Supplementary Figure Legend

Supplementary Figure 1. Dose- and time-dependent accumulation of poly-ubiquitinated proteins following RA-9 exposure. A, *left* dose-dependent accumulation of high-molecular weight ubiquitin species in ES-2 ovarian cancer cell line exposed to the indicated concentrations of RA-9 over a period of 24 hours. Amido black staining was used as loading control. *Right,* quantification of the ubiquitin/total protein (amido) ratio expressed as % of t_0. B, time-dependent accumulation of high-molecular weight ubiquitin species and concomitant reduction in mono, tri and tetraubiquitin species in SKOV-3 (*left*) and TOV-21G (*right*) ovarian cancer cell line exposed to 10μM RA-9 for 4h, 8h, 16h and 24 h. Amido black staining was used as loading control.

Supplementary Figure 2. Ovarian cancer cells sensitivity to cisplatin and to RA 9/cisplatin combination. A, cell viability of ES-2 (*left*) and TOV-21G (*right*) ovarian cancer cell lines exposed at the indicated concentration of ciplatin (*cis*-Diamineplatinum(II) dichloride) for 48 hours. Cell viability was measured by WST-1 assay and it is expressed as % of control. B, Simultaneous treatment with RA-9 and cisplatin induces synergistic killing of ovarian cancer cells. Dose-dependent inhibition of the cell viability of the cisplatin resistant HEY ovarian cancer cell line in the absence (-) or in the presence (+) of 50μM cisplatin and RA-9 at the indicated concentrations. CI=combination index. Cell viability was measured after a 48-h incubation by WST-1 assay and the percentage of viable cells is presented relative to mock-treated controls.

Supplementary Figure 3. UPR stress levels in ovarian surface epithelial cells (OSEs). A, *left* levels of poly-ubiquitinated proteins in lysates of OSEs cells exposed to the indicated concentrations of RA-9 over a period of 24 hours. Amido black staining was used as loading

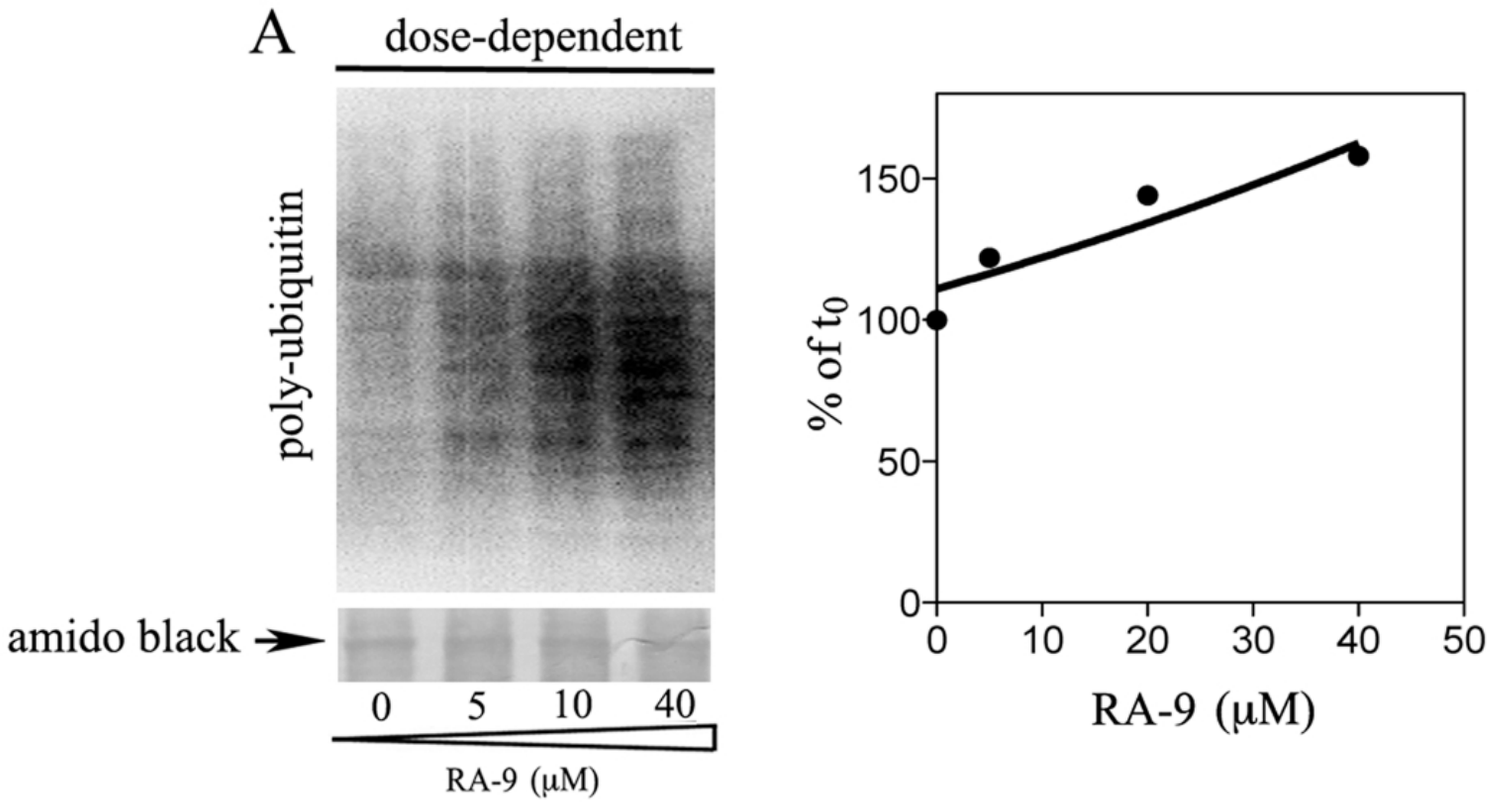
control. *Right,* quantification of the ubiquitin/total protein (amido) ratio expressed as % of t_0. B, *left panel*, OSEs cells were exposed to 5 μM of RA-9 over a period of 24 h following Western blot analysis with specific antibodies against the ER stress-associated protein Ero1L-α. Amido black was used as loading control. *Right panel,* quantification of Ero1L-α/ total protein (amido) ratio.

