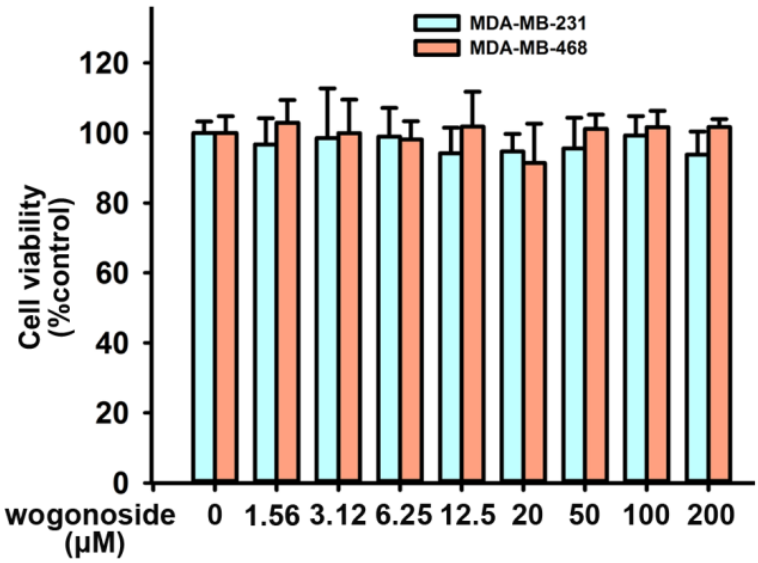

Figure S1 (**Related to Figure 2).** Effects of wogonoside on the viability of MDA-MB-231 and MDA-MB-468 cell lines were examined by MTT assay. Cells were treated with various concentrations of wogonoside (0, 25, 50 and 100 μM) for 24 h. Data are presented as mean ± SD.

