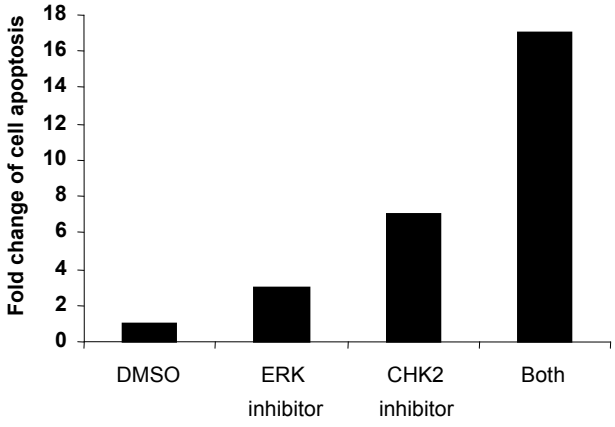
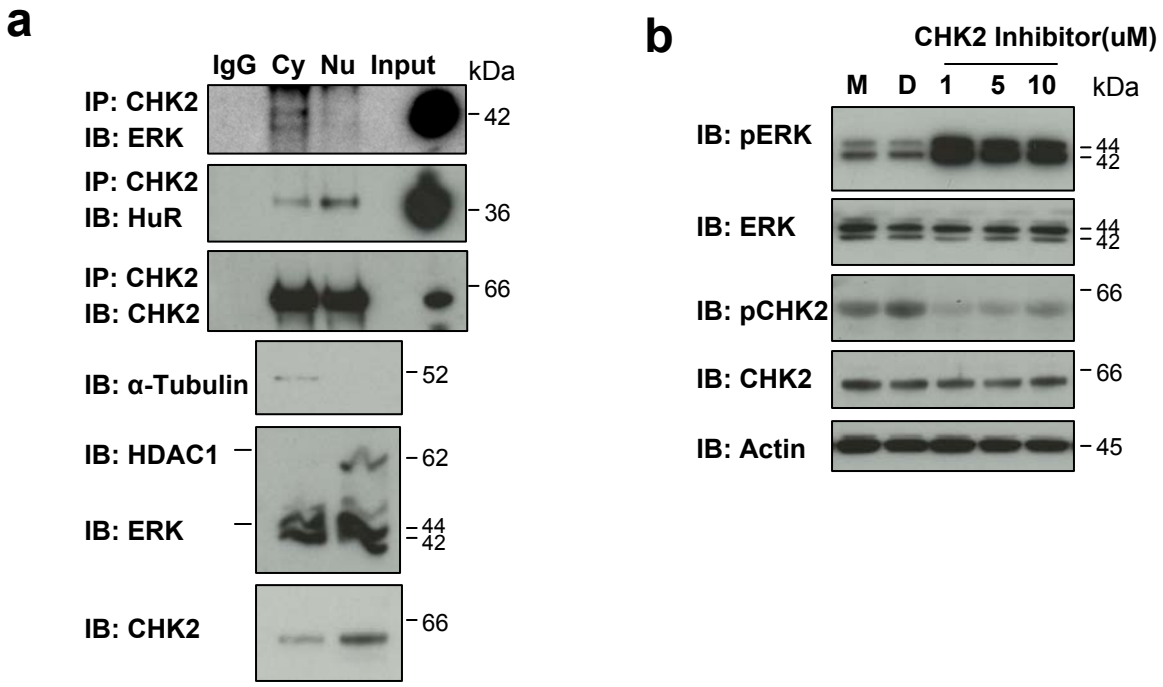
