Figure S1. AGTR1 knockdown decreases the chemosensitivity of EC109 EC cells to cisplatin *in vivo*. Control EC109 cells and AGTR1-knockdown EC109 cells were used to inoculate nude mice. Cells were injected subcutaneously into the right flank of nude mice ($1x10^6$ cells/mouse) to establish the xenograft model. Mice were treated with an intraperitoneal injection of vehicle (PBS) or cisplatin (5 mg/kg body weight) twice every week. Tumor volume was monitored once per week and tumor tissues were collected at 36 days after tumor inoculation. The (A) tumor images, (B) tumor growth curves and (C) tumor weight at end time-point. The (D) cell proliferation and (E and F) apoptosis in tumor tissues of the indicated four groups are shown. (G) The protein level of N-cadherin, E-cadherin and Vimentin were detected by western blotting. n=5 for each group; $^{*}P<0.05$, $^{**}P<0.01$, $^{***}P<0.001$. AGTR1, angiotensin II receptor type 1; NC, negative control; siRNA, small interfering RNA.

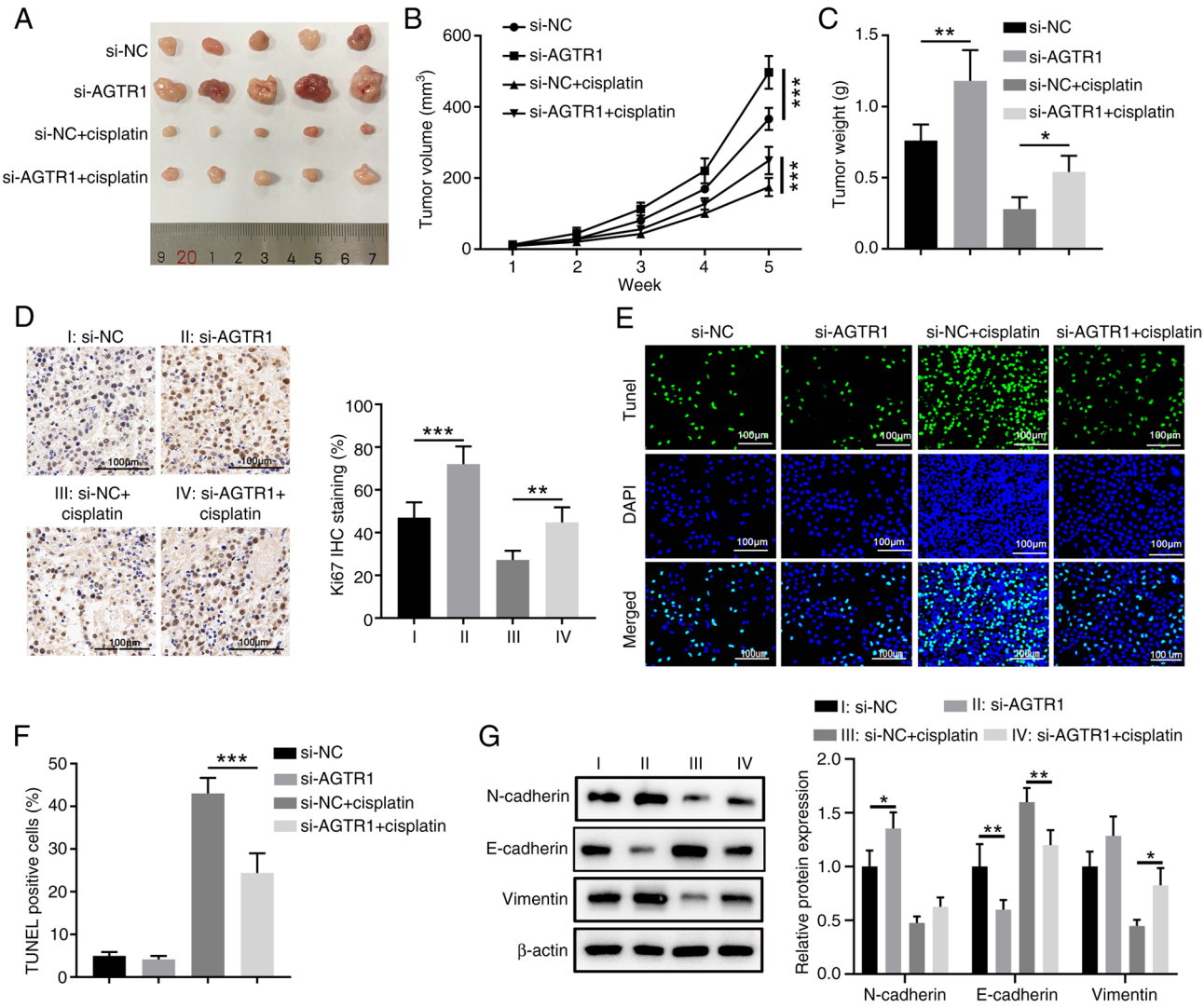

Figure S2. Representative plots of the Fluo-3 AM and the Annexin V/PI staining detected by flow cytometry. Upper panels: KYSE-150 cells were transfected with empty vector plasmid or AGTR1-expressing plasmid and treated with or without cisplatin. Lower panels: EC109 cells were transfected with NC siRNA oligos, AGTR1-specific siRNA oligos and treated with or without cisplatin. The (A) intracellular Ca^{2+} levels and (B) apoptosis of the indicated eight groups were determined by flow cytometry with the calcium indicator, Fluo-3 AM, and Annexin V/PI staining, respectively. (C) Control KYSE-150 cells and AGTR1-overexpressing KYSE-150 cells were untreated or treated with the calcium channel blocker, fendiline. The intracellular Ca^{2+} levels of the indicated eight groups were determined by flow cytometry with the calcium