

Supplemental Materials and Methods

Antibody-mediated neutralization

HDP spheroids were treated with 20 $\mu\text{g}/\text{mL}$ loliolide and/or 1 $\mu\text{g}/\text{mL}$ neutralizing antibody against VEGF, IGF-1, KGF and normal mouse IgG (R&D System, Minneapolis, MN, USA) for 48 h. After treatment, the diameters of spheroids were quantified using phase contrast images.

Supplemental Figure legends

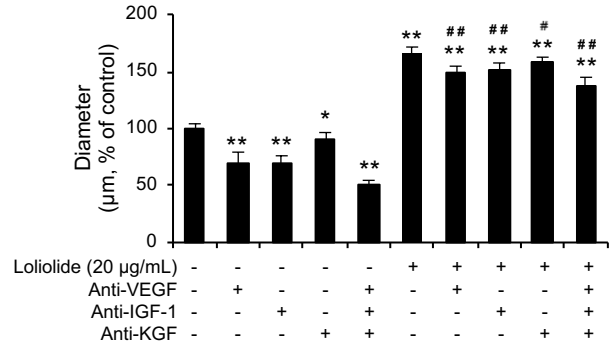
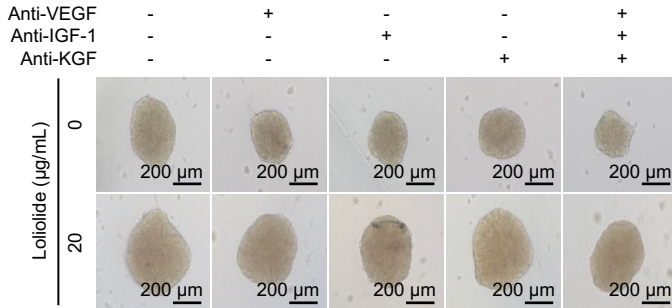
Fig S1. Effects of loliolide on regulation of growth factors in HDP spheroids.

(A) Neutralization of growth factors was analyzed by neutralizing antibodies, Anti-VEGF, Anti-IGF-1 and Anti-KGF, and normal mouse IgG. Cells were treated with 20 µg/mL loliolide and/or 1 µg/mL neutralizing antibodies for 48 h, and phase-contrast images of spheroids were captured.

(B) Cells were treated with 20 µg/mL loliolide with or without 20 µM LY249002 for 48 h, and the mRNA levels of *VEGF*, *IGF-1* and *KGF* were assessed using qRT-PCR. *GAPDH* served as an endogenous control. The data represents the means of three independent samples ± SD *p < 0.05, **p < 0.005 versus DMSO-treated control and #p < 0.05, ##p < 0.05 versus loliolide-treated HDP spheroids. Scale bars represent: A 200 µm.

Supplemental Data_Figure_S1

A



B

