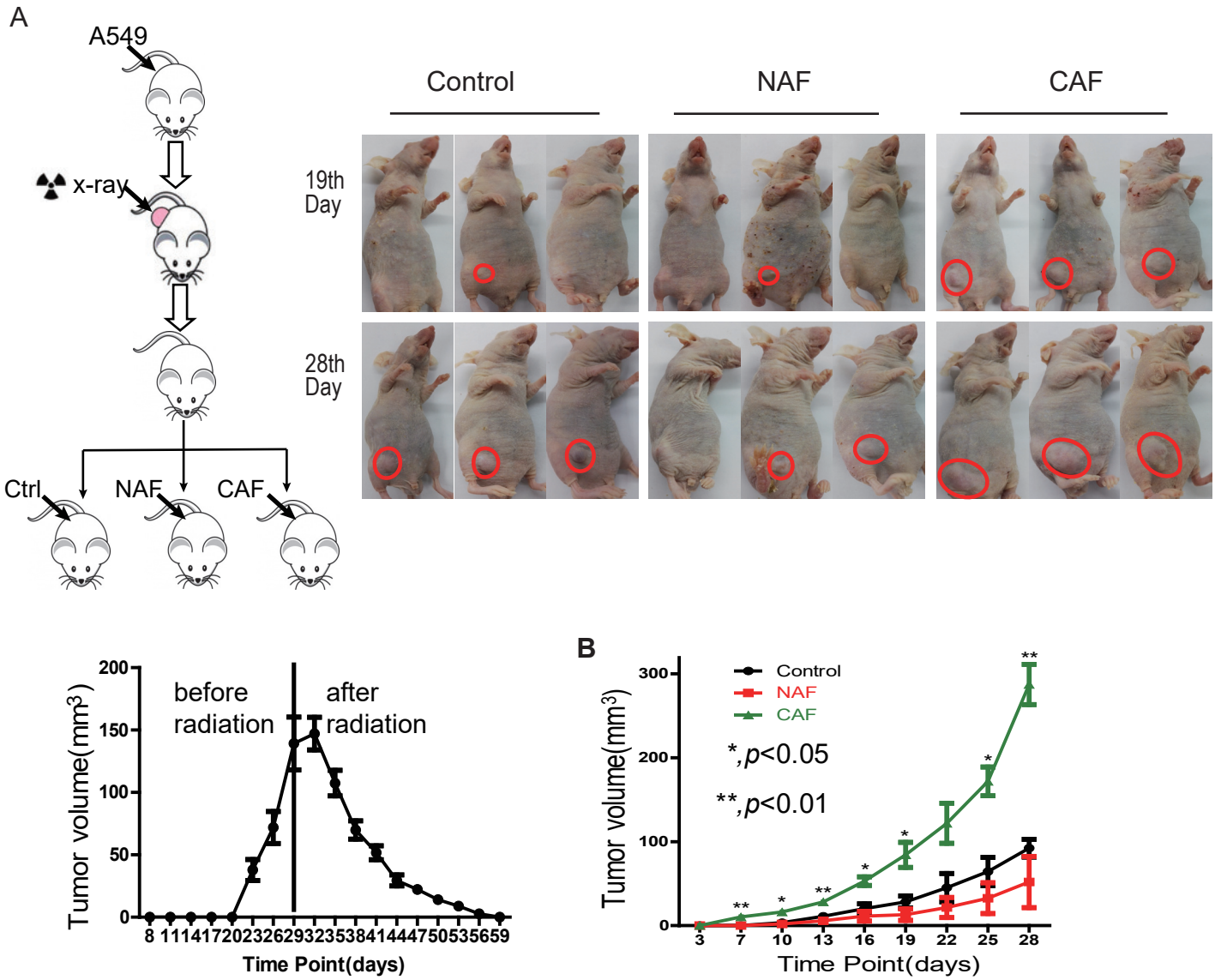


Figure S1 CAF promotes lung cancer recurrence post-radiation in the xenografted mouse model.

A. The representative tumors at the indicated time points post-radiation in the group of CAF, NAF and control. Tumors were locally recevied radiation at a total dose of 30 Gy in 5 fractions of 6 Gy.

