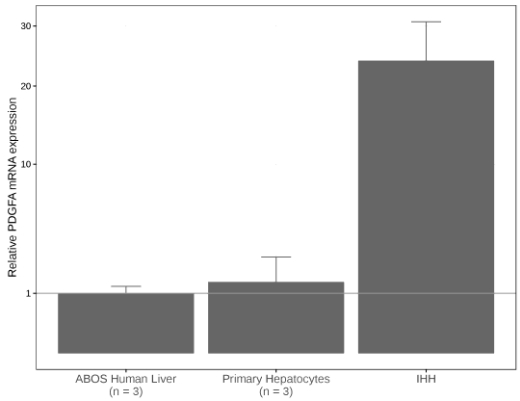
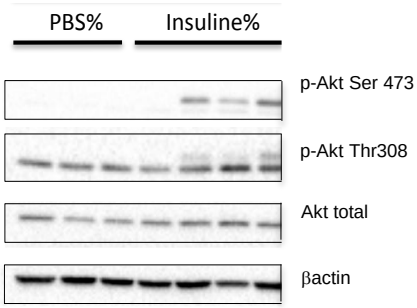
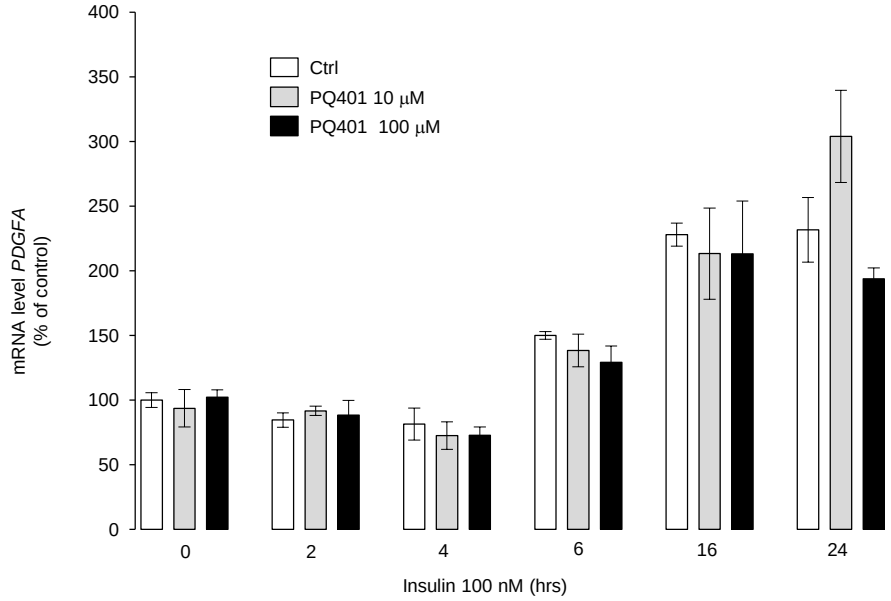


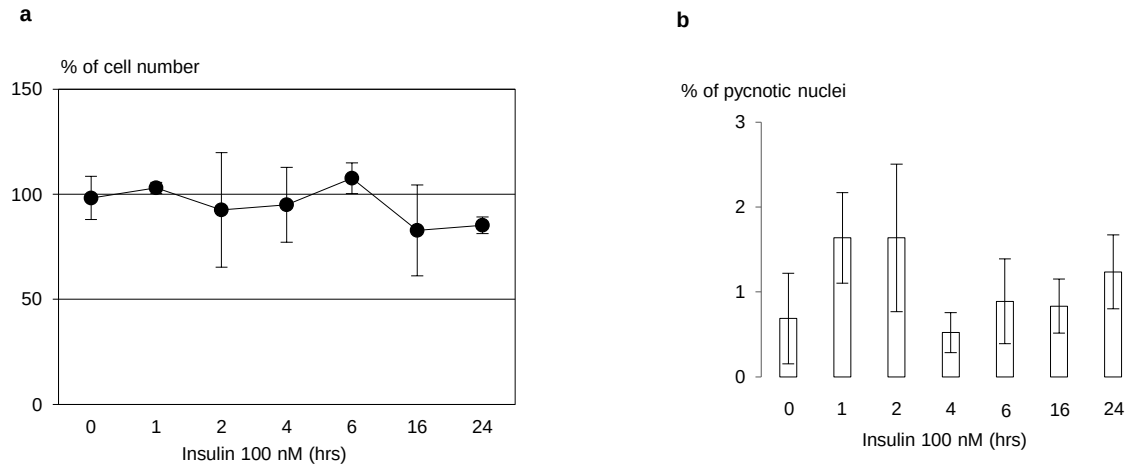
Extended Data Figure 1. Expression of *PDGFA* in IHH cells and freshly isolated human primary hepatocytes. The *PDGFA* mRNA level was quantified by quantitative real-time PCR (qRT-PCR) in immortalized human hepatocytes (IHH), liver biopsies and freshly isolated human primary hepatocytes. The mRNA level was normalized against the glucuronidase beta (*GUSB)*.



