

Figure S1. Metabolic changes regulate CD36 expression through MEK5/ERK5 pathway. A-C) CD36 mRNA or CD36 membrane protein were analyzed in different cell types treated with 5 mM DCA for 3 days or as indicated in (B). D-E) Different cell lines were treated with siRNA for ERK5 or with the ERK5 inhibitor XMD-892 (5 μ M) or the MEK5 inhibitor PD02189 (5 μ M) for 24 hours and CD36 mRNA (D) or protein (E) were analyzed. F) Jurkat cells were transfected with an ERK5 expression plasmid and 3 days later CD36 expression was analyzed. Bar graphs represent means \pm SD of at least 3 independent experiments performed in triplicate. * p<0.05, ** p<0.01, *** p<0.005 compare to control cells.

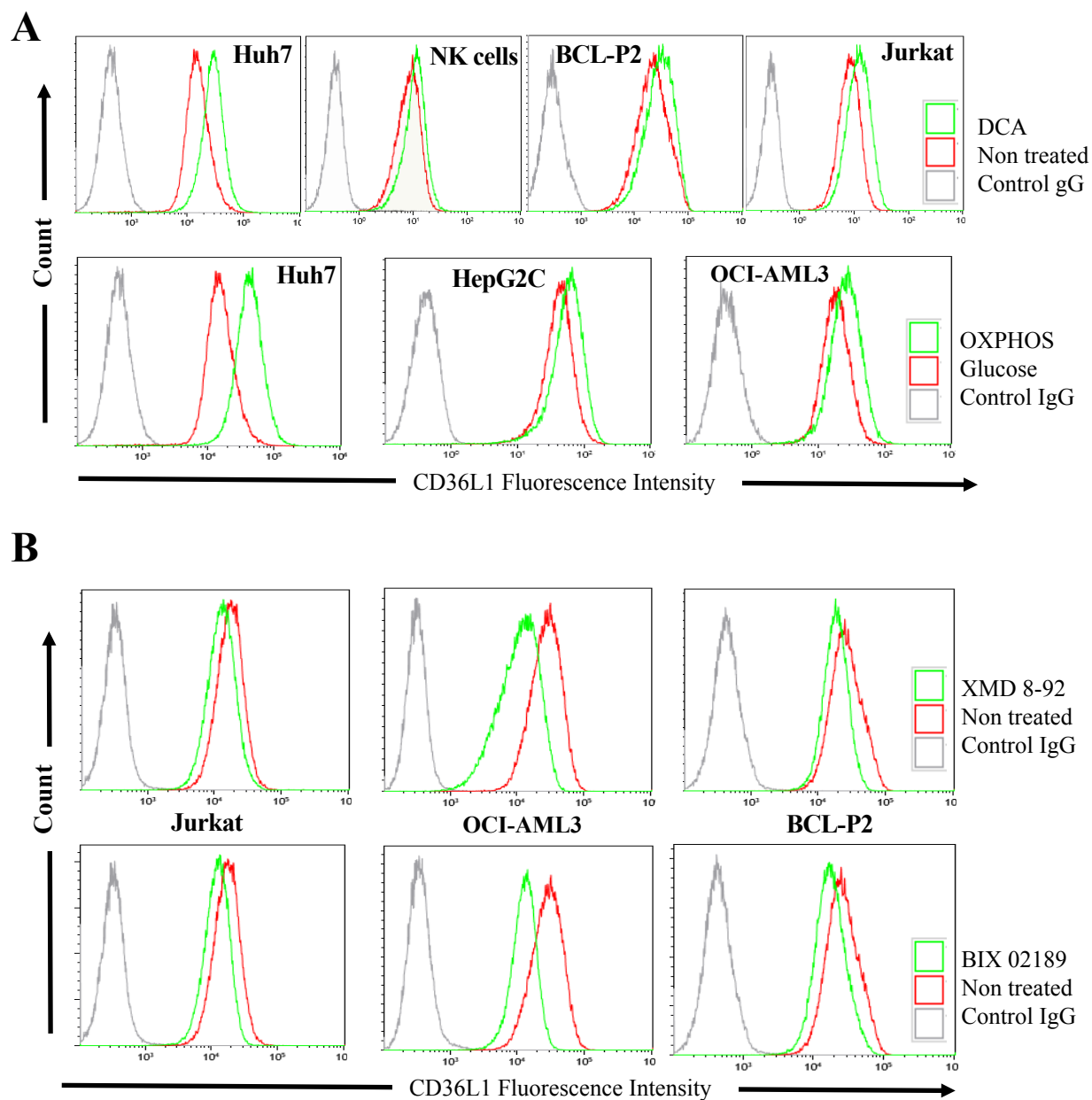
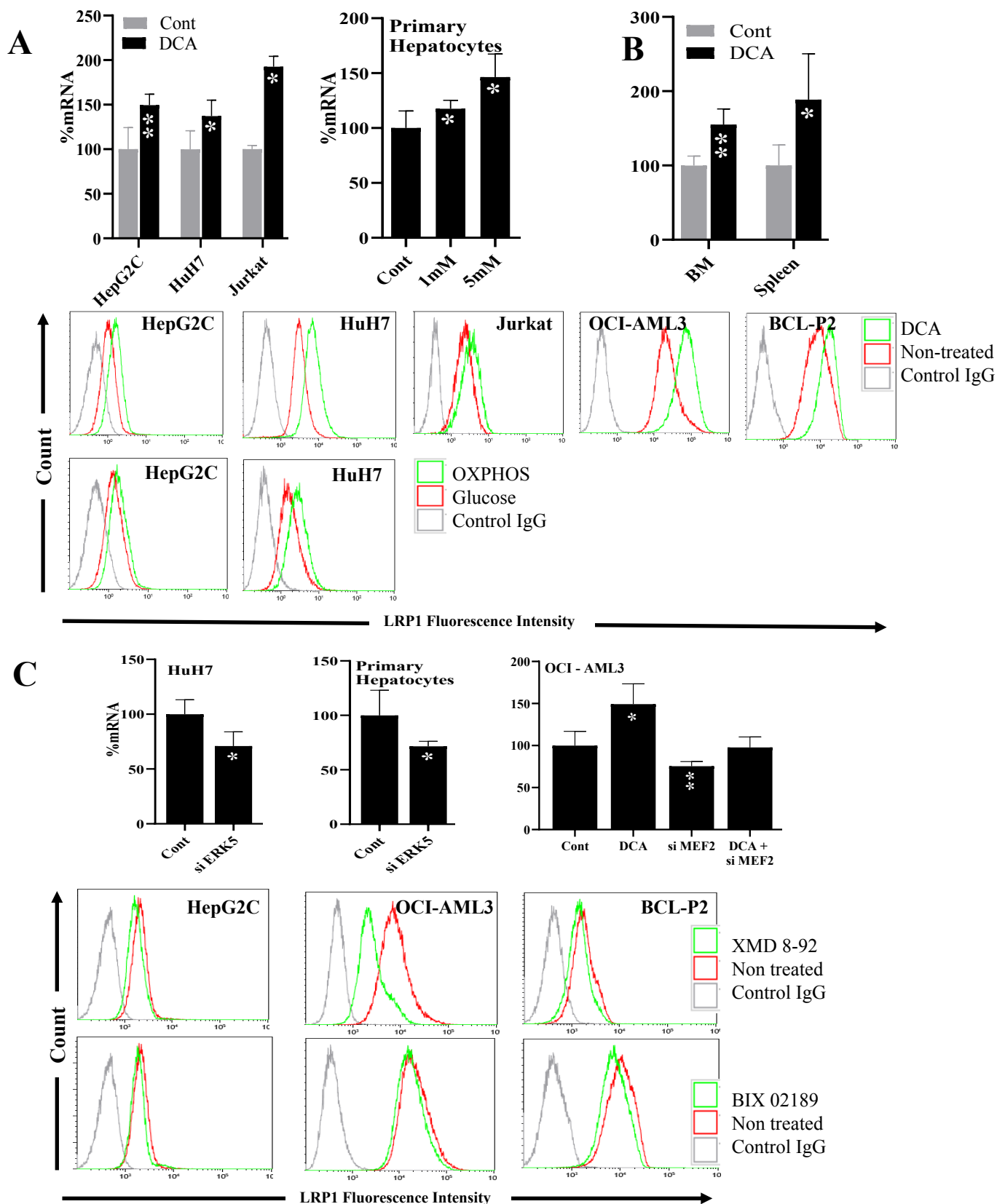


Figure S2. Changes in cell metabolism regulate SCARB1/CD36L1 expression. CD36L membrane protein was analyzed in different cell types treated for 3 days with DCA (5 mM) or growing in a free-glucose medium for 5-7 days (A) or treated with the ERK5 (XMD 892 10 μ M) or with the MEK5 (BIX 02189 5 μ M) inhibitors for 24 h (B).



