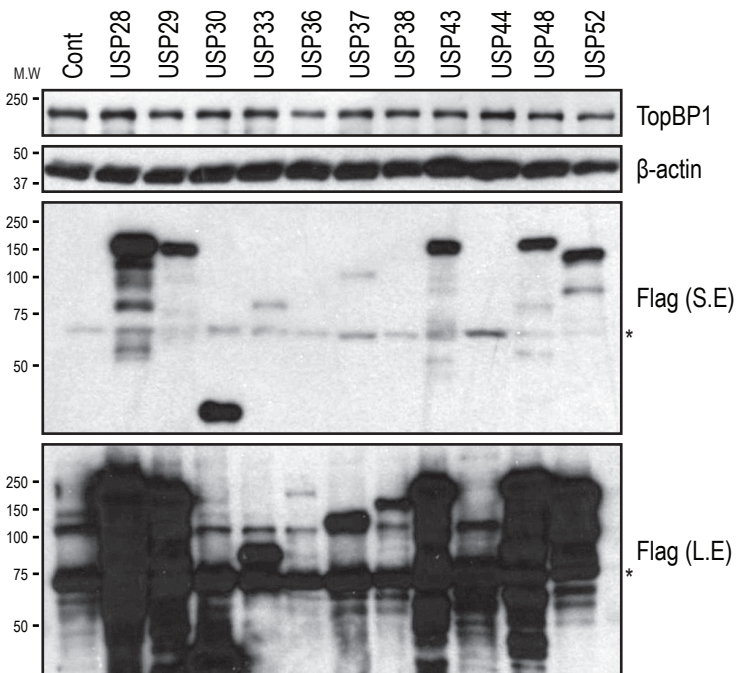
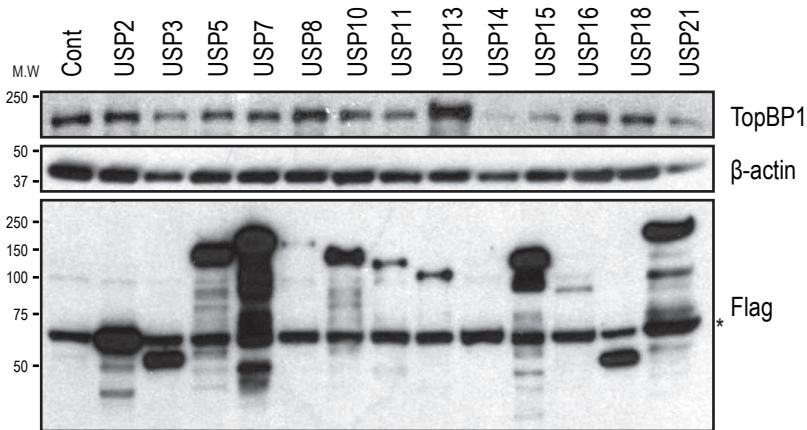
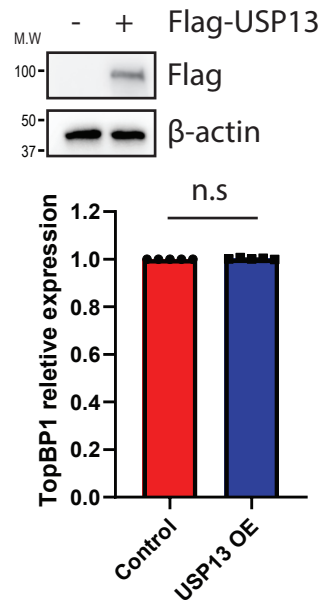
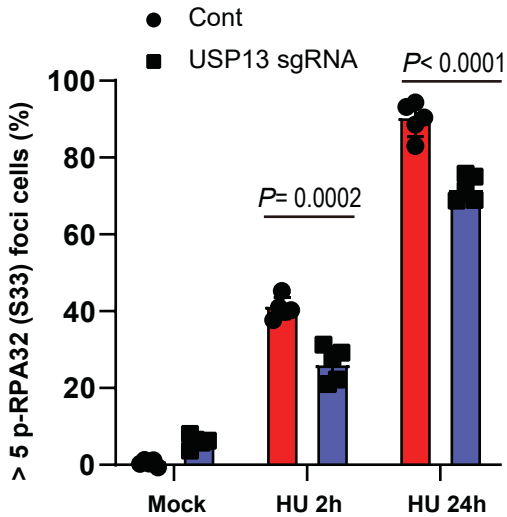