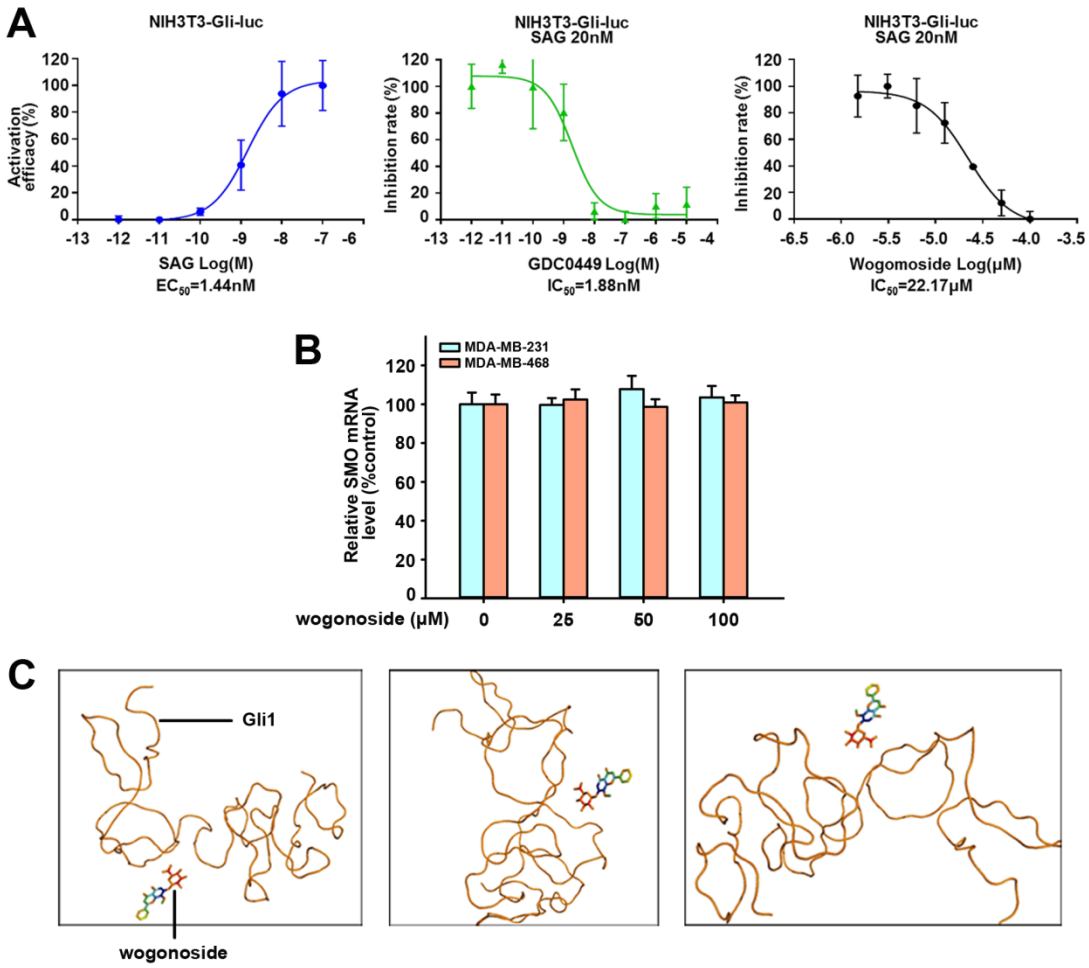

Figure S2 (Related to Figures 3 and 5). Effect of wogonoside on Gli and SMO.

(**A**) Effect of wogonoside on the transcription activity of Gli was detected by Gli-luciferase reporter assay. NIH3T3 cells were transfected with 8 x Gli firefly luciferase reporter plasmid, then maintained in DMEM medium with 0.5% FBS and different concentrations of wogonoside in the presence of SAG (20 nM) as indicated. Data were analyzed by GraphPad Prism 7 software (GraphPad, La Jolla, CA). Results are representative of three independent experiments. (**B**) The mRNA level of SMO was investigated by RT-PCR. MDA-MB-231 or MDA-MB-468 cells pretreated with wogonoside (0, 25, 50 and 100 μM) for 24 h as indicated. Data are presented as mean ± SD. (**C**) The binding mode of wogonoside with Gli1 was shown according to the molecular docking simulation. Molecular docking simulation didn't show a significant interaction between wogonoside with Gli1. Results are representative of three independent experiments.

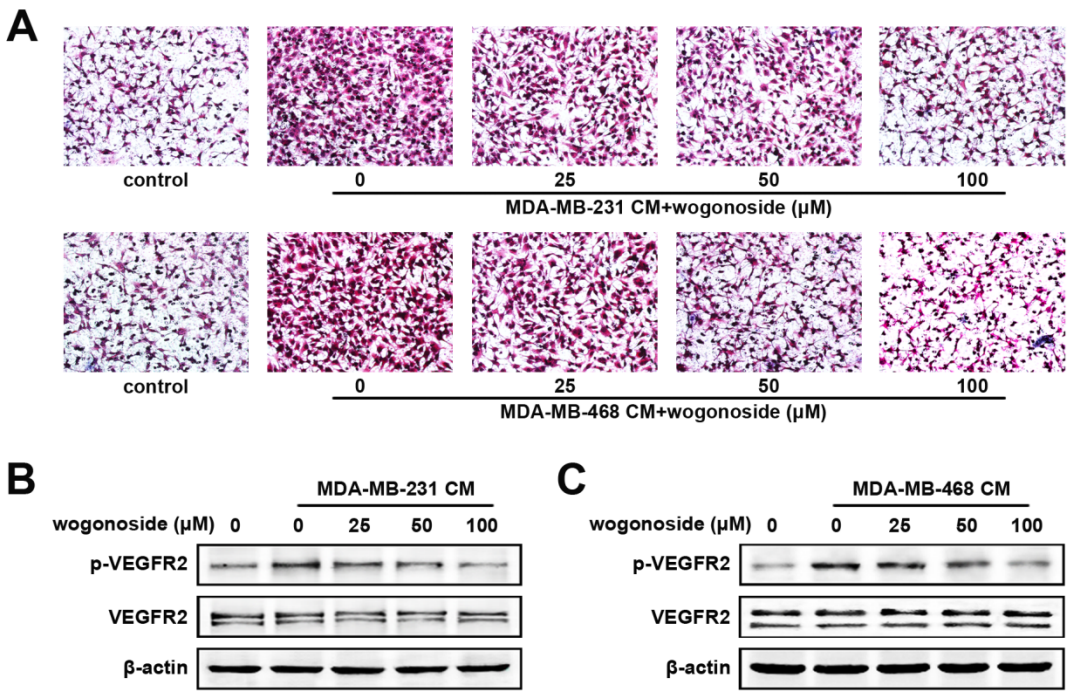

Figure S3 (Related to Figure 6). Effect of wogonoside on the invasion and protein expression of endothelial cells.

