Supplemental Figures and Figure Legends

Figure S1

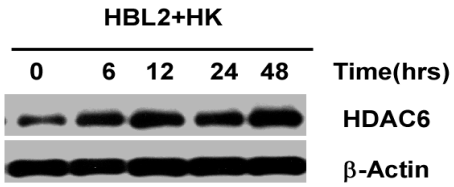

Figure S1. The time course of stromal cells (HK)-induced HDAC6 expression in HBL-2 cells. Western Blot shows HDAC6 expression after HBL-2 and HK cell co-cultured at the indicated time. Result is representative of at least 3 independent experiments.

Figure S2

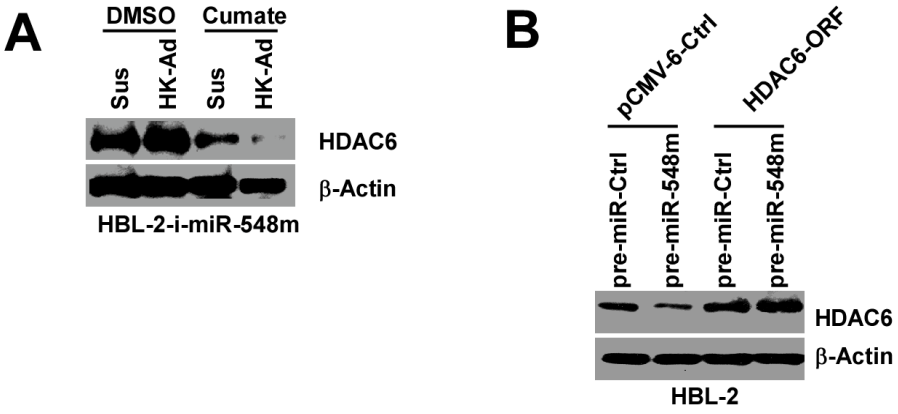

Figure S2. (**A**) Induction of miR-548m decreases HDAC6 expression with and without HK cell adhesion. HBL-2-i-miR-548m cells were co-cultured with and without HK cells, treated with DMSO or cumate (30ug/ML) for 48hrs and HDAC6 expression was measured by western blot. Result is representative of at least 3 independent experiments. (**B**) Overexpression of HDAC6 by HDAC6-ORF construct blocked the miR-548m induced inhibition of HDAC6 expression. Two stable cell lines were established by

using two pCMV6-Entry constructs (ORIGENE): one containing HDAC6 open reading frame (ORF, without the 3′UTR) and one control construct. After puromycin selection, these two stable cell lines were transfected with pre-miR-548m and pre-miR-control respectively and HDAC6 level was examined by Western blot. Result is representative of at least 3 independent experiments.