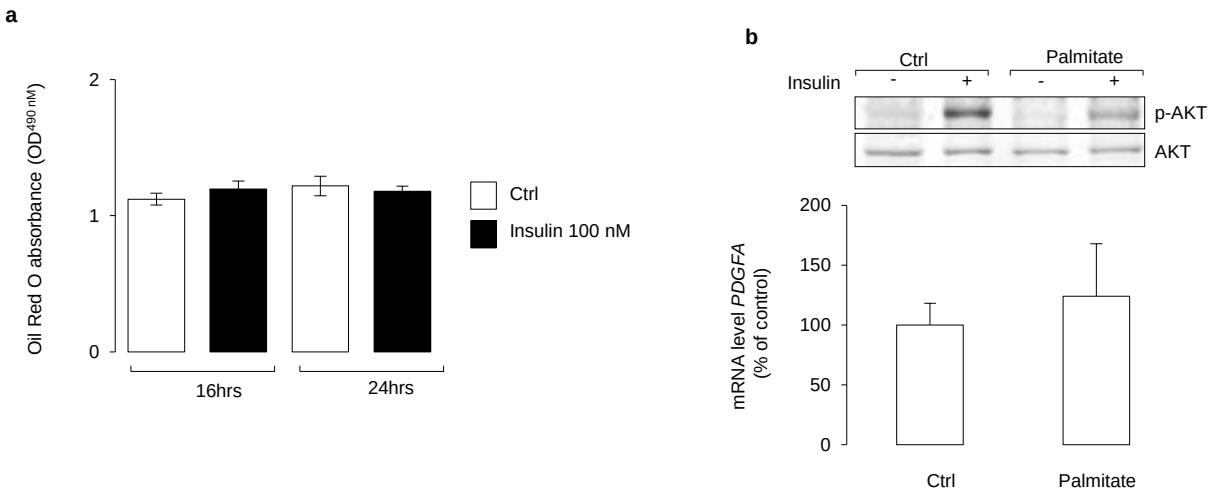
Extended Data Figure 2: insulin-induced Akt activation in liver of mice. C57Bl/6 mice (n=5/groups) received either insulin (I.P. 5U/kg) or vehicle PBS for 10 minutes. Total proteins from the liver biopsies were subjected to Western Blotting analysis. Immunoblotting was done using the anti-phospho-AKT (Thr-308 and Ser 473), anti-AKT and anti-bactin antibodies.



Extended Data Figure 3. Effect of the IGF-1R inhibitor PQ401 on the expression of *PDGFA* in IHH cells. The *PDGFA* mRNA level was quantified by quantitative real-time PCR (qRT-PCR) in immortalized human hepatocytes (IHH) that were cultured with 100 nM insulin plus or minus 10 or 100 mM PQ401 for the indicated incubation times. The *PDGFA* mRNA level was quantified by qRT-PCR and normalized against *GUSB*. The expression levels from untreated cells were set to 100 %. Data are the mean ± SEM (n=3 independent experiments).



