

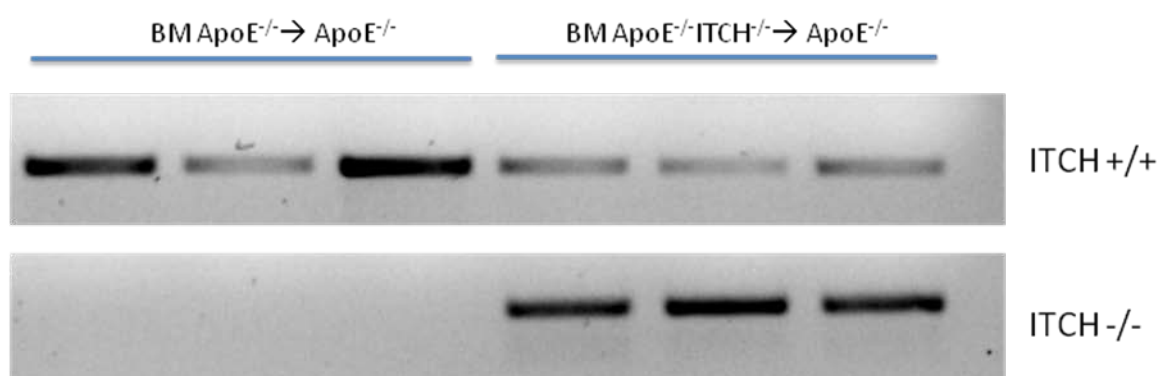
ITCH modulates SIRT6 and SREBP2 to influence lipid metabolism and atherosclerosis in ApoE null mice

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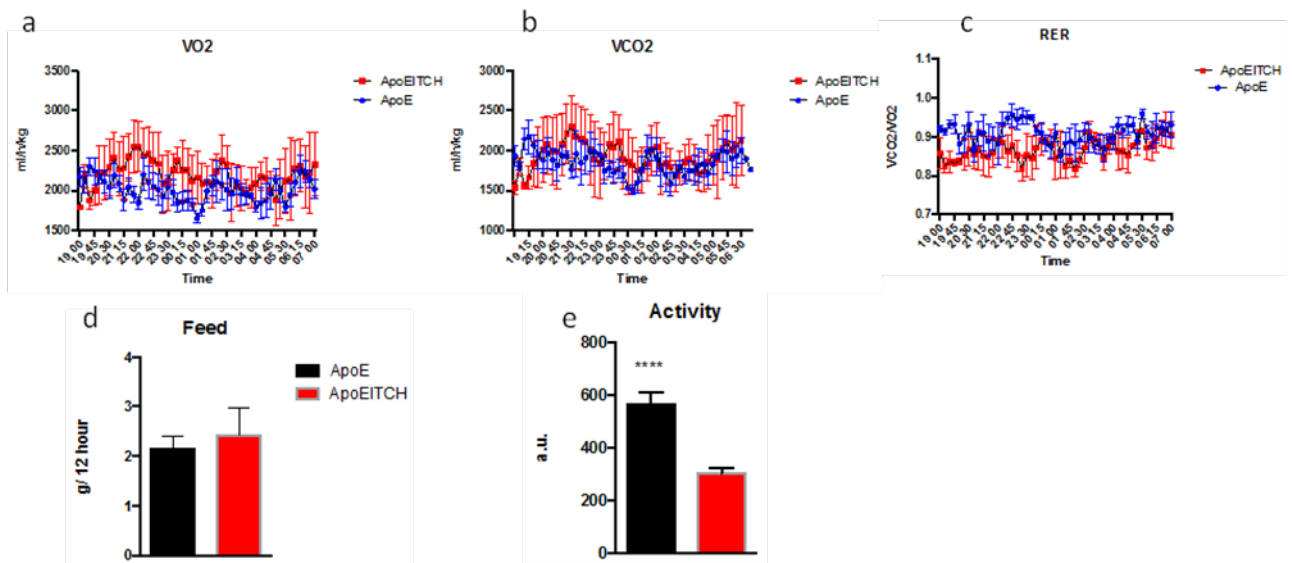
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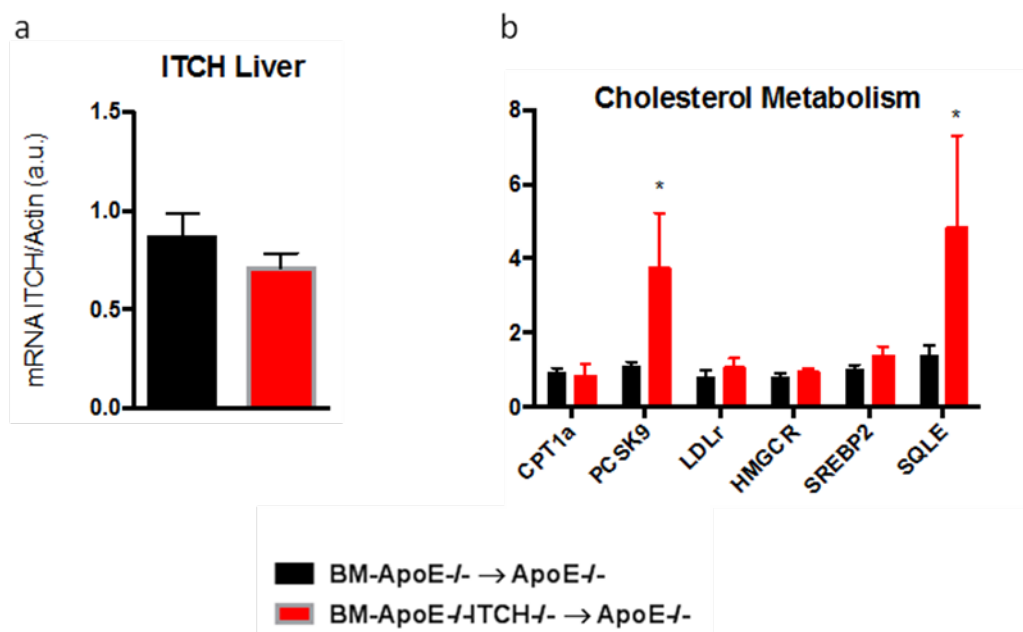


