**A** qRT-PCR analysis of the indicated genes in HT-29 cells expressing APC shRNA, compared to a non-silencing shRNA (NonS) control. Cells were treated with DOX for 72 hours. Shown are mean values ± SD (n=3). * p < 0.05, ** p < 0.01.

**B** Immunoblot analysis of APC and β-actin on WCL from Colo205 cells treated with 500 ng/ml DOX to induce expression of APC-targeting shRNA or NonS control.

**C, D** qRT-PCR analysis of the indicated genes in Colo205 cells (C) or HT-29 cells (D) expressing APC-targeting shRNA. Cells were treated with DOX for 96 and 54 hours, respectively. Mean values ± SD (n=3) are shown. ** p < 0.01, **** p < 0.0001.

**E, F** qRT-PCR analysis of the indicated genes in LS174T (E) or SW480 (F)-NE or -E cells, treated with 400 nM 4-OHT for 24 or 36 hours. Expression was compared to untreated cells (LS174T) or ERT control (SW480). Mean values (n=3) are depicted as mean ± SD., *** p < 0.001, **** p < 0.0001.

**G** Mutation detection assay on genomic DNA from stably transduced SW480 cell pools edited via CRISPR/Cas9 to visualize targeting of the TCF7L2_BS (guides: g1, g2) against control (Ctrl).

**H** qChIP analysis on genomic DNA from SW480 cells, wild-type (Ctrl) or mutant for TCF7L2_BS (BSg2). The amount of DNA immunoprecipitated with TCF7L2 antibody or rabbit control IgG in each sample is shown as percentage of chromatin input. Results are shown as mean (n=3) ± SD. * p < 0.1; ** p < 0.05; *** p < 0.01 **** p < 0.001.

**I** Luciferase reporter assay in SW480 cells, transfected with equimolar amounts of control pBV-Luc vector, the vector containing wt or mutated TCF7L2_BS. A Renilla luciferase vector was used as a transfection control., luciferase activity was measured 36 hrs after transfection. Results are shown as mean (n=3) ± SD. ** p < 0.01, *** p < 0.001.