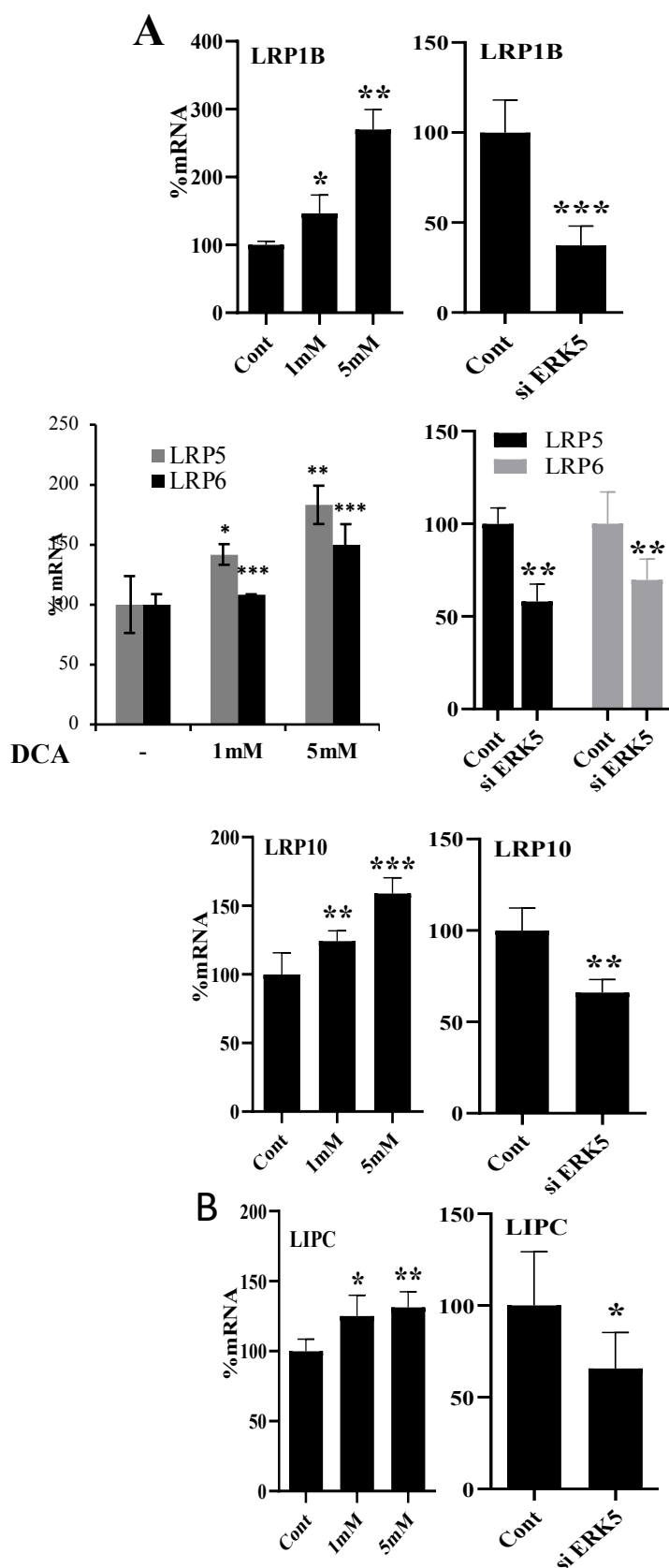


Figure S4. Metabolic changes regulate LRP1B, LRP5/6, LIRP10, and LIPC expression through the MEK5/ERK5 pathway. The *LRP1B*, *LIRP10*, *LRP5/6* (A) and *LIPC* (B) mRNA was analyzed in primary hepatocytes treated with the indicated doses of DCA for 48h or transfected with siRNA of ERK5. Bar graphs represent means \pm SD of at least 3 independent experiments performed in triplicate. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.005$ compare to control cells.

