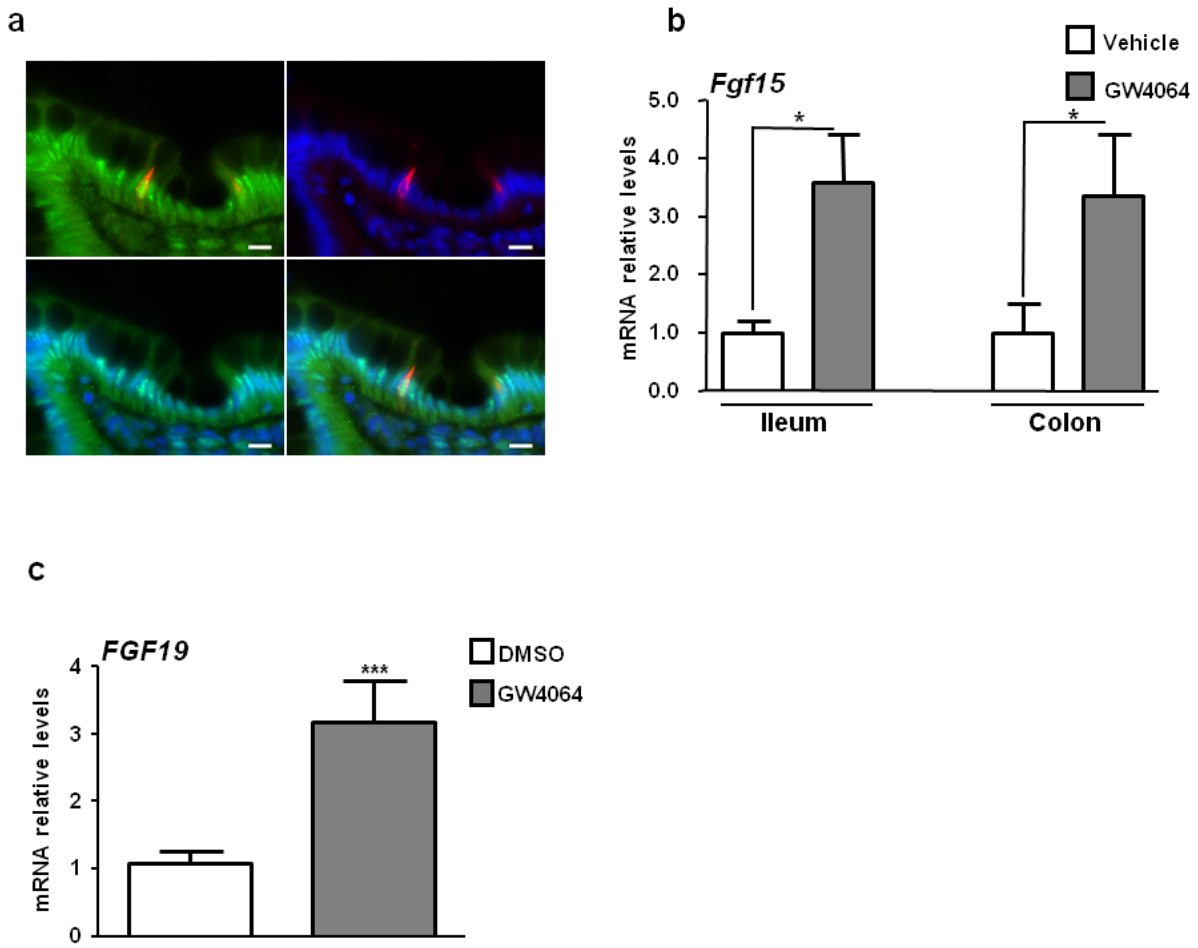
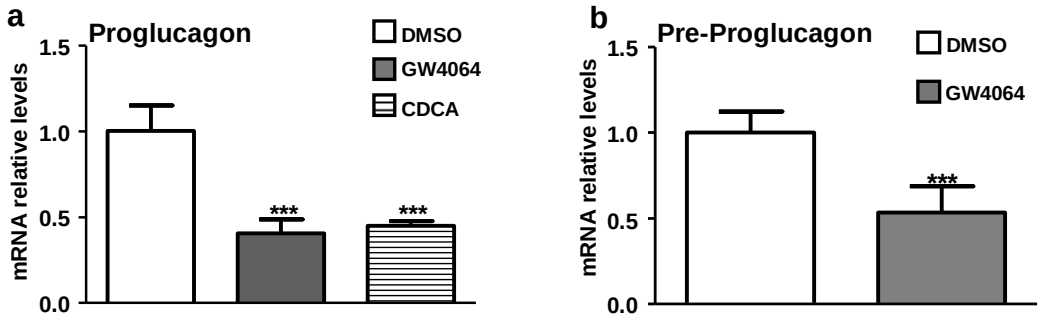
Supplementary Figures

