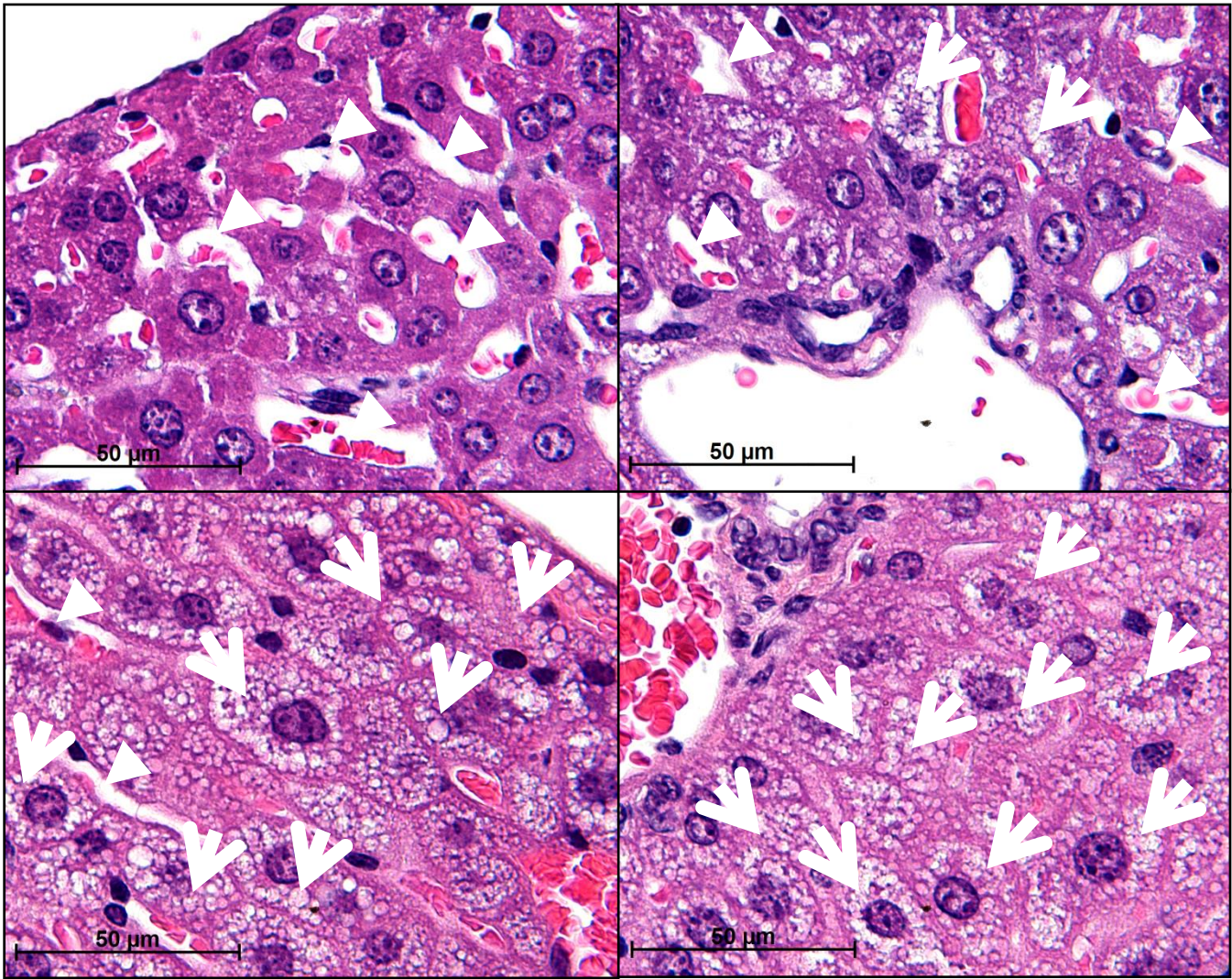


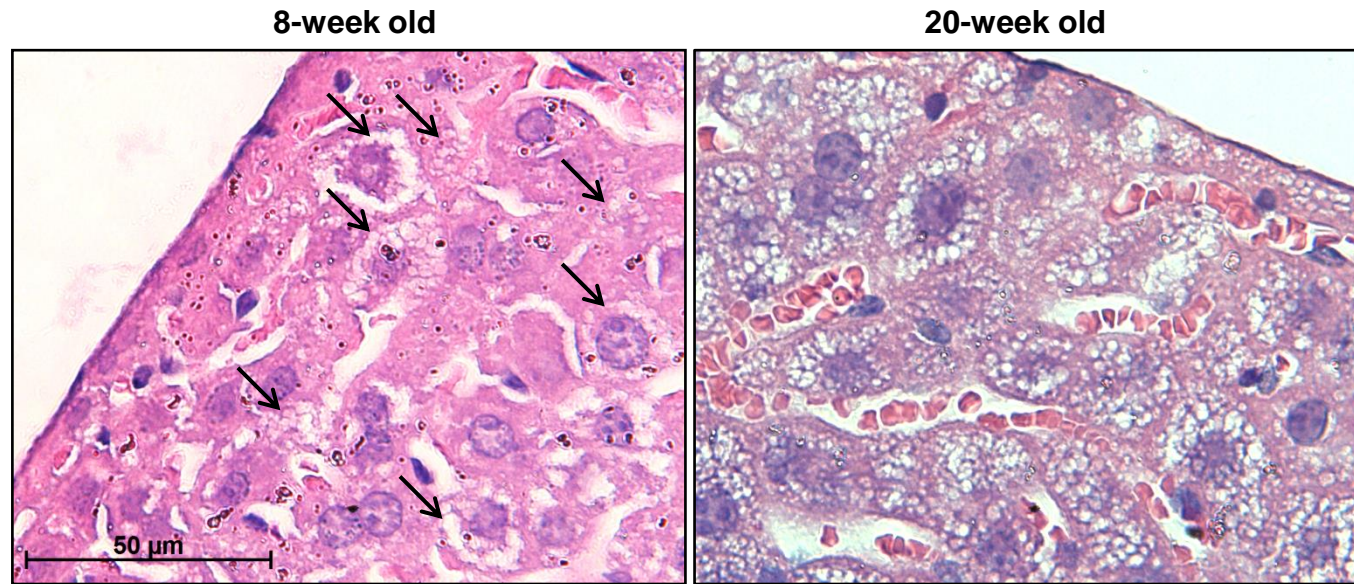
## **Supplementary Figures**

**p73 regulates autophagy and hepatocellular lipid metabolism through transcriptional activation