

## **Supplementary Information**

### **TRABID overexpression enables synthetic lethality to PARP inhibitor via prolonging 53BP1 retention at double-strand breaks**

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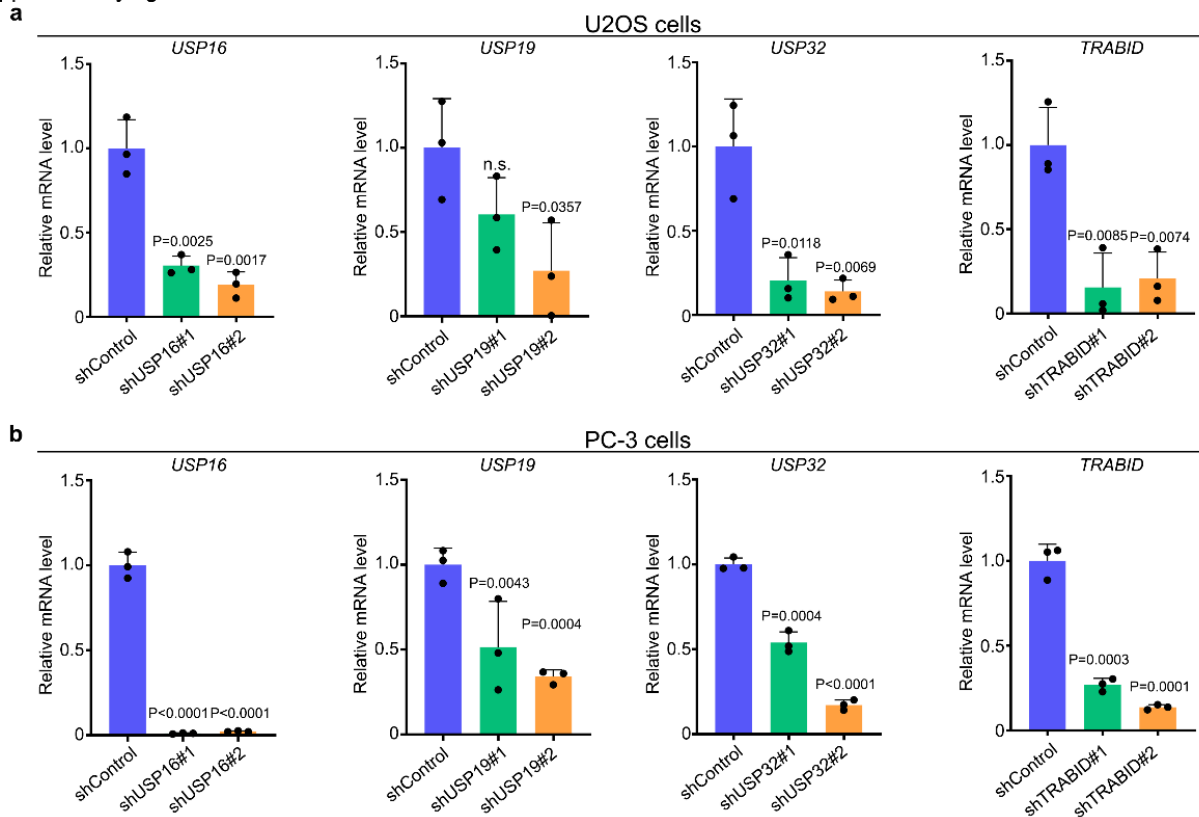
**This PDF file includes:**

