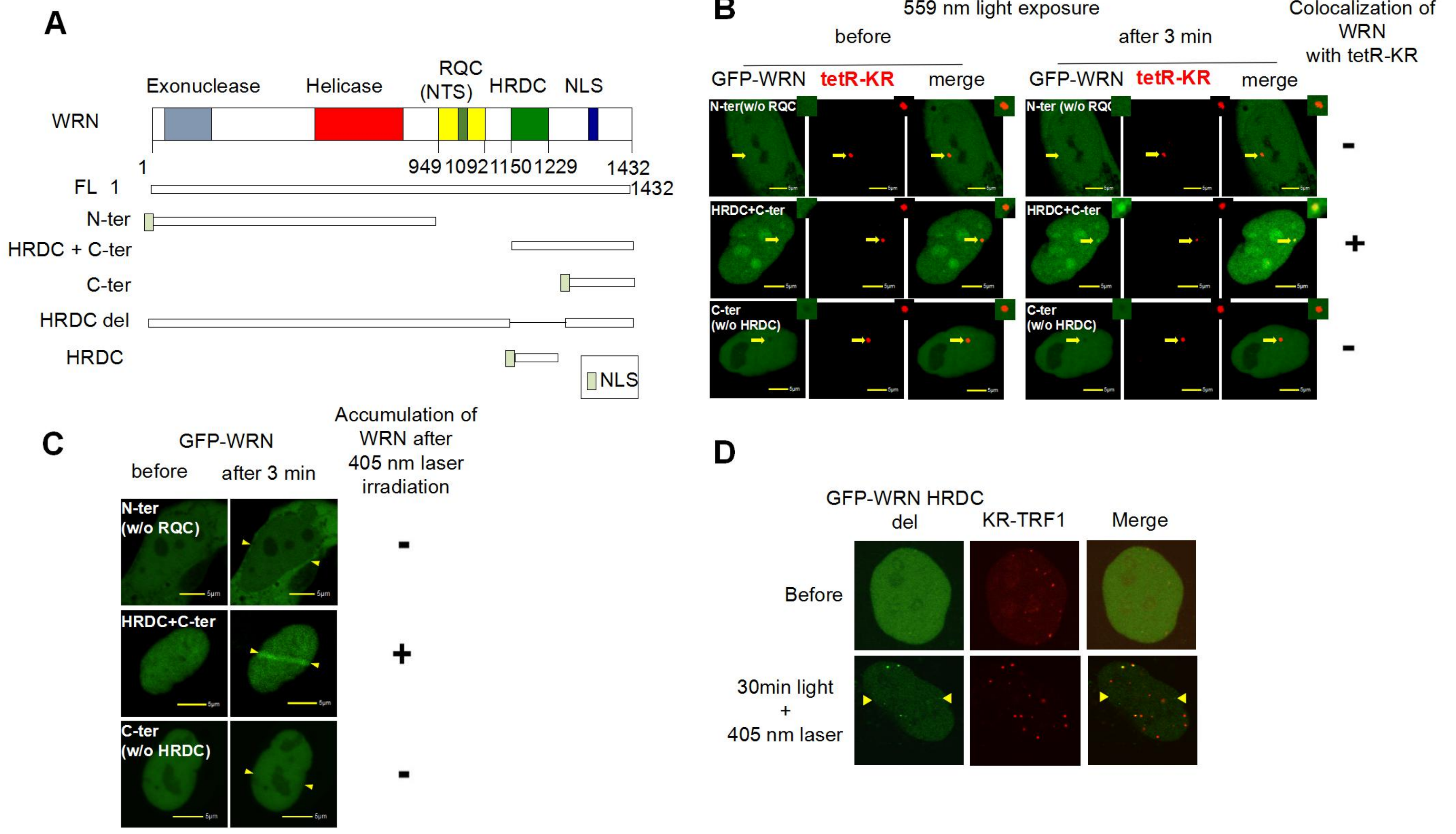