B. Tumour volumes (median ± SD) at the indicated time points.

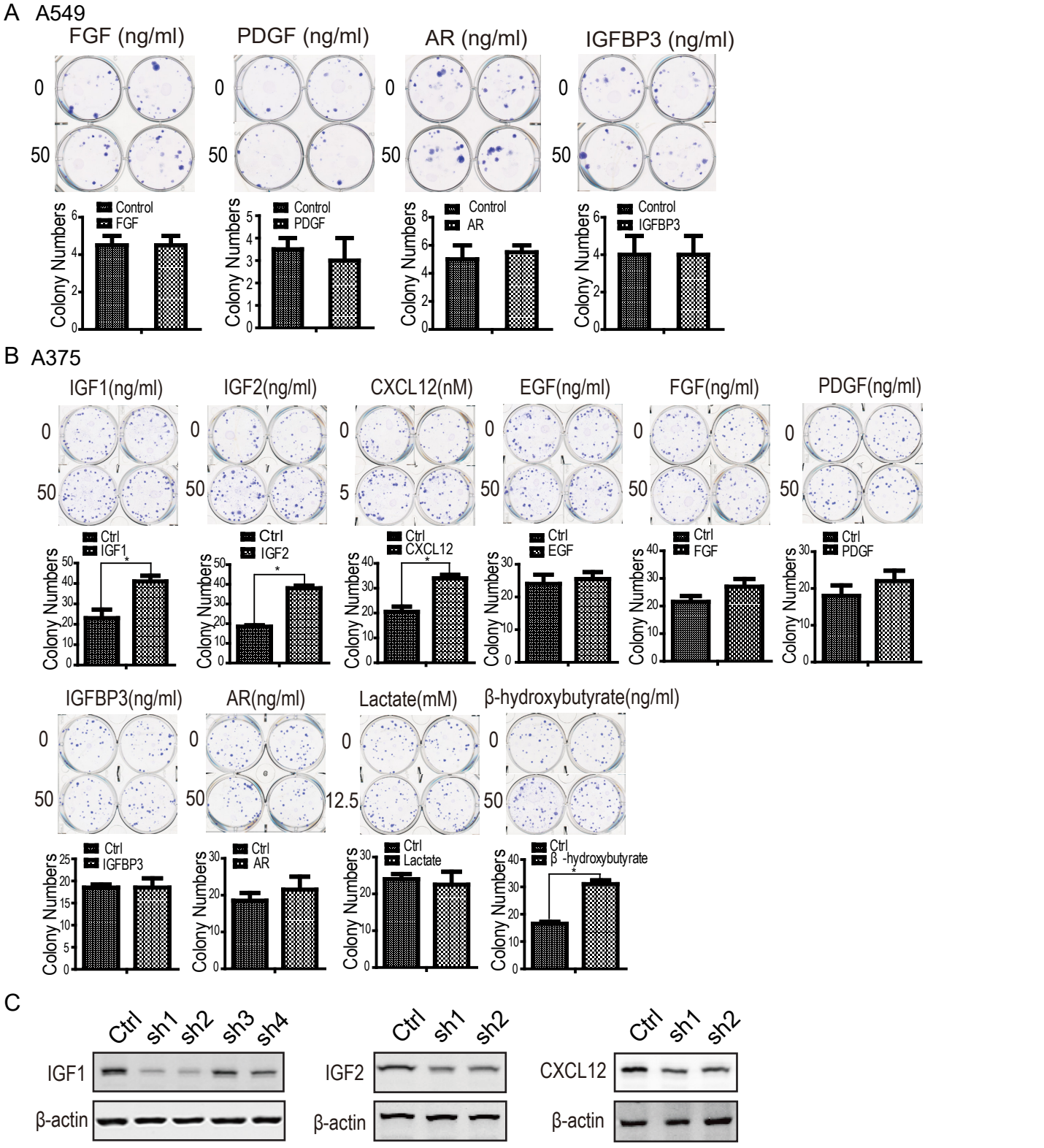


Figure S2 CAF-derived cytokines promote cancer cell recovery post-radiation

A. The other upregulated cytokines, such as FGF, PDGF, AR or IGFBP3, did not promote A549 cell recovery from radiation-induced damage. **B.** IGF1/2 and CXCL12 also mediated CAF-promoted melanoma A375 cell recovery post-radiation. Cytokines/chemokines were added into culture medium rigth after radiation. C. Knockdown efficiency analysis by Western blotting.

