**Supplementary Figure legends**

**Supplementary Figure S1. Anti-proliferative and pro-apoptotic effects of CuB against different NSCLC cells.** *A)* Effect of CuB treatment on the cellular proliferation of A549, H1299 and H1650 cells. Cells were treated with varying concentrations of CuB (0.01-40 µM) for 24, 48 and 72 h. Percent cellular proliferation was assessed using MTT assay. *B)* Cell cycle analysis was performed by PI staining followed by FACS analysis after 48 h of CuB treatment in NSCLC A549 cells. The numerical values given in the figure show the percentage of cells in each phases of cell cycle compared to vehicle-treated control. *C)* CuB treatment leads to dose-dependent induction of apoptosis in A549 cells at 48 h. The graphical representation shows the percentage of apoptotic cells. *D)* CuB treatment leads to inhibition of DNMTs and HDACs activities in A549 cells. Cells were treated with varying concentrations of CuB for 48 h and nuclear extracts were used to assess DNMTs and HDACs activities. Experiments were performed in triplicates. Results are represented as percentage DNMTs or HDACs activity compared to respective control. *\*P<0.05,* respective to vehicle-treated control.

**Supplementary Figure S2. CuB alters the global as well as gene-specific pattern of methylation in H1299 cells.** *A)* The genomic DNA was extracted from H1299 cells treated with different concentrations of CuB for 48 h. South-western dot-blot analysis was performed for the presence of 5-methyl cytosine (5-mC). The blots are representatives of three independent experiments. Graphical representation shows the relative band intensity of 5-mC expression in H1299 cells. *B and C)* Effect ofCuB-treatment decreases the degree of methylation at the *p21CIP1/WAF1* and *hTERT* promoters, respectively, in human NSCLC H1299 cells at 48 h. The degree of methylation was assessed by MSP analysis followed by agarose gel electrophoresis. Gel images show methylated (M) and unmethylated (U) DNA bands of the selected genes and the graphs represent their relative band intensities. Untreated H1299 cells were used as controls. Results represent mean of two independent experiments (mean±SE). \**P<0.05* with respect to control.

**Supplementary Figure S3. Average body weights and representative lung histology of different animal groups.** *A)* Body weights of the mice were recorded twice a week and average weight per group was plotted as mean±SD. *B)* Representative lung histology (20x) of different animal groups using Hematoxylin and eosin staining (color images). The arrows represent angiogenesis; circles represent microadenomas; and squares represent tumor hyperplasia.