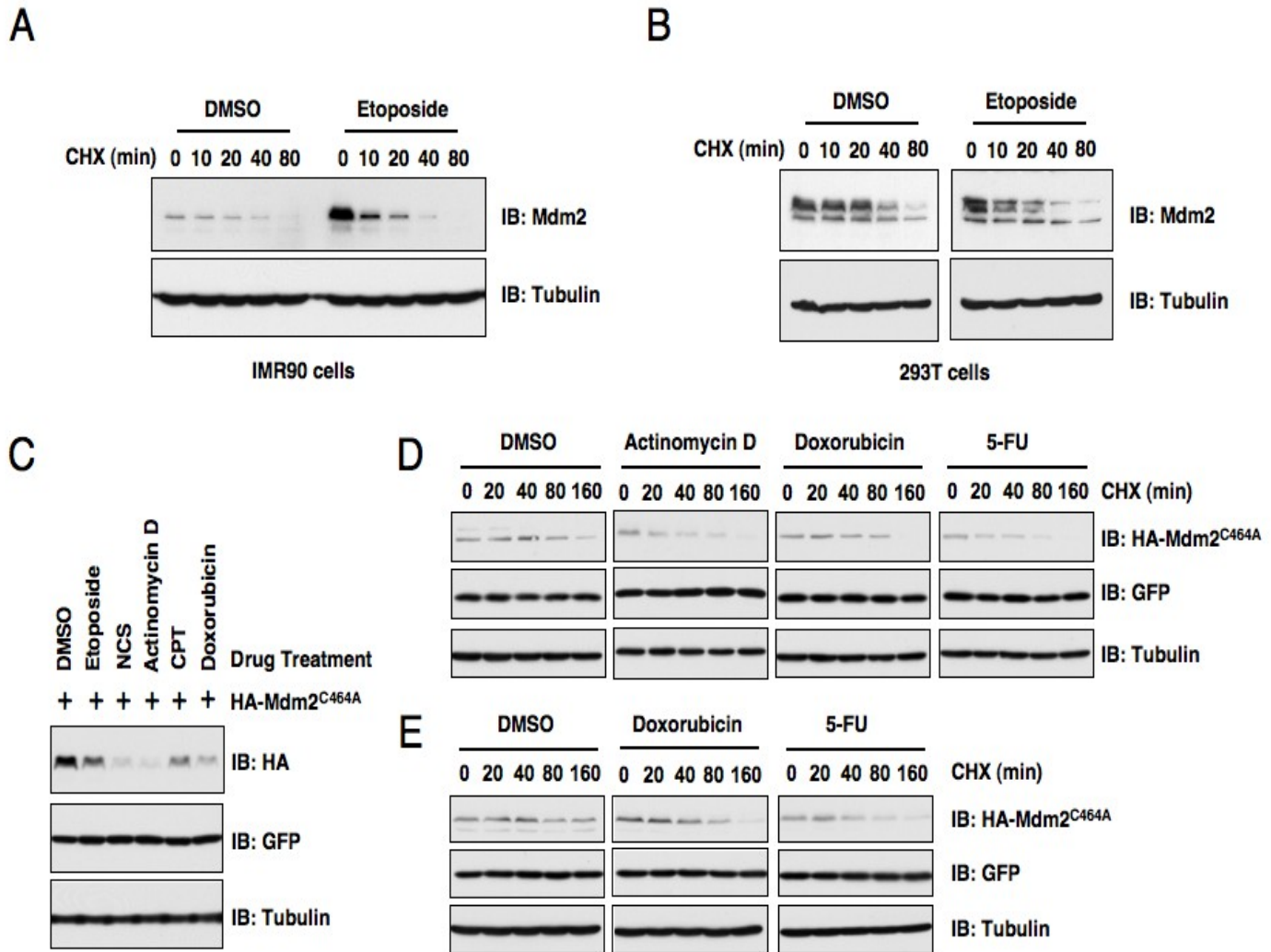


**DNA damage-induced activation of ATM promotes  $\beta$ -TRCP-mediated Mdm2 ubiquitination and destruction – Wang et al**