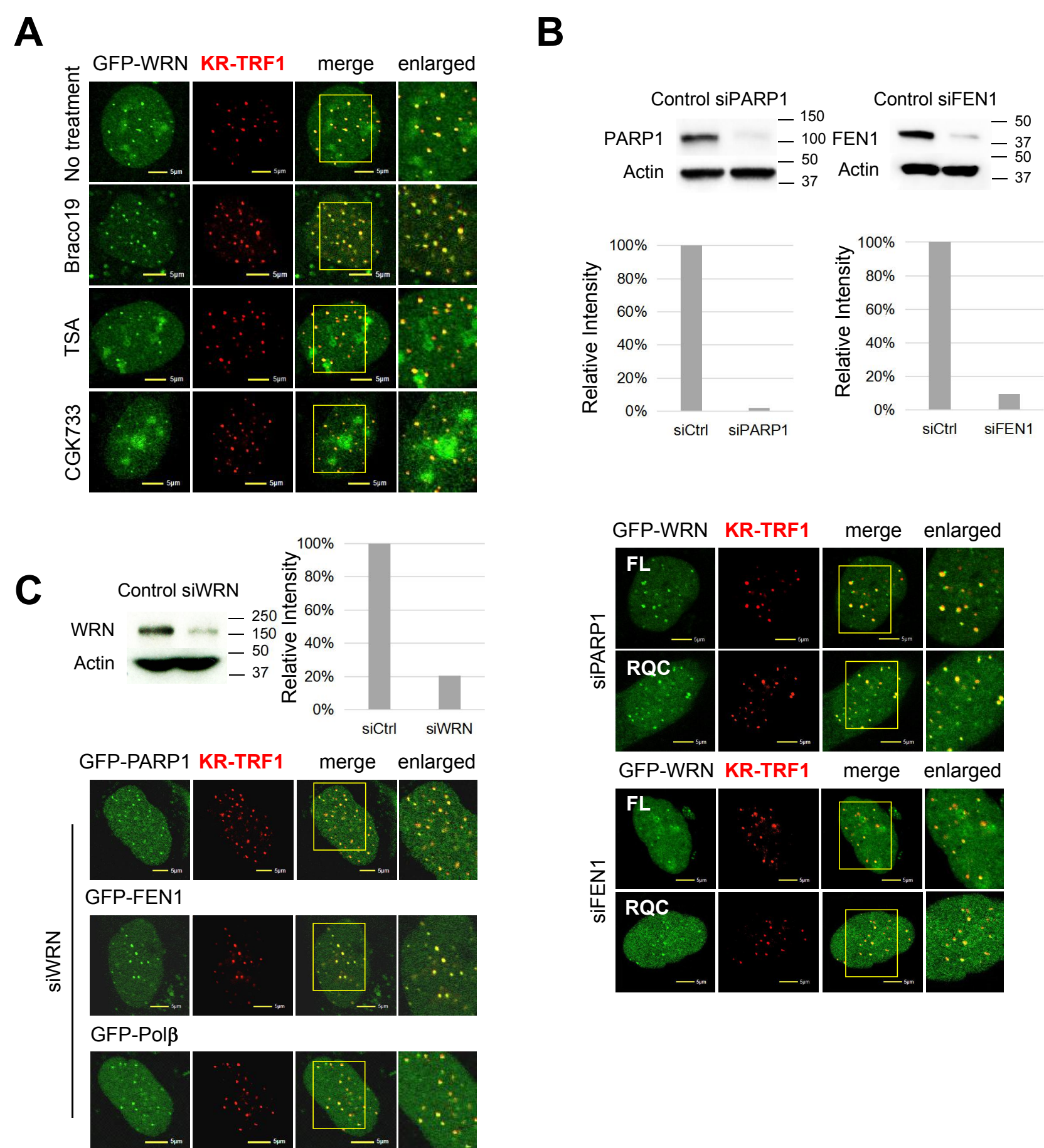