**Supplementary Figure 1 to 4**

**Supplementary Figure Legends**

**References cited in Supplementary Information**

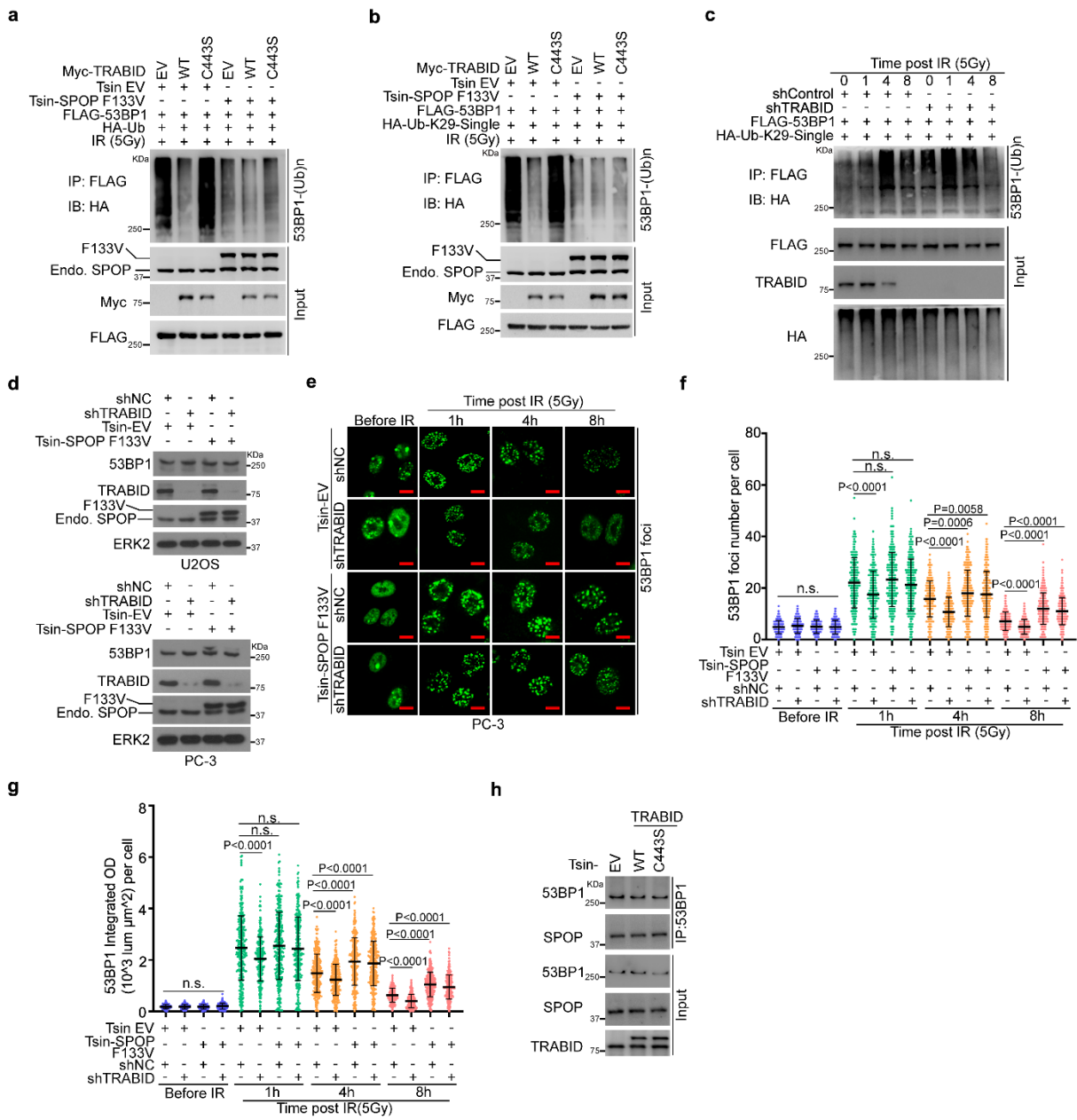
Supplementary figure 1



**Supplementary Fig. 1 Knockdown efficiencies of deubiquitinase genes, Related to Figure 1**

U2OS (**a**) and PC-3 (**b**) cells were infected with lentivirus expressing indicated shRNAs and harvested for RT-qPCR. Data are shown as mean  $\pm$  SD (n=3). Two-tailed unpaired Student's t-test. P values based on the order of appearance: in **a** (0.0025, 0.0017, 0.1323, 0.0357, 0.0118, 0.0069, 0.0085, 0.0074) and in **b** (2.4E-5, 2.5E-5, 0.0043, 0.0004, 0.0004, 6.8E-6, 0.0003, 0.0001). n.s., not significant. Source data are provided in this paper.

Supplementary figure 2



**Supplementary Fig. 2 TRABID antagonizes SPOP-mediated removal of 53BP1 from DSB sites, Related to Figure 3**

**a, b** Ubiquitination assay in 293T cells transfected with HA-WT (**a**) or K29-only (**b**) ubiquitin together with other indicated plasmids and treated with IR (5 Gy) for 1 hour.

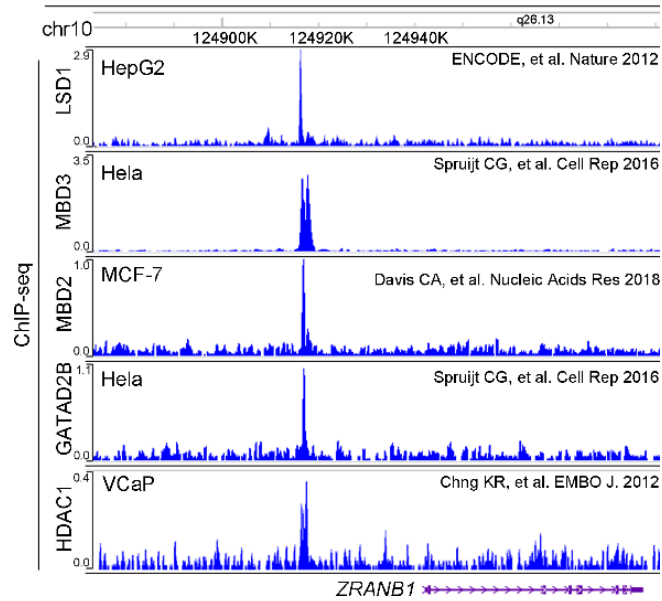
**c** Ubiquitination assay in 293T cells transfected with indicated plasmids. Cells were harvested at different time points after IR.

