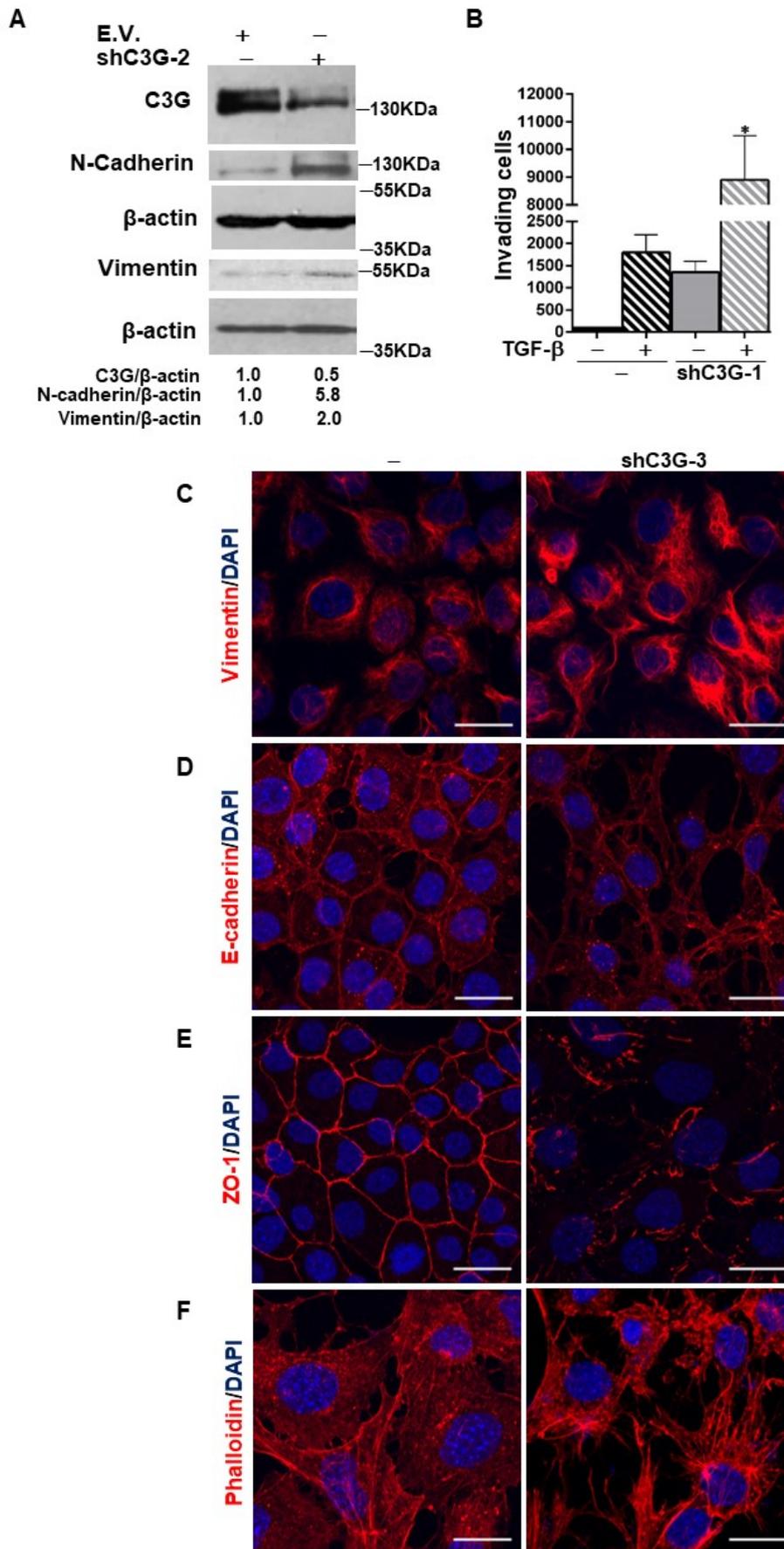
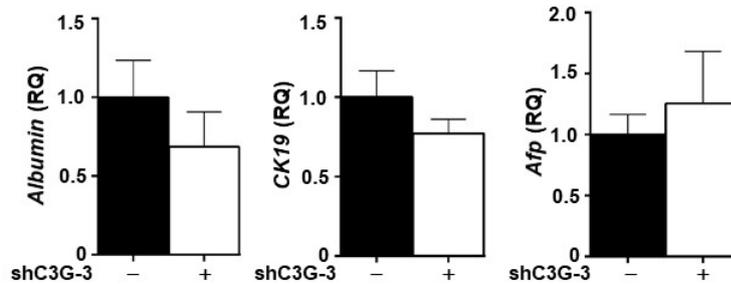


