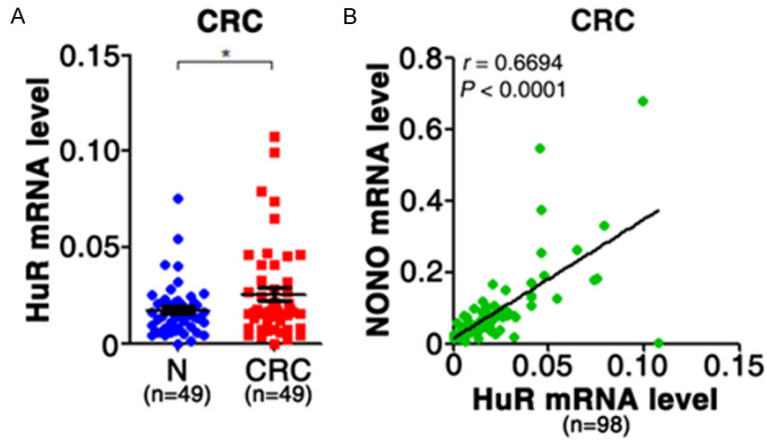
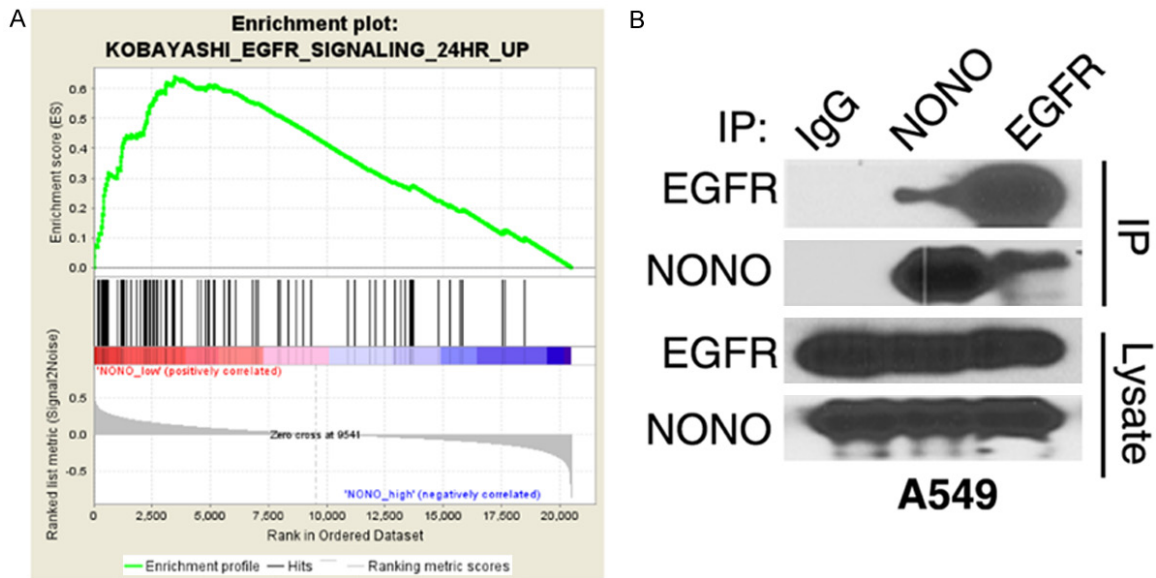