of the ATG5 gene**

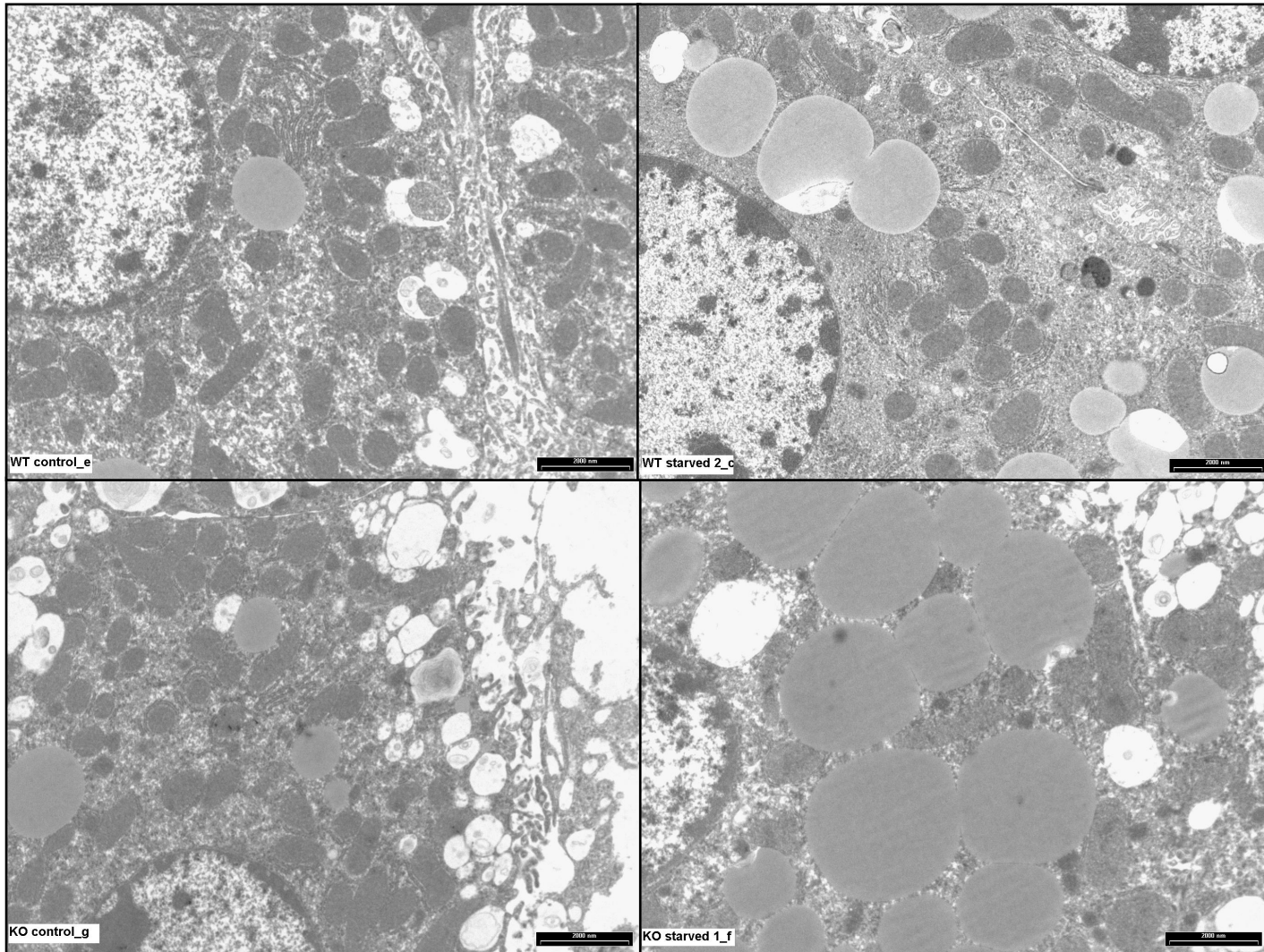
**Zhaoyue He, He Liu, Massimiliano Agostini, Shida Yousefi,  
Aurel Perren, Mario P. Tschan, Tak Wah Mak, Gerry Melino  
and Hans-Uwe Simon**