Figure S3

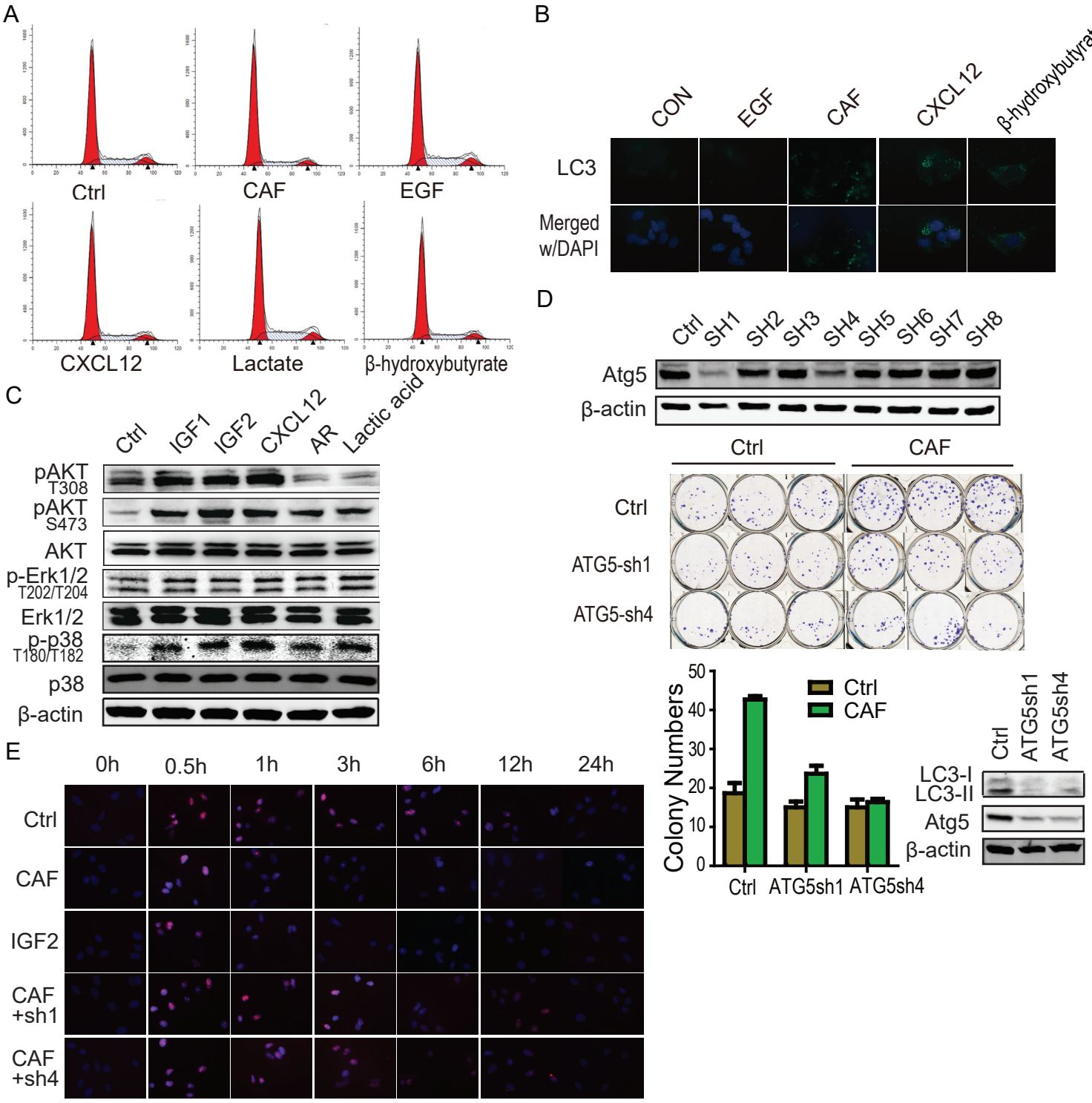


Figure S3 CAF induces autophagy, but not dormancy in cancer cell post-radiation

A. Representative cell cycle analysis data of A549 cells 24 hours post-radiation. The cells were co -cultured with CAF-conditioned medium or its-secreted cytokines.