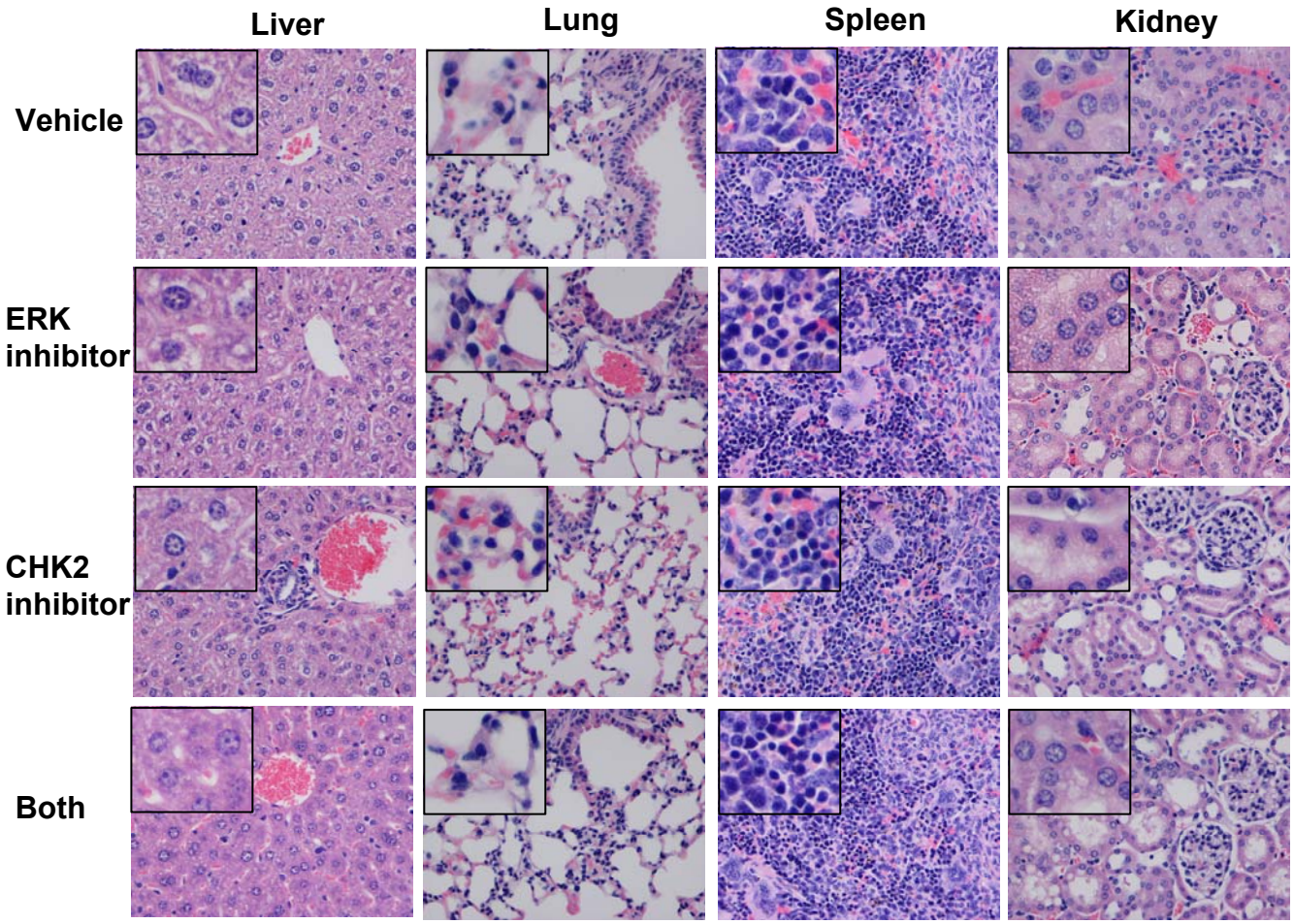
Supplementary information