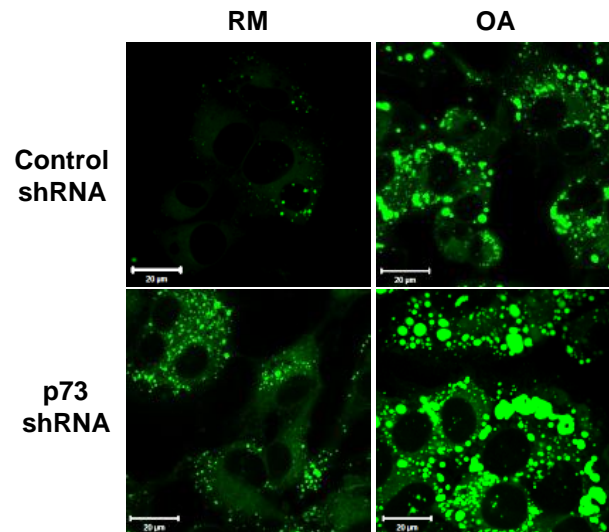
**Figure S1** Enlarged images of Figure 1a.



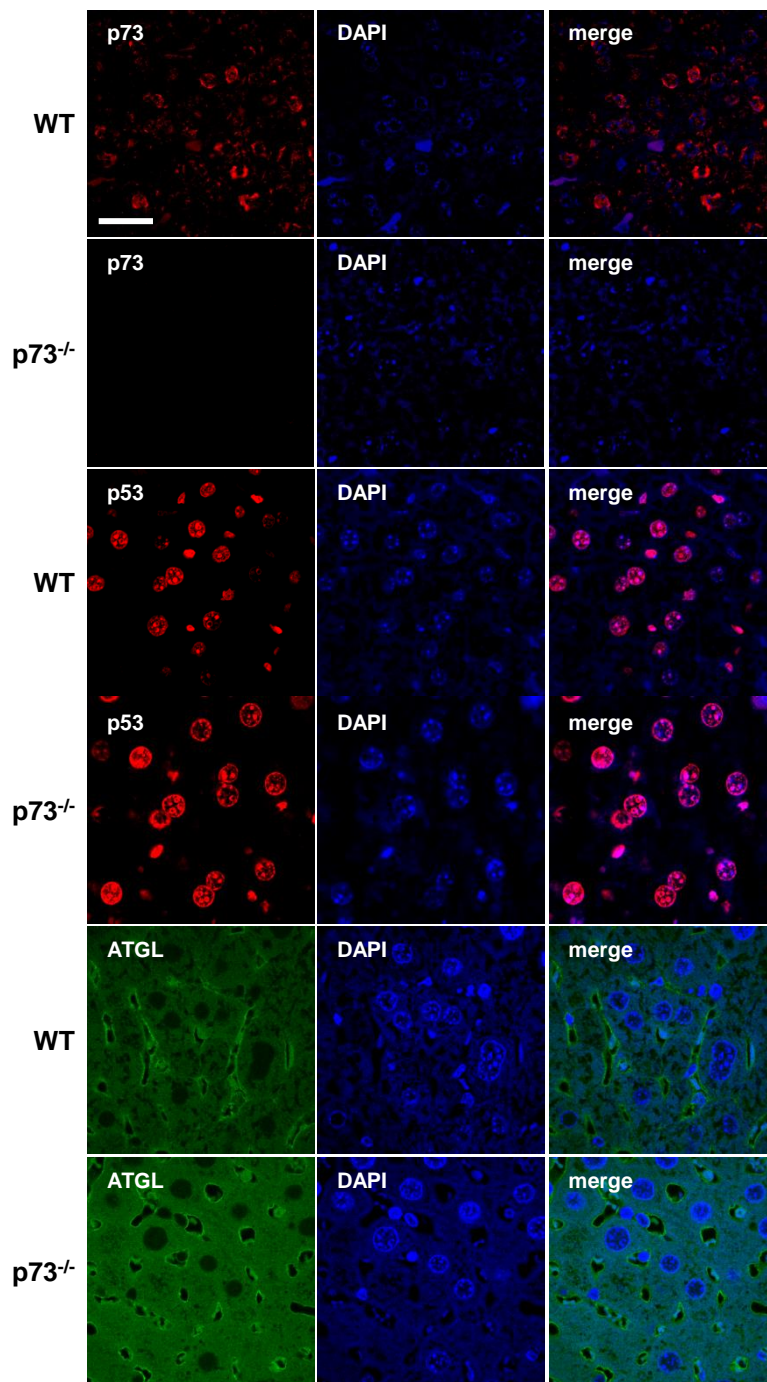
**Figure S2** Age-dependent accumulation of LDs in p73-deficient mice. Histology. Liver sections from starved p73-deficient mice of the indicated age were stained with H&E. 20-week old mice demonstrated  $3.3 \pm 0.63$  more vacuoles compared with 8-week old mice ( $n=3$  in each group). Quantification was performed as in Figure 1A. For better visibility, vacuoles in the younger mice are marked with black arrows. Bar, 50  $\mu\text{m}$ .