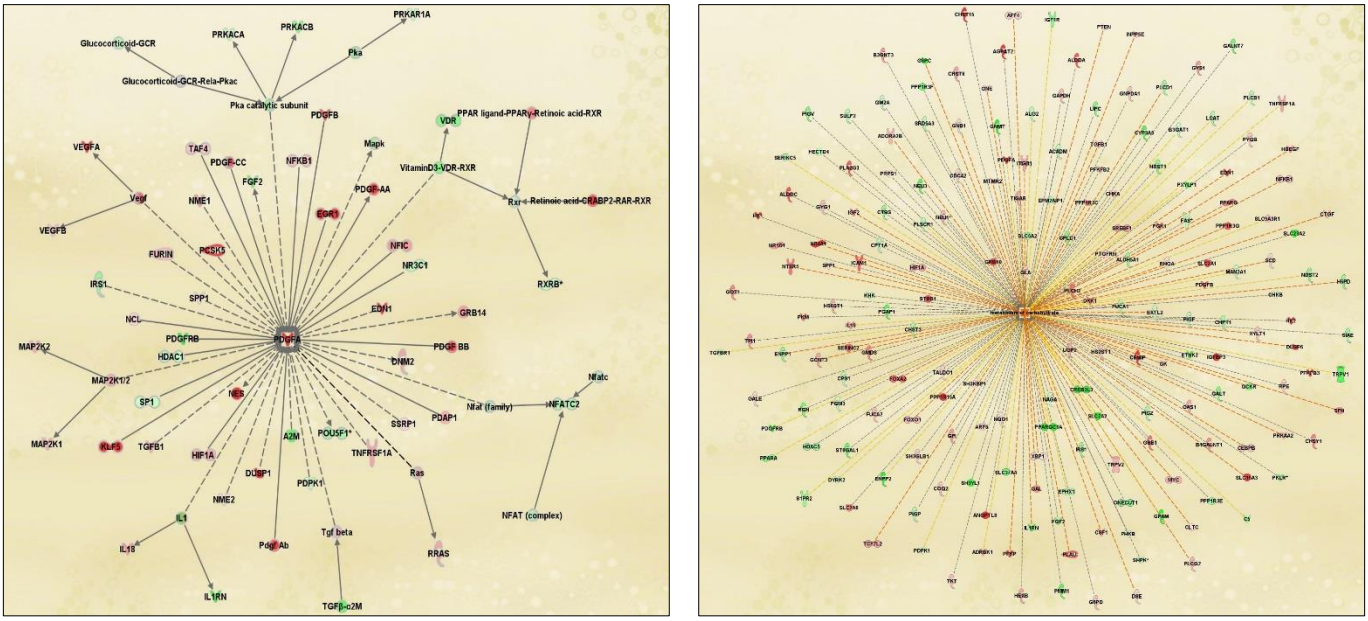
Extended Data Figure 4. Cell proliferation and death in response to insulin. IHH Cells were cultured with 100 nM insulin for the indicated times. **a**) Cell number and **b**) apoptosis were counted.



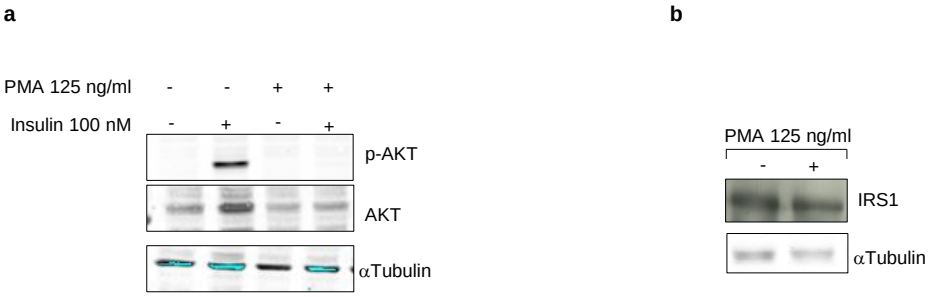
Extended Data Figure 5. Role of lipids in IHH cells a) Lipid accumulation in IHH cells. Cells were cultured with 100 nM insulin for the indicated times. Intracellular fat drops were read with spectrophotometer at 490 nm with Oil Red O staining, representing the mean ± SD of 3 independent experiments. **b) effect of palmitate on the *PDGFA* mRNA level.** IHH cells were cultured with 0.5 mM Palmitate (coupled to BSA) for 24 hrs. Impaired insulin-induced Akt activation was monitored by western blotting experiments (upper panel) using the anti-phospho-AKT (Thr-308) and anti-Akt antibodies. The The *PDGFA* mRNA level was quantified by qRT-PCR and normalized against *GUSB.* The expression levels from untreated cells were set to 100 %. Data are the mean ± SEM (n=3 independent experiments).

