

1 **Supplementary Fig. S1. S1A** Related to Fig 1C: Screening for DUBs stabilizing Cdt2 in HeLa  
2 cells. **S1B.** Related to Fig 2B: SiHa, HeLa or U2OS cell lysates were immuno-precipitated with  
3 control IgG or anti-Cdt2 antibodies, and immunoblotted. **S1C.** Related to Fig. 4D and 4E:  
4 Quantitation of signal presented in Fig. 4D and 4E. USP46 localization was calculated in cells  
5 which showed expression of both USP46-His (red signal) and E6-myc (green signal). A  
6 minimum of 25 such cells were counted for each data set and localization type is expressed as  
7 percentage. **S1D.** Related to fig 3F:HEK293T cells were transfected with indicated plasmids  
8 and were treated with MG132 for 6 hours before harvesting at 48 hours of transfection. Flag-  
9 Cdt2 immunoprecipitates were immunoblotted with anti-HA antibody (top) and cell lysates with  
10 indicated antibodies (bottom). **S1E.** Related to Fig. 3A: Blots corresponding to figure 3A  
11 indicating that cycloheximide treated siGI2 and siE6 as well as siGI2 and siUSP46 were run on  
12 the same gel.

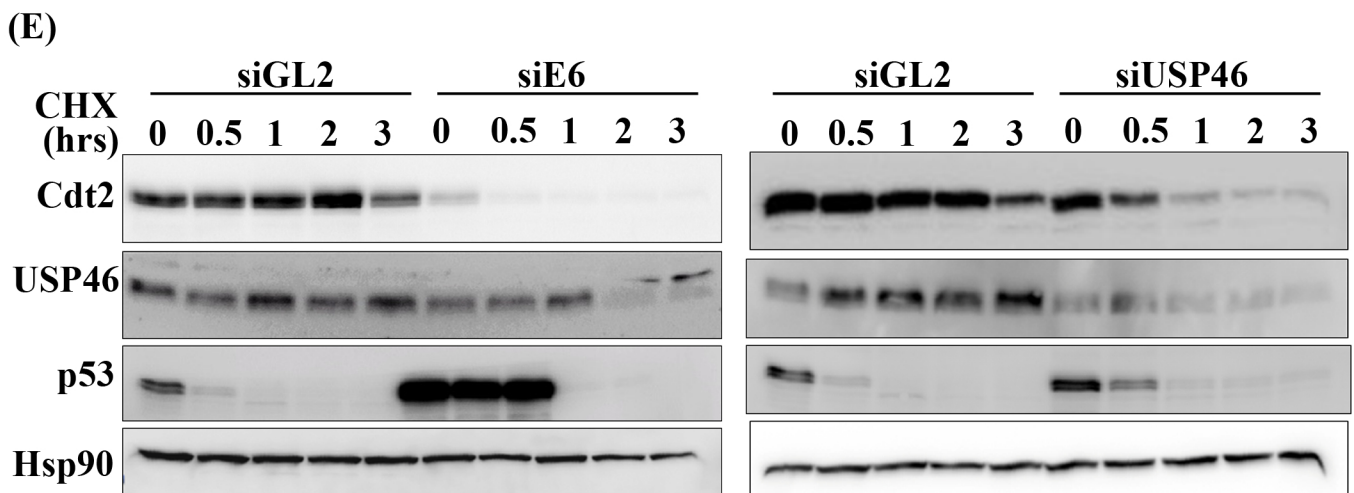
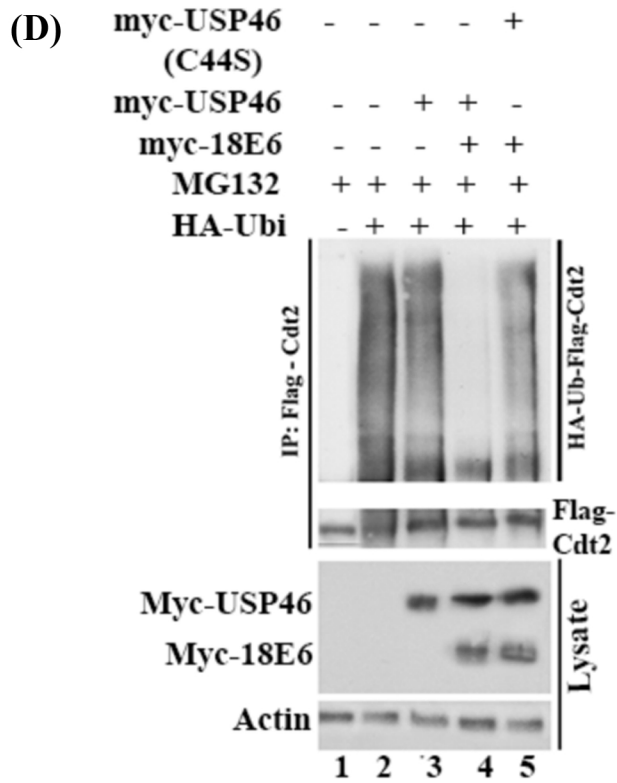
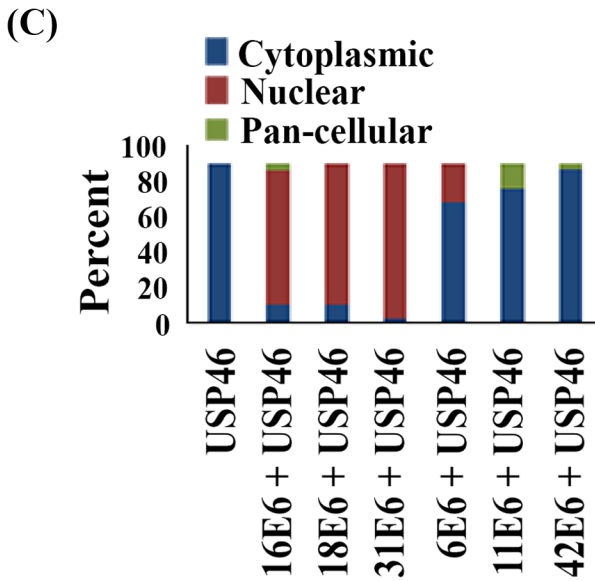
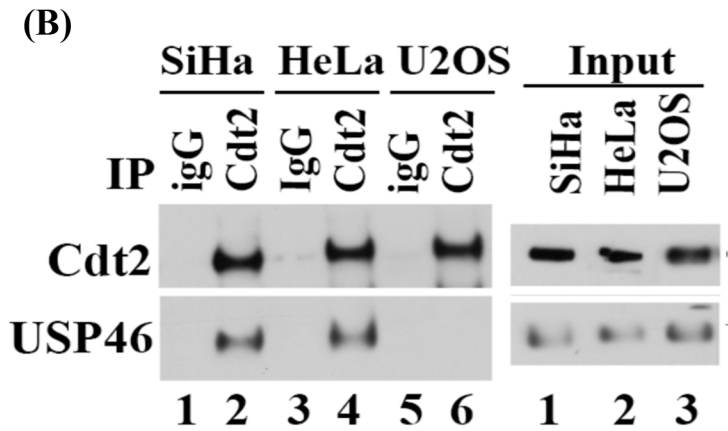
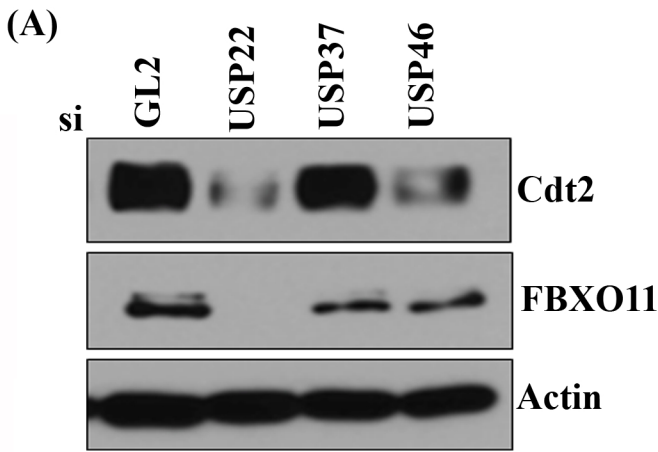
