

## Supplementary Figure legends

### **Supplementary Figure S1. Change of cytokine release of HepG2 cells under treatment.**

Cytokine release into the supernatant by HepG2 cells after treatment with 20  $\mu\text{M}$  of 5-aza-CR or 5-aza-dC for 72 h was measured by antibody array. This method simultaneously profiles relative levels of 36 human cytokines. Array images from one minute exposure to x-ray film and the position of sICAM-1 (1), IL-1ra (2) and IL-8 (3) on the nitrocellulose membranes are shown.

### **Supplementary Figure S2. Induction of apoptosis and activation of caspase 3/7 by 5-aza-CR but not 5-aza-dC in hepatoma cell lines.**

(A, B) Determination of sub2N fractions as marker for apoptosis after treatment of HepG2 and Hep3B cells with 100  $\mu\text{M}$  of 5-aza-CR or 5-aza-dC for (A) 48 h or (B) 72 h. Bars represent mean  $\pm$  SD of three independent experiments, each performed in triplicate. (C, D) Activation of effector caspases 3 and 7 was measured (C) 36 h and (D) 48 h after treatment of HepG2 and Hep3B cells with vehicle (control) or 5  $\mu\text{M}$ , 10  $\mu\text{M}$ , 20  $\mu\text{M}$ , 50  $\mu\text{M}$  and 100  $\mu\text{M}$  5-aza-CR or 5-aza-dC. As a positive control for apoptosis induction, 5  $\mu\text{M}$  staurosporine (STS) was used. Three independent experiments were performed each in duplicates.

**Supplementary Figure S3. p53 expression of HepG2 and Hep3B cells.** Western blot analyses of p53 content in cell lysates of HepG2 (p53 wild-type) and Hep3B (p53-deficient) hepatoma cells. Vinculin expression served as a loading control.

**Supplementary Figure S4. 5-aza-CR induces a decrease of p53 protein levels, whereas 5-aza-dC increases  $\beta$ -galactosidase in various tumor entities.** (A, C) Western blot and densitometric analyses of p53 contents in cell lysates of A-498 renal cancer and A549 lung

cancer tumor cell, treated with vehicle or increasing concentrations of 5-aza-CR or 5-aza-dC over a 24 h time period. Vinculin expression served as a loading control. (B, D) After 96 h of incubation with vehicle or 20  $\mu$ M 5-aza-CR or 5-aza-dC, A-498 and A549 cells positive for senescence-associated  $\beta$ -galactosidase (SA- $\beta$ -gal) and nuclei were counted via microscopy. Bars represent mean  $\pm$  SD of three independent experiments; Student's t-test,  $**P < 0.01$ ,  $***P < 0.001$ ; ns: not significant.