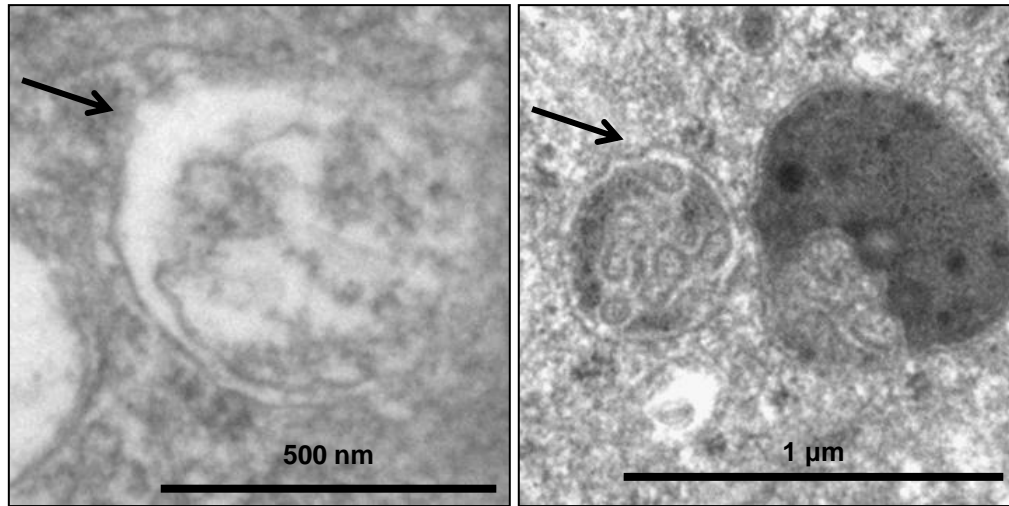
**Figure S3** Enlarged images of Figure 1b.