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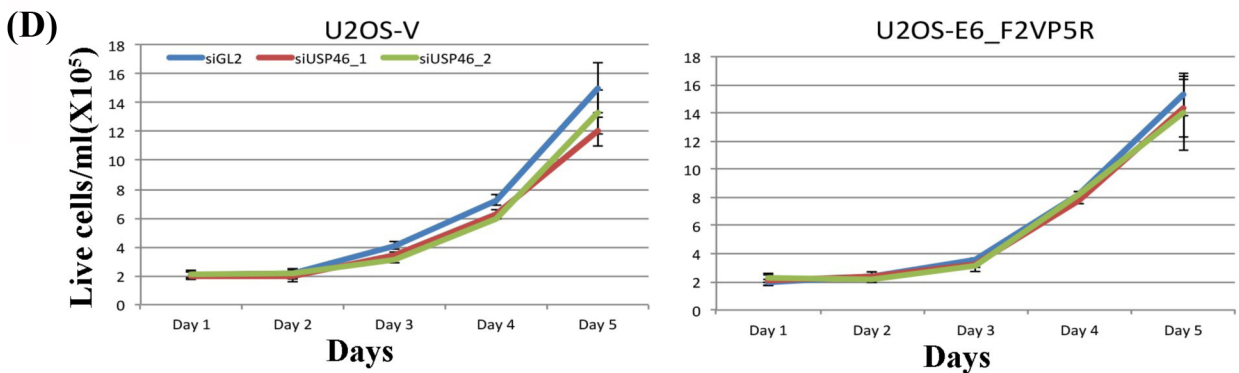
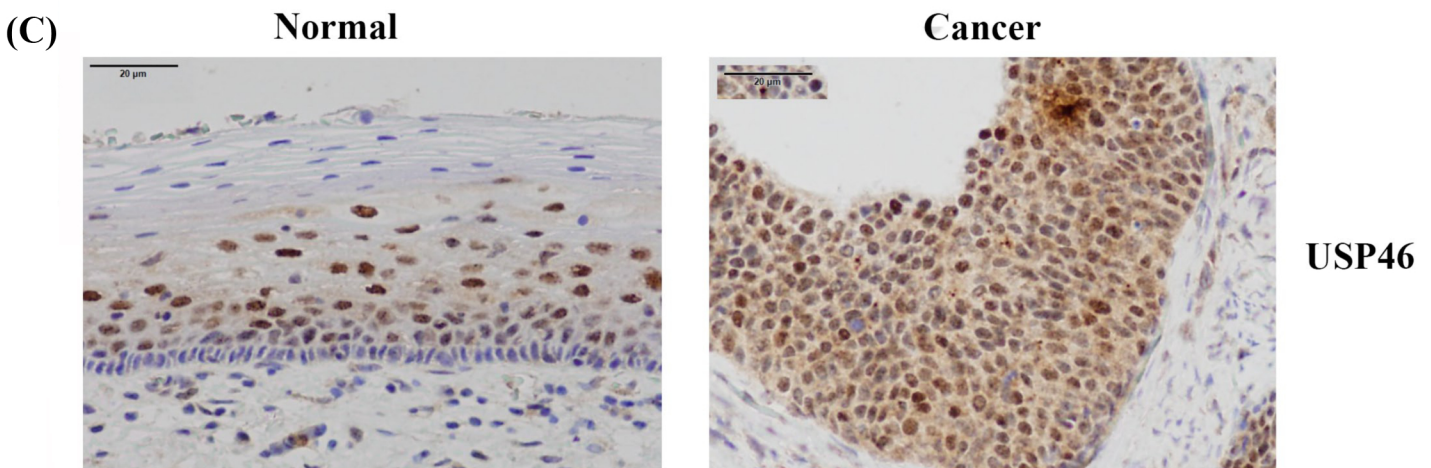
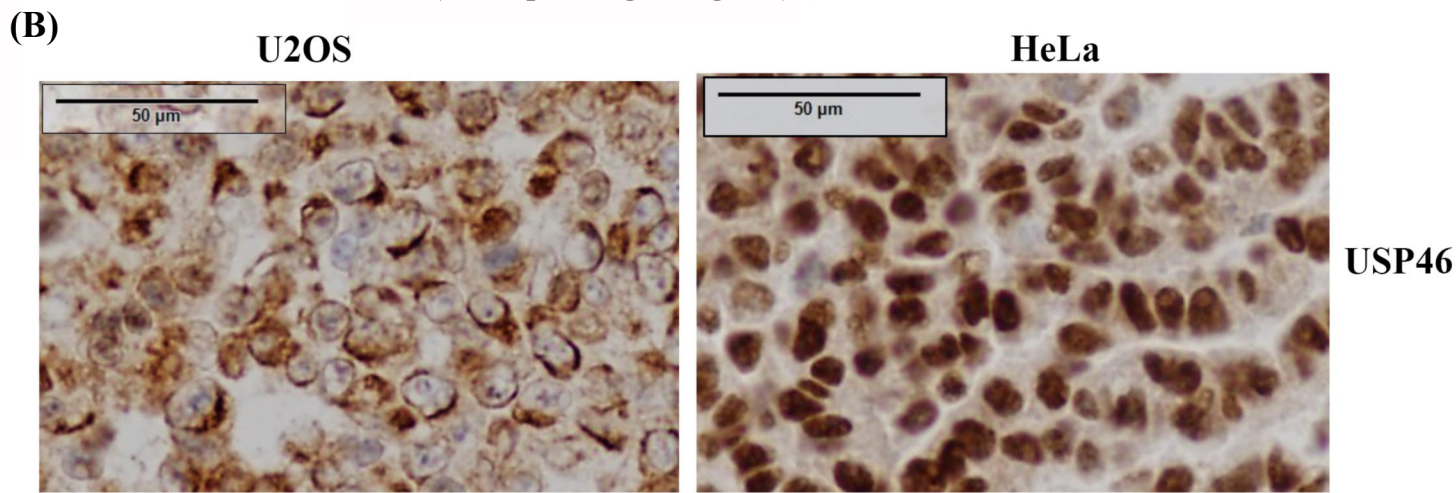
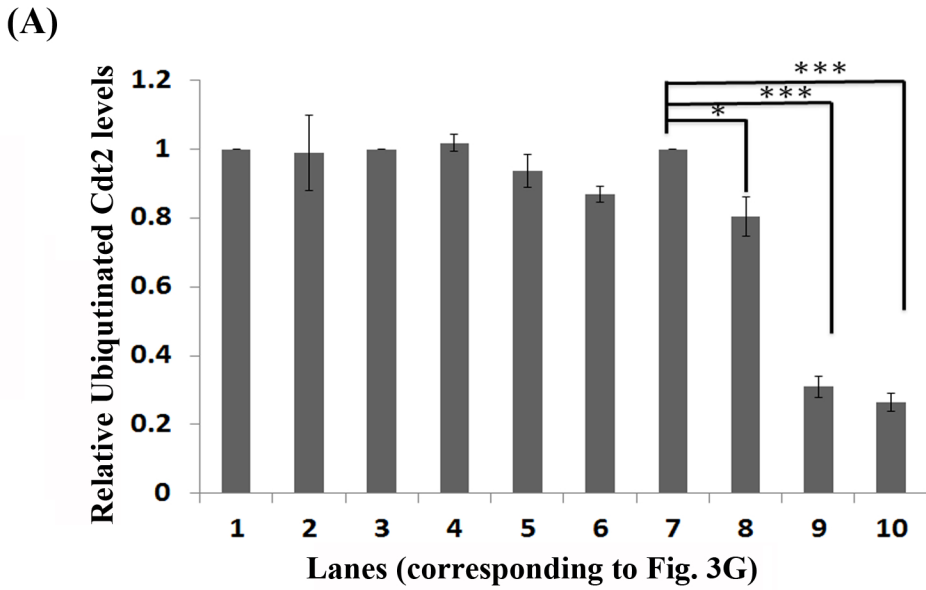
14 **Supplementary Fig. S2. S2A.** Related to Fig 3G: Quantification of 3G over five replicate  
15 experiments. Cdt2 ubiquitination signal as well total Cdt2 signal was quantified for each lane  
16 using imageJ software and for each lane ubiquitination signals were normalized to total Cdt2  
17 levels. Following this, lane 2 is normalized to lane 1; lanes 4, 5, 6 are normalized to lane 3 and  
18 lanes 8, 9, 10 are normalized to lane 7. \*:  $p < .05$  ; \*\*\* $p < 0.0005$  in one tailed student's t-test.  
19 **S2B.**Related to Fig 4C: Localization of endogenous USP46 as revealed by  
20 immunohistochemistry of formalin fixed paraffin embedded sections of cell pellets of U2OS and  
21 HeLa cells. **S2C.** Related to Fig 7D: Representative immunohistochemistry staining of USP46  
22 in cervical normal and tumor sections. **S2D.** Related to Fig 7B: Proliferation rates of U2OS  
23 cells transfected with vector control or mutant E6 (F2VP5R), after transfection of siGL2 (blue  
24 line) or siUSP46 (red and green lines). Mean and s.d. of 3 replicates.