NONO phase separation promotes tumor radioresistance

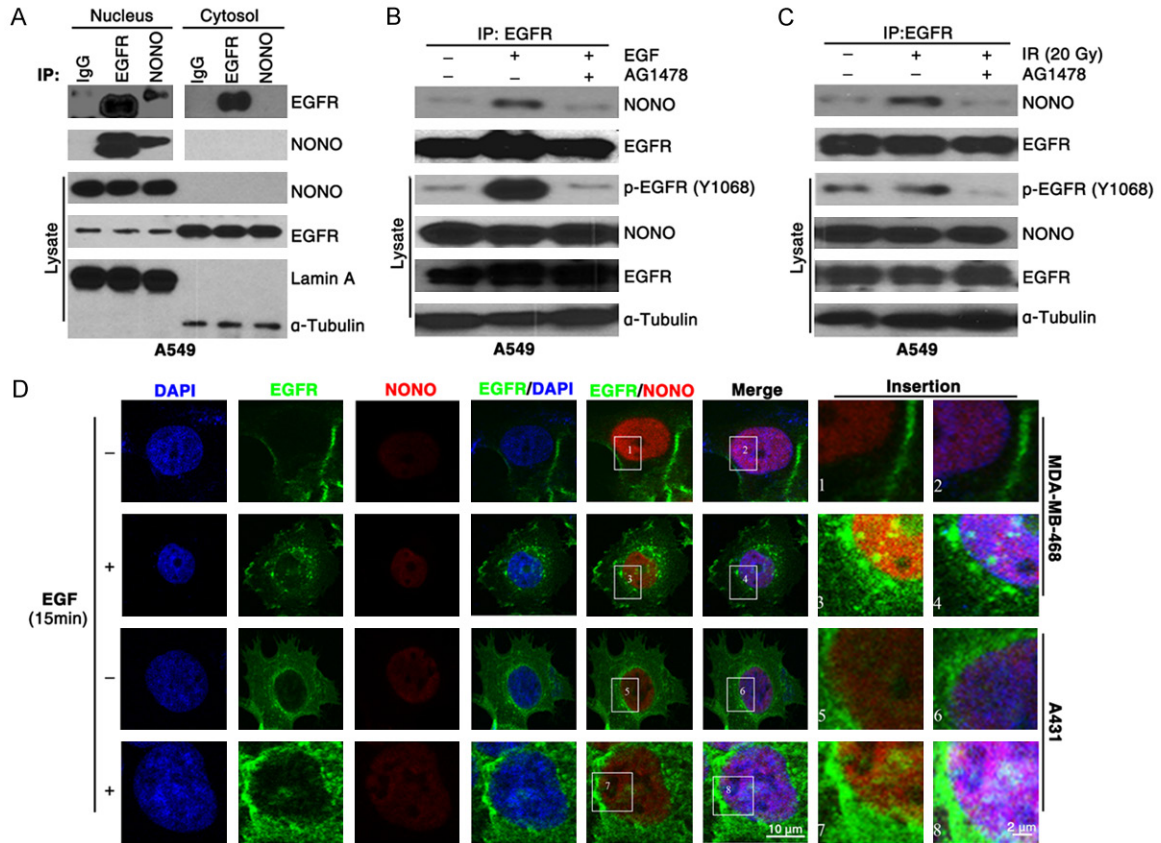


**Figure S1.** HuR was upregulated in CRC tissues and its level was correlated with NONO expression. A. HuR mRNA level of CRC tissue was examined with qPCR. B. HuR mRNA level was positively correlated with NONO mRNA level in CRC tissues. \*,  $P < 0.05$ .

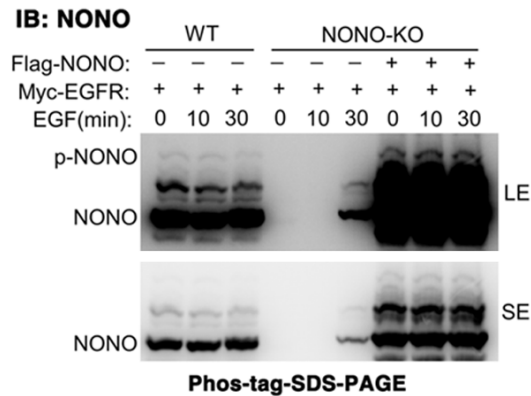


**Figure S2.** Association of NONO and EGFR. A. NONO-correlated genes were enriched in EGFR pathway. B. The association of NONO and EGFR in A549 cells were investigated using CoIP assay.

