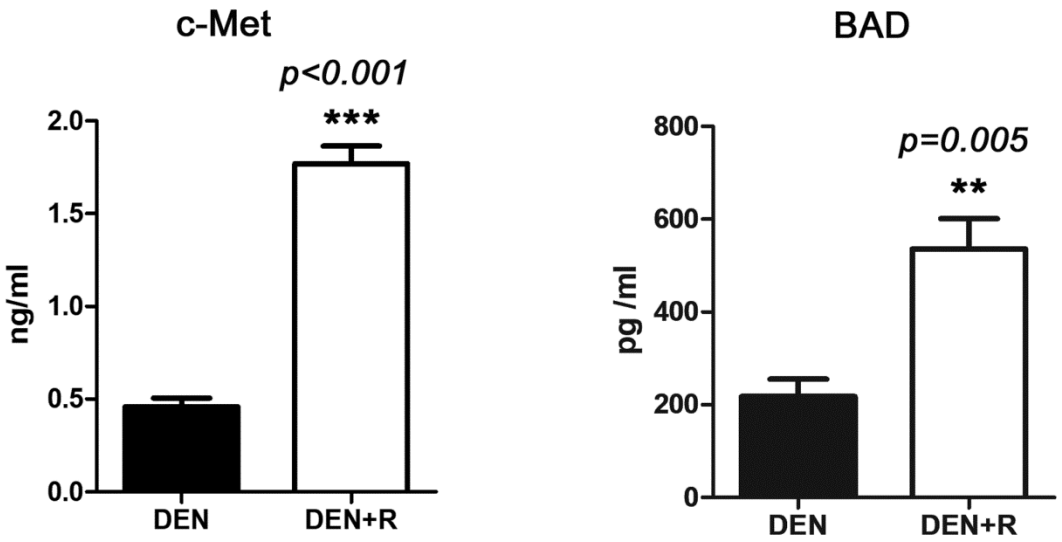

Figure S1

Serum ELISA analysis of c-met and BAD. Romidepsin-treated mice have significantly increased levels of both c-Met and BAD by comparison with untreated controls.Numbers on the y-axis of bar graphs correspond to the mean±SEM of the parameters assessed. *p<0.05, ** p<0.001.BAD: Bcl2-associated agonist of cell death; c-Met: met proto-oncogene; DEN: diethylnitrosamine; R: Romidepsin