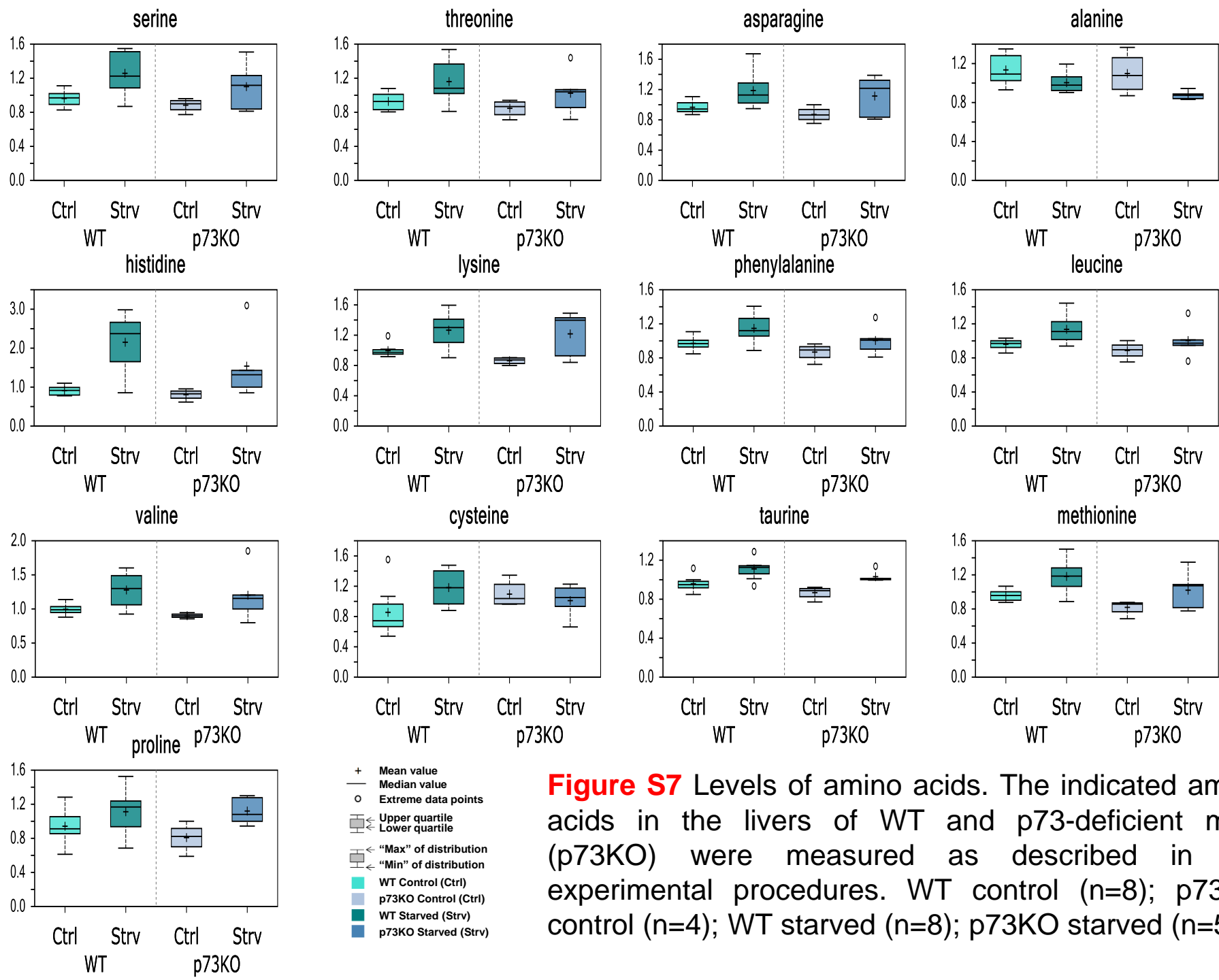
**Figure S4** Visualization of LDs using BODIPY staining. HepG2 cells were infected with either control shRNA or p73 shRNA and then kept in regular medium (RM) or exposed to oleic acid (OA). LDs were detected by BODIPY staining and analysed by confocal microscopy. Bars, 20  $\mu$ m.



**Figure S5** Expression levels of p73, p53, and ATGL in WT and p73-deficient mice. Liver sections were analyzed by immunofluorescence. Bar, 20  $\mu$ m. Results are representative of 3 independent experiments.

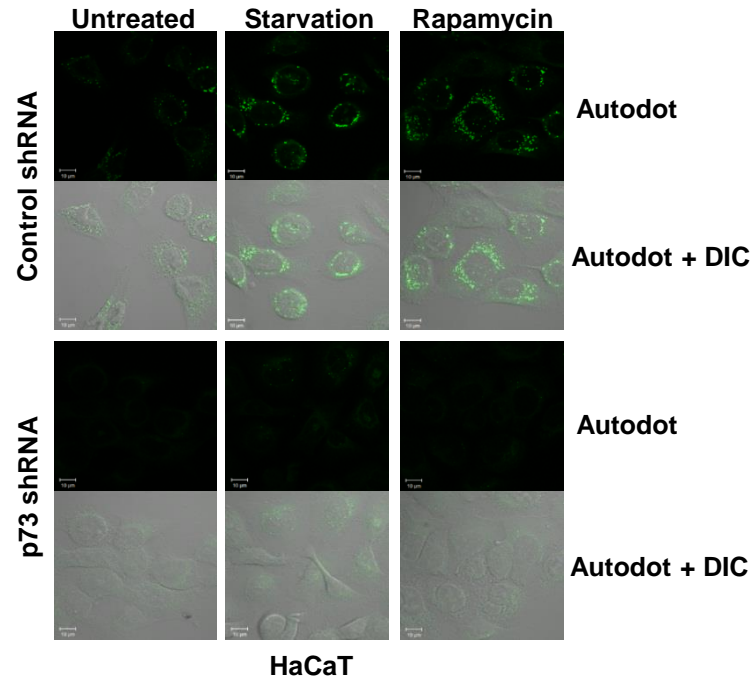


**Figure S6** Autophagosome detection in the liver of starved wild-type mice using transmission electron microscopy. Liver sections from 24-h starved mice are shown. Autophagosomes and autolysosomes, respectively, are indicated with black arrows. Bars, 500 nm and 1  $\mu\text{m}$ , respectively.

