

Sterol Sensing and Cholesterol-bile Acid Homeostasis in NAFLD

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Genes Regulated by SREBPs

SREBP-2

SREBP-1

Acetyl CoA

30 Enzymes

PCSK9

**LDL
Receptor**

Cholesterol



4 Enzymes

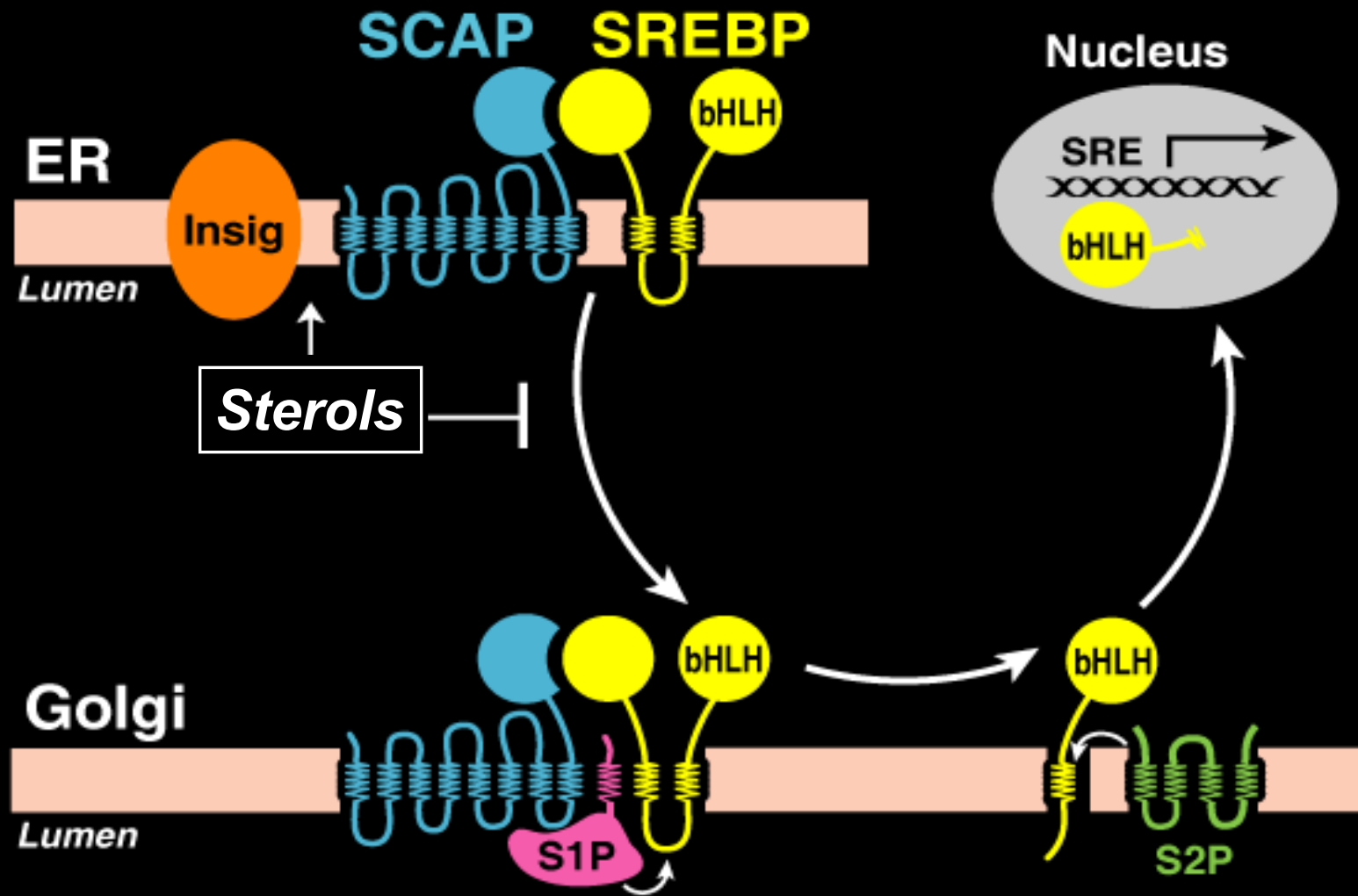
Fatty Acids

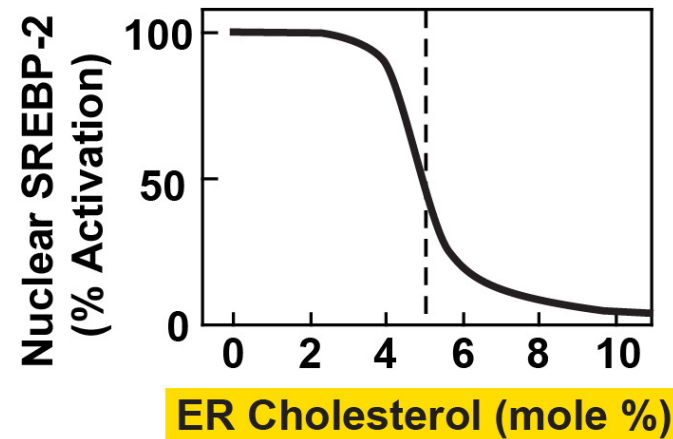
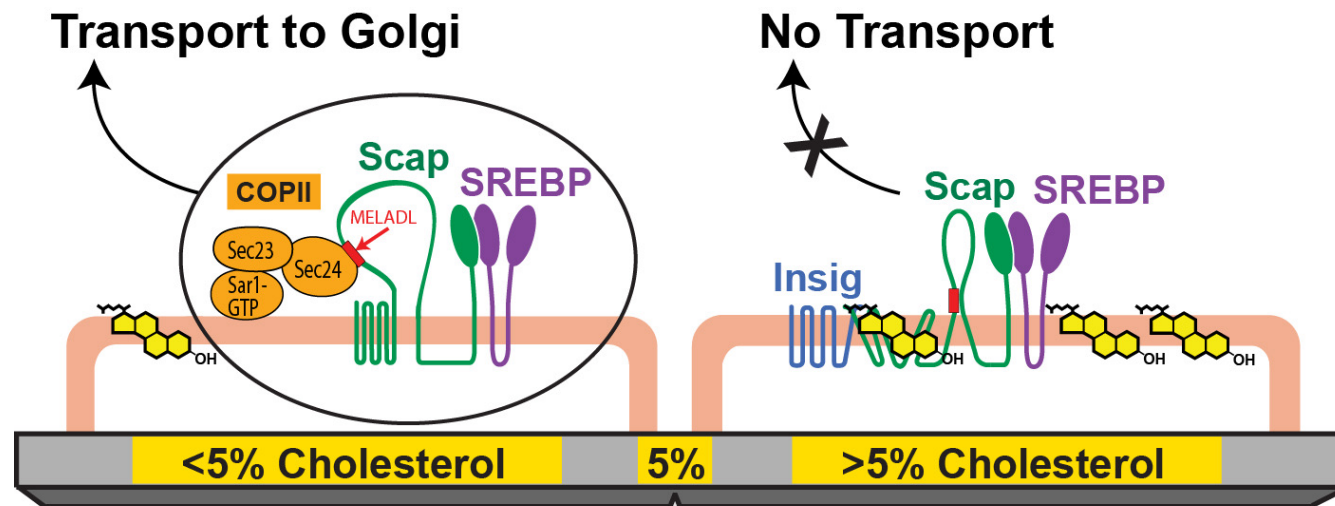
1 Enzyme