indicator, Fluo-3 AM. (D) Control EC109 cells and AGTR1-knockdown EC109 cells were used. The intracellular Ca^{2+} levels were determined by flow cytometry with the calcium indicator, Fluo-3 AM. AGTR1, angiotensin II receptor type 1; NC, negative control; siRNA, small interfering RNA; PI, propidium iodide.

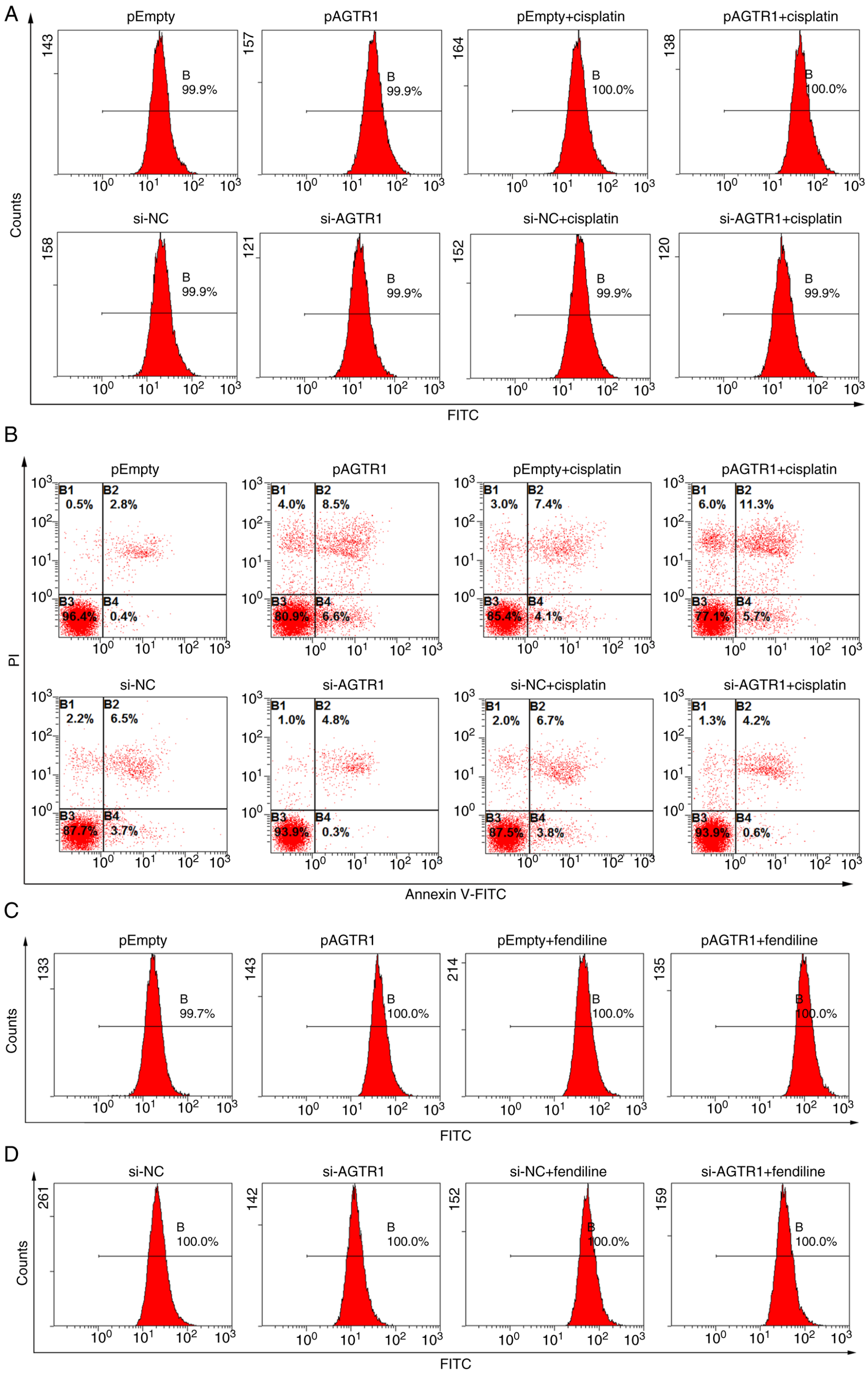

Figure S3. AGTR1 knockdown in EC109 cells downregulates intracellular Ca^{2+} levels and inhibits mitochondria-dependent apoptosis. The control EC109 cells and AGTR1-knockdown EC109 cells were treated with/without fendiline. The (A) intracellular Ca^{2+} levels, (B) ATP levels, (C) mitochondrial membrane potentials and (D) mitochondria pathway-dependent apoptosis of the indicated four groups were summarized. n=5 for each group. $^{*}P<0.05$, $^{**}P<0.01$, $^{***}P<0.001$. AGTR1, angiotensin II receptor type 1; NC, negative control; siRNA, small interfering RNA; PI, propidium iodide.