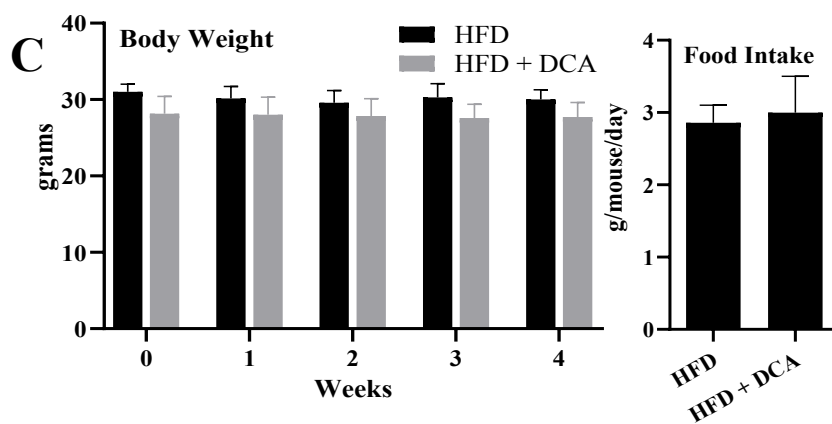
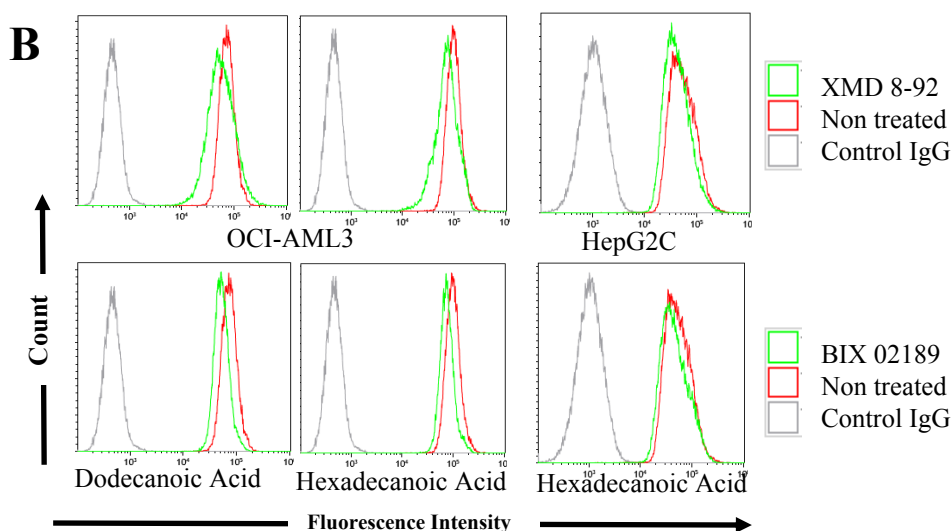
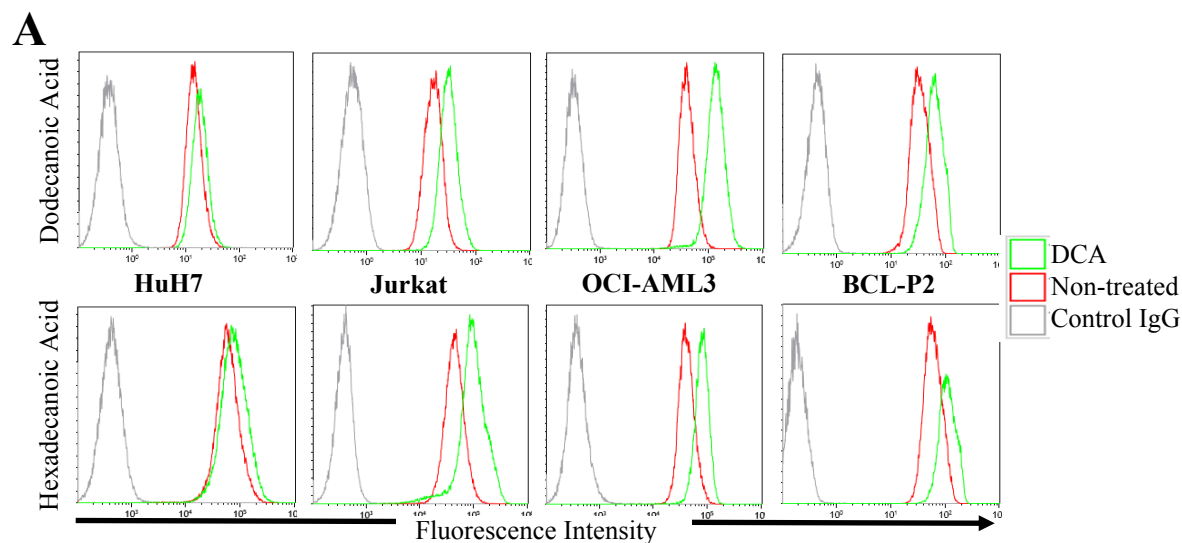


