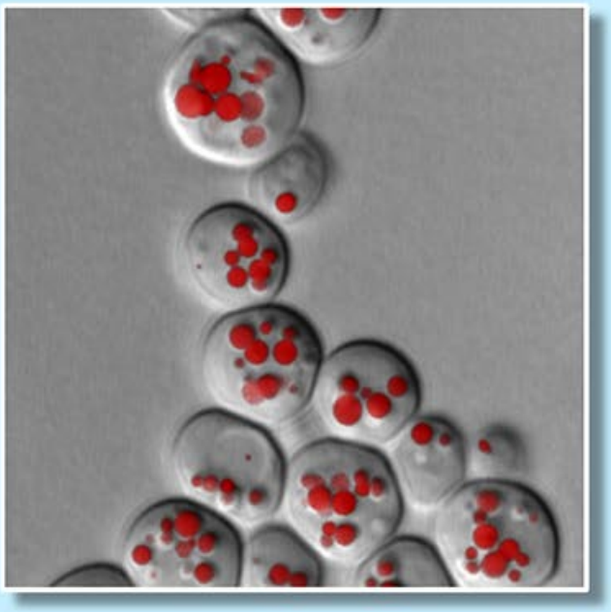

Lipid Droplets (Red) in Budding Yeast
(Image credit: www.leica-microsystems.com/science-lab/obese-and-slim-yeast-cells/)

AGPAT Enzyme Activity Increases in the Absence of GPAT3 and GPAT4 in Murine Liver and Adipose

Triacylglycerol (TAG) is a fat that serves as a vital energy source in eukaryotes. TAG is synthesized *de novo* in the liver and fat cells through a pathway that is initiated by the enzyme glycerol-3-phosphate acyltransferase (GPAT) and next catalyzed by acylglycerol-phosphate acyltransferase (AGPAT). It was hypothesized the deletion of GPAT would result in decreased activity in the TAG synthesis pathway and therefore decreased AGPAT activity. To investigate this idea, the activity of AGPAT was assayed in tissue homogenate from liver and adipose of mice lacking GPAT3 or GPAT4, the main GPAT isoforms. Contrary to the hypothesis, AGPAT activity was elevated in GPAT3-deficient and GPAT4-deficient liver samples and adipose samples compared to those prepared from wild type mice. This result suggests the activity of the TAG synthesis pathway increases to compensate for the absence of the rate limiting enzyme, GPAT. In addition to AGPAT's responsiveness to GPAT, the sub-cellular localization of AGPAT was also explored. AGPAT was known to localize to the ER membrane, but it is hypothesized that the ER shares membranes with lipid droplets, the organelles that store TAG. Thus, we predicted that AGPAT activity would be detectable in isolated lipid droplets. AGPAT activity was measured in lipid droplet and microsomal fractions of murine wild type, GPAT3-deficient and GPAT4-deficient livers. AGPAT activity was indeed detected in the lipid droplet fraction, supporting our hypothesis that the ER membranes are contiguous with lipid droplets. AGPAT activity was higher in lipid droplet and microsomal fractions in GPAT3-deficient and GPAT4-deficient tissues compared to wild type mice, consistent with our results above and suggesting a general cellular response to the absence of GPAT3 or GPAT4. Understanding the functions and interactions of the enzymes along the *de novo* TAG synthesis pathway can provide insights that will inform the development of treatments for metabolic conditions such as heart disease, obesity, and diabetes, in which it is desirable to control TAG synthesis.