Supplementary Figure 1

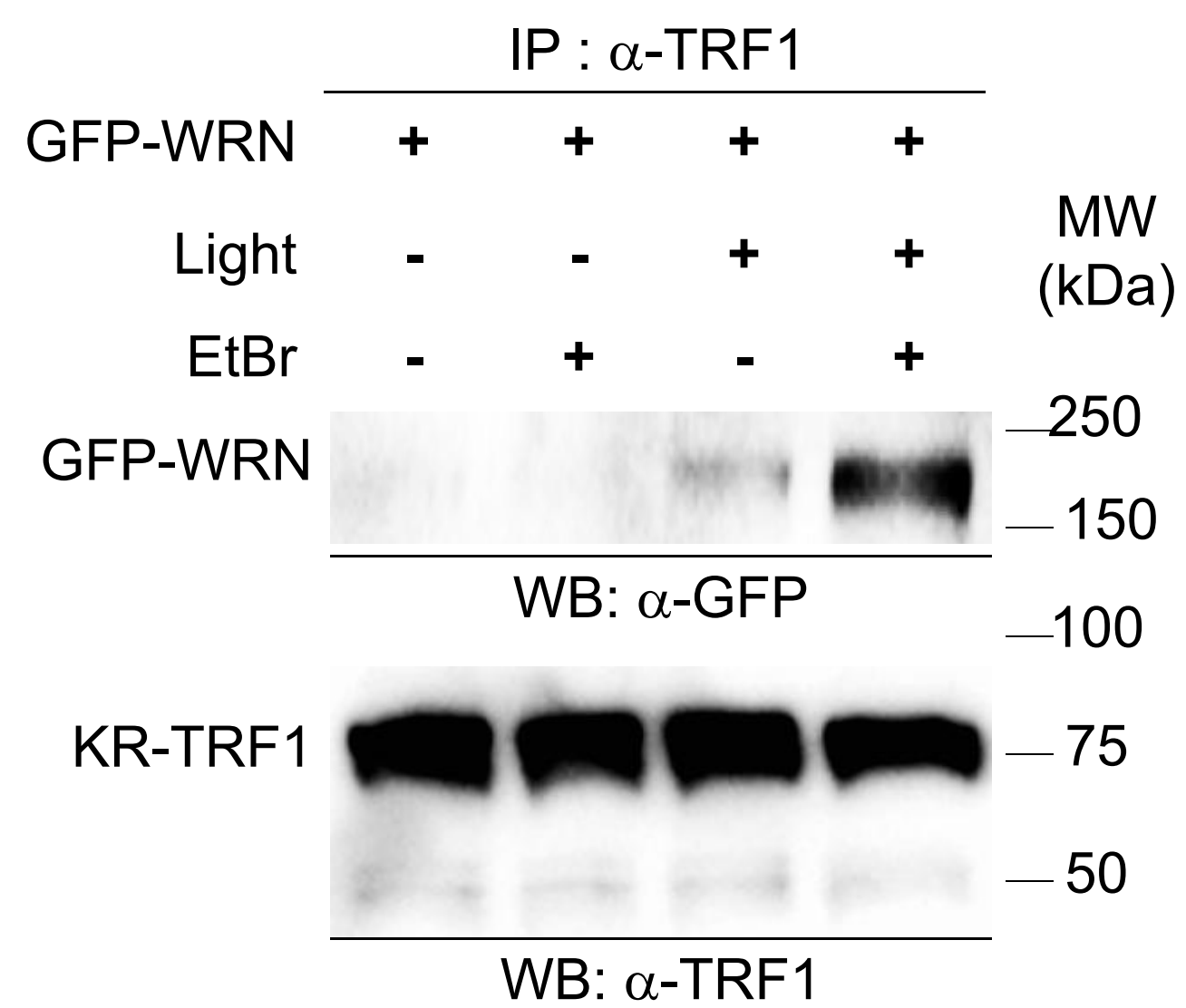
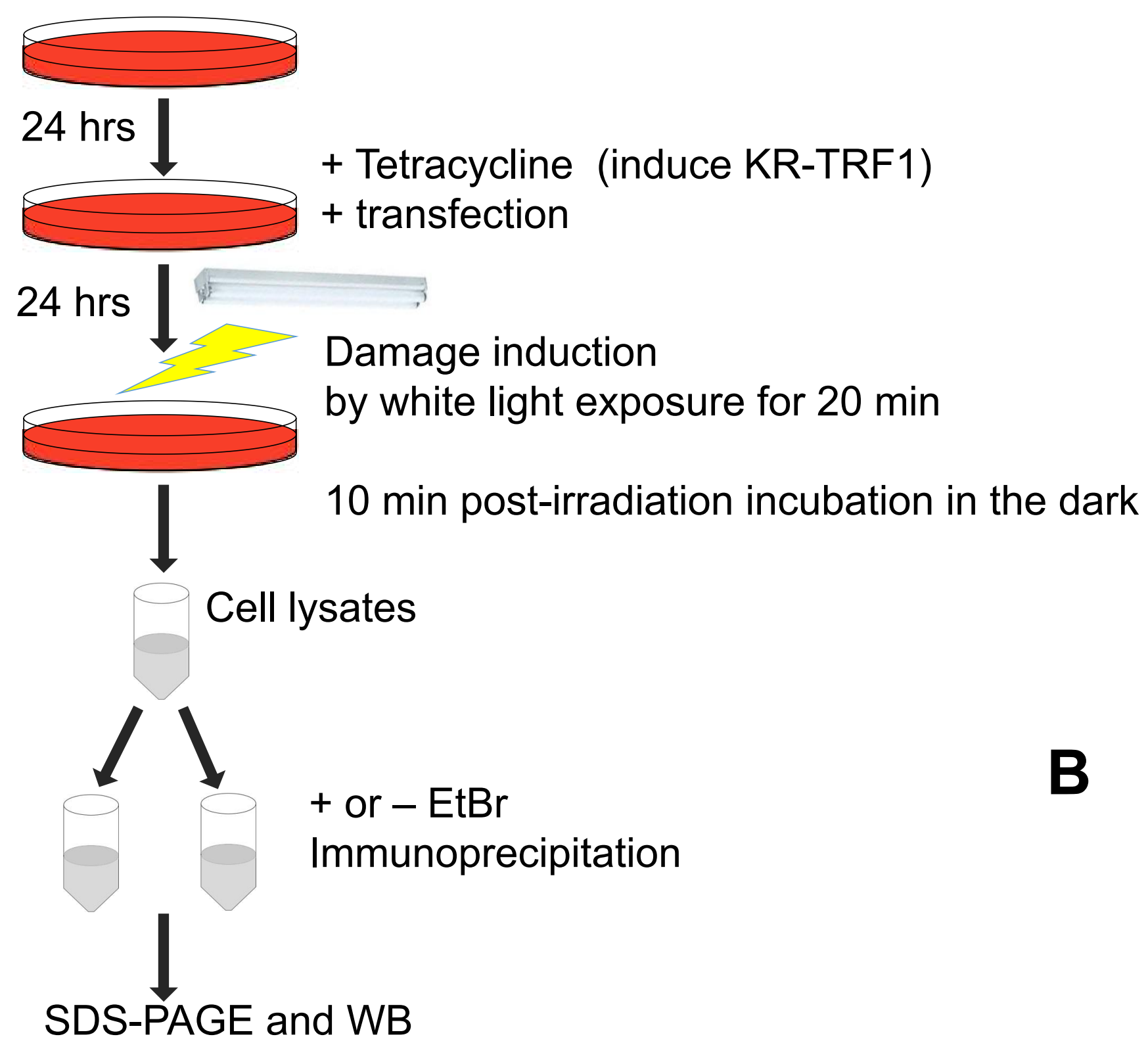