Figure S5. Metabolic changes regulate FA transport through the MEK5/ERK5 pathway. A) Fluorescent hexadecanoic and dodecanoic acid transport was analyzed in different cell types treated with DCA (5 mM for 5 days). B) Cells were treated with ERK5 (10 μ M) and MEK5 (5 μ M) inhibitors for 24 h before analyzing FA transport. C) DCA treatment does not affect body weight or food intake in mice. Mice were treated with DCA (50 mg/kg per day) for four weeks. Bar graphs represent means \pm SD of at least 3 independent experiments performed in triplicate.

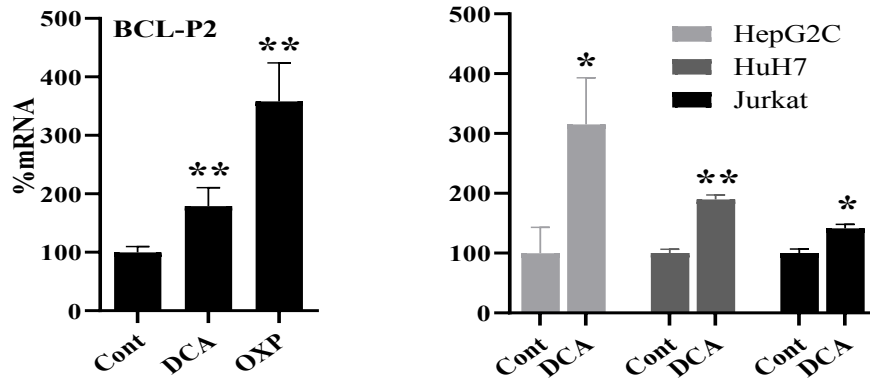
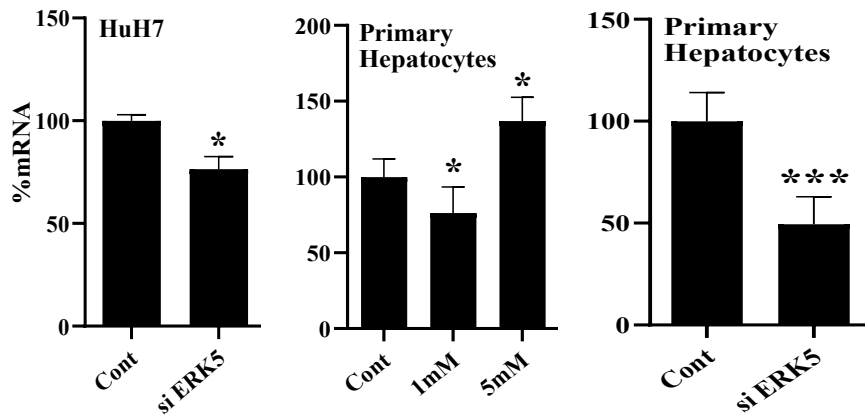
A**B**

Figure S6. Metabolic changes regulate the expression of the ACSL family of ligases through the MEK5/ERK5 pathway. A) The *ACSL1* and B) *ACSL6* mRNA was analyzed in different cell types treated with 5 mM DCA for 3 days or growing in a free-glucose medium that induced OXPHOS for 5-7 days or in cells treated for 72 h with siRNA for ERK5 or MEF2. Bar graphs represent means \pm SD of at least 3 independent experiments performed in triplicate. * $p<0.05$, ** $p<0.01$, *** $p<0.005$ compare to control cells.