Figure S3

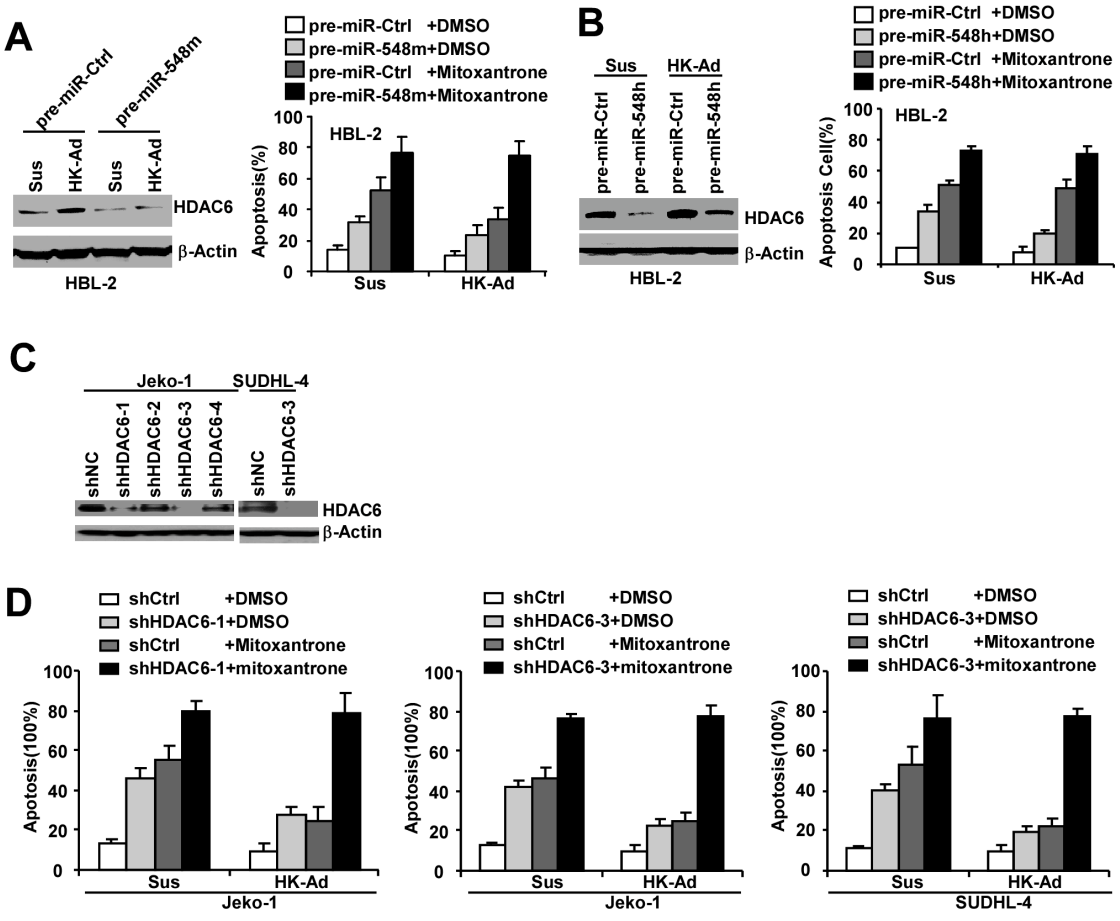

Figure S3. (**A-B**) Overexpression of miR-548m (A) and miR-548h (B) induces HDAC6 down-regulation, lymphoma cell apoptosis and enhances mitoxantrone-induced cell apoptosis in HBL-2 cells in the presence and absence of HK adhesion. HBL-2 cells transfected with pre-miR-548m/h or pre-miR-control (pre-miR-Ctrl) were treated with vehicle control (DMSO) or mitoxantrone (0.2 μM) for 24 hours with or without HK cell

adhesion. HDAC6 expression levels (left panel) were then analyzed by Western blot, and cell apoptosis (right panel) was analyzed by flow cytometry using Annexin V. (**C-D**) Knockdown of HDAC6 induces lymphoma cell apoptosis and enhances mitoxantrone-induced cell apoptosis in Jeko-1 and SUDHL-4 cells in the presence and absence of HK adhesion. Jeko-1 transfected with HDAC6 shRNA-1, 3 (shHDAC6) and SUDHL-4 cells transfected with HDAC6 shRNA-3 (shHDAC6) or control shRNA (shCtrl) were incubated for 48 hours and then treated with vehicle control (DMSO) or mitoxantrone (0.2 μM) for another 24 hours. HDAC6 expression levels (C) were then analyzed by Western blot and cell apoptosis (D) was analyzed by flow cytometry using Annexin V. Results are representatives of at least 3 independent experiments and means ± SD.