Supplementary Figure 2

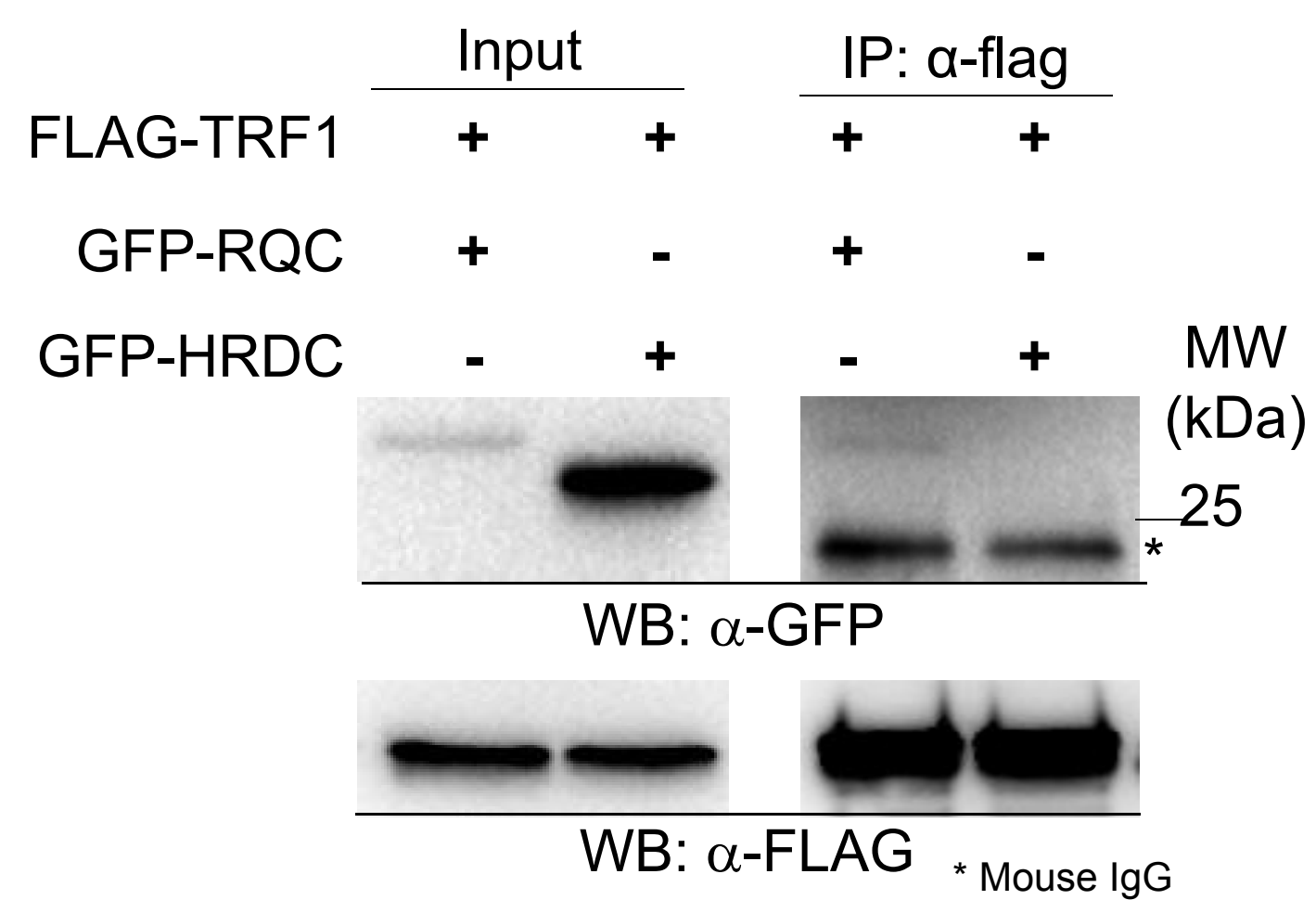


Supplementary Figure 3

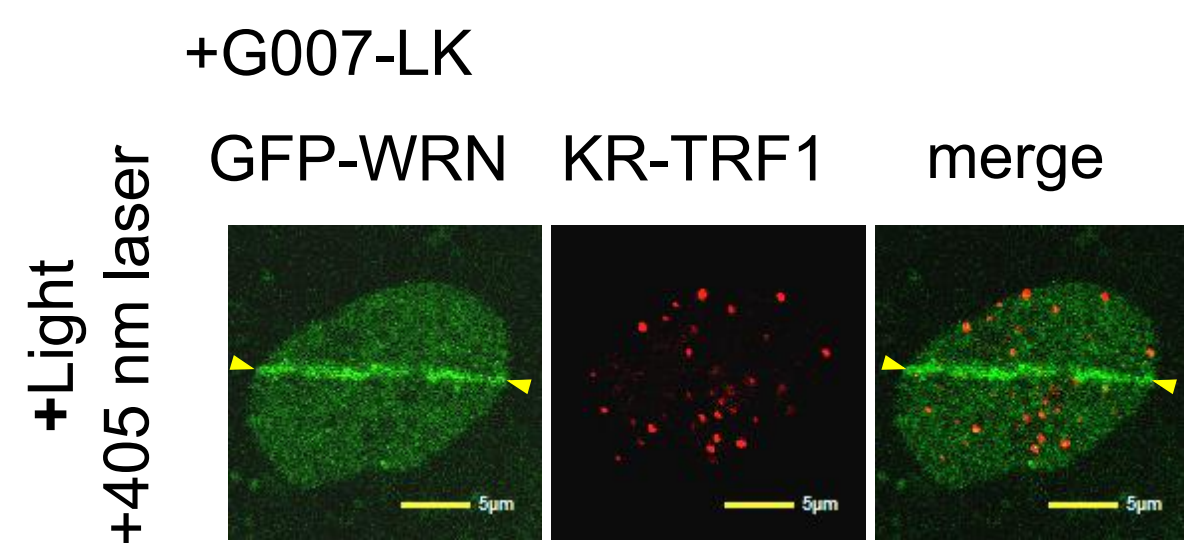