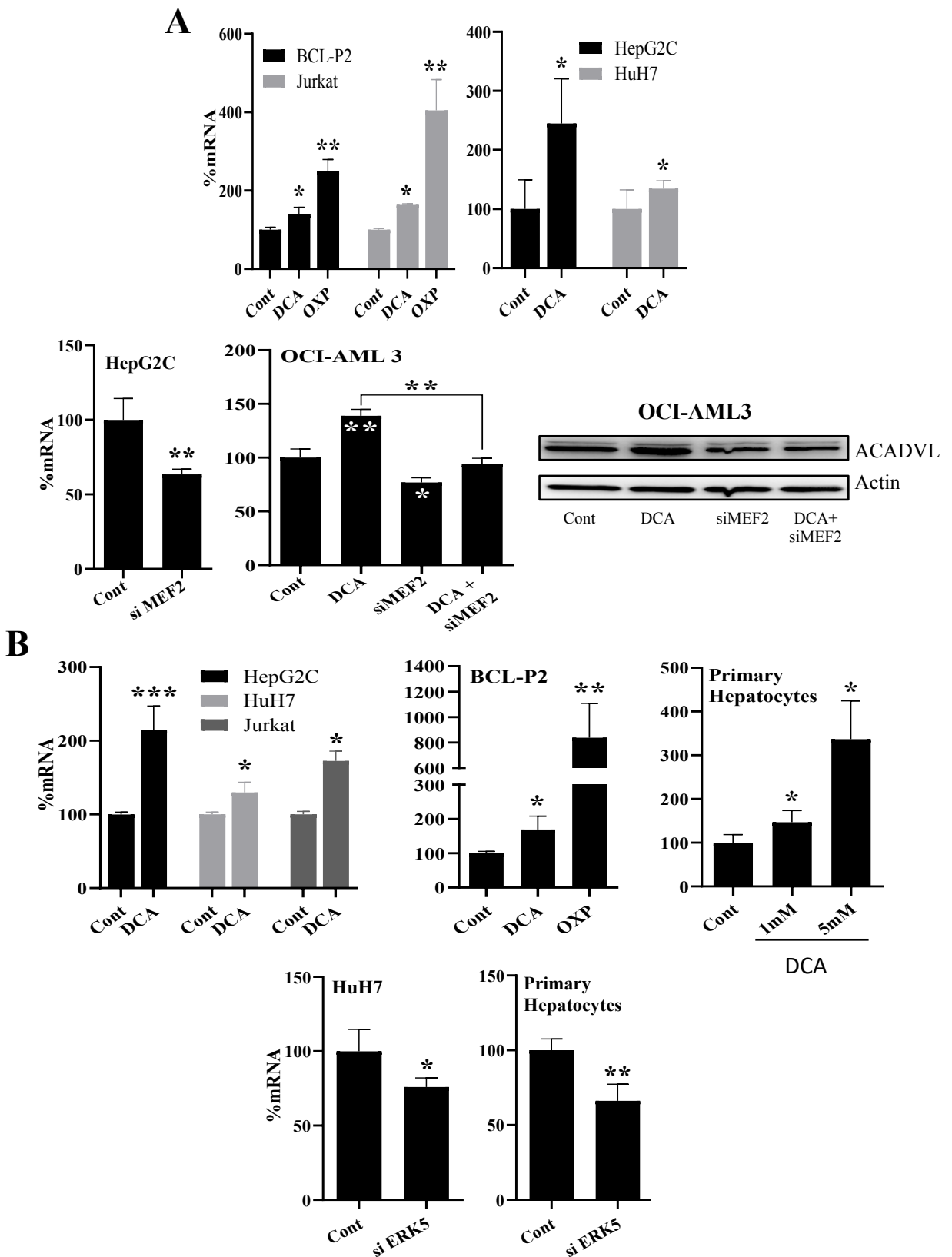


Figure S7. Metabolic changes regulate the expression of the acyl-CoA dehydrogenases through the MEK5/ERK5 pathway. A) The *ACADVL1* and B) *ACADM* mRNA or protein were analyzed in different cell types treated with DCA or growing in a free-glucose medium for 5-7 days or in cells treated with siRNA for ERK5 or MEF2 for 72 hours. Bar graphs represent means \pm SD of at least 3 independent experiments performed in triplicate. * p<0.05, ** p<0.01, *** p<0.005 compare to control cells or as depicted.