Triglycerides

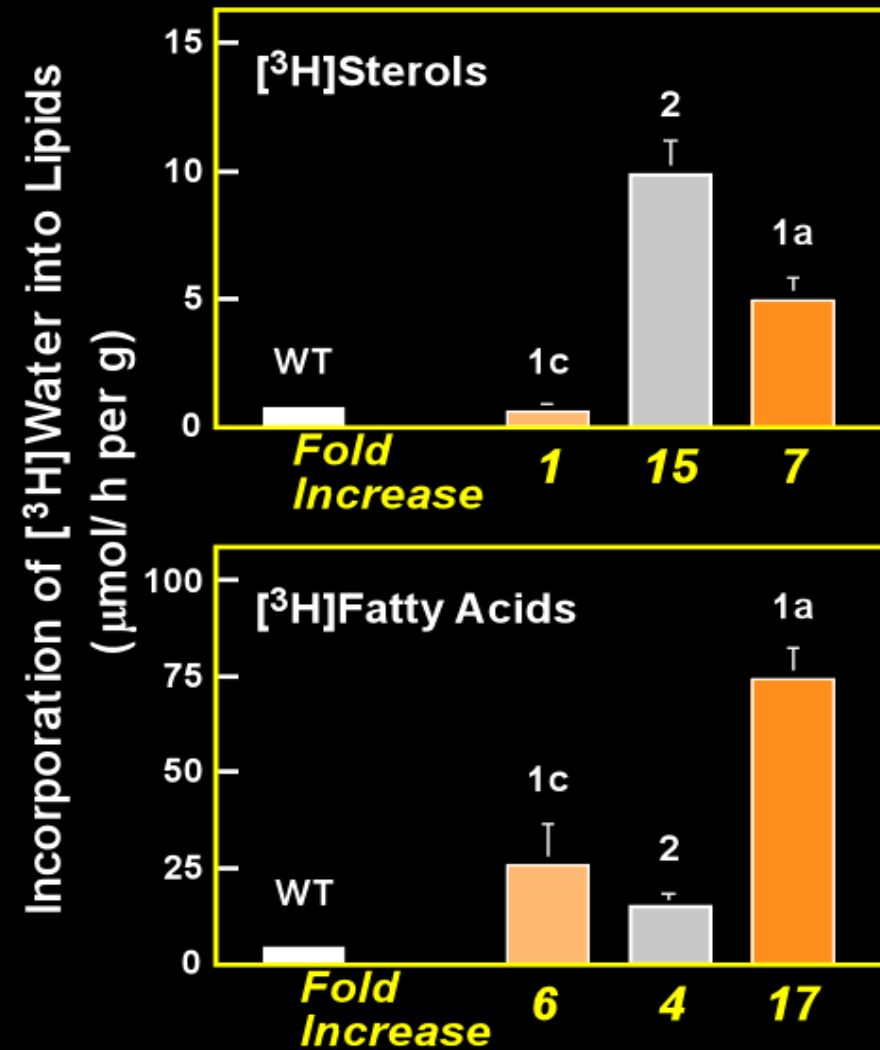


The SREBP Pathway

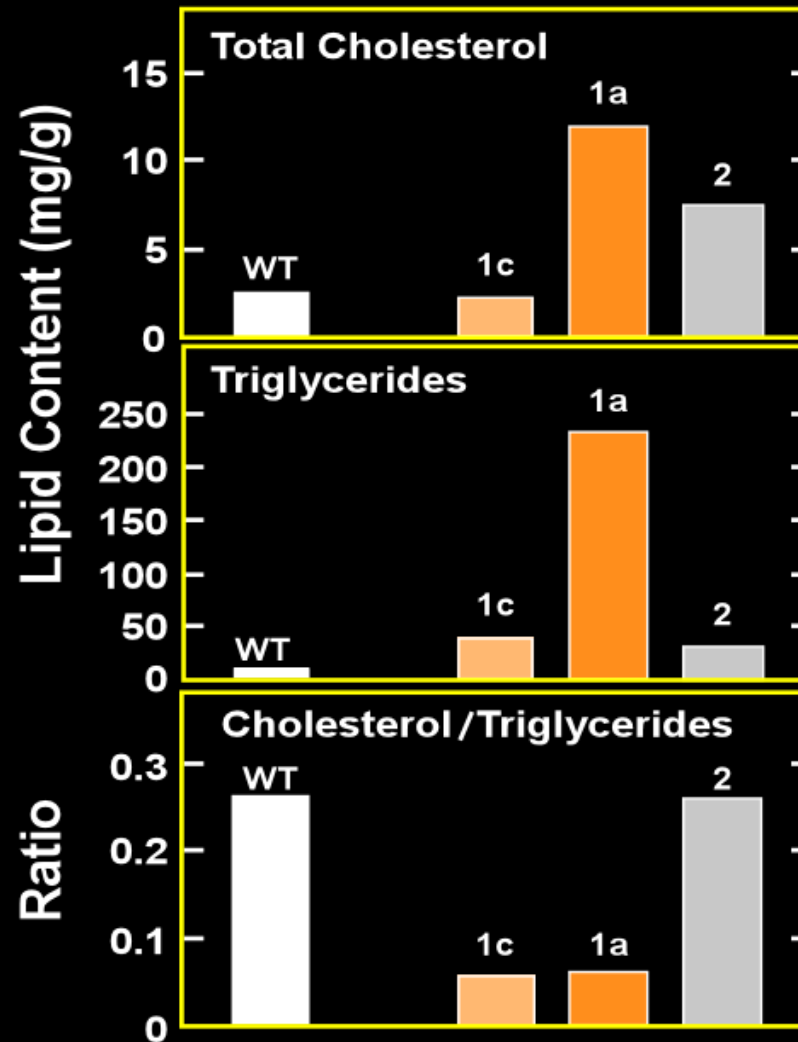




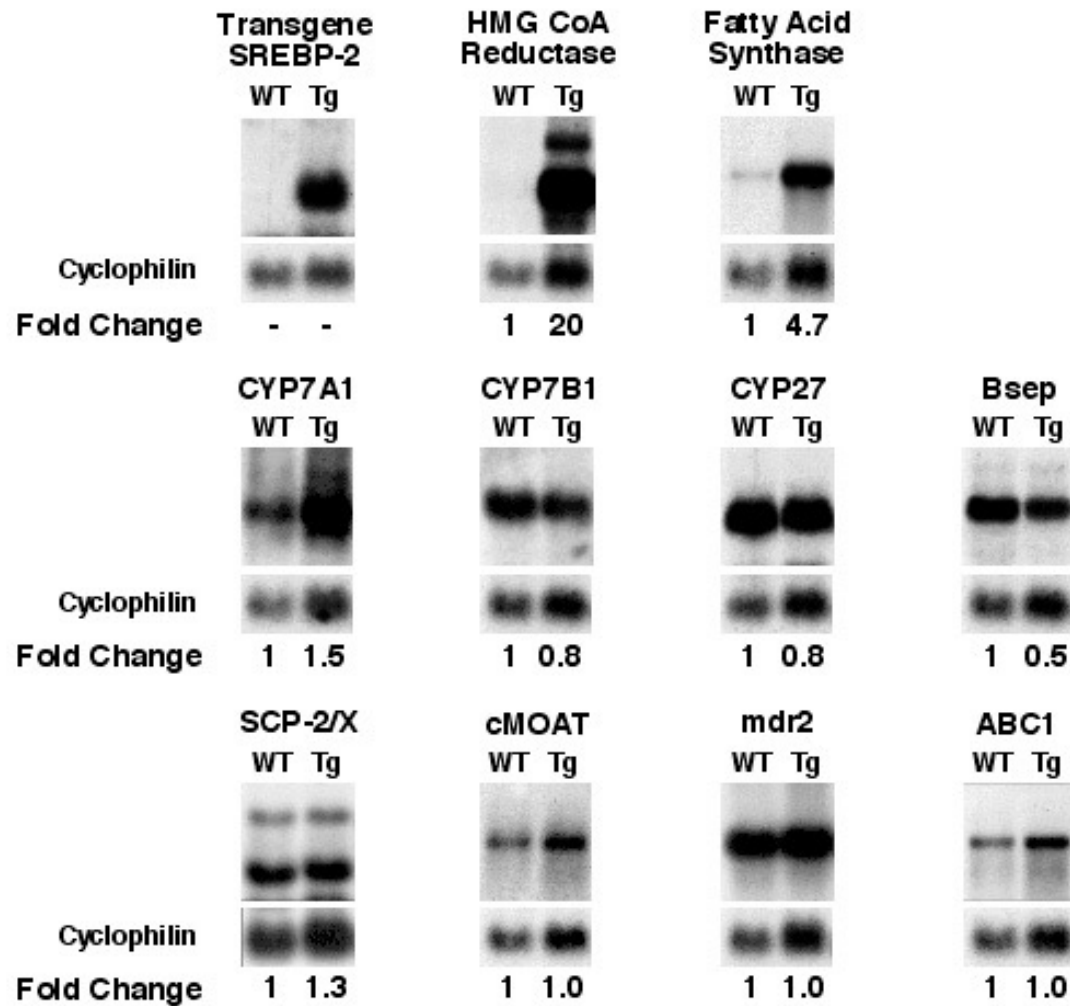