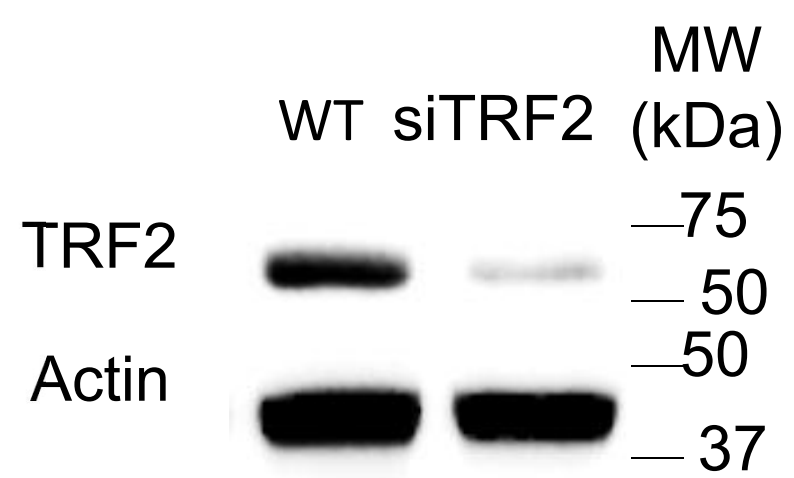
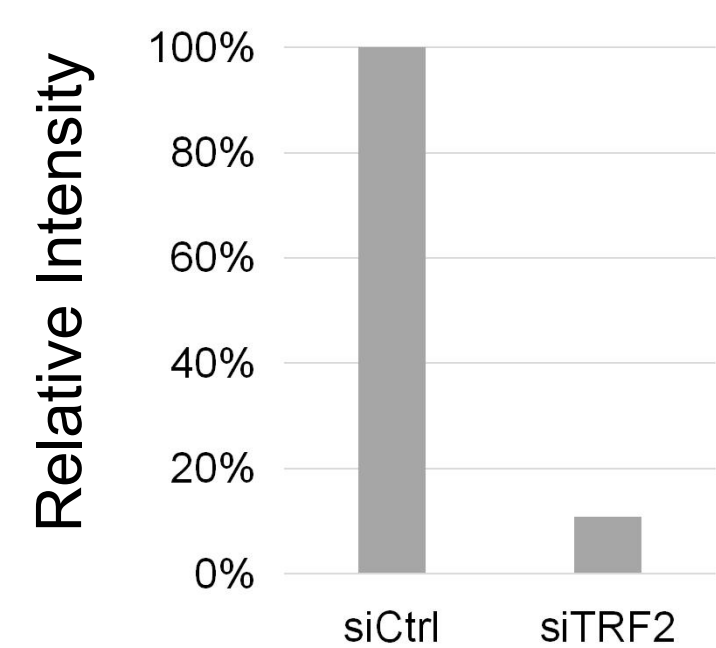
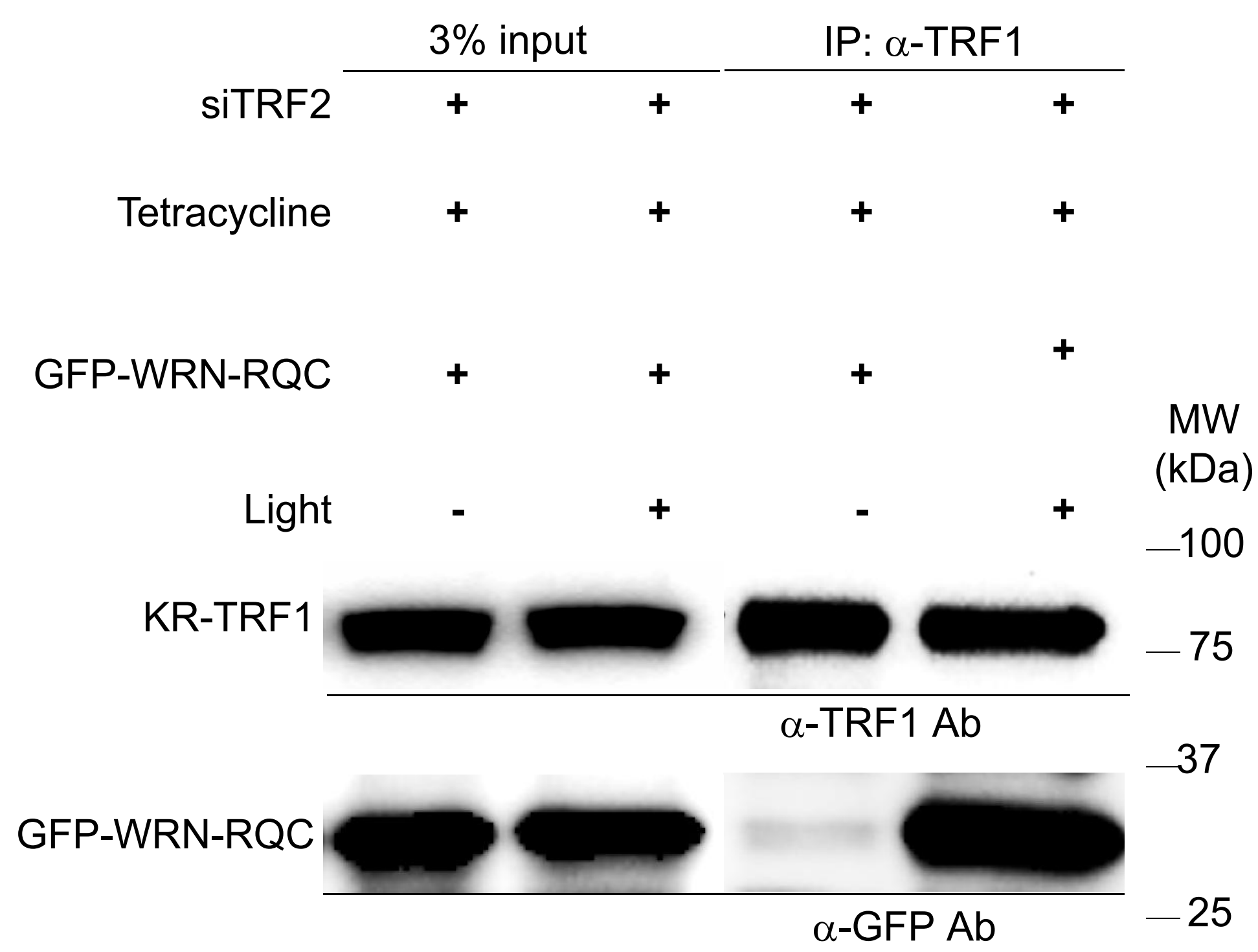
A