SUPPLEMENTARY INFORMATION

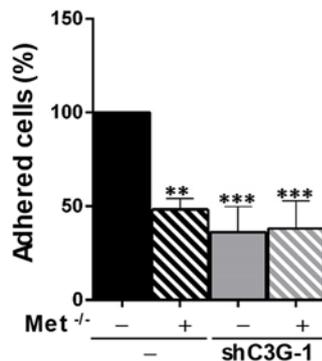
Supplementary figures



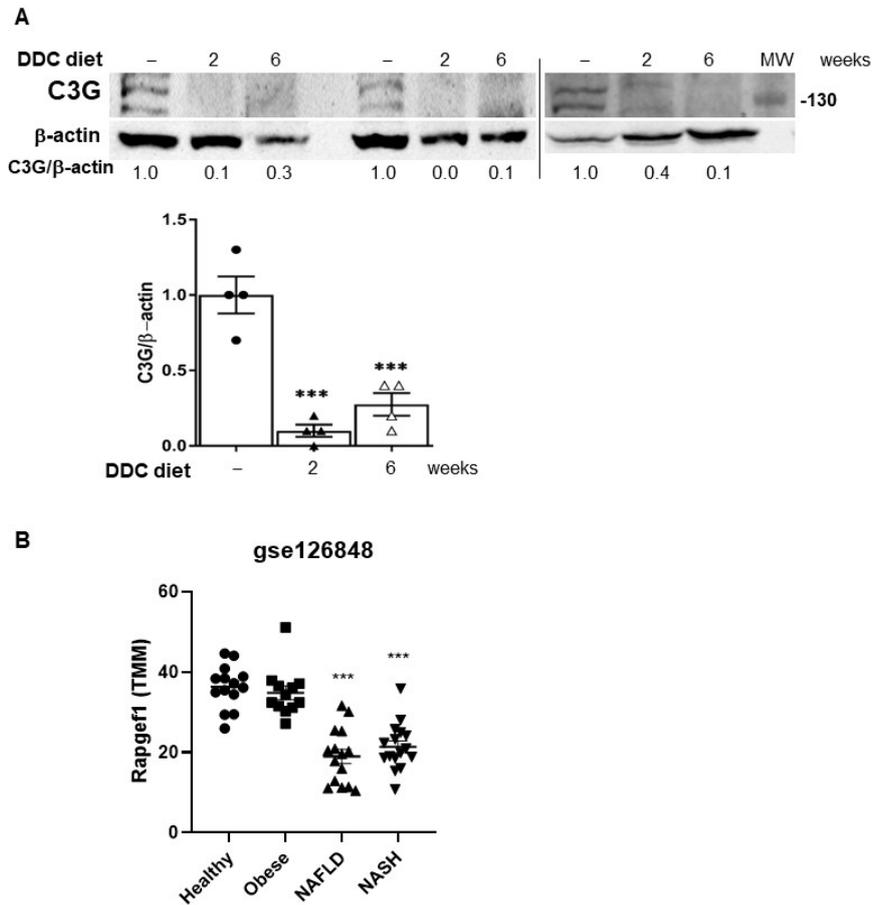
Supplementary figure 1-Chronic treatment with TGF- β mimicked the effect of C3G knock-down enhancing invasiveness of oval cells. Oval cells (C3G-silenced (shC3G-1, 2 or 3) and non-silenced (EV (transfected with the empty vector)) were maintained untreated in a medium supplemented with 10% FBS or chronically treated with TGF- β to induced EMT. **A)** Western-blot analysis of C3G, N-Cadherin and Vimentin protein levels normalized with β -Actin. **B)** Invasion assay through Matrigel using 10% FBS as chemoattractant. Histograms show the mean \pm S.E.M. of number of invading cells (n=3). Confocal microscopy images of Vimentin **(C)**, E-cadherin **(D)**, ZO-1 **(E)** and Phalloidin F-actin **(F)** staining in cells maintained in the absence of serum. Scale bars: 20 μ m.



Supplementary figure 2-Effect of C3G knock-down on the expression of cytokeratin 19, albumin and alpha-fetoprotein mRNAs by oval cells. Levels of *CK19* (*KRT19*), *Albumin* and *Afp* mRNAs quantified by RT-qPCR in C3G-silenced (shC3G-3) and non-silenced oval cells. Histograms show RQ mean value \pm S.E.M. (n=3).



Supplementary figure 3-Lack of a functional MET receptor mimics the reduced adhesion of C3G knock-down in oval cells. Adhesion assay in oval cells with either C3G knock-down (shC3G) or lacking a functional MET receptor (Met^{-/-}) (described in ref 5) and non-silenced wt cells. Histogram showing the mean value \pm S.E.M. of the percentage of adhered cells at 15 min (n=3).



Supplementary figure 4-C3G expression is down-regulated in the liver upon chronic damage. (A) Western-blot analysis of C3G protein levels normalized with β -actin in liver samples from 3,5-Diethoxycarbonyl-1,4-Dihydrocollidine (DDC)-treated mice to induce oval cell expansion. Upper panel, images of representative western-blot showing different C3G isoforms with a line separating different blots; lower panel, histogram showing the quantification (mean value \pm S.E.M.) of different blots referred to an untreated control, corresponding to 4 independent experiments. (B) Graphic showing *RapGEF1* mRNA expression in liver biopsies obtained from healthy normal weight (n=14) and obese (n=12) individuals, non-alcoholic fatty liver disease (NAFLD) with simple steatosis (n=15) and non-alcoholic steatohepatitis (NASH) (n=16) patients expressed as the median TMM (Trimmed Mean of M-values (counts per million normalized to TMM)). These data were extracted from NCBI GEO repository, accession number GSE 126848. *** $p \leq 0.001$ versus healthy samples.