Rewiring of lipid metabolism in yeast suppressor mutants devoid of phosphatidylcholine

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The composition of the membrane lipid matrix determines the physical properties of a biological membrane including membrane surface charge, membrane fluidity and membrane intrinsic curvature. For proper membrane function it is essential that these parameters are maintained in the proper range. Yeast is the eukaryote of choice for investigating the regulatory mechanisms governing membrane lipid composition because the organism is extremely tolerant to manipulation of membrane lipid biosynthesis. We interrogate regulation of membrane lipid composition by manipulating phospholipid acyl chain or head group composition.

Phosphatidylcholine (PC) is a highly abundant membrane lipid in the vast majority of eukaryotes and is considered essential for viability. The yeast mutant *cho2opi3* lacks the methyltransferases that convert phosphatidylethanolamine (PE) into PC, and is a choline-auxotroph: it relies on supplementation with choline for PC synthesis by the CDP-choline route. We picked up *cho2opi3* suppressor clones that lost the auxotrophy for choline. These clones exhibit decent growth in the absence of choline or choline substitutes. Whole genome sequencing and FACS analysis of DNA content revealed that all suppressors tested had been subject to genome duplication and that most acquired 2n-1 aneuploidy. The phenotypic hallmarks of the first PC-free eukaryotes will be presented and discussed in the context of membrane lipid homeostasis.