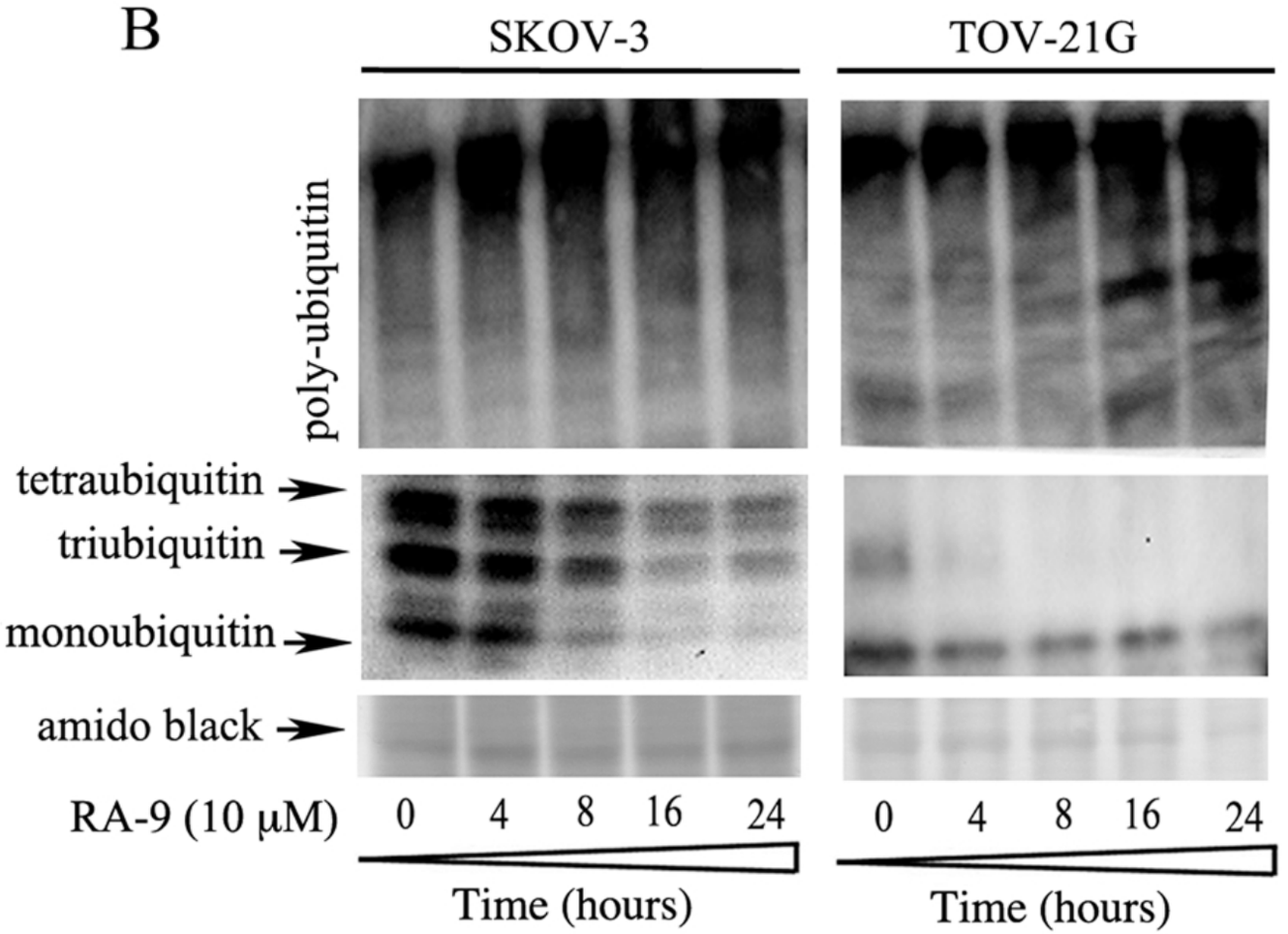
Supplementary Figure 4. Effect of RA-9 treatment on GCN2 expression levels. ES-2 (*top*) and TOV-21G (*bottom*) ovarian cancer cells were exposed to 5 μM of RA-9 over a period of 24 h following Western blot analysis with specific antibodies against the GCN2 protein. Amido black was used as loading control.