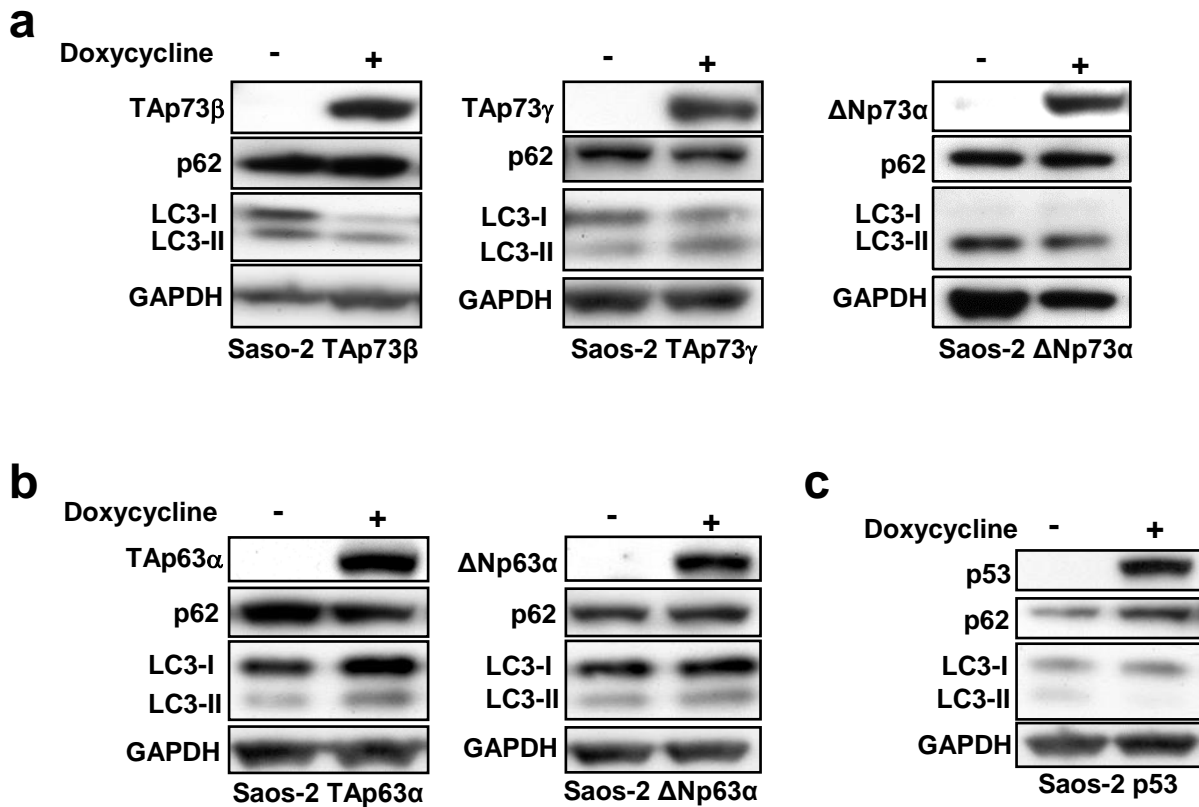


**Figure S7** Levels of amino acids. The indicated amino acids in the livers of WT and p73-deficient mice (p73KO) were measured as described in the experimental procedures. WT control (n=8); p73KO control (n=4); WT starved (n=8); p73KO starved (n=5).

