S02-4 **Perturbation of phospholipid catabolism by the PNPLA family leads to hepatic dysfunction**

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A large fraction of choline, an essential nutrient, exists in cellular membranes as a form of phosphatidylcholine (PC). Choline supplies methyl groups for regeneration of methionine and its metabolite *S*-adenosylmethionine (SAM), a universal methyl donor, mainly in the liver. Theoretically, the enzymatic removal of two fatty acyl chains and glycerol phosphate from PC can give rise to free choline, yet the pathway for PC catabolism that generates the endogenous choline pool remains largely unknown. Here we show that two particular members of the PNPLA/iPLA$_2$ family, PNPLA7 and PNPLA8, take part in this PC-catabolic process in the liver. PNPLA8, a phospholipase A (PLA) that converts PC to lysophosphatidylcholine (LPC), and PNPLA7, a lysophopholipase that hydrolyzes LPC to glycerophosphocholine (GPC), are sequentially coupled with the generation of endogenous choline, whose methyl group is preferentially fluxed into the methionine cycle. Mice deficient in either PNPLA7 or PNPLA8 show marked decreases in hepatic GPC and choline, accompanied by a series of signs of methionine insufficiency. Accordingly, mutant mice are lean, display growth retardation, and die within a few months, features reminiscent of premature aging. Our results highlight that the metabolic flow from membrane PC to choline through the PNPLA8-PNPLA7 axis is crucial for proper hepatic function and systemic energy homeostasis, and uncover a novel functional aspect of the PLA$_2$ family as a regulator of phospholipid recycling.