

Supplementary Figure Legends

Supplementary Figure 1. (A) Cre expression and recombination of the Rb and p53 genes were determined by PCR analysis of genomic DNA. Since the recombined region of the Rb gene consists of a single exon (exon 19), both the full-length Rb gene (unrecombined) and the recombined Rb gene products are detected from a single PCR primer set. The recombined region of the p53 gene consists of exons 2-10; thus, two PCR primer sets are utilized to characterize the recombination event. First, amplification outside of the floxed region is performed to simply detect the presence of the p53 gene (unfloxed region). Second, amplification specifically across the newly recombined region of the p53 gene is performed (recombined). To directly measure gene expression of the p53 gene, semi-quantitative PCR was performed from cDNA, along with Gapdh gene expression as a control. Quantification of p53 gene expression relative to Gapdh expression is shown. (B) Total protein lysates from 14-day old livers were immunoblotted for the indicated proteins. Lamin B served as a loading control. (C) Kegg pathway analysis demonstrating those genes significantly associated with deregulated cell cycle control ($p=1.6E-13$).

Supplementary Figure 2. (A) Quantification of average liver weights of 1-year old mice expressed as a percentage of total body weight (** $p=0.005$). (B) DNA content analyzed via propidium iodide (PI) staining and flow cytometry. Percentage of hepatocytes harboring 2N, 4N and >4N was quantified (* $p=0.04$). (C) *Left*, Ki67 staining in 5-week old livers. *Center*, percentage of Ki67-positive hepatocytes. *Right*, Total protein lysates from 5-week old livers were immunoblotted for the indicated proteins. Lamin B served as a loading control.

Supplementary Figure 3. qPCR validation of select up-regulated (Top) and down-regulated (Bottom) genes from microarray analyses of 14-day old, DEN-treated livers.

Supplementary Figure 4. *Left*, representative images of DEN-treated, 3-month old livers. *Right*, quantification of average liver weight expressed as a percentage of total body weight.

Supplementary Figure 5. Statistically significant gain/loss segments identified in CGH analyses are displayed. CHR refers to the chromosome in which the gain/loss was identified. The locations of the gain/loss segments are indicated by the START and END positions along the chromosome, and the overall size of the segments are indicated in LENGTH column. The P-value and false discovery rate (FDR) for each segment is displayed. C1-2 indicates non-tumor liver tissue samples from a pool of wild-type mice. T1-5 indicates individual tumor tissue samples from mice 6-months post-DEN exposure.