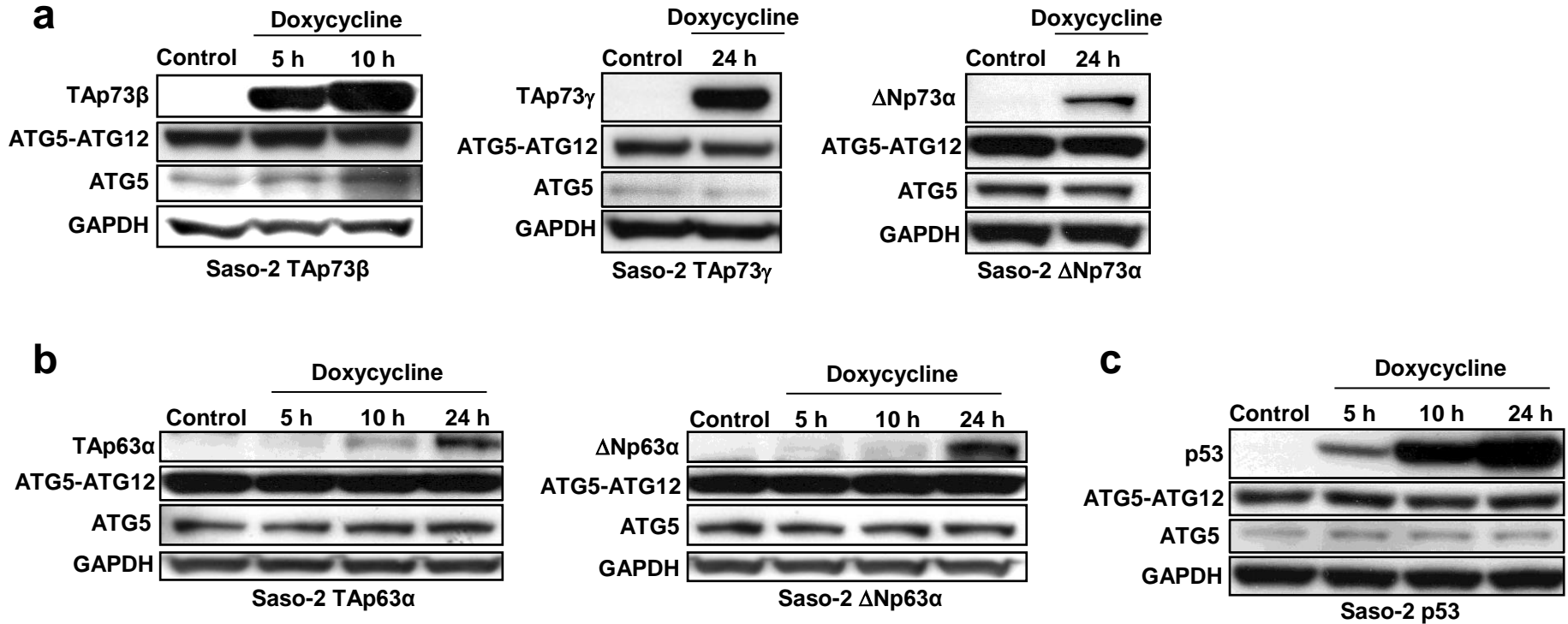




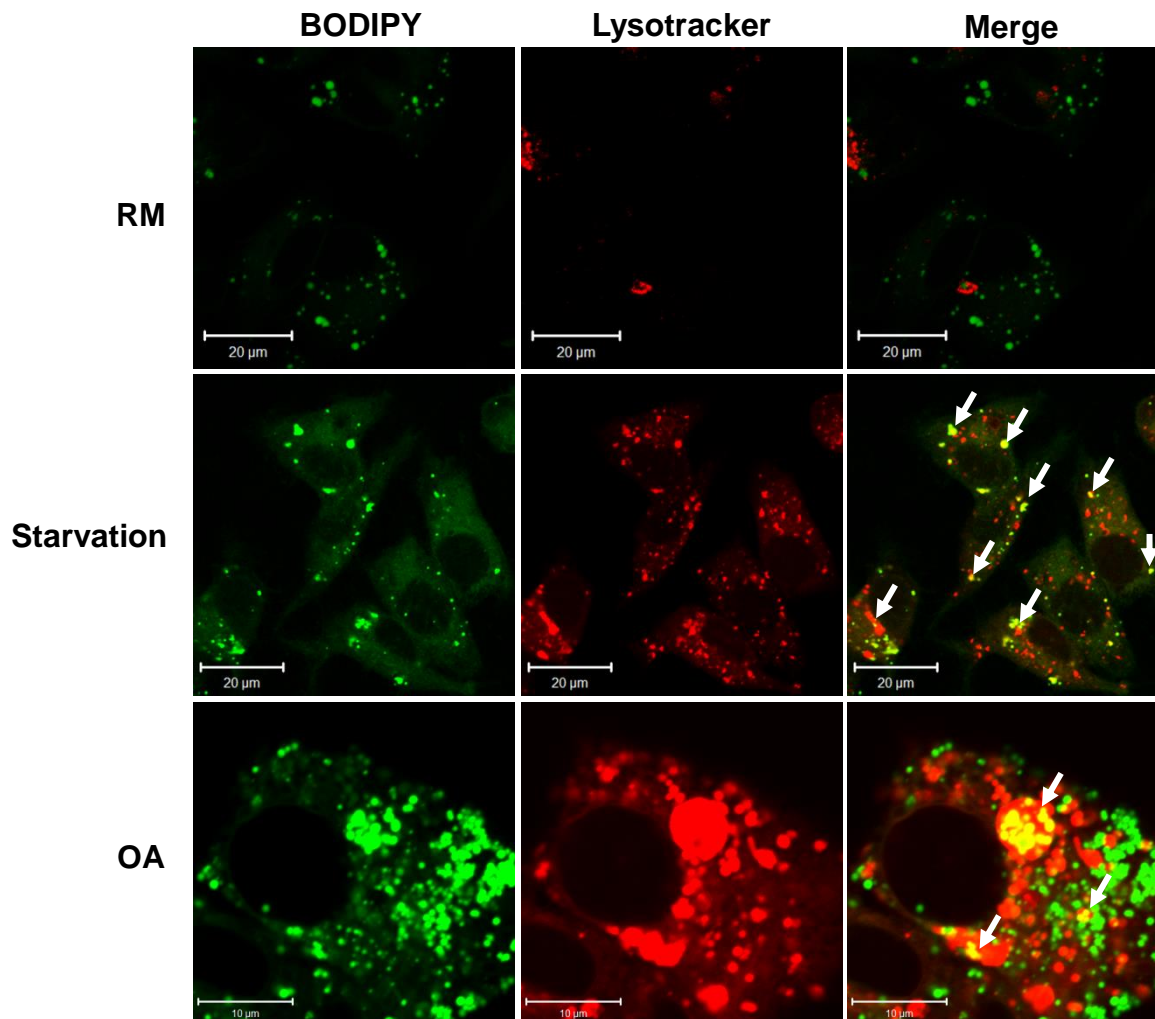
**Figure S8** Autophagosome detection in HaCaT cells using autodot staining. HaCaT cells were infected with either control shRNA or p73 shRNA. 48 post infection, cells were either starved for 1 h or treated with 10  $\mu$ M rapamycin for 24 h, and stained with Autodot. Cells were observed with confocal microscopy. Bars, 10  $\mu$ M.