MDA-MB-231 or MDA-MB-468 cells (5×10^6cells/culture flask) pretreated with wogonoside (0, 25, 50 and 100 μM) for 24 h were cultured for another 12 h with low serum media containing 1% FBS, and then the condition medium (MDA-MB-231 or MDA-MB-468 CM) was collected. The human umbilical vein endothelial cells (HUVECs) were stimulated with CM or 1% FBS medium in control group. (**A**) Effect of wogonoside on HUVECs invasion induced by MDA-MB-231 or MDA-MB-468 CM as indicated was tested by endothelial cell invasion assay. (**B**) Effect of conditioned media (CM) on VEGFR2 and p-VEGFR2 expression in HUVECs was detected by Western blot assay. Results are representative of three independent experiments.

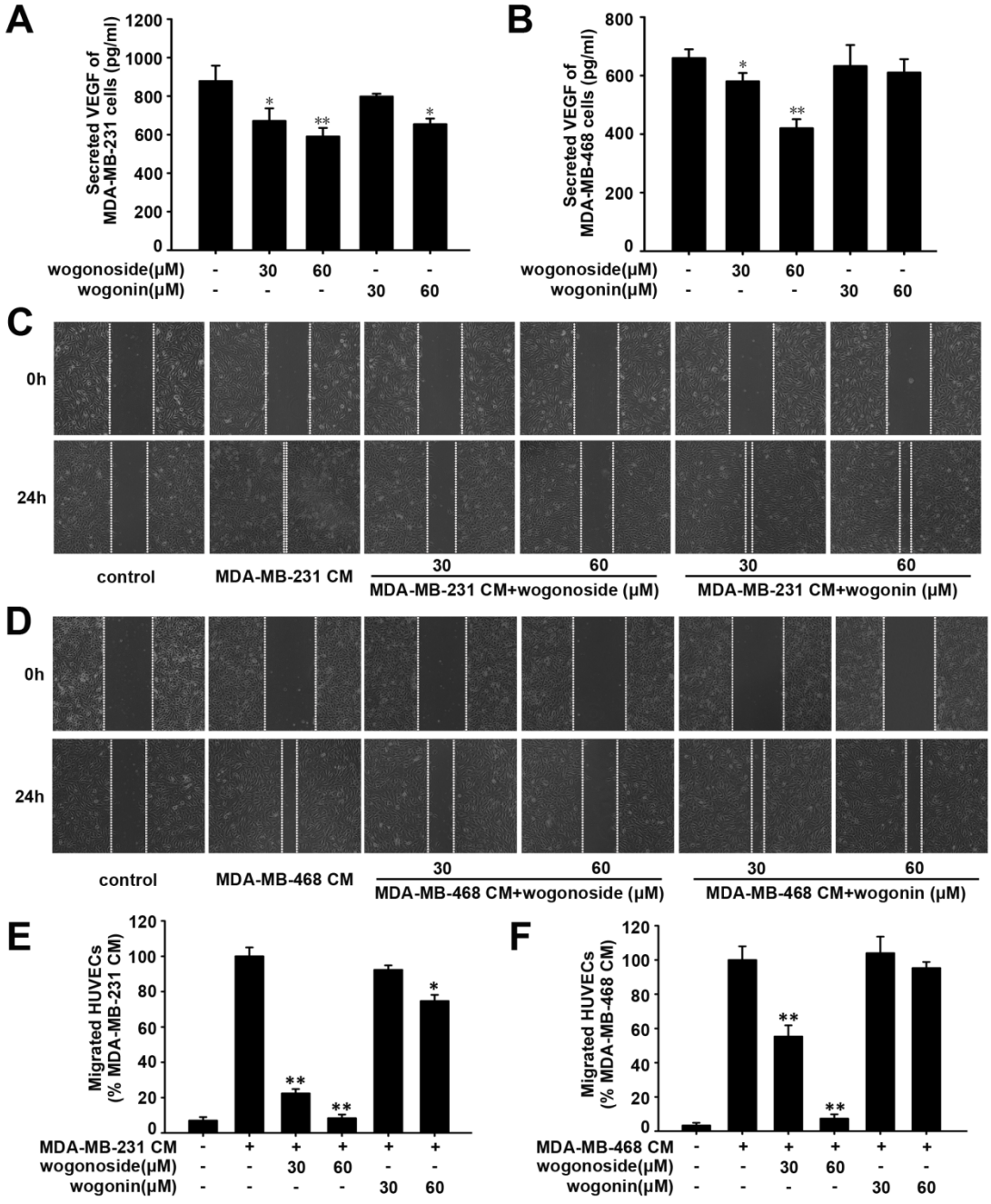

Figure S4 (Related to Figure 7). Effects of wogonoside and wogonin on VEGF secretion and endothelial cell migration.