Supplementary figure 1



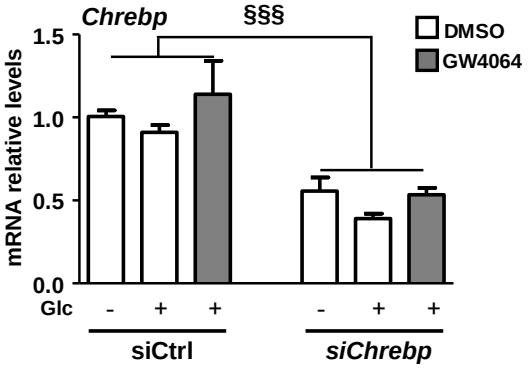
Supplementary figure 1. (**a**) Twelve µm-thick slices from human colonic biopsies were incubated with antibodies against FXR (in green) and GLP-1 (in red). Nuclei are in blue. This experiment is representative of 3 different FXR/GLP-1 immunostainings. Scale bar represents 100 µm. Magnification 63X. (**b**) *Fgf15* qPCR on cDNA from ileum and colon of 8-week old WT mice treated by gavage for 5 days with GW4064 (30 mg/kg, n=5 mice/group). (**c**) *FGF19* qPCR on cDNA of human jejunal biopsies from 4 normoglycemic patients *ex vivo* treated for 16h with GW4064 (5 µmol L^{-1}) (n=3/group). Data are represented as mean +/- SD. Student t test, **P*≤0.05 & ****P*≤0.001.

Supplementary figure 2



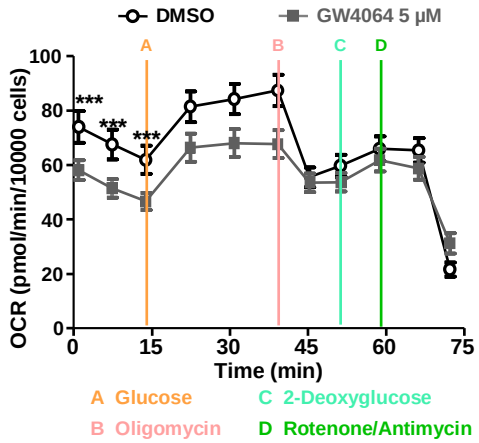
Supplementary figure 2. (**a**) Proglucagon qPCR on cDNA from GLUTag cells treated for 24h with GW4064 (10 µmol L^{-1}) or CDCA (100 µmol L^{-1}) (n=3; representative of 4 different experiments). Data are represented as mean +/- SD. One-Way ANOVA followed by Tukey's post-hoc test. ****P*≤0.001 vs DMSO. (**b**) Proglucagon pre-mRNA quantification on cDNA from GLUTag cells treated for 24h with GW4064 (5 µmol L^{-1}) (n=3; representative of 4 different experiments). Data are represented as mean +/- SD. Student t test, ****P*≤0.001.