B

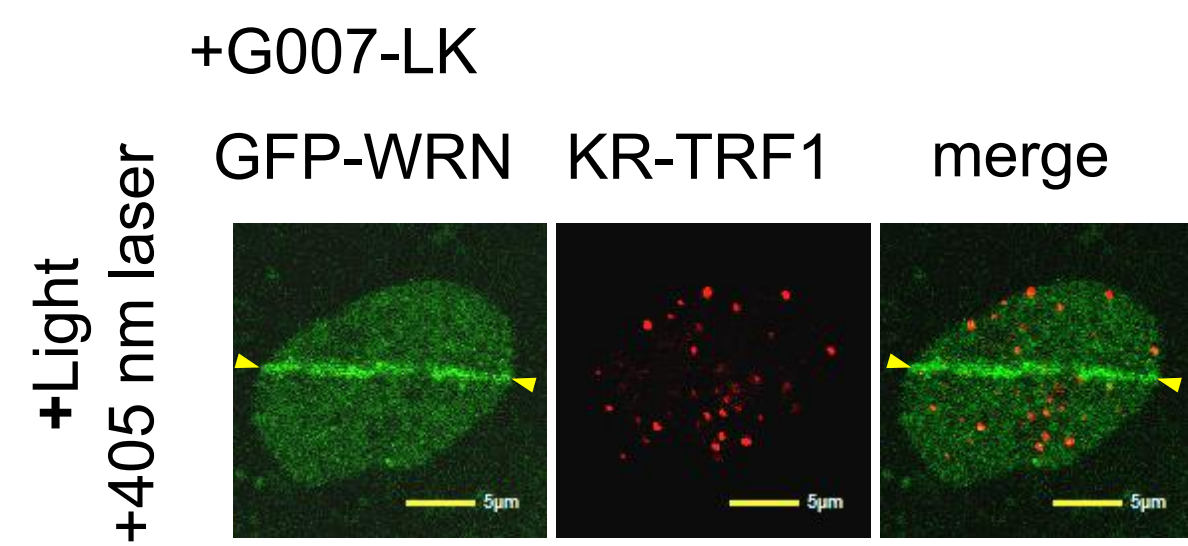


Supplementary Figure 4