**A****B**

**Fig. S1 USP13 regulates TopBP1 protein level**

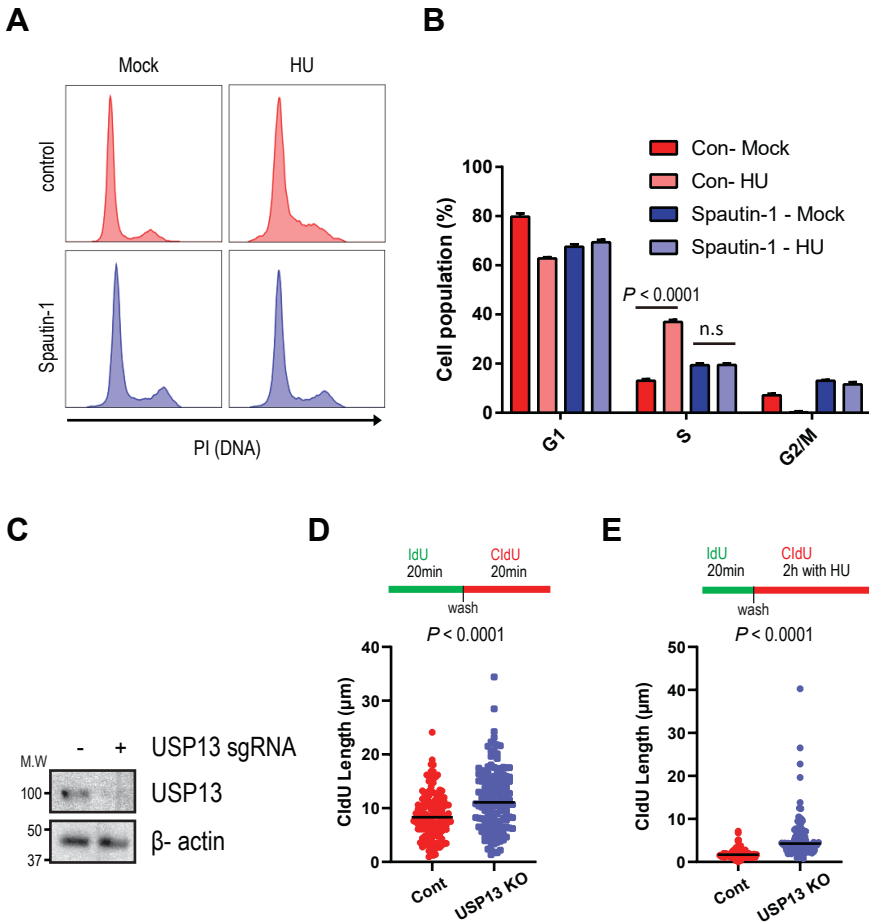
A. 293T cells were transfected with USP superfamily and screened for TopBP1 protein levels.

Unspecific proteins were indicated by \*. B. TopBP1 mRNA measured in USP13 overexpressed cells.



