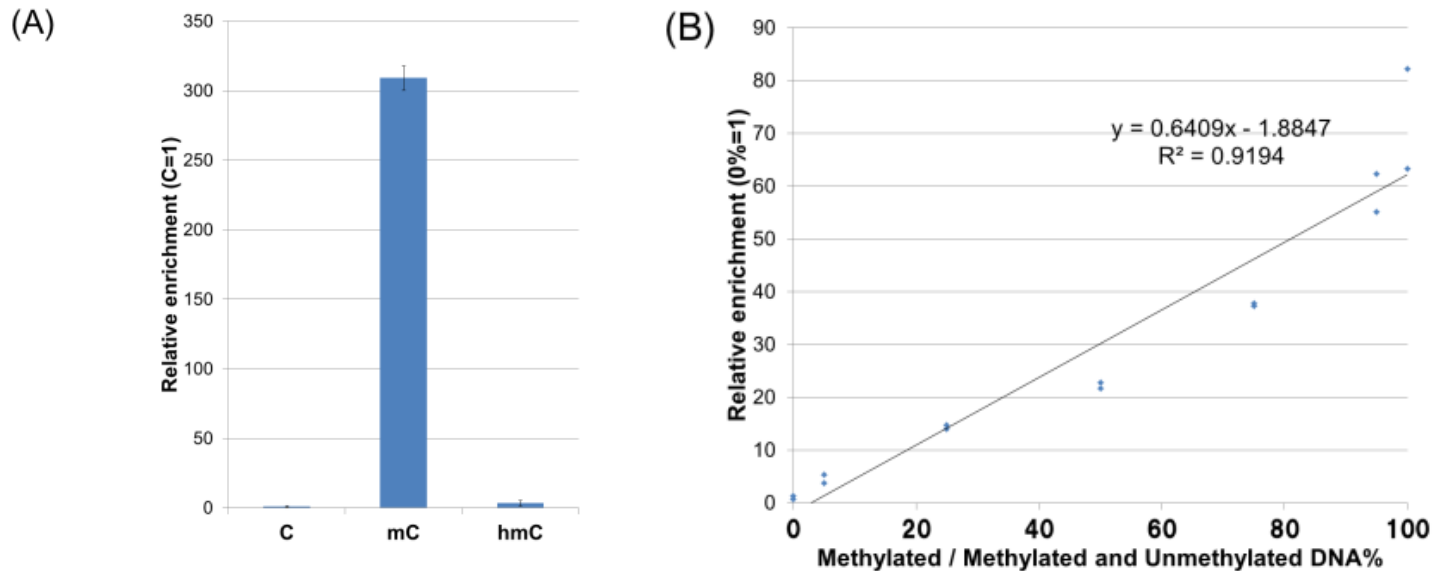


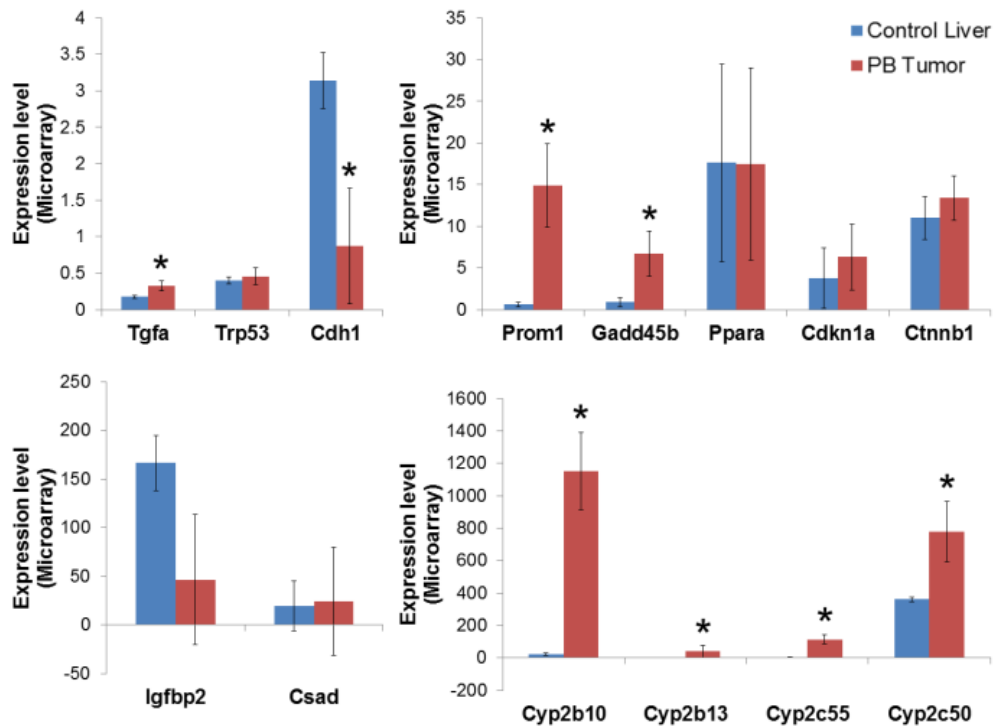
Supplementary Figure S1.

Histopathology of liver in control animals (DEN/NaPB(-)) and treated animals (DEN/NaPB(500 ppm)) selected for global analyses of gene expression, DNA methylation and DNA hydroxymethylation. In three control animals analyzed, no histological changes were observed in adjacent tissue of the sample for the global analyses mentioned above. In three DEN/NaPB(500ppm) treated animals analyzed, hepatocellular adenoma, focus of cellular alteration and hepatocytic hypertrophy were observed in adjacent tissue of the sample for the global analyses mentioned above. From each group, photos of the each two animals are presented as representative.



Supplementary Figure S2.

Validation data for the specificity of 5mC antibody. (A) Unmethylated, 5mC and 5hmC DNA standards of Methylated DNA Standard Kit (Active Motif) were spiked separately into genomic DNA in the proportion of 1 part to 20000, removed 1% of DNA as input sample and the other were subjected to MeDIP. Immunoprecipitated and input DNA were analyzed by quantitative PCR with standard-specific primers (Active Motif). Data are mean \pm SD from triplicate experiments. (B) Methylated DNA was mixed by 0, 5, 25, 50, 75, 95 and 100% with unmethylated DNA. These mixtures were subjected to MeDIP and analyzed by quantitative PCR for confirming linearity of response. Data are obtained from duplicate experiments.



Supplementary Figure S3.

The expression profiles of genes related to cell signaling, cancer progression and xenobiotic response. These genes were selected in reference to Thomson et al., 2016. Data are mean \pm SD from three replicates of each group. * $p < 0.05$, Student's t-test.