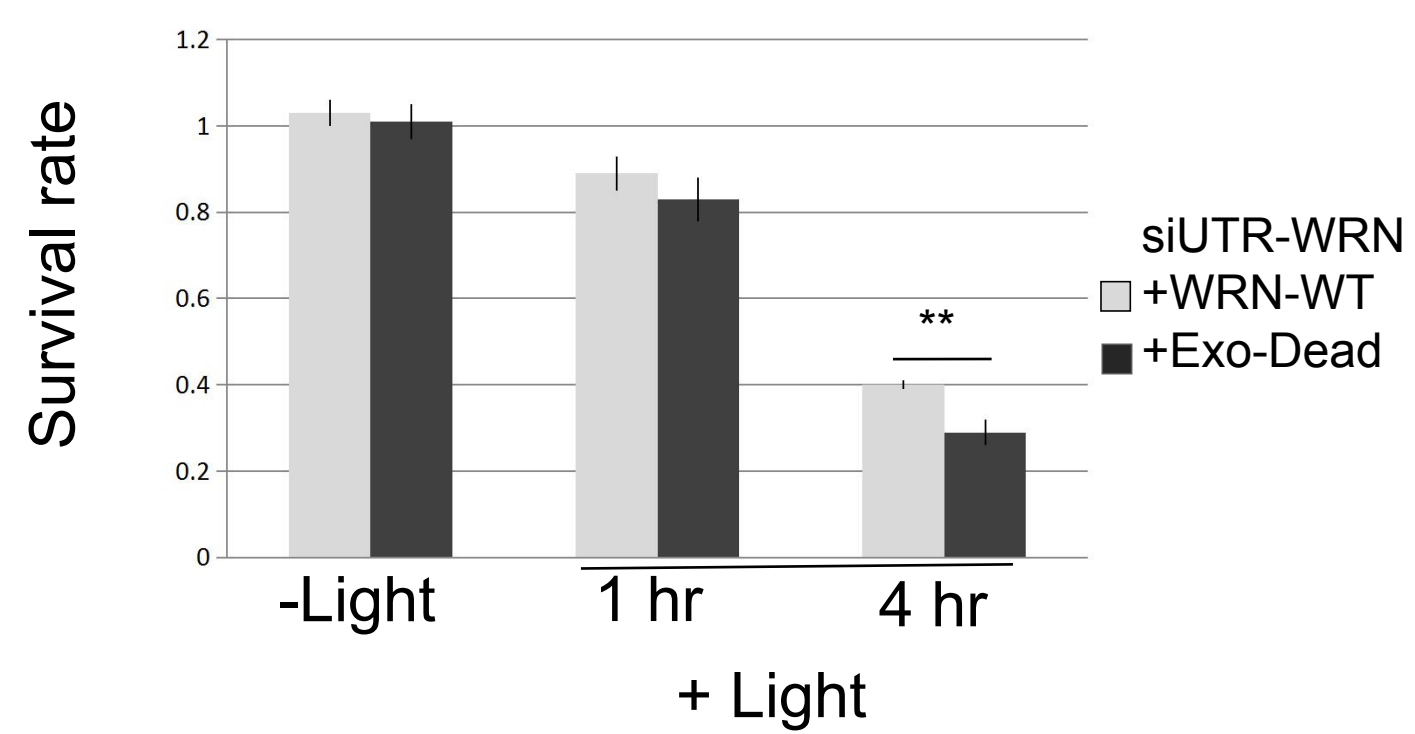
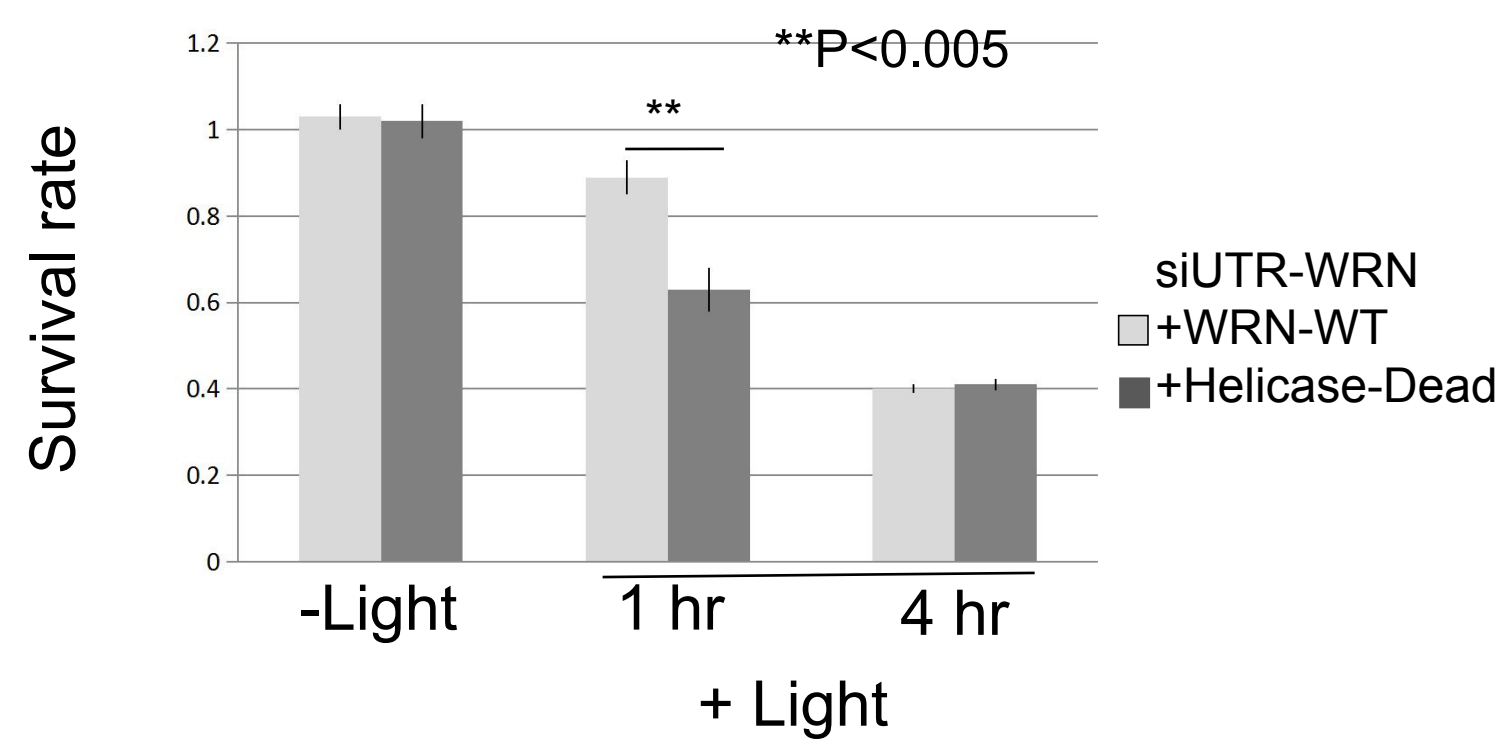