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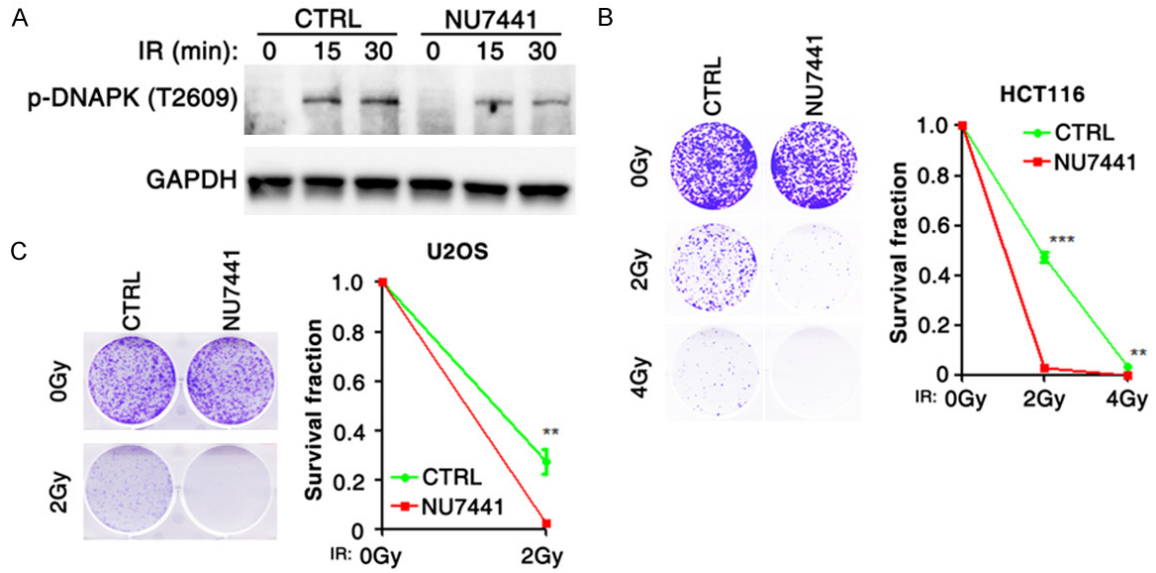


**Figure S3.** NONO and nEGFR are associated in nucleus. (A) the cytoplasmic and nuclear proteins were fractionated from A549 cells and subjected to CoIP assay with anti-NONO and anti-EGFR antibodies. (B, C) EGF treatment (B) and irradiation (C) enhance the interaction of NONO and EGFR. After EGF (10 ng/mL) or irradiation (20 Gy) treatment, CoIP assay was conducted with anti-EGFR antibody. (D) EGF treatment enhances the association of NONO and EGFR in nucleus. IF assay was conducted with anti-EGFR and anti-NONO antibodies in MDA-MB-468 and A431 cell lines.

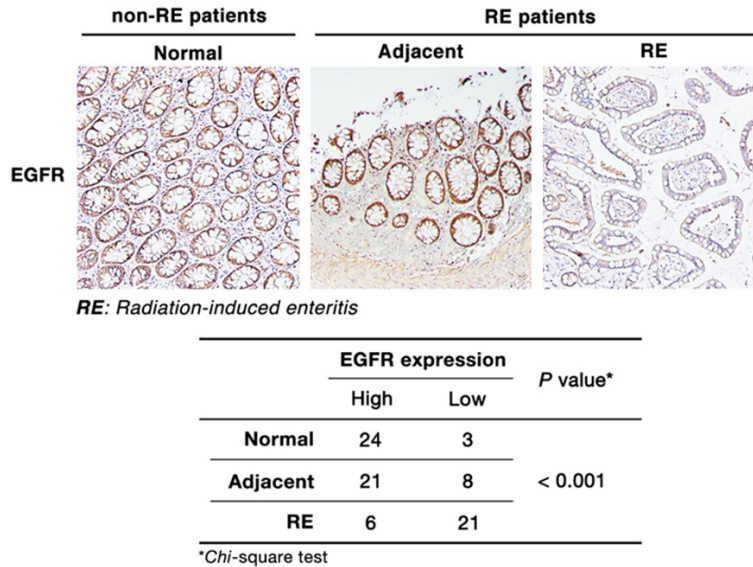


**Figure S4.** Phosphorylated NONO was detected in NONO re-expressing NONO-KO cells. HEK 293T cells were transfected with indicated plasmid and treated with EGF before Phos-tag-SDS-PAGE analysis.

## NONO phase separation promotes tumor radioresistance



**Figure S5.** NU7441 sensitized tumor cells to radiation. A. NU7441 reduced the radiation-induced p-DNA-PK-T2609 in U2OS cells. B, C. NU7441 sensitized HCT116 and U2OS cells to radiotherapy. \*\*,  $P < 0.01$ ; \*\*\*,  $P < 0.001$ .



**Figure S6.** EGFR was down-regulated in radiation-induced enteritis tissues. The expression of EGFR protein in RE or adjacent normal tissues from RE patients, as well as normal colon tissues from CRC patients without radiotherapy, were examined with IHC assay.