**d** U2OS (**top**) and PC-3 (**bottom**) cells were infected with lentivirus expressing indicated shRNA and harvested for WB analysis. ERK2 was used as a loading control.

**e-g** PC-3 cells infected with lentivirus expressing indicated shRNA were treated with IR followed by IFC of 53BP1 at the indicated time points after IR (**e**). Scale bar, 10  $\mu$ m. The average 53BP1 foci number (**f**) and foci density (**g**) in each cell were quantified. Data are presented as means  $\pm$  SD of more than 300 cells from three biological replicates. Two-tailed unpaired Student's t-test. n.s., not significant. P values based on the order of appearance: in **f** (0.33, 0.5657, 0.9126, 4.7E-9, 0.1316, 0.3342, 1.6E-20, 0.0006, 0.0058, 4E-15, 5.7E-30, 9.9E-25) and in **g** (0.5466, 0.7991, 0.0932, 1.9E-6, 0.4184, 0.7657, 4.7E-6, 1.1E-10, 1.8E-8, 4.3E-23, 3.3E-34, 3.4E-22).

**h** PC-3 cells were infected with lentivirus expressing indicated plasmids and harvested for co-IP analysis. Source data are provided in this paper or Mendeley database (<https://data.mendeley.com/datasets/n9txt6y5cj/1>). Similar results for (**a-d**) and (**h**) panels were obtained in three independent experiments.