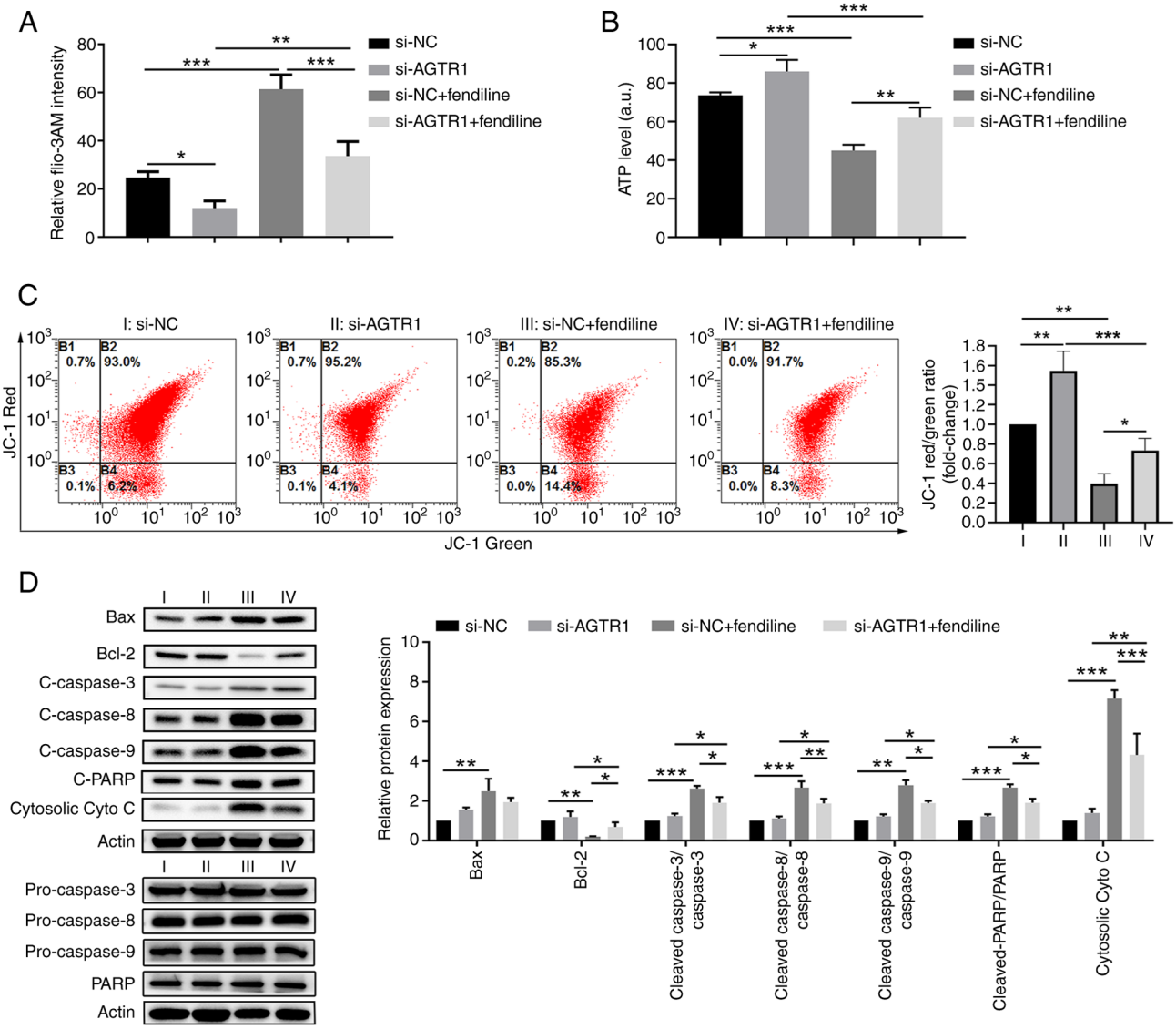

Figure S4. Representative plots of the Fluo-3 AM and the Annexin V/PI staining detected by flow cytometry. (A) A stable KYSE-150 cell line (pTet-On-AGTR1) with Dox-inducible expression of AGTR1 was generated by transfection of a plasmid bearing the Tet-On system. Control KYSE-150 cells and AGTR1 Tet-on KYSE-150 cells were treated with Dox or without Dox as indicated, and the protein levels of AGTR1 were semi-quantified by western blotting. Representative western blot results for the validation of inducible AGTR1 expression in KYSE-150 cells. (B and C) Cells were treated with cisplatin alone, cisplatin + fendiline, cisplatin + Dox or cisplatin + fendiline + Dox for 48 h. (B) The intracellular Ca^{2+} levels of the indicated four groups were determined by flow cytometry with the calcium indicator, Fluo-3 AM. (C) The apoptosis of the indicated four groups were determined by flow cytometry with the Annexin V/PI staining. AGTR1, angiotensin II receptor type 1; PI, propidium iodide; Dox, doxycycline.