Supplementary figure 3



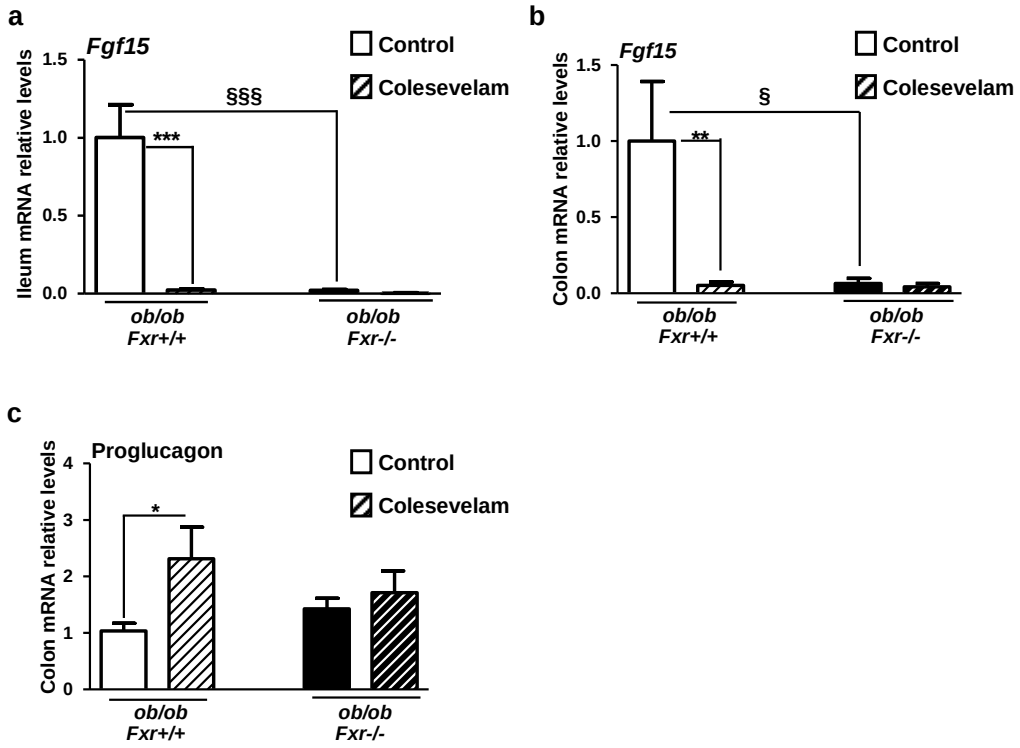
Supplementary figure 3. *Chrebp* qPCR on cDNA from GLUTag cells electroporated with a siCtrl or si*Chrebp*, starved for 12h with lactate (10 mmol L^{-1}) and then incubated for 24h in lactate 10 mmol L^{-1} (Glc -) or glucose 5.6 mmol L^{-1} (Glc +) media supplemented with DMSO or GW4064 (5 µmol L^{-1}) (n=3; representative of 4 different experiments). Data are represented as mean +/- SD. Two-Way ANOVA analysis followed by Bonferronni's posthoc test. §§§*P*≤0.001: effect of si*Chrebp* in each treatment condition.

Supplementary figure 4



Supplementary figure 4. Oxygen consumption rate (OCR) after successive injection of glucose (10 mmol L^{-1}), oligomycin (1µmol L^{-1}), 2-deoxyglucose (100 mmol L^{-1}) and rotenone (1µmol L^{-1}) / antimycin A (1 µmol L^{-1}) on GLUTag cells incubated 24h with DMSO or GW4064 (5 µmol L^{-1}) (n=3; representative of 4 different experiments). Data are represented as mean +/- SD. Two-Way ANOVA analysis followed by Bonferronni's posthoc test. ***$P \leq 0.001$: effect of GW4064 on OCR from t=0min to t=15min.

Supplementary figure 5



Supplementary figure 5. *Fgf15* qPCR on cDNA from ileum (**a**) or from colon (**b**) of 8 week-old *Fxr+/+*, *Fxr-/-* male mice on an *ob/ob* background fed for 2 weeks with a diet enriched or not with 2% colesevelam (n=6-7 mice/group). Data are represented as mean +/- SEM. (**c**) Proglucagon qPCR on cDNA from colon of 8 week-old *Fxr+/+*, *Fxr-/-* male mice on an *ob/ob* background fed for 2 weeks with a diet enriched or not with 2% colesevelam (n=6-7 mice/group). Data are represented as mean +/- SEM. Two-Way ANOVA analysis followed by Bonferronni's posthoc test. **P*≤0.05, ***P*≤0.01 and ****P*≤0.001: effect of Colesevelam treatment on gene expression in each genotype. $^{§}P$≤0.05 and $^{§§§}P$≤0.001: effect of FXR-deficiency on gene expression in each treatment condition.