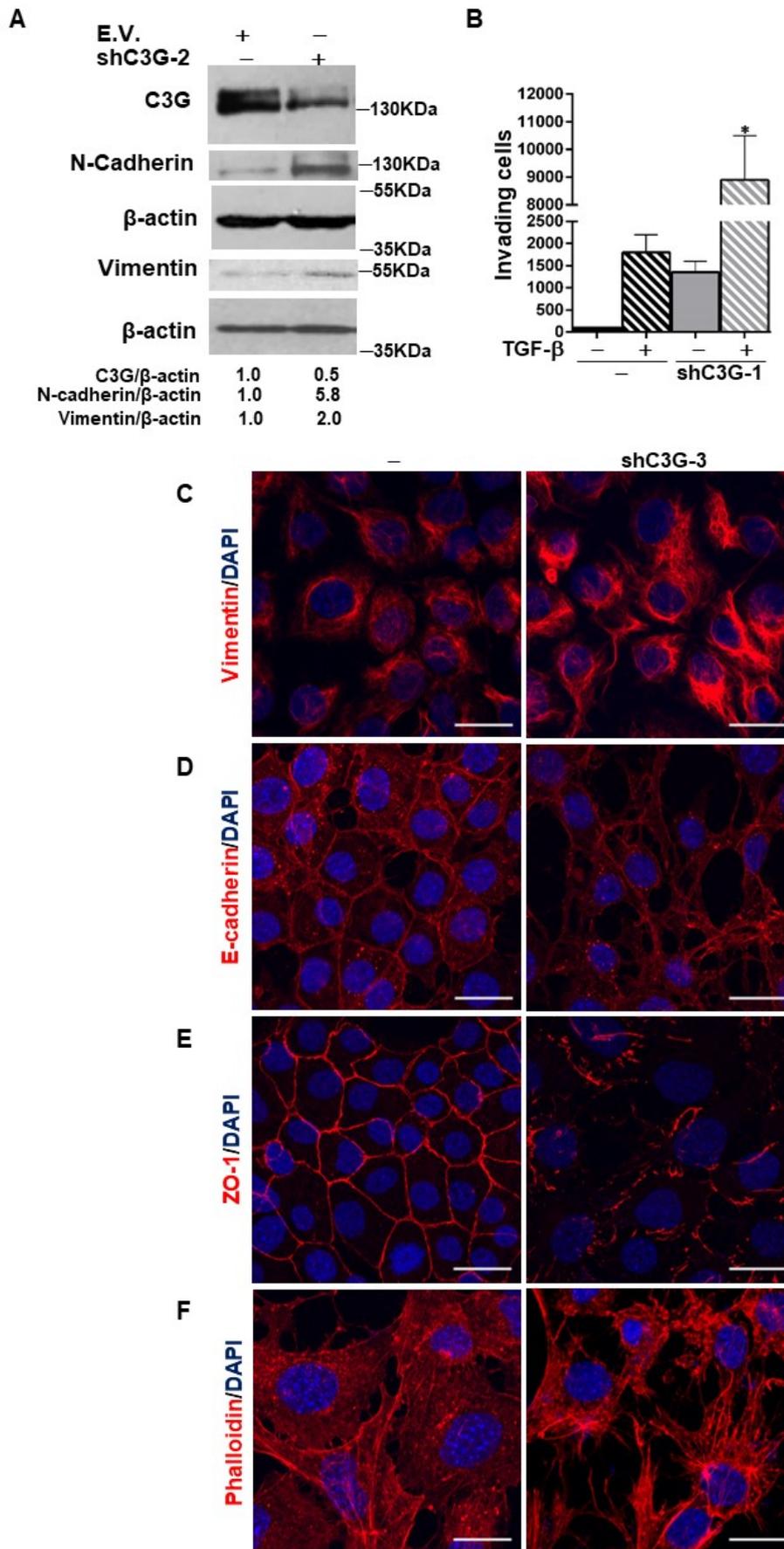
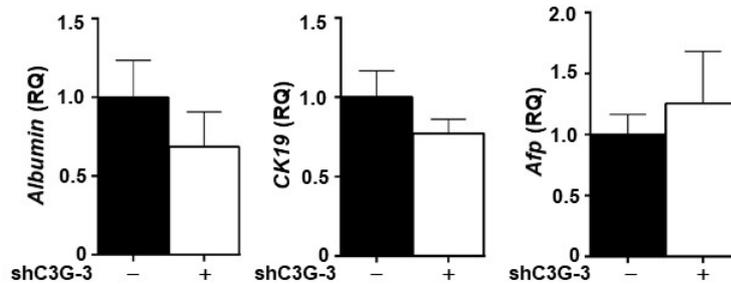