In Vivo Cholesterol and Fatty Acid Synthesis in Livers of Transgenic Mice



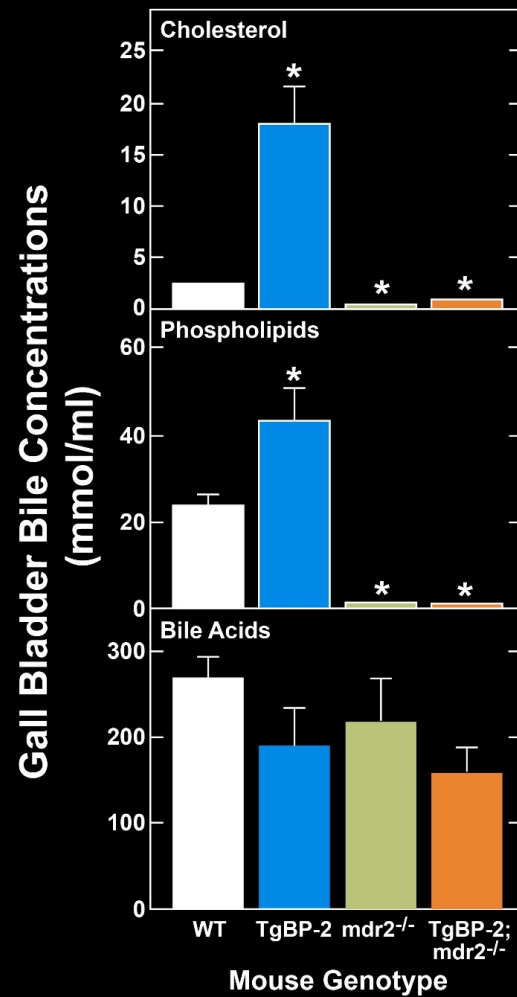
Hepatic Lipid Concentrations in Transgenic Mice Expressing nSREBP-1 c,-1 a, and -2