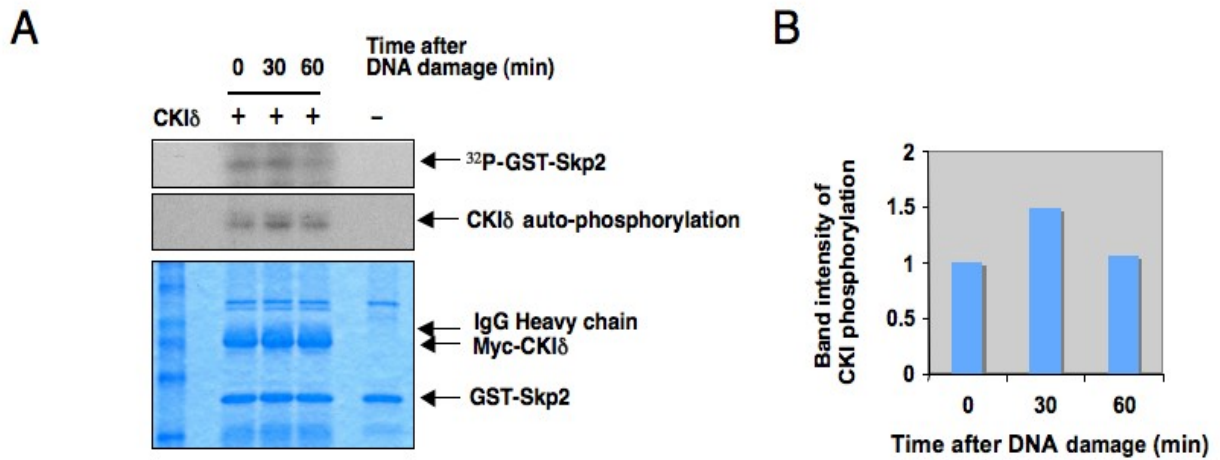


**Supplementary Figure 1: DNA damage destabilizes Mdm2.**

**A-B.** IMR90 (**A**) and 293T (**B**) cells were treated with 25  $\mu$ M etoposide for 1.5 hours before 20  $\mu$ g/ml cycloheximide was added. At the indicated time points, whole cell lysates were prepared and immunoblots were probed with the indicated antibodies.

**C.** HeLa cells were transfected with the C464A mutant HA-Mdm2 plasmid. Twenty hours post-transfection, cells were split into 60 mm dishes, and after another 20 hours, treated with the indicated DNA damaging drugs for 3 hours. Afterwards, whole-cell lysates were prepared and immunoblots were probed with the indicated antibodies.

**D-E.** HeLa cells (**D**) and 293T cells (**E**) were transfected with the C464A mutant HA-Mdm2 plasmid. Twenty hours post-transfection, cells were split into 60 mm dishes, and after another 20 hours, treated with the indicated DNA damaging drugs for 3 hours. Afterwards, cells were treated with 20  $\mu$ g/ml cycloheximide. At the indicated time points, whole cell lysates were prepared and immunoblots were probed with the indicated antibodies.



**Supplementary Figure 2: DNA damage does not lead to a significant induction in CKI $\delta$  kinase activities.**

**A.** Detection of CKI $\delta$  kinase activity changes in response to DNA damage by *in vitro* kinase assay. CKI $\delta$  kinase was purified by CKI $\delta$ -immunoprecipitation from U2OS cells after treatment with etoposide for the indicated times, and then incubated with 5  $\mu\text{g}$  of the GST-Skp2 protein in the presence of  $\gamma$ - $^{32}\text{P}$ -ATP. The kinase reaction products were resolved by SDS-PAGE and phosphorylation was detected by autoradiography.

**B.** Quantification of the band intensities in **A**. The CKI $\delta$  auto-phosphorylation band intensity was normalized to Myc-CKI $\delta$  immunoprecipitation band, then normalized to the t=0 controls.