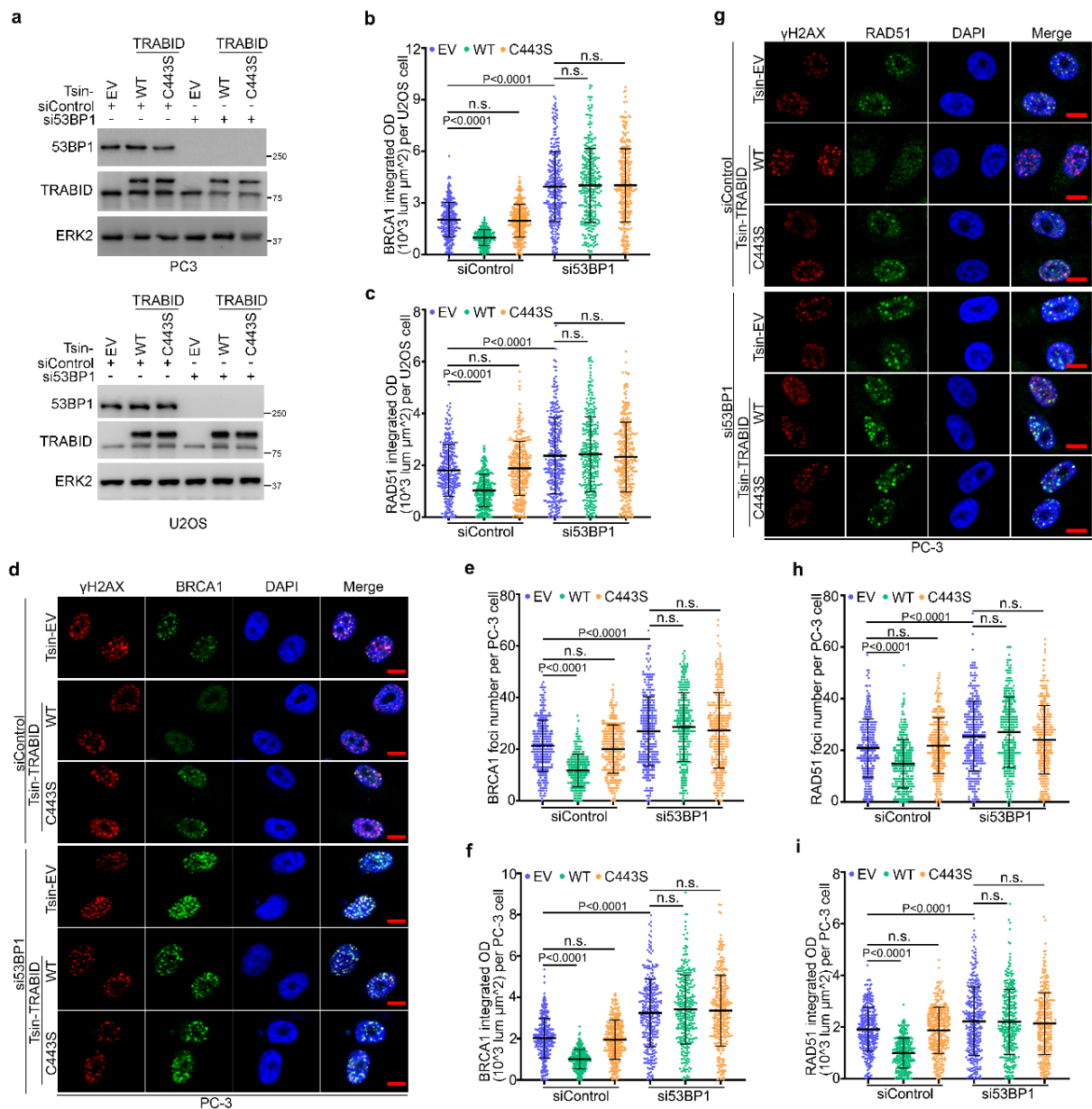
### Supplementary figure 3



**Supplementary Fig. 3 ChIP-seq signal showing the occupancy of the indicated components of the NuRD complex in the ZRANB1 gene locus, Related to Figure 4**

Screenshot of the Cistrome Data Browser (<http://cistrome.org/db/#/>) showing ChIP-seq signal profiles of the indicated components of the NuRD complex (reported previously<sup>1-4</sup>) in the ZRANB1 gene locus in different human cell lines. The accession codes from Cistrome Data Browser: 101921 (GEO: GSM2825431), 71069 (GEO: GSM2104436), 64901 (ENCODE: ENCSR940MHE\_2), 71067 (GEO: GSM2104440), and 8658 (GEO: GSM717399).

Supplementary figure 4



**Supplementary Fig. 4 TRABID overexpression inhibits HR activity, Related to Figure 5**

**a** PC-3 (**top**) and U2OS (**bottom**) cells were infected with lentivirus expressing the indicated plasmids and treated with the indicated siRNAs and harvested for WB analysis. ERK2 was used as a loading control. Similar results were obtained in three independent experiments.

**b, c** U2OS cells infected with lentivirus expressing EV, TRABID-WT or TRABID-C443S and treated with siControl or si53BP1 were exposed to IR. Cells were subjected to IFC of BRCA1 and RAD51 at 1 hour after IR and IFC results are shown in Fig. 5d, f. The average foci density of BRCA1 (**b**) and RAD51 (**c**) in each cell are shown. Data are presented as means  $\pm$  SD of more than 300 cells from three biological replicates. Two-tailed unpaired Student's t-test. n.s., not significant. P values based on the order of appearance: in **b** (9.6E-50, 0.4198, 4.6E-42, 0.6769, 0.6318) and in **c** (6.5E-28, 0.3313, 4.8E-8, 0.661, 0.6374).

**d-i** PC-3 cells infected with lentivirus expressing EV, TRABID-WT or TRABID-C443S and treated with siControl or si53BP1 were exposed to IR followed by IFC of BRCA1 (**d**) and RAD51 (**g**) 1 h after IR. Scale bar, 10  $\mu$ m. The average foci number (**e, h**) and foci density (**f, i**) in each cell were quantified. Data are presented as means  $\pm$  SD of more than 300 cells from three biological replicates. Two-tailed unpaired Student's t-test. n.s., not significant. P values based on the order of appearance: in **e** (5.1E-39, 0.1121, 1E-8, 0.1259, 0.7436), in **f** (8.6E-51, 0.3748, 7.1E-27, 0.2346, 0.4682), in **h** (2.5E-12, 0.3563, 1.3E-5, 0.119, 0.2067) and in **i** (6.5E-46, 0.5748, 0.0007, 0.8471, 0.3907). Source data are provided in this paper or Mendeley database (<https://data.mendeley.com/datasets/n9txt6y5cj/1>).

## References cited in Supplementary Information

1. Consortium, E.P. An integrated encyclopedia of DNA elements in the human genome. *Nature* **489**, 57-74 (2012).
2. Spruijt, C.G. *et al.* ZMYND8 Co-localizes with NuRD on Target Genes and Regulates Poly(ADP-Ribose)-Dependent Recruitment of GATAD2A/NuRD to Sites of DNA Damage. *Cell Rep* **17**, 783-798 (2016).
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4. Chng, K.R. *et al.* A transcriptional repressor co-regulatory network governing androgen response in prostate cancers. *EMBO J* **31**, 2810-2823 (2012).