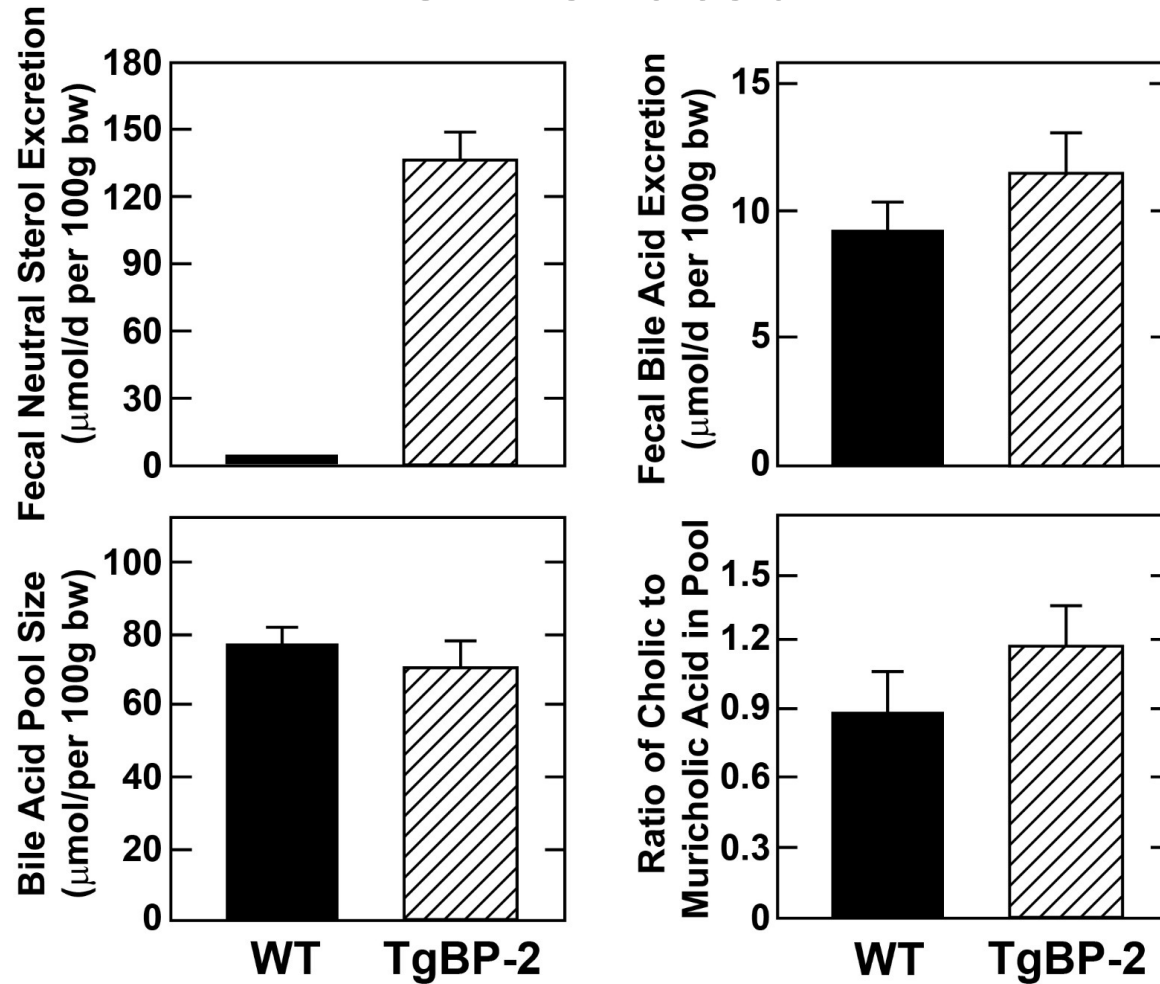
Relative mRNA Levels for Genes Involved in Biliary Lipid Metabolism in Livers of SREBP-2 Transgenic Mice



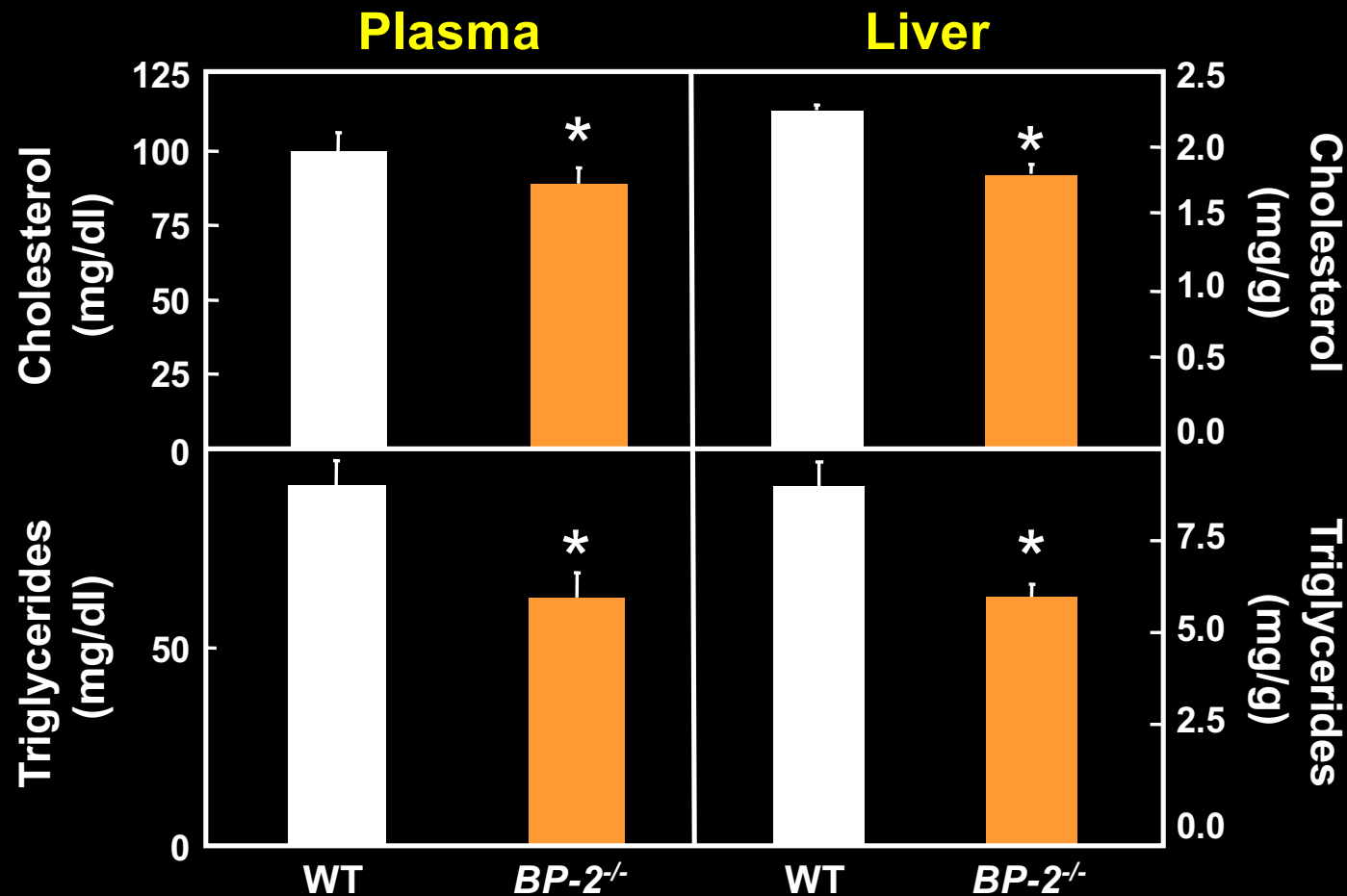
Gallbladder Bile Lipid Concentrations in Wild-type and TgBP-2 Mice