B. Immunofluorescency staining of autophagy marker LC3.

C. CAF did not induce dormancy in lung cancer A549 cells 2 hrs post-radiation. Three dormancy markers were analyzed by immunoblots in A549 cells treated with IGF1/II, CXCL12, AR or lactate.

D. Depletion of Atg 5 abolished rapamycin-induced autophagy. Atg 5 successfully knocked down in A549 tumor cells by the 1st and 4th lentiviruses-mediated shRNA.

E. Images of γ-H2Ax merged with DAPI.

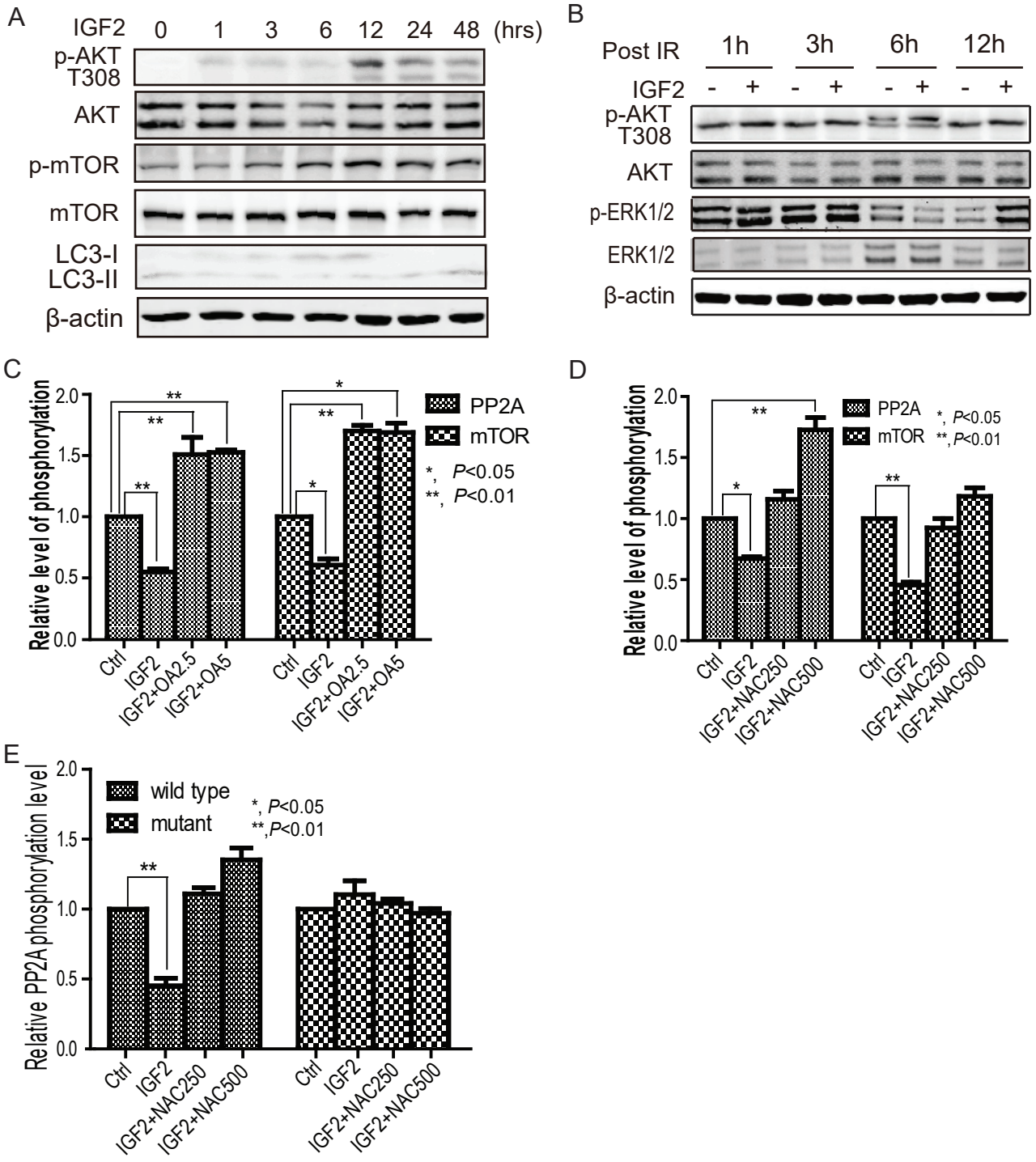


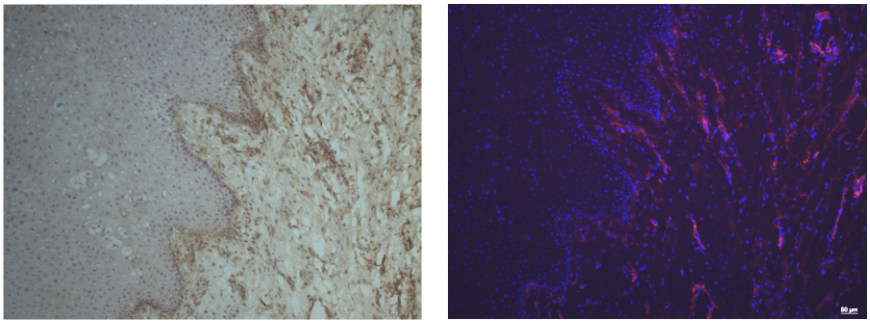
Figure S4

A. IGF2 activates AKT-mTOR pathway without radiation.

B. IGF2 did not supress the upstream kinase activity of mTOR post radiation. The phosphorylation of AKT and ERK were detected by Western blot.

C-E. Quantitative analysis of phosphorylation level of PP2A and mTOR by densitometry.

A

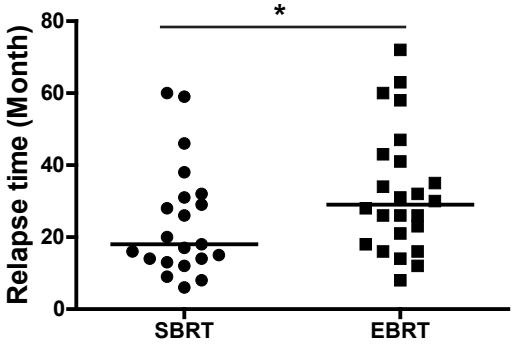


FAP (IHC) FAP (IF)