**SUPPLEMENTARY INFORMATION**

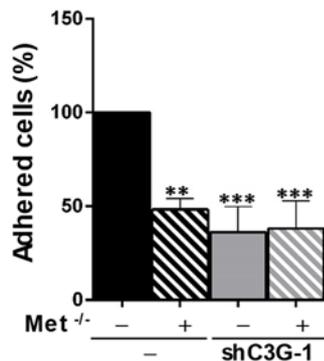
**Supplementary figures**



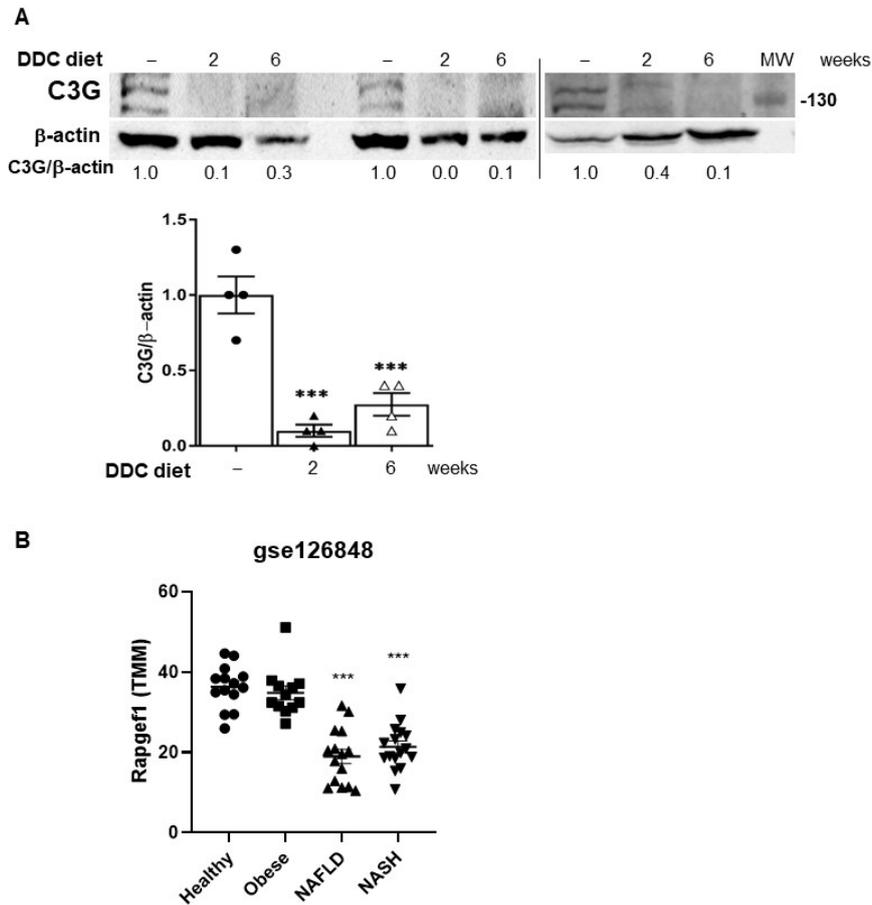
**Supplementary figure 1-Chronic treatment with TGF- $\beta$  mimicked the effect of C3G knock-down enhancing invasiveness of oval cells.** Oval cells (C3G-silenced (shC3G-1, 2 or 3) and non-silenced (EV (transfected with the empty vector)) were maintained untreated in a medium supplemented with 10% FBS or chronically treated with TGF- $\beta$  to induced EMT. **A)** Western-blot analysis of C3G, N-Cadherin and Vimentin protein levels normalized with  $\beta$ -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 $\mu$ 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<sup>-/-</sup>) (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  $\beta$ -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.