Figure S4

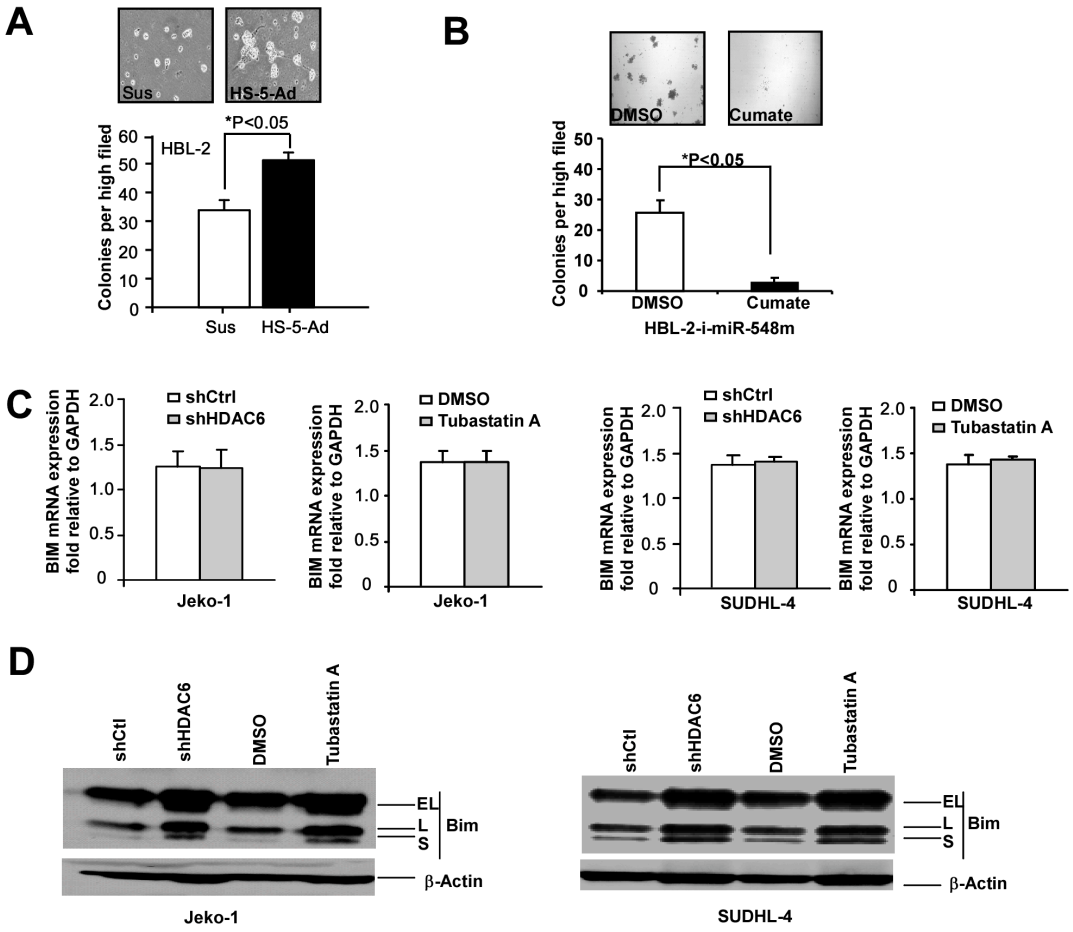

Figure S4. (**A**) HBL-2 cells were plated without (Sus) and with (HS-5-Ad) HS-5 cells at ratio of 1:2 in methycellulose medium. Colonies from HBL-2 cells in suspension versus adhesion to HS-5 cells are shown in micrographs in methylcellulose. (**B**) HBL-2-i-miR-548m cells were plated in the methycellulose medium and then treated with cumate (30ug/ML) or DMSO. The numbers of HBL-2 tumor cell colonies were enumerated microscopically after 2 weeks of culture. Colonies are shown in micrographs in methylcellulose. (**C**) Bim mRNA expression levels in Jeko-1 and SUDHL4 cells were analyzed by TaqMan qRT-PCR assays after 48 hours of transfection with either HDAC6 shRNA constructs 2 (shHDAC6 construct 2) or non-silencing control shRNA (sh.Ctrl-) as well as treatment with DMSO or tubastatin A (0.5 μM). Results in fold were obtained and expressed relative to GAPDH expression levels. **(D)** Bim protein expression levels in Jeko-1 and SUDHL4 cells were analyzed by Western blot after 48 hours of transfection with either HDAC6 shRNA constructs 2 (shHDAC6 construct 2) or non-silencing control shRNA (shCtrl-) as well as treatment with DMSO or tubastatin A (0.5 μM). Results are representative of at least 3 independent experiments and means $\pm$ SD.