B

	Cases	Age (Median)	Stage II/Stage I
SBRT	40	73	33/7
EBRT	33	67	25/8

C



D

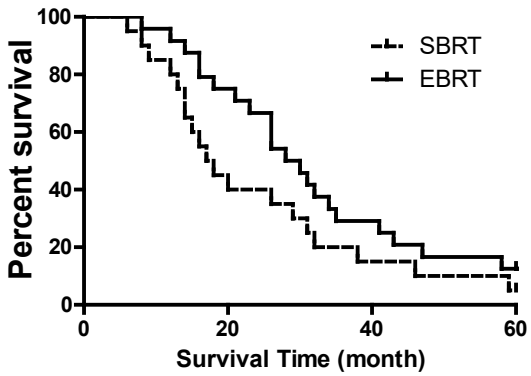


Figure S6 The SBRT therapy accelerated the liver cancer recurrence and shortened the survival of patients.

A. FAP immunohistochemistry and immunofluoresence analysis at the edge of breast cancer. Two sections were sequentially adjacent. The magnification was 100 X.

B. The statistical information for lung cancer patients involved in the clinical study.

C. The SBRT treatment accelerated the recurrence of patients beard with liver cancer, compared to the EBRT treatment (*, $p<0.05$). The cancers were unresectable; the total radiation dose was 65 ± 5 Gy.

D. The SBRT treatment shortened the survival of patients beard with liver cancer ($p<0.05$), compared to the patients with the EBRT treatment. The survival was analyze by the Kaplan-Meier method.