a

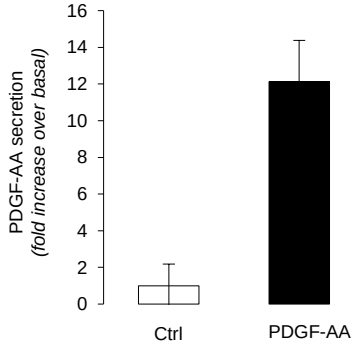
b



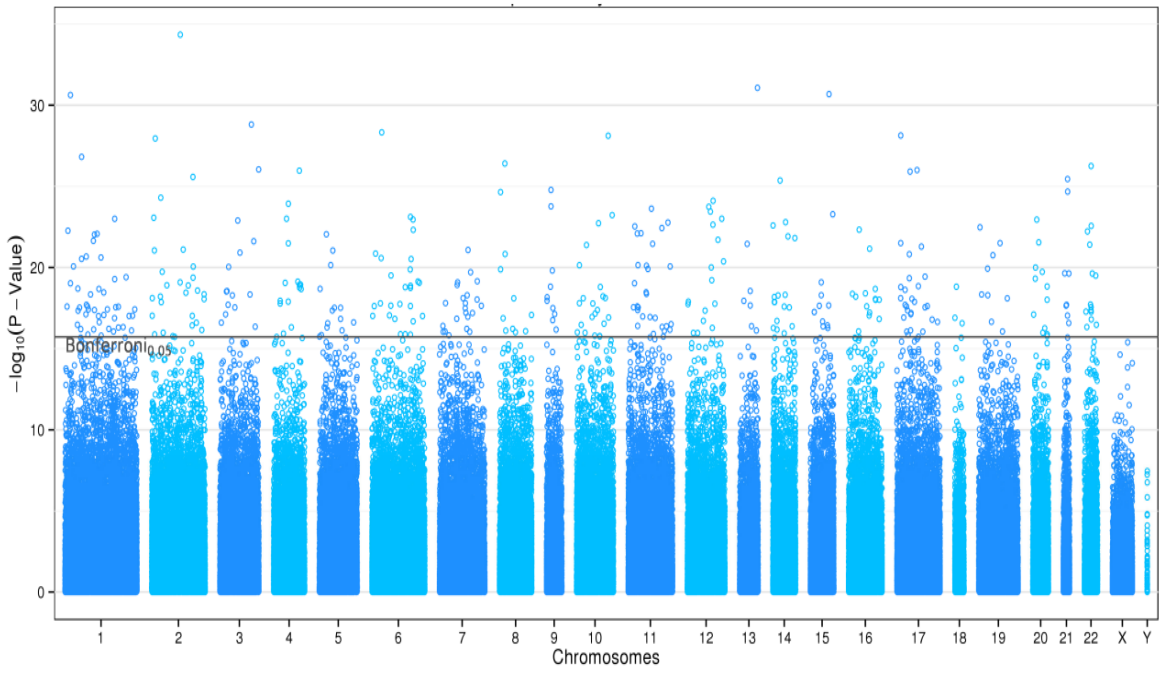
Extended Data Figure 6. a) Dysregulated genes within the network of PDGFA. Red and green colors mean increased and decreased gene expression, respectively. Solid lines embody direct interaction, while dotted lines embody indirect interactions. **b) Dysregulated genes within the network related to the carbohydrates metabolism.** Red and green colors mean increased and decreased gene expression, respectively. Each line embodies a predicted relationship: an orange line leads to activation, a blue line leads to inhibition, a yellow line highlights that the findings are inconsistent with state of downstream molecule, and a gray line highlight that the effect is not predicted.



