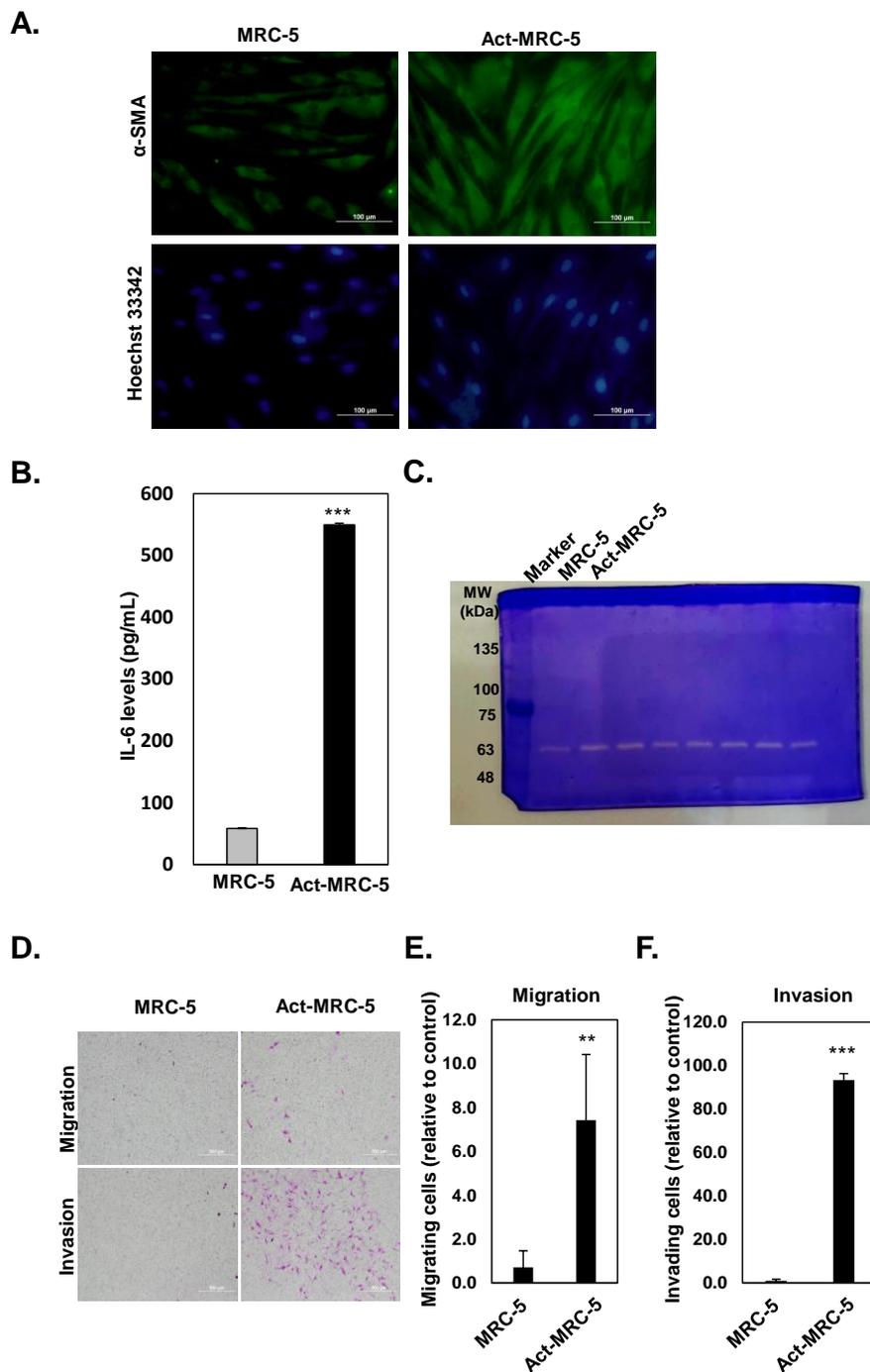


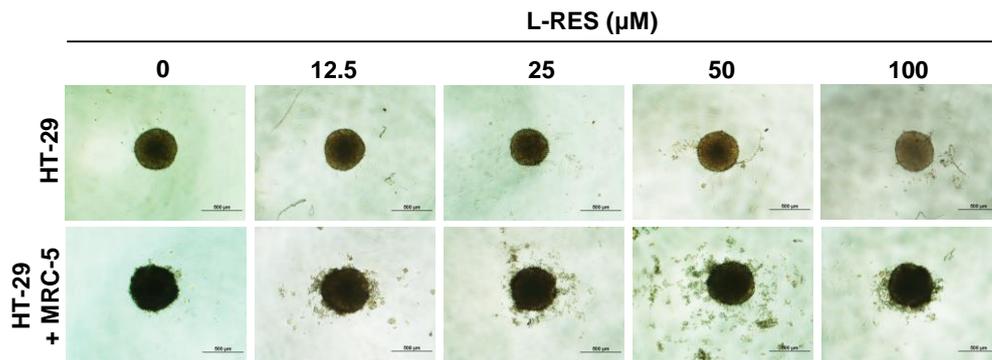
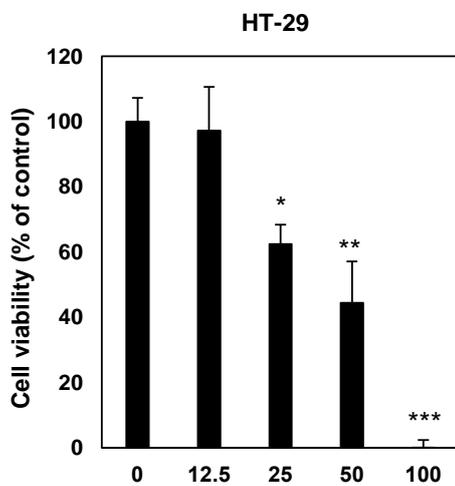
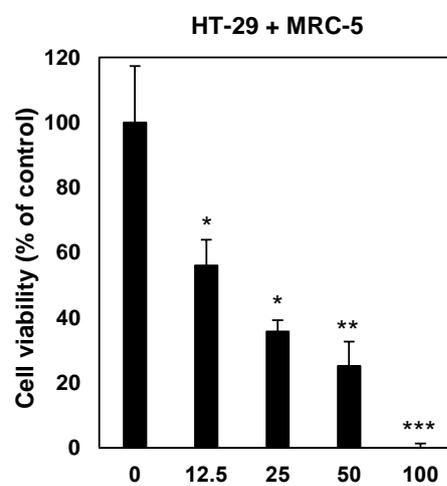
## Supplementary file



**Figure. S1. CRC-cell-derived conditioned medium used to induce activated fibroblasts.**

Normal human fibroblast cells (MRC-5 cells) were treated with HT-29 cells derived conditioned medium for 24 h. (A) Expression of  $\alpha$ -SMA in the MRC-5 normal human fibroblast cells was determined by immunocytofluorescent labeling. (B) IL-6 levels in

conditioned medium of MRC-5-treated cells analyzed by ELISA. (C) MMPs 2/9 activities (D) Cell migration and cell invasion abilities of MRC-5-treated cells analyzed by Boyden chamber assay. The migrated and invaded cells were captured using an inverted microscope with 5 fields/well, in triplicated well at 10× magnification. Relative of migrated cells (E) and invaded cells (F) are presented (untreated control cells = 100%). The data are means ± SD from the representative experiments. \*\* $P < 0.01$ .,\*\*\* $P < 0.001$ .

**A****B****C**

**Figure. S2. Activated-fibroblast-containing tumor spheroid was more sensitized to L-RES.** The tumor spheroids of monoculture of HT-29 tumor spheroid (upper panel) or co-cultured HT-29 and MRC-5 cells (lower panel) were established. Three-day-old spheroids were treated with L-RES at various concentrations (12.5–100  $\mu\text{M}$ ) for 48 h. (A) The morphology of the tumor spheroid was observed under inverted microscope at 4 $\times$  magnification. Scale bar = 500  $\mu\text{m}$ . Dot boxes emphasize the minimum concentration in which spheroid deformity was observed. (B) Quantitative analysis of cell viability of monoculture tumor spheroid or (C) Quantitative analysis of co-cultured tumor spheroid was determined using ATPlite luminescence assay. The data are means  $\pm$  SD from the representative experiments. \* $P < 0.05$ ., \*\* $P < 0.01$ , \*\*\* $P < 0.001$ .