Figure S5

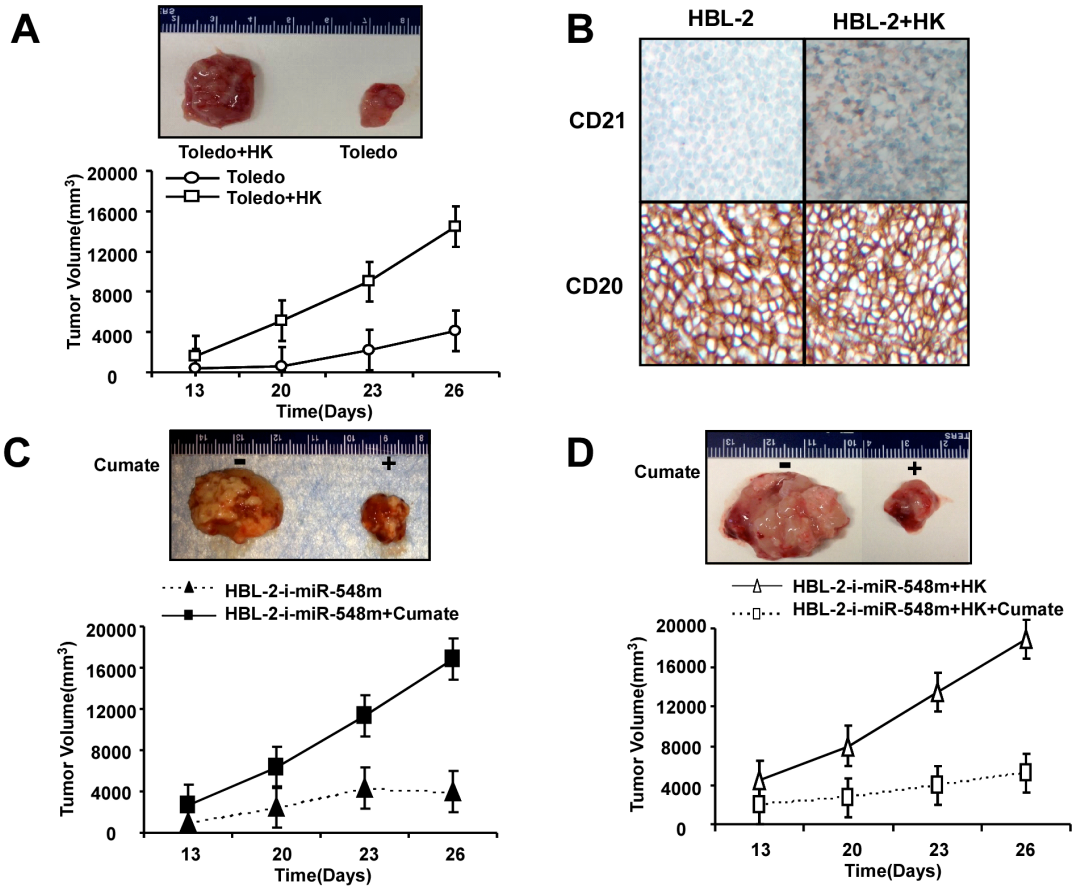

Figure S5. **(A)** HK cells support diffuse large B-cell lymphoma formation in vivo in NOD-SCID mice. Toledo cells (1×10^6) were subcutaneously injected with or without HK cells (5×10^5) into the posterior flank of nude mice. Graph shows tumor size measured with a caliper in three dimensions at the indicated days after cell injection. Inset in A shows photographed tumors innoculated by Toledo alone (Sus) or Toledo co-innoculated with HK (HK-Ad) on day 26. (**B**) Immunohistochemical stains showed the presence of dispersed single and clusters of HK cells (CD21) in lymphoma derived from co-injection of HBL-2 with HK cells (upper right) and absence of HK in tumor derived from injection with HBL-2 cell only (upper left).CD20 is used to stain for lymphoma cells. Original Magnification, 200×. (**C-D**) HBL-2-i-miR-548m cells were treated with DMSO or 30ug/ML

Cumate (System Biosciences) for twenty-four hours. Then the NOD-SCID mice were inoculate subcutaneously in the right flanks with 1 x 10^6 HBL-2-i-miR-548m cells suspended in 100 ul of PBS without (C) or with (D) HK with cells at ratio of 1:2. Graph shows tumor size measured with a caliper in three dimensions at the indicated days after cell injection. Insets show photographed tumors on day 26.