Figure S7

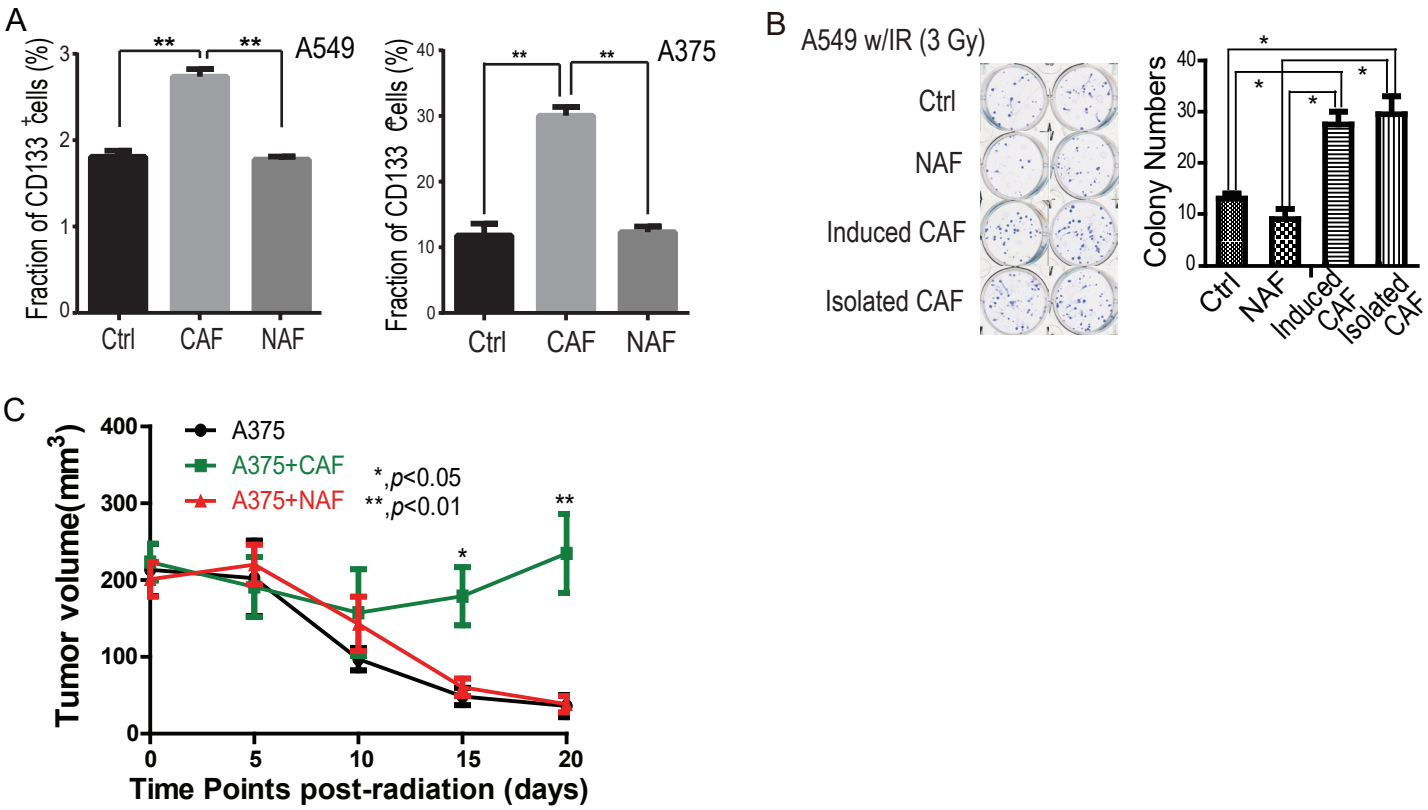


Figure S7 Pre-existing of CAFs promote radiation resistance of cancer cells.

A. FACS analysis on the CD133⁺ tumour stem-like cell in lung cancer A549 cells and melanoma A375 cells *in vitro* (**: p<0.01); Tumour cells were cultured in the CAF- or NAF- conditioned medium for 96 hours, fresh medium was considered as control.

B. Coloney formation analysis of A549 cells post-radiation. A549 cells were cultured in CAF- or NAF -conditioned medium 48 hours before radiation treatment. The colonies were counted and visualized by histogram (mean ± SD).

C. Tumor growth post-radiotherapy. Melanoma A375 cells were inoculated into nude mice at the 1 X 10^6 cells per injection.