Supplementary Figure 1 PCR analysis of Bone marrow transplantation experiments shows chimerism of the transplanted animals.



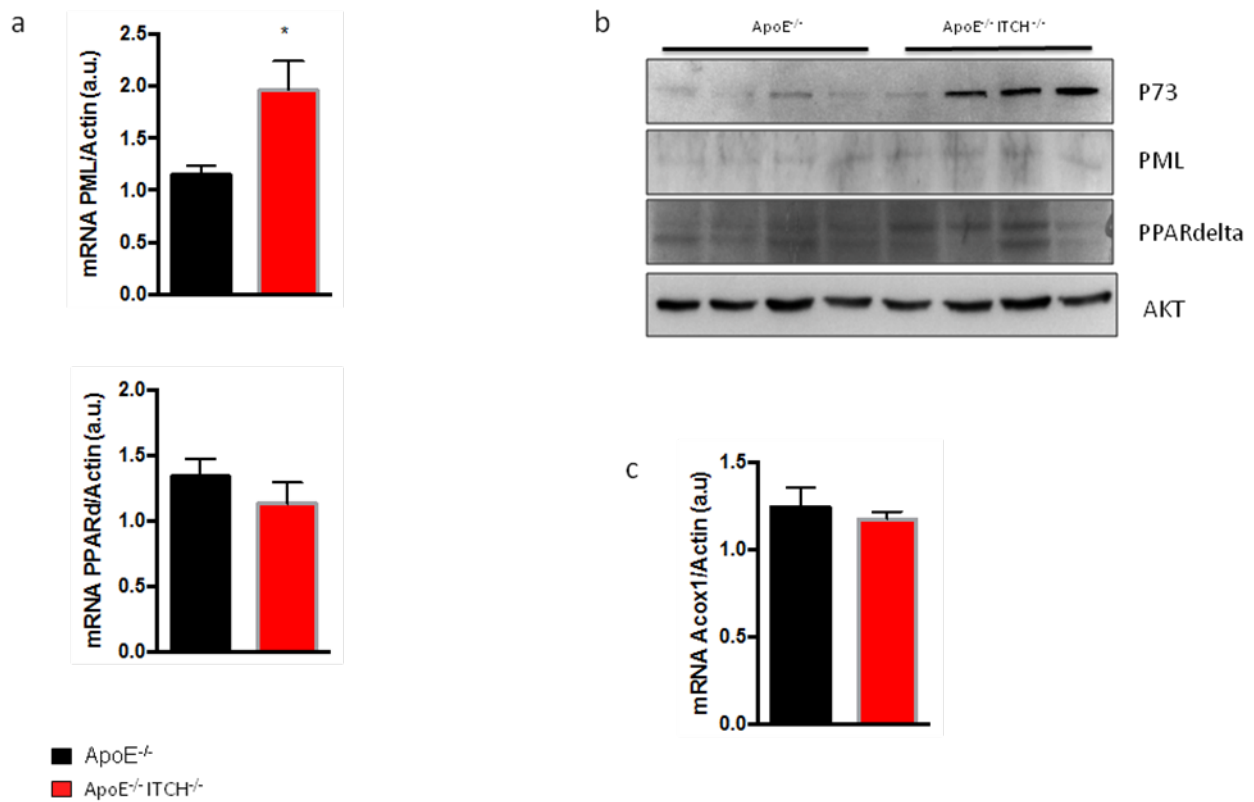
S2

Supplementary Figure 2 Loss of ITCH increases reliance on fatty acids as an energy source. ApoE^{-/-} ITCH^{-/-} animals show increased levels of O₂ consumption (A) and CO₂ (B) production with a lowered Respiratory Exchange Ratio (RER) (C). No changes were seen in food consumption (D) while activity was reduced in the ApoE^{-/-} ITCH^{-/-} animals (N=4 per group)



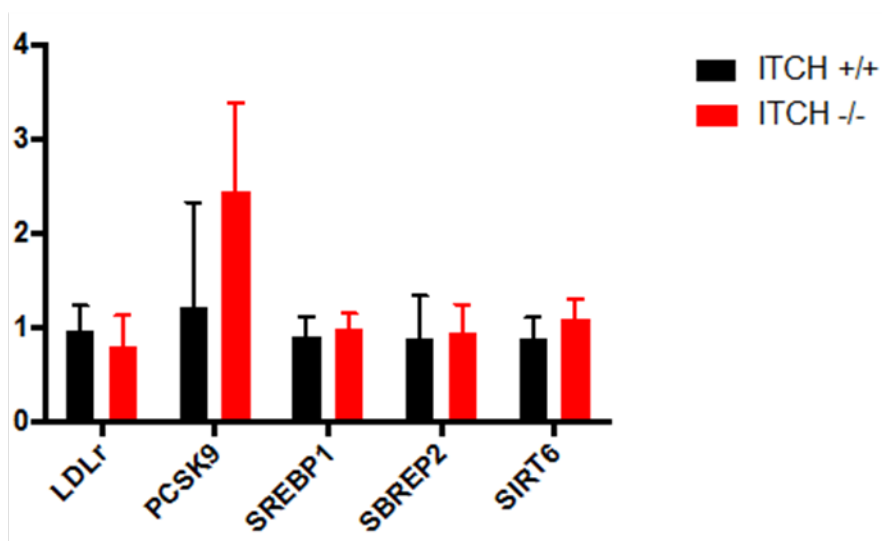
S3

Supplementary Figure 3 Bone marrow transplantation does not affect ITCH liver levels. Bone marrow transplantation does not result in a downregulation of ITCH in the liver (A) and consequently does not affect the cholesterol metabolism in the same manner as the total body knockout (B) (N=4 per group)



S4

Supplementary Figure 4: A) RT-PCR and **B)** western blots of liver tissue show that the P73-PML-PPAR δ is not affected in the livers of ApoE^{-/-} ITCH^{-/-} mice. While there is the expected increase in the protein content of P73 in the livers of ApoE^{-/-} ITCH^{-/-} there is no upregulation of the protein content of PML and PPAR δ . **C)** Furthermore, the direct target of PPAR δ , Acox1 is unaffected in the livers of ApoE^{-/-} ITCH^{-/-} mice.



S5

Supplementary Figure 5: RT-PCR of liver tissue from ITCH^{-/-} mice does not show any alterations in the expression of genes related to cholesterol metabolism. .