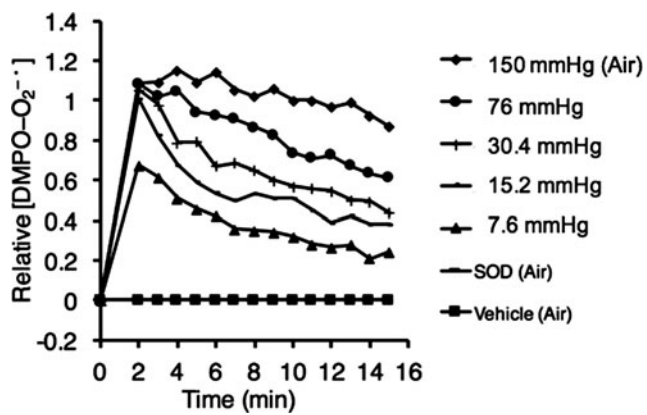
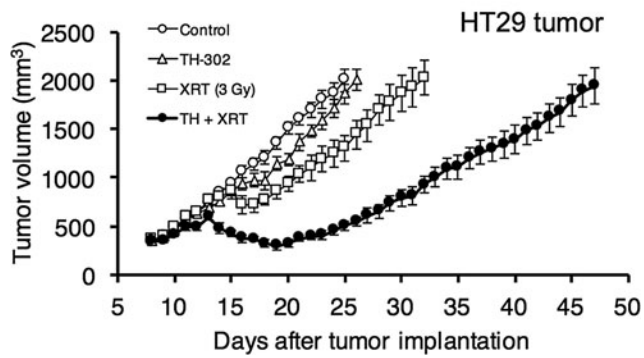
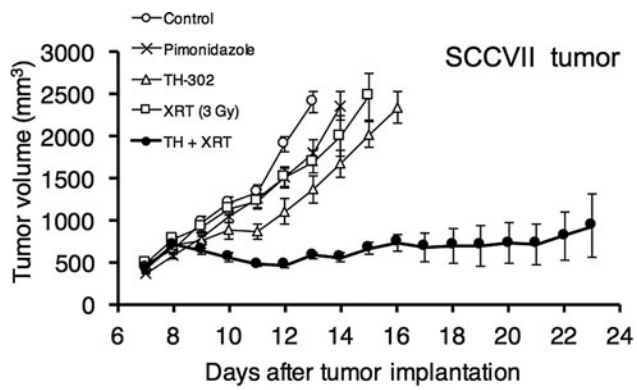


**SUPPLEMENTARY FIG. S2. Effect of PEG catalase on the toxicity of TH-302.** A total of  $5 \times 10^4$  SCCVII cells and  $2 \times 10^5$  HT29 cells were plated on a six-well plate 24 h before treatment. Cells were treated with TH-302 and PEG catalase at various concentrations, as indicated in the figure. The plates were then placed in a desiccator set at 0% oxygen by flowing 5% CO<sub>2</sub> 95% N<sub>2</sub> gas for 2 h. After treatment, the culture media were replaced and the plates were incubated for 48 h and the number of cells were counted. The Y axis represents the number of cells when the no drug treatment group was scaled to 1. PEG, polyethylene glycol.



**SUPPLEMENTARY FIG. S3.** A plot of [DMPO-O<sub>2</sub><sup>-</sup>] signal (every 1 min) recorded for 15 min under the indicated condition of enzymatic reaction at 37°C using pimonidazole (1 mM). Experimental condition is identical to Figure 1D.



**SUPPLEMENTARY FIG. S4. Tumor growth data of Figure 4.** SCCVII data include the pimonidazole treatment group that showed weak–none antitumor effect compared with TH-302.