25

26 **Supplementary Fig. S3. S3A.** Related to Fig 7H: Plot showing tumors resulting from  
27 xenografts of CaSki cells engineered to express tetracycline-induced shUSP46. Although  
28 statistically significant, the mice did not tolerate gavaging with doxycycline, resulting in  
29 premature death and a decrease in the number of tumors at later time points. Each data point  
30 represents median tumor volume and error bars represent median absolute deviation (MAD),  
31 black and red fonts for “n” denote number of xenografts tumors in study at those time points.

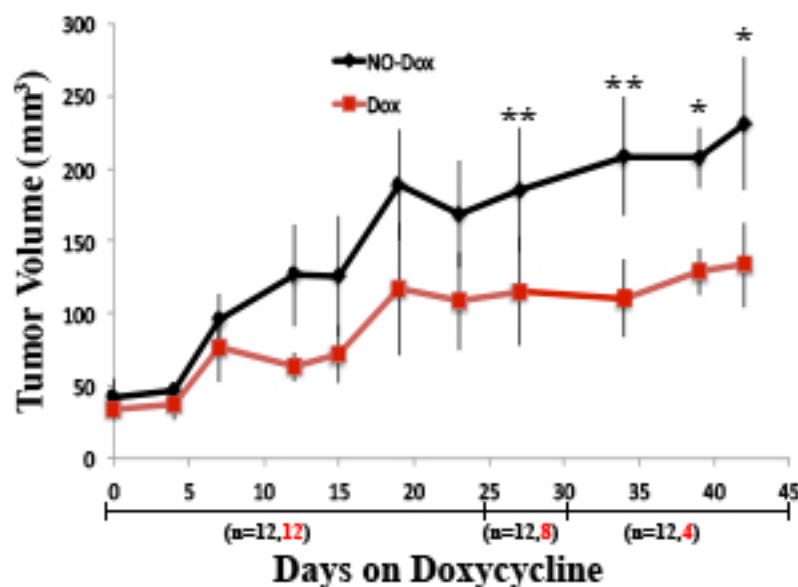
32 Mice were sacrificed once the tumor size grew to 1500 mm<sup>3</sup>. \*,p<0.05 ; \*\*p<0.005. **S3B, S3C.**  
33 Related to discussion: siCdt2 decreases proliferation of HeLa cells. **S3D, S3E.** Related to  
34 discussion: Colony forming ability of HeLA cells after knockdown of Cdt2, quantified in S3E.  
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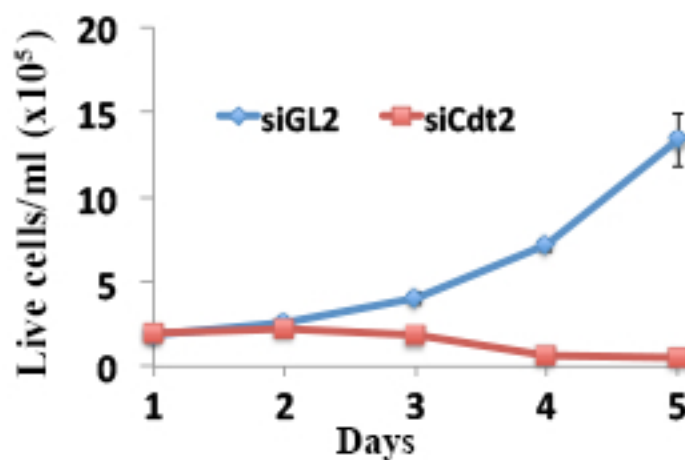


## Supplementary-S3

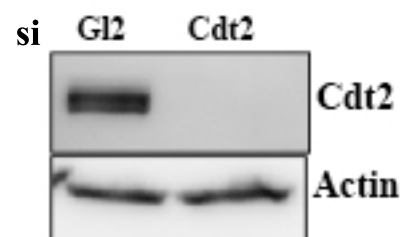
(A)



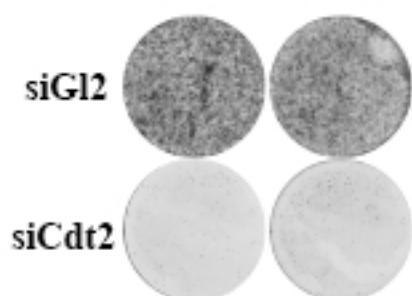
(B)



(C)



(D)



(E)