Supplementary Figure 5. RA-9 inhibits tumor growth *in vivo.* Athymic nude mice inoculated with 100,000 GFP expressing ES-2 ovarian cancer cell lines intraperitoneally and treated with i.p injection of 5mg/kg RA-9 (n=10) or saline (control n=9) on a one-day on, two-days off schedule. Representative images of control or RA-9 treated mice at day 5 of treatment.

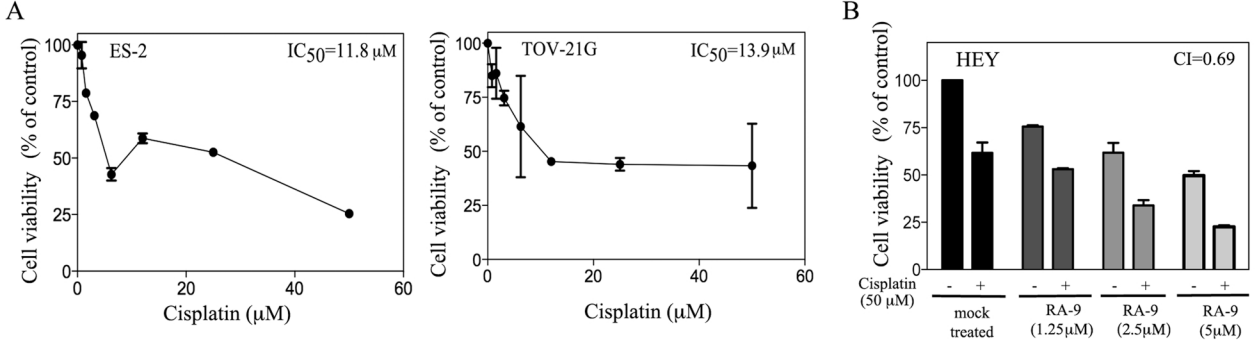
Supplementary Figure 6. Effect of RA-9 treatment on total body weight. Body weight in RA-9 or saline treated mice was recorded prior each treatment and is expressed in grams.

Supplementary Figure 1