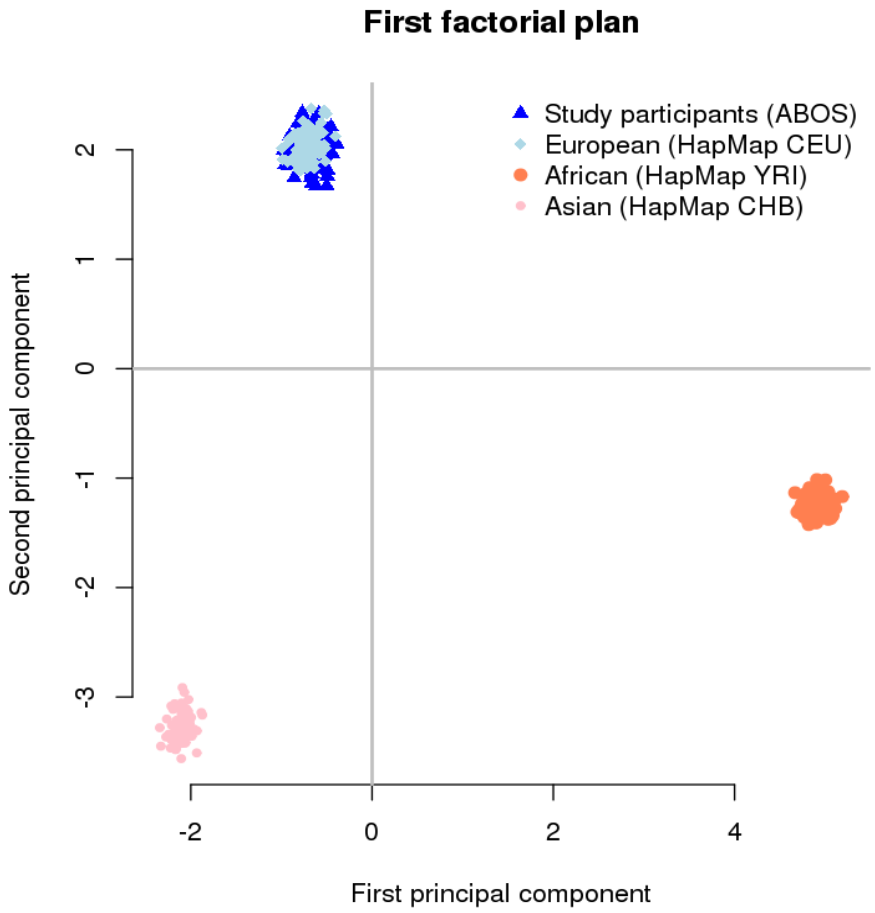
Extended Data Figure 7. Effect of PMA on a) insulin-induced AKT activation and b) IRS1 abundance. IHH cells were incubated in a culture medium containing 5 mM Glucose, 2 % FCS with or without 100 nM human insulin and 125 ng/ml PMA for 30 minutes. Immunoblotting was done using the anti-phospho-AKT (Thr-308), anti-AKT and anti αTubulin antibodies. For measuring the IRS1 content, IHH cells were cultured with 125 ng/ml PMA for 16 hrs.



Extended Data Figure 8. Effect of exogenous PDGF-AA on the PDGF-AA secretion. IHH cells were cultured with 100 ng/ml human PDGF-AA or vehicle (Ctrl) for 24 hrs. PDGF-AA in the supernatant was measured by ELISA.



Extended Data Figure 9. CpG sites differentially methylated in livers of obese diabetic vs normoglycemic individuals. Liver methylome of 192 individuals revealed 381 differentially methylated CpG sites in 96 obese diabetic vs 96 normoglycemic.



Extended Data Figure 10. HapMap samples of European ancestries. Principal component analysis on a combined dataset including 192 study participants and 272 samples from HapMap Project database and showing that study participants clustered well with HapMap samples of European ancestries (CEU).