Figure S6

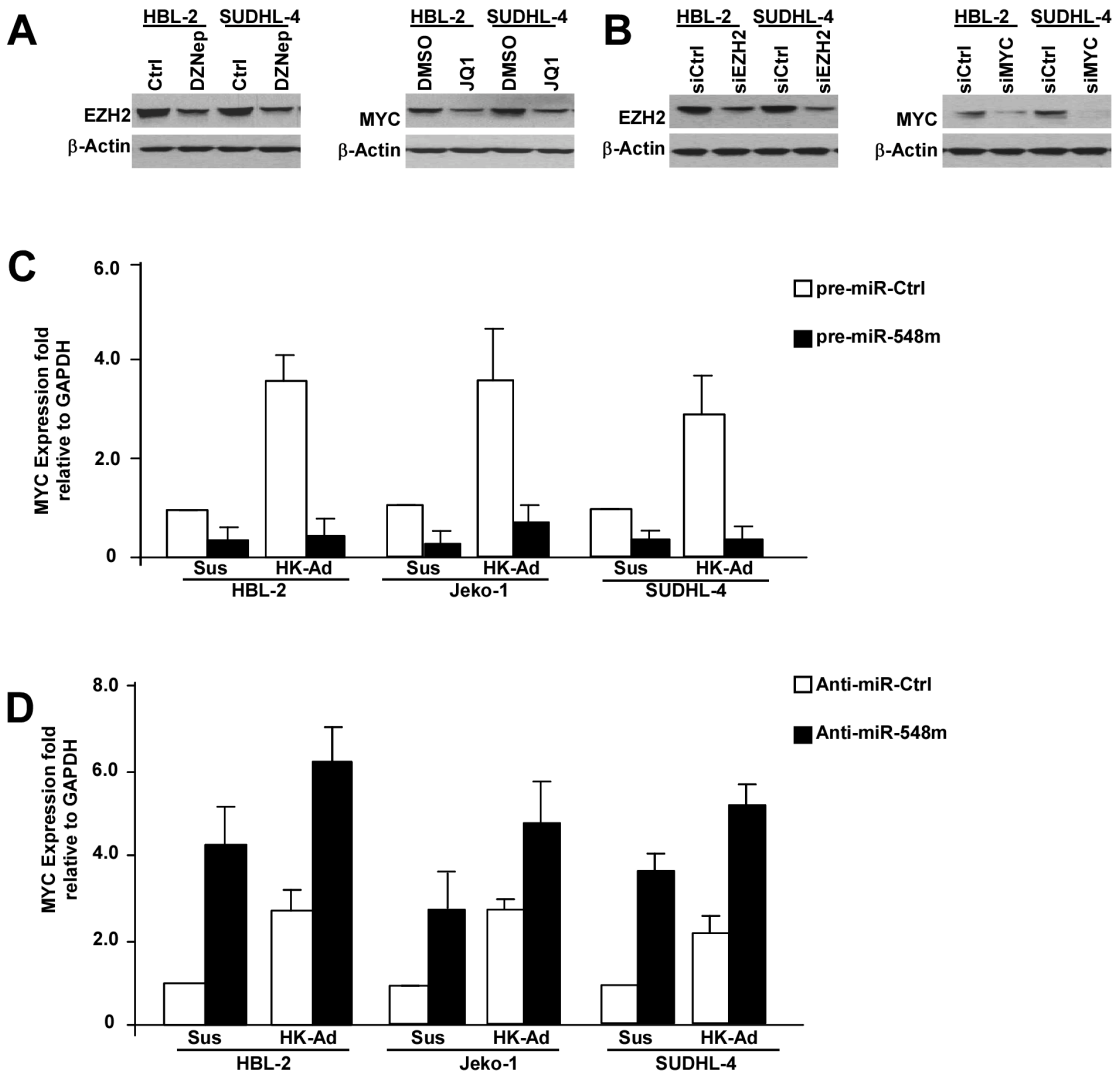

Figure S6. **(A-B)** Inhibition of c-Myc and EZH2 induces miR-548m expression in HBL-2 and SUDHL4 cells. HBL-2 and SUDHL4 were treated with JQ1 (1uM) for 48 hours or

DZNep (1 uM) for 24 hours (A), or c-Myc and EZH2 were knocked down with c-Myc siRNA (siMyc) or EZH2 siRNA (siEZH2). siCtrl, control non-specific siRNA (B). The protein levels of c-Myc and EZH2 were detected with Western blot. Results are representative of at least 3 independent experiments.(**C**-**D**) Overexpression of miR-548m with pre-miR-548m decreases c-Myc mRNA expression (C), and knock-down of miR-548m by anti-miR-548m increases c-Myc mRNA expression in the absence and presence of HK cells in HBL-2, Jeko-1 and SUDHL-4 cells. A-B, representative of at least 3 independent experiments; C-D, Results are means ± SD of at least 3 independent experiments.