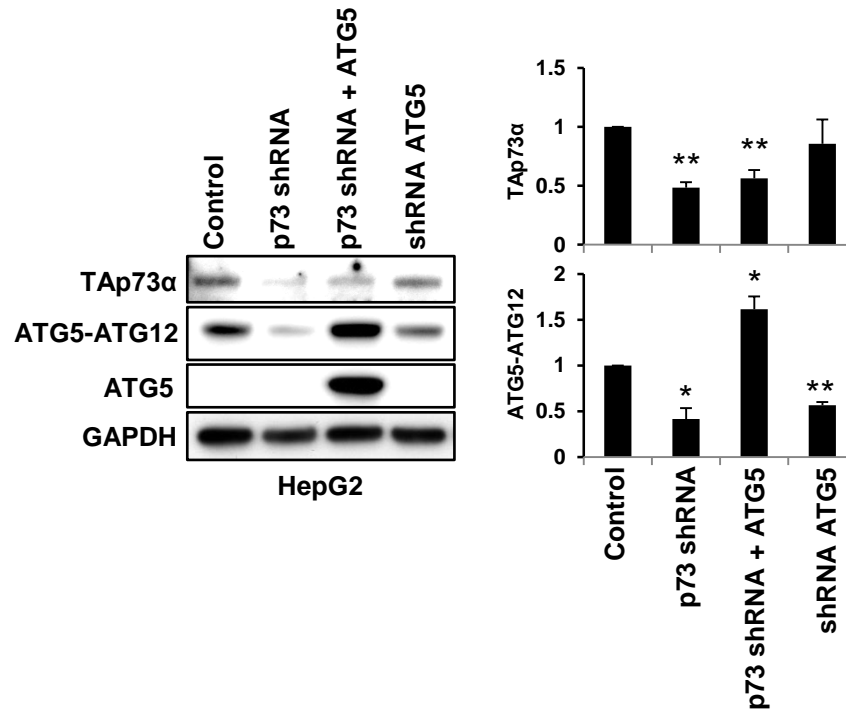
**Figure S9** No or minimal effects on autophagy following induction of members of the p53 family other than TAp73 $\alpha$ . Saos-2 cells transfected with the indicated inducible constructs of other members of the p53 family were treated with 2.5  $\mu$ g/ml doxycycline for 24 h. Immunoblots were performed to detect p62 and LC3 after induction of TAp73 $\beta$ , TAp73 $\gamma$  and  $\Delta$ NP73 $\alpha$  (panel a), TAp63 $\alpha$  and  $\Delta$ NP63 $\alpha$  (panel b), and p53 (panel c).



**Figure S10** No or minimal effects on ATG5 protein expression following induction of members of the p53 family other than TAp73 $\alpha$ . Saos-2 cells transfected with the indicated inducible constructs of other members of the p53 family were treated with 2.5  $\mu$ g/ml doxycycline for the indicated time periods. Immunoblots were performed to detect ATG5 protein expression after induction of TAp73 $\beta$ , TAp73 $\gamma$  and  $\Delta$ NP73 $\alpha$  (panel a), TAp63 $\alpha$  and  $\Delta$ NP63 $\alpha$  (panel b), and p53 (panel c).



**Figure S11** LDs are degraded by the lysosomal pathway. HepG2 cells were cultured in regular medium (RM) or either starved or treated with oleic acid (OA). LDs were visualized by BODIPY staining (green) and lysosomes stained by Lysotracker (red). Engulfment of LDs by lysosomes is indicated by white arrows. Bars, 20 or 10  $\mu\text{m}$ .



**Figure S12** Expression levels of p73 and ATG5 in genetically modified HepG2 cells. Cells were treated as indicated and protein expression of TAp73α and ATG5 was determined by immunoblotting. *Right*: The fold changes in expression levels compared with the control conditions are presented. \*,  $p < 0.05$ ; \*\*,  $p < 0.01$ ,  $n = 3$ .