Upregulation of Hepatic Lipogenic Gene Expression does not Result in Lipid Accumulation in PUFA-deficient Elovl2 KO Mice.

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The potential beneficial role of diet derived polyunsaturated fatty acids (PUFAs) is one of the most intensively studied fields in a lipid research whereas the function of endogenously synthesized PUFAs still remains neglected. Elongation of very long–chain fatty acids in mammals is catalyzed by the elongase enzymes family (ELOVL) to which ELOVL2 belongs. In our study we have investigated how global ablation of highly expressed in the liver ELOVL2 affects hepatic lipid composition and *de novo* lipogenesis. In the liver of Elovl2 KO in comparison to WT we have observed accumulation of 22:4 (n-6) docosatetraenoic acid and 22:5 (n-3) docosapentaenoic acid as well as decreased levels of 22:5 (n-6) docosapentaenoic acid (DPA) and 22:6 (n-3) docosahexaenoic acid (DHA). These data suggest that ELOVL2 is involved in the elongation process of fatty acids with 22 carbons to produce 24 carbons precursors for DPA (n-6) and DHA (n-3). Moreover, we found that impaired levels of polyunsaturated fatty acids in Elovl2 KO positively influenced the hepatic mRNA and protein levels of the key lipogenic transcriptional regulator sterol regulatory element-binding protein 1c (SREBP1c) as well as its downstream genes such as fatty acid synthase (FAS) and stearoyl-CoA desaturase (SCD1) (2.1-fold and 2.3-fold increase respectively). Interestingly, this was not followed by accumulation of triglycerides in the liver and development of hepatic steatosis. Therefore our findings imply that disrupted hepatic PUFA synthesis in Elovl2 KO mice, except stimulation of *de novo* lipogenesis, presumably activates some compensatory mechanisms to prevent storage of lipids.