After MDA-MB-231 or MDA-MB-468 cells were treated with wogonoside or wogonin (30 and 60 μM) for 24 h, the supernatant was collected and referred to as TNBC cell derived conditioned medium (MDA-MB-231 CM or MDA-MB-468 CM), then VEGF concentration in the conditioned medium was measured by ELISA kits. (**A**) Effect of wogonoside and wogonin on VEGF secretion of

MDA-MB-231 cells. (**B**) Effect of wogonoside and wogonin on VEGF secretion of MDA-MB-468 cells. The wound-healing assay and the conditional cell culture system were established to evaluate the effect of compounds on angiogenesis in TNBC cells. In the wound-healing assay, human umbilical vein endothelial cells (HUVECs) were stimulated with MDA-MB-231 CM or MDA-MB-468 CM. (**C**) Effect of wogonoside and wogonin on MDA-MB-231 CM-induced HUVECs migration tested by wound healing assay. (**D**) Effect of wogonoside and wogonin on MDA-MB-468 CM-induced HUVECs migration tested by wound-healing assay. (**E-F**) Wound healing was quantified by measuring the migrated distance of HUVECs. Data are presented as mean ± SD. The comparisons were made relative to MDA-MB-231 or MDA-MB-468 CM group and significance of difference is indicated as **P* value < 0.05 and ***P* value < 0.01.

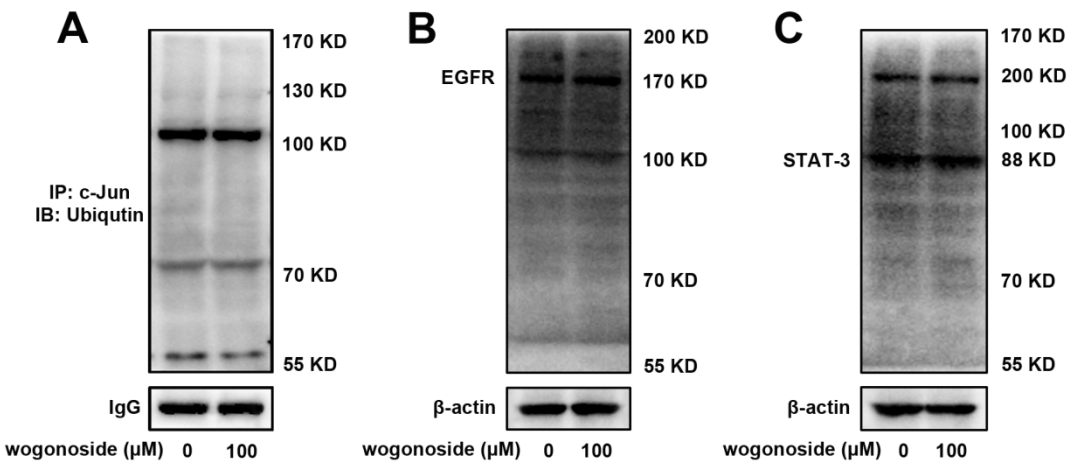

Figure S5 (Related to Figure 5). Effects of wogonoside on the ubiquitination level of c-Jun, EGFR and STAT-3.

MDA-MB-231 cells were treated by wogonoside (100 μM) for 24 h. (**A**) c-Jun ubiquitination was determined by protein immunoprecipitation assay. c-Jun protein of MDA-MB-231 cells was immunoprecipitated and detected by ubiquitin antibody using western blotting. (**B**) The ubiquitination level of EGFR was detected with specific antibodies by Western Blot Analysis. (**C**) The ubiquitination level of STAT-3 was detected with specific antibodies by Western Blot Analysis. Results are representative of three independent experiments.