



**Supplementary Figure 6. Lipid raft integrity is necessary for TGF- $\beta$ -mediated activation of TACE/ADAM17.** Cav1<sup>+/+</sup> hepatocytes treated with TGF- $\beta$  (2 ng/ml) at different times after previous FBS starvation (16 h). Metalloprotease TACE/ADAM17 activity expressed as percentage of activity/untreated control. A: Cells were treated in the absence (Cav1<sup>+/+</sup>) or presence (Cav1<sup>+/+</sup> + M $\beta$ C) of M $\beta$ C for 30 minutes. After this time, in half of the cells in each treatment group, medium was removed and fresh medium with cholesterol (1 mM) was added (Cav1<sup>+/+</sup> + Chol; Cav1<sup>+/+</sup> + M $\beta$ C + Chol). After 1 hour, cells were treated with TGF- $\beta$  and collected for TACE/ADAM17 activity analysis at the times indicated in the figure (N=3). B: Cells were treated with the cholesterol-binding agents nystatin (Nyst, 25  $\mu$ M) and filipin (0.5  $\mu$ M) added 30 minutes before TGF- $\beta$  treatment (N=3). Results expressed as mean  $\pm$  SEM. Statistical comparison using two-way ANOVA with Bonferroni post-hoc test: \*p<0.05; \*\*p<0.01; \*\*\*p<0.001 (A: (\*) Cav1<sup>+/+</sup> + M $\beta$ C + Col vs. Cav1<sup>+/+</sup> + M $\beta$ C; B: (\*) Cav1<sup>+/+</sup> vs. Cav1<sup>+/+</sup> + Nyst and (#) Cav1<sup>+/+</sup> vs. Cav1<sup>+/+</sup> + Filipin).