Supplementary Figure S1.
Inhibition of ERK and CHK2 increases apoptosis in OCI-LY3 cells. OCI-LY3 cells were exposed to 5μM CHK2 inhibitor II or 20μM ERK inhibitor alone or in combination for 72hrs after which the percentage of apoptotic cells was determined by Annexin V analysis as described in Materials and Methods.

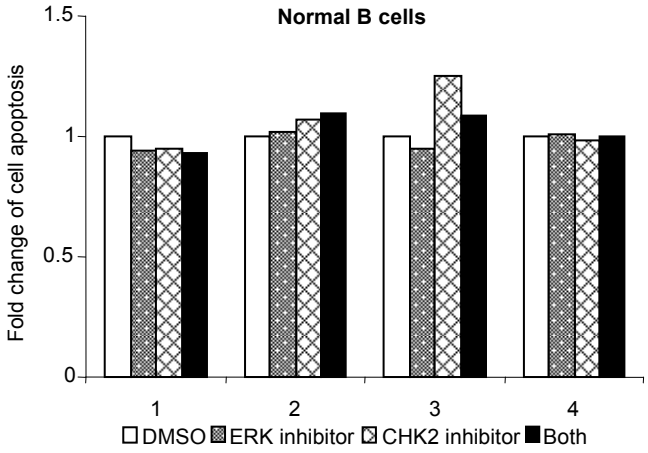


Supplementary Figure S2.
ERK1/2 associates with CHK2 and CHK2 inhibition increases ERK1/2 phosphorylation in OCI-LY3 cells. (a) Equal amounts of cytoplasmic (Cy) and nuclear fraction (Nu) from OCI-LY3 cells were immunoprecipitated with anti-CHK2 antibody followed by immunoblotting with anti-ERK1/2, anti-HuR or anti-CHK2 an tibody. Tubulin and HDAC1 were u sed as markers of the cytop lasmic and nuclear fractions respectively. (b) OCI-LY3 cells were treated w ith CHK2 inh ibitor II in R PMI 1640 complete medium f or 4 h. T he l evels of pCHK2, CHK 2, pERK1/2 or E RK1/2 i n the t otal cell lysates were monitored by immunoblotting with the indicated antibodies. M, media; D, DMSO.

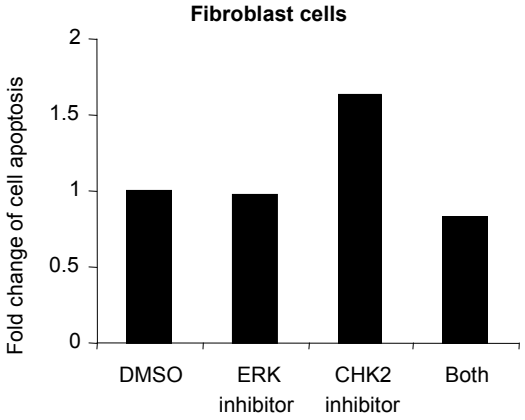


Supplementary Figure S3.
Absence of changes in tissue architecture in mice exposed to ERK inhibitor, CHK2 inhibitor or the combination. Representative microscopic images (magnification, ×400) (Hematoxylin & eosin staining) of the tissues harvested from 28 mice treated with vehicle, ERK inhibitor, CHK2 inhibitor or the combination for 20 days.

a



b



Supplementary Figure S4.
Normal B cells and immortalized untransformed fibroblast (GM04390) cells were relatively resistant to co-administration of ERK inhibitor and CHK2 inhibitor II. Normal B cells were isolated from healthy donors by immunodepletion of normal T cells from PBLs and then treated with IL-4 (80 U/mL) to expand a B-cell population. Immortalized untransformed fibroblast cell line GM04390 was purchased from Coriell cell Repositories and cultured in minimum essential medium (Invitrogen) supplemented with 20% fetal bovine serum and antibiotics. (a) Four cases of normal B cells from different donors and (b) fibroblast (GM04390) cells were exposed to 5 μM CHK2 inhibitor II or 20μM ERK inhibitor alone or in combination for 48hrs after which the percentage of apoptotic cells was determined by Annexin V analysis as described in Materials and Methods.