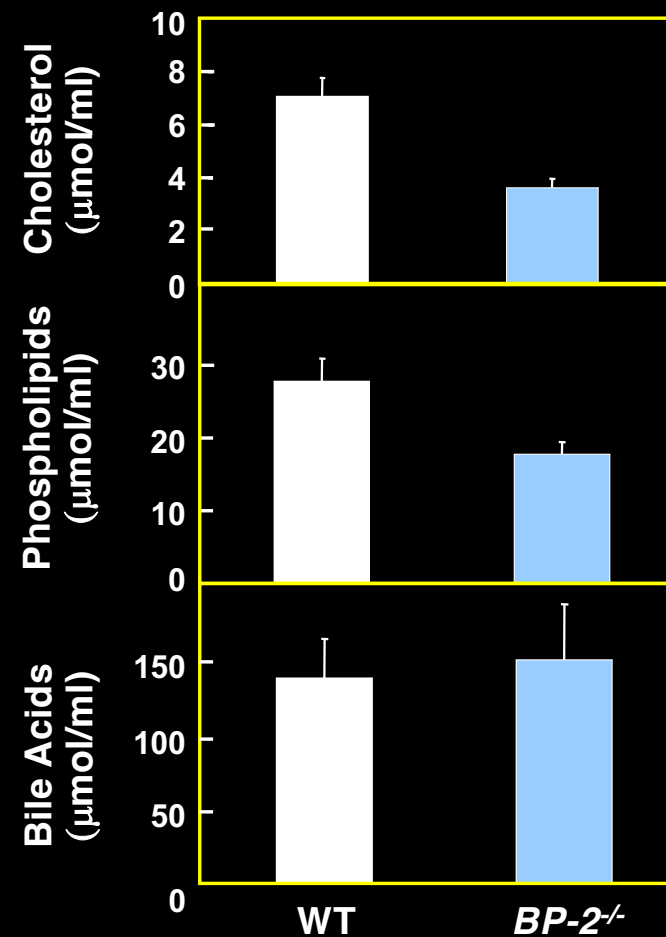
Bile Acid Homeostasis when Cholesterol Synthesis is Elevated



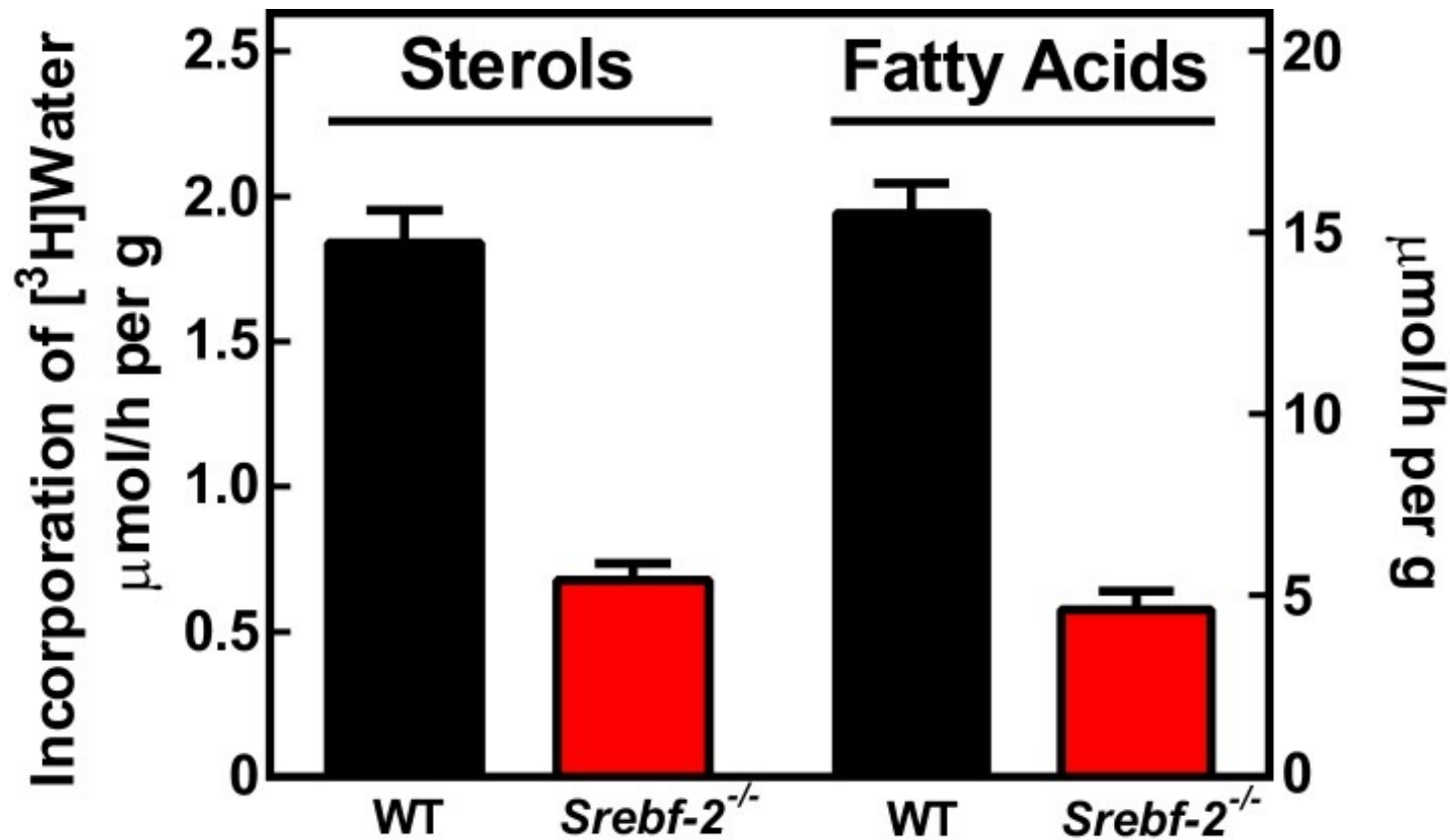
Plasma and Liver Lipid Levels in WT and *L-SREBP-2*^{-/-} Knockout Mice