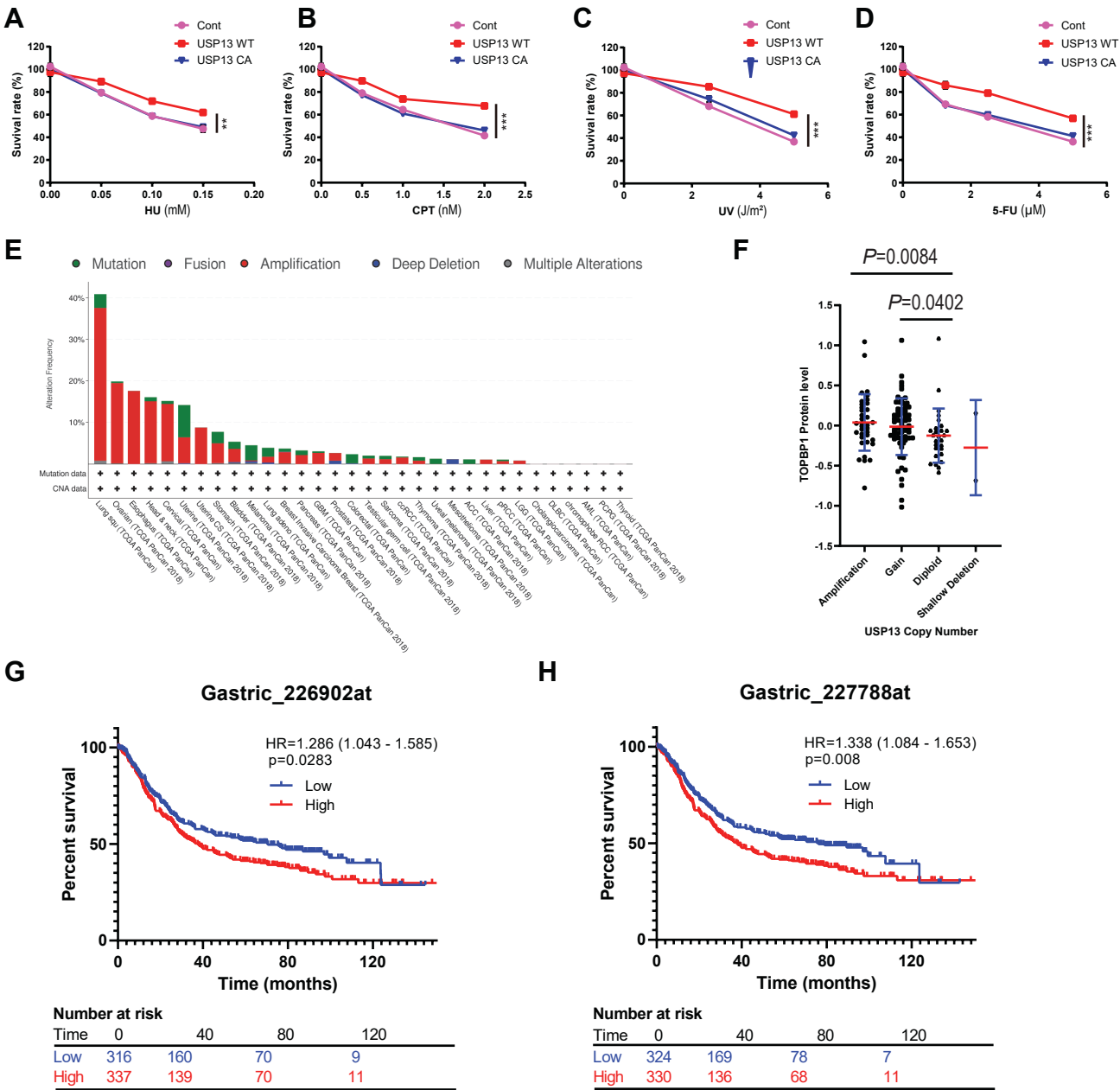
**Fig. S2 USP13 is involved in the ATR signaling pathway**

The phospho-RPA32 (S33) was determined by immunofluorescence in control or USP13-deficient cells after HU 2h and 24h treatment. Foci numbers were counted by Image-Xpress confocal High-content imaging system (molecular device). The graphs represent mean  $\pm$  S.D., two-tailed, unpaired t-test. n = 3 independent experiments.



**Fig. S3 USP13 is important for DNA-damage checkpoint activation**

A. Cell cycle distribution was determined by flow cytometry in SK-OV3 cells B. Population fractions were analyzed by Modfit. C. Knockout efficiency of USP13. D-E. Cells were labeled with IdU and CldU. Fork speeds (D), and DNA synthesis (E) were determined by measuring DNA fiber length. All fiber lengths were measured using Image J. The graphs represent mean  $\pm$  S.D., two-tailed, unpaired t-test. n = 3 independent experiments.



**Fig. S4 USP13 maintains genomic stability**

A-D. USP13 overexpressed SK-OV-3 cells were plated and treated with hydroxyurea (HU, mM) (A), camptothecin (CPT, nM) (B), ultraviolet (UV,  $J/m^2$ ) (C), and fluorouracil (5-FU,  $\mu M$ ) (D). After 14 days, colony numbers were counted. E. USP13 expression and mutation status were analyzed using cBioPortal platform. F. Analysis of USP13 copy number and TopBP1 protein levels. G-H. Survival analysis produced from gastric cancer specimens by KM-plot.