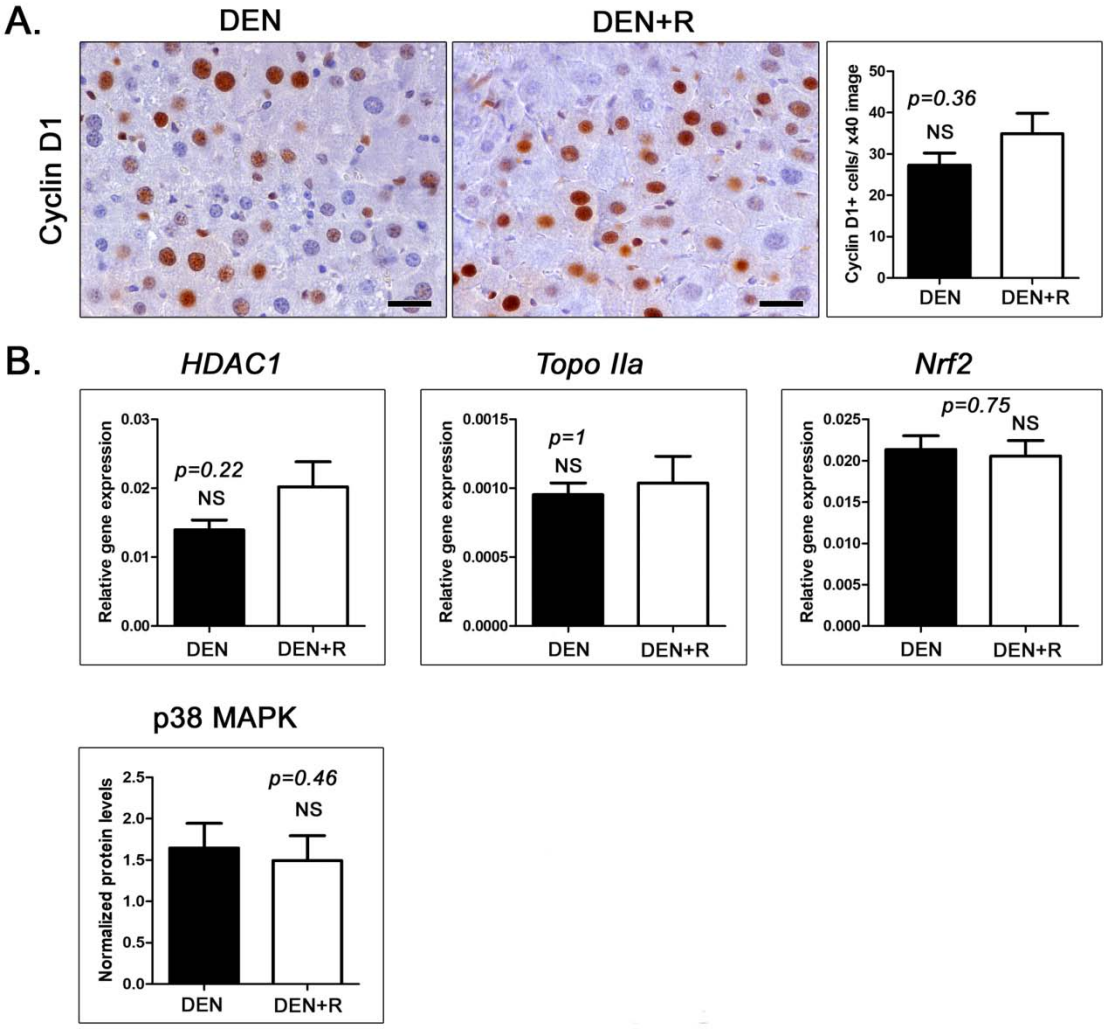

Figure S2

A. HDAC1/2 depletion did not affected numbers of neoplastic liver cells showing positive nuclear Cyclin D1 immunohistochemical signal. B. Likewise, it did not alter theexpression of *HDAC1*, *Topo IIa*, *Nrf2* and p38 MAPK.IHC; Diaminobenzidine chromogen, Hematoxylin counterstain. Scale bars: 25 μm. Numbers on the y-axis of bar graphs correspond to the mean±SEM of the parameters assessed. NS p>0.05. DEN: diethylnitrosamine; HDAC1: histone deacetylase 1; Nrf2: nuclear factor, erythroid derived 2, like 2; p38 MAPK: mitogen-activated protein kinase 14; R: Romidepsin; Topo IIa: topoisomerase (DNA) II alpha

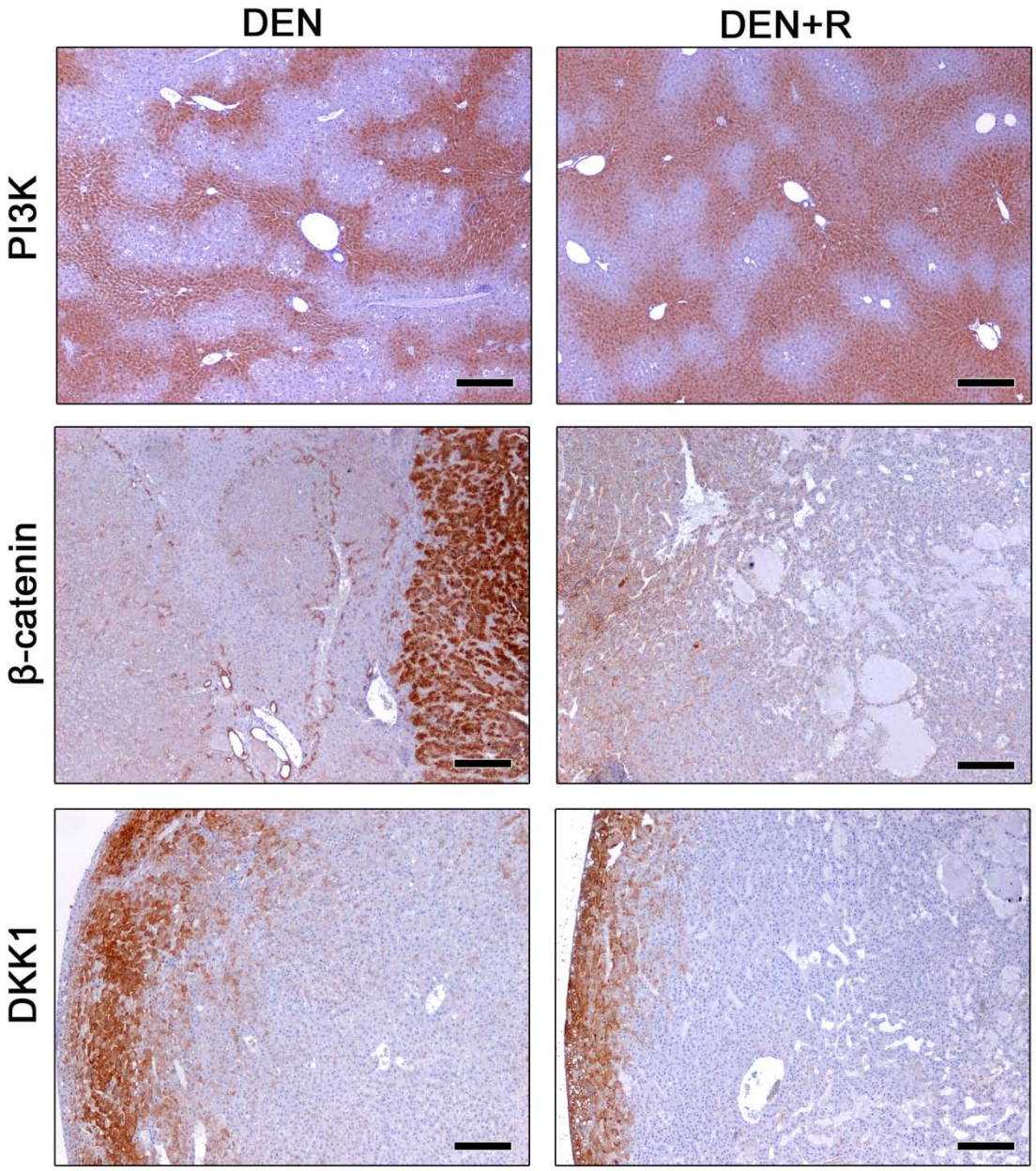

Figure S3

Romidepsin treatment affected neither the presence nor the topographical distribution of PI3K expression in the non-tumoral liver of mice. Poorly differentiated areas in advanced HCC lesions show scarce β-catenin expression. In large HCC tumors DKK1-positivity is seen mostly at the margins and invasive fronts of tumors. IHC; Diaminobenzidine chromogen, Hematoxylin counterstain. Scale bars: 250 μm.DEN:

diethylnitrosamine; DKK1: dickkopf WNT signaling pathway inhibitor 1; PI3K: phosphoinositide-3-kinase regulatory subunit 1; R: Romidepsin