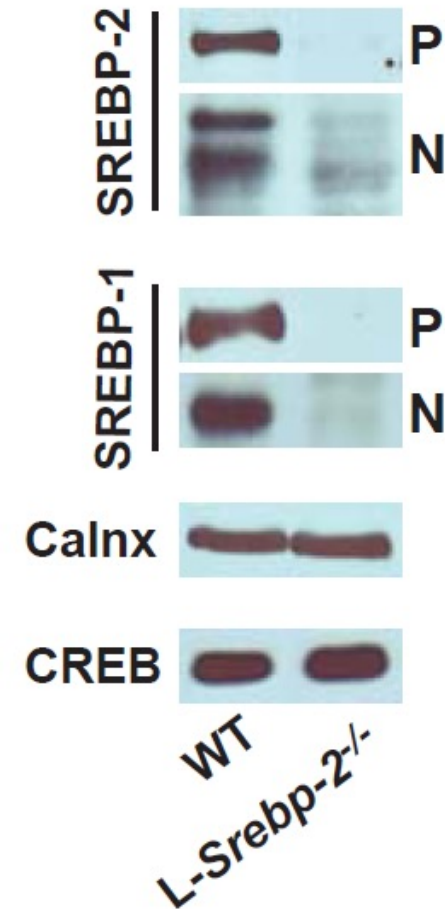
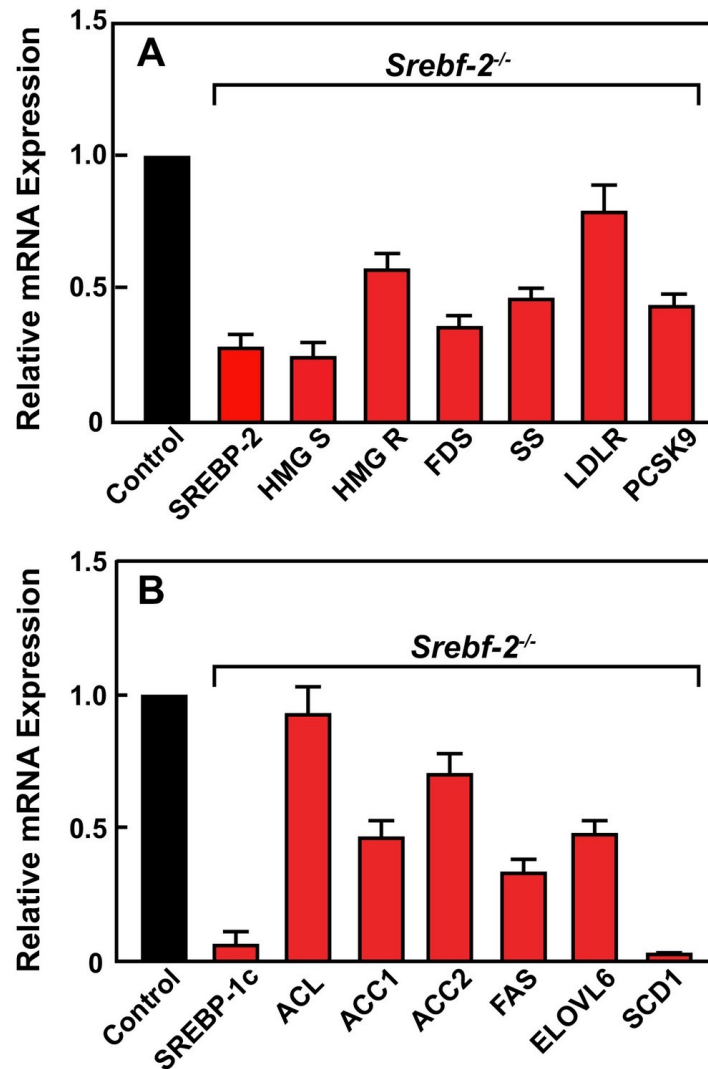
Gallbladder Bile Lipid Concentrations in Wild-type and *L-SREBP-2*^{-/-} Mice



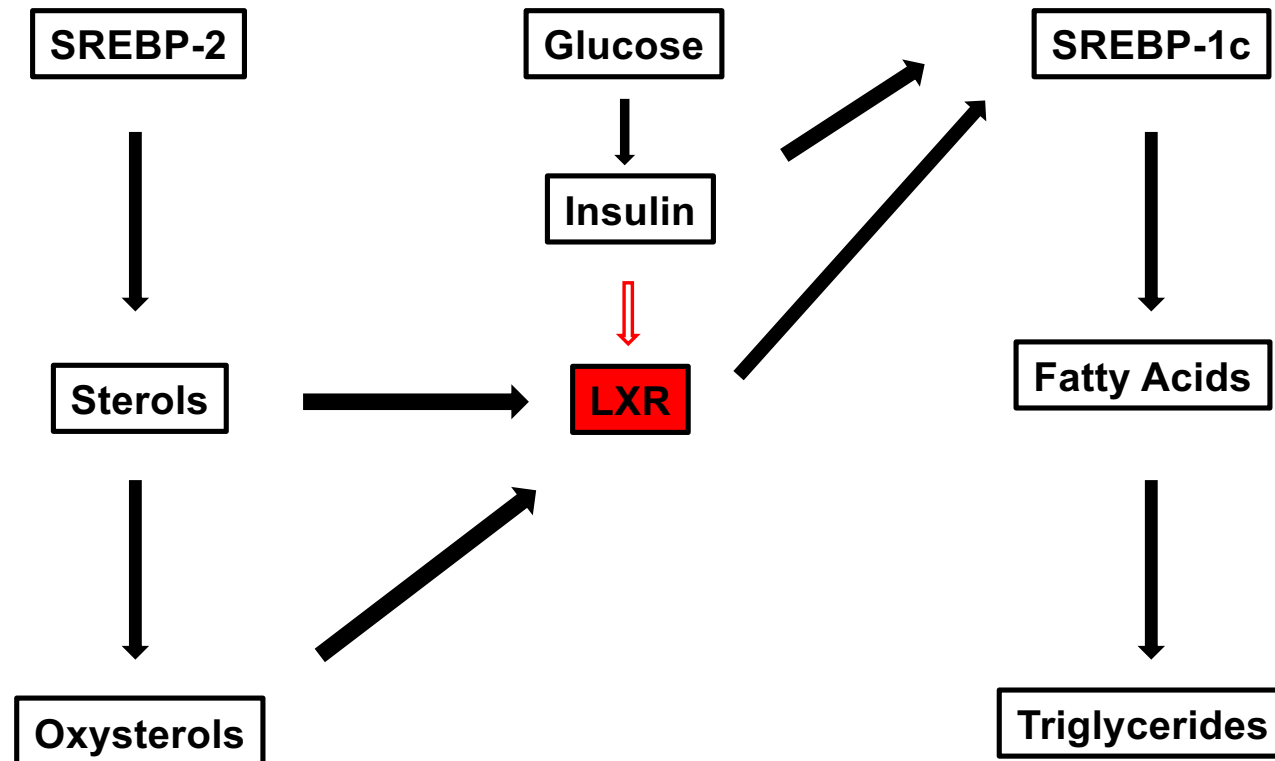
Sterol and Fatty Acid Synthesis are Reduced in L-SREBP-2 Deficient Livers



SREBP-1c is Dramatically Reduced in L-SREBP-2 Deficient Mice



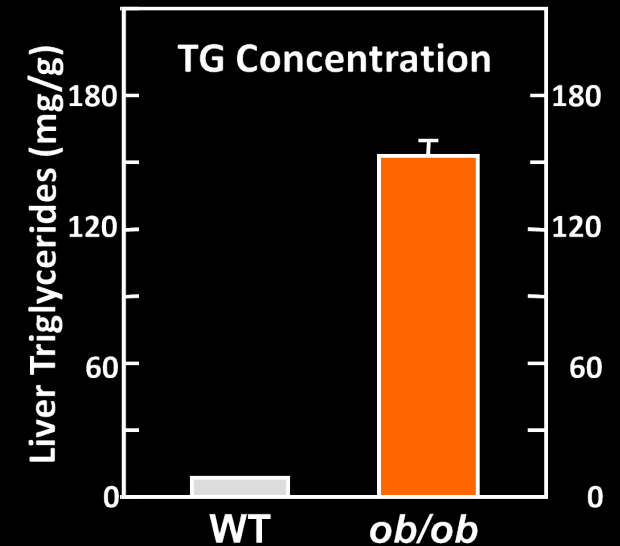
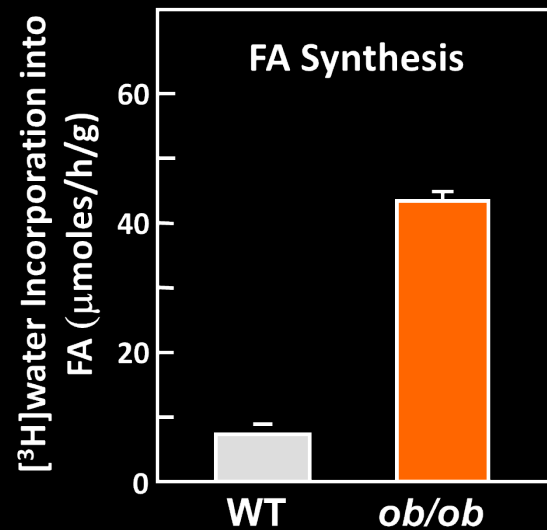
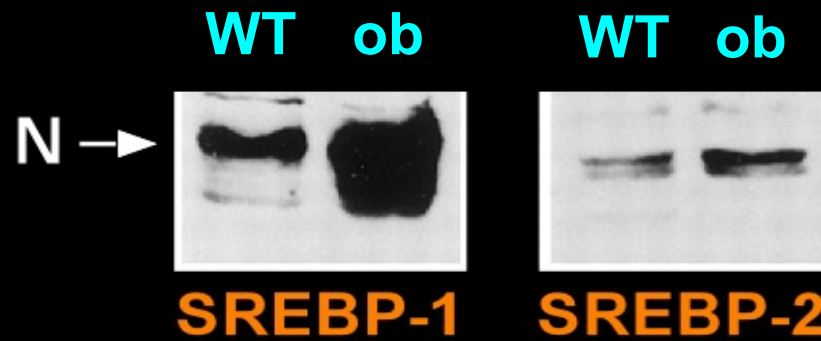
Regulation of SREBP-1c Activity by LXR Ligands from SREBP-2 Pathway



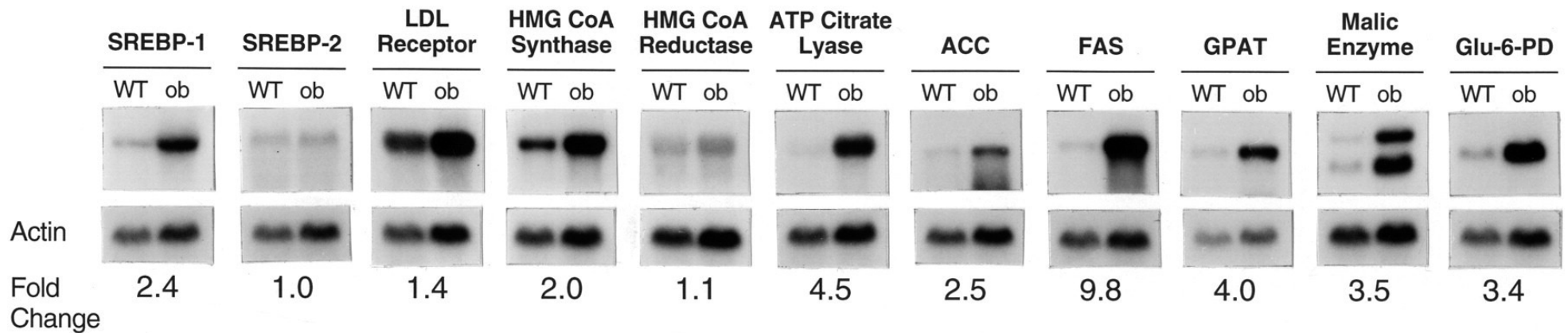
SREBP-1 Levels are Elevated in Livers of *ob/ob* Mice



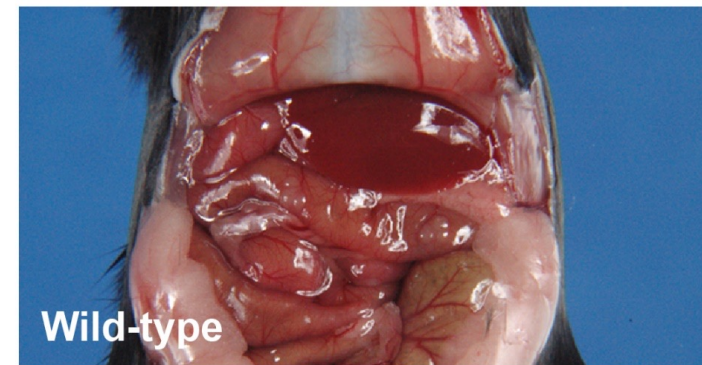
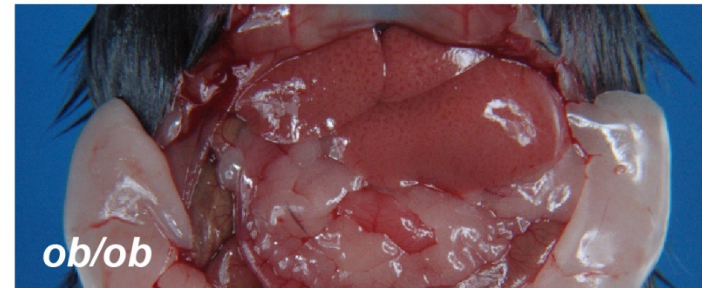
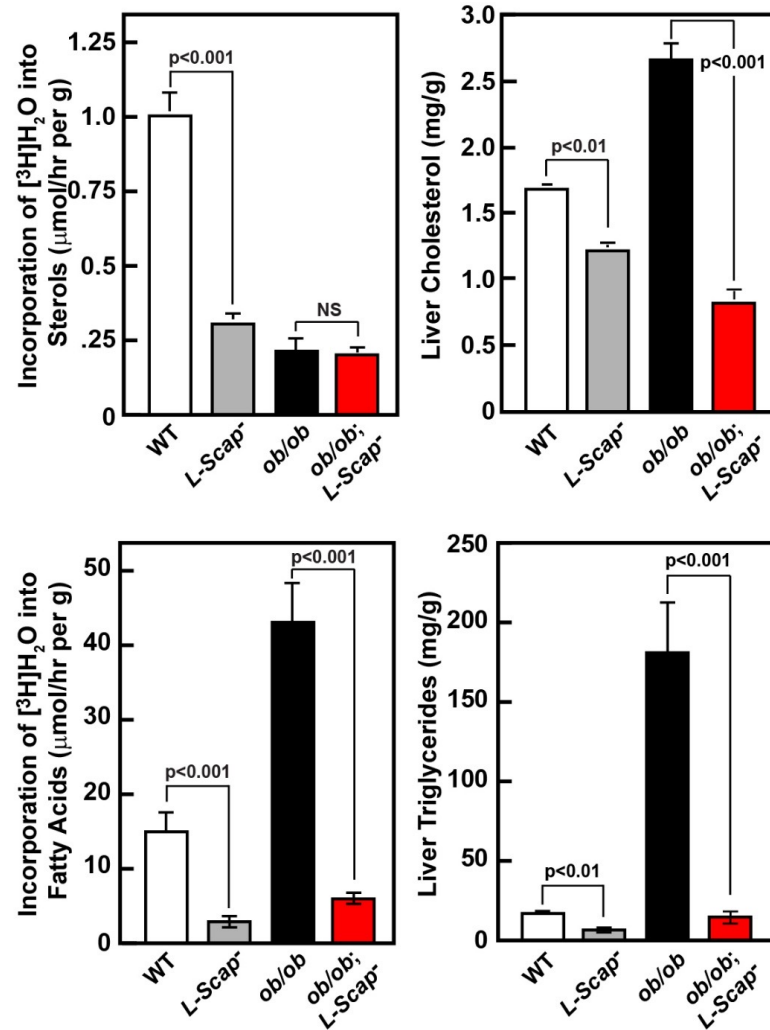
Shimomura et al. 1999. J. Biol. Chem. 274:30028-32



Cholesterol Synthesis Genes are Not Suppressed in *ob/ob* Mice

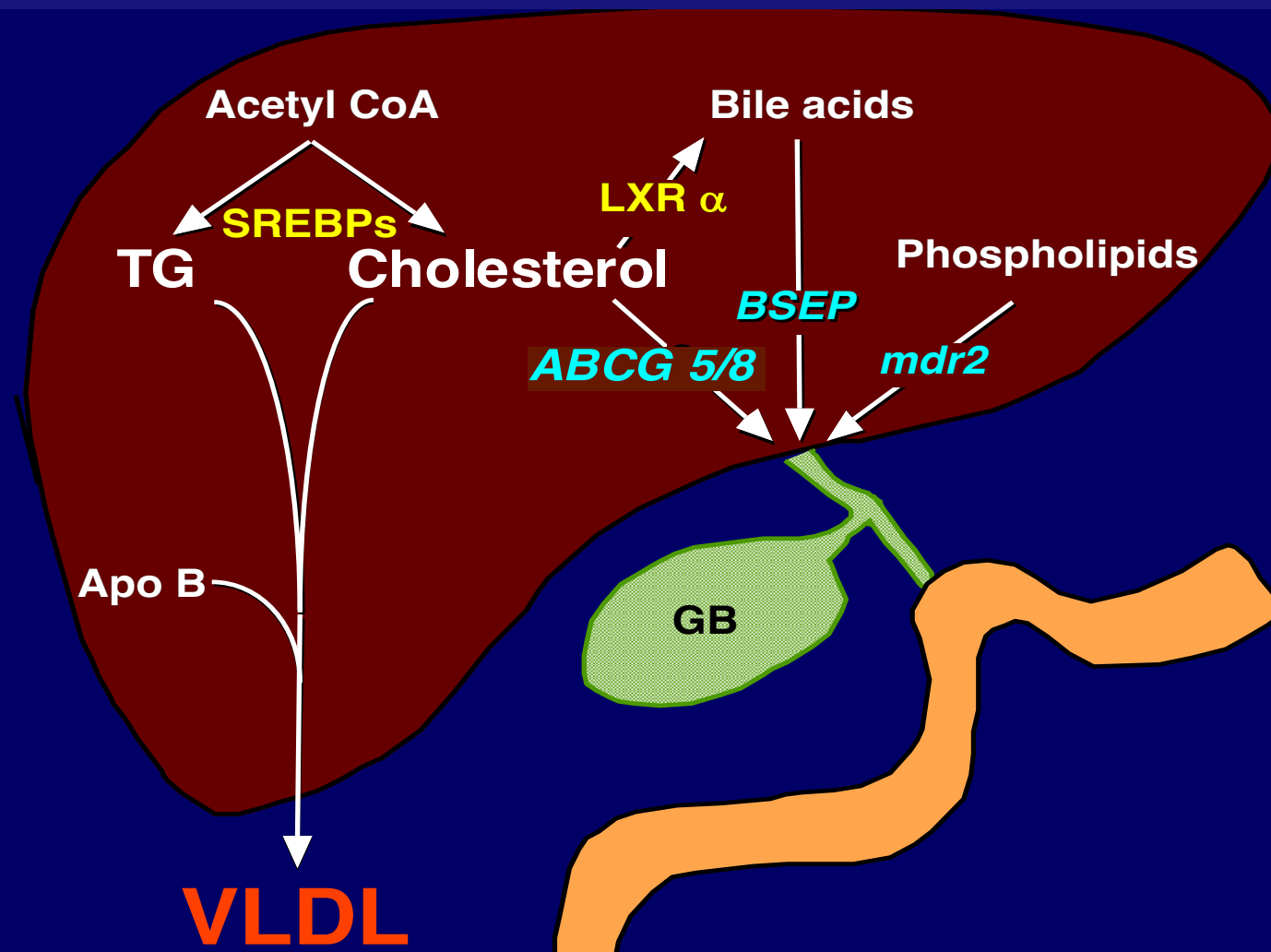


Cholesterol Synthesis is Suppressed in Livers of *ob/ob* Mice



Moon *et al.* 2012. *Cell Metab.* 15(2):240-6.

Molecular Pathways Linking Cholesterol, Fatty Acids, and Bile Acids



Acknowledgements