Supplementary Figure 5

A



B



Supplemental Information

Supplementary Data

Figure S1. Damage response of WRN domains at sites of tetR-KR and 405 nm laser induced damage. **A.** Schematic representation of HRDC related domains of WRN. Recruitment of the GFP-tagged WRN N-terminal without the RQC domain, C-terminal with the HRDC domain (HRDC), and C-terminal without the HRDC domain to sites of tetR-KR induced damage before (left) and 3 min after (right) 559 nm laser bleaching. **B.** Recruitment of truncated WRN described in (A) to 405 nm laser induced damage before (left) and 3 min after (right) 405 nm laser irradiation for 500 msec. The laser bleaching area is indicated with a yellow arrowhead. **C.** Recruitment of truncated WRN HRDC-Del described in (A) to 405 nm laser-induced damage and KR-TRF1 induced telomeric damage. **D.** HRDC is not recruited to KR-TRF1 induced telomeric damage after 559 laser bleaching.

Figure S2. The damage response of WRN domains at sites of KR-TRF1 is not affected by repair factor deficiency. **A.** U2OS cells were transiently transfected with GFP-tagged WRN FL and KR-TRF1 followed by treatment with the indicated inhibitors. Recruitment of GFP-tagged WRN FL to KR-TRF1 induced damage at telomeres is shown. **B.** The recruitment of WRN FL and the RQC domain to oxidative damage at telomeres is not affected by PARP1 and FEN1 suppression. Recruitment of WRN FL and RQC was observed in U2OS cells after siPARP1 and siFEN1 treatment. Images at 3 min after 559 nm laser light exposure or without laser light exposure of KR-TRF1 are shown. Yellow rectangles indicate the enlarged area. Suppression of PARP1 and FEN1 in U2OS cells is shown by WB. **C.** Recruitment of GFP-tagged PARP1, FEN1 and Pol β was observed in U2OS cells after siWRN treatment. Images at 3 min after 559 nm laser light exposure of KR-TRF1 are shown. Yellow rectangles indicate the enlarged area.

Figure S3. The interaction between WRN and TRF1 is not mediated by DNA. **A.** Schematic representation of the experimental procedure for immunoprecipitation with EtBr treatment. KR-TRF1 stably expressing Flp-in T-REx 293 cells were treated with or without 20 min cool white fluorescent bulb light exposure to activate KR and incubated in the dark for 10 min. Cell lysates were aliquoted and treated with or without 100 μ g/ml ethidium bromide (EtBr) throughout the entire immunoprecipitation process. Cell lysates were immunoprecipitated with α -TRF1. The precipitates and 3% of the lysate (input) were immunoblotted with α -GFP and α -TRF1. **B.** KR-TRF1 stably expressing Flp-in T-REx 293 cells were cotransfected with FLAG-tagged TRF1 and GFP-WRN-RQC or GFP-WRN-HRDC. Cell lysates were immunoprecipitated with α -FLAG and immunoblotted with α -FLAG and α -GFP.

Figure S4. The interaction between WRN and TRF1 is not mediated by TRF2. The interaction of WRN-RQC and TRF1 is not mediated by TRF2. KR-TRF1 stably expressing Flp-in T-REx 293 cells were treated with or without siTRF2 to suppress TRF2. Twenty-four hours post siRNA transfection, cells were transfected with GFP-WRN-RQC and tetracycline was added to induce KR-TRF1 expression. Cells were treated with or without 20 min cool white fluorescent bulb light exposure to activate KR and incubated in the dark for 10 min. Cell lysates were immunoprecipitated with α -TRF1. The precipitates and 3% of the lysate (input) were immunoblotted with α -GFP and α -TRF1. A western blot of siTRF2 is shown (bottom).

Figure S5. Recruitment of GFP-WRN FL to 405 nm laser induced damage is not affected by the TNKS1 inhibitor, G007-LK. **A.** U2OS cells were transfected with GFP-WRN and KR-TRF1, followed by treatment with G007-LK. Recruitment of GFP-WRN FL to 405 nm laser-induced damage for 500 msec is shown. The laser bleaching area is indicated with a yellow arrowhead. **B.** Clonogenic survival assay of HeLa cells with stably expressed KR-TRF1 after siUTR-WRN with the expression of WRN-WT, exonuclease dead (E84A) or helicase dead (K577M). Cells were exposed to cool white fluorescent light for the indicated time. Data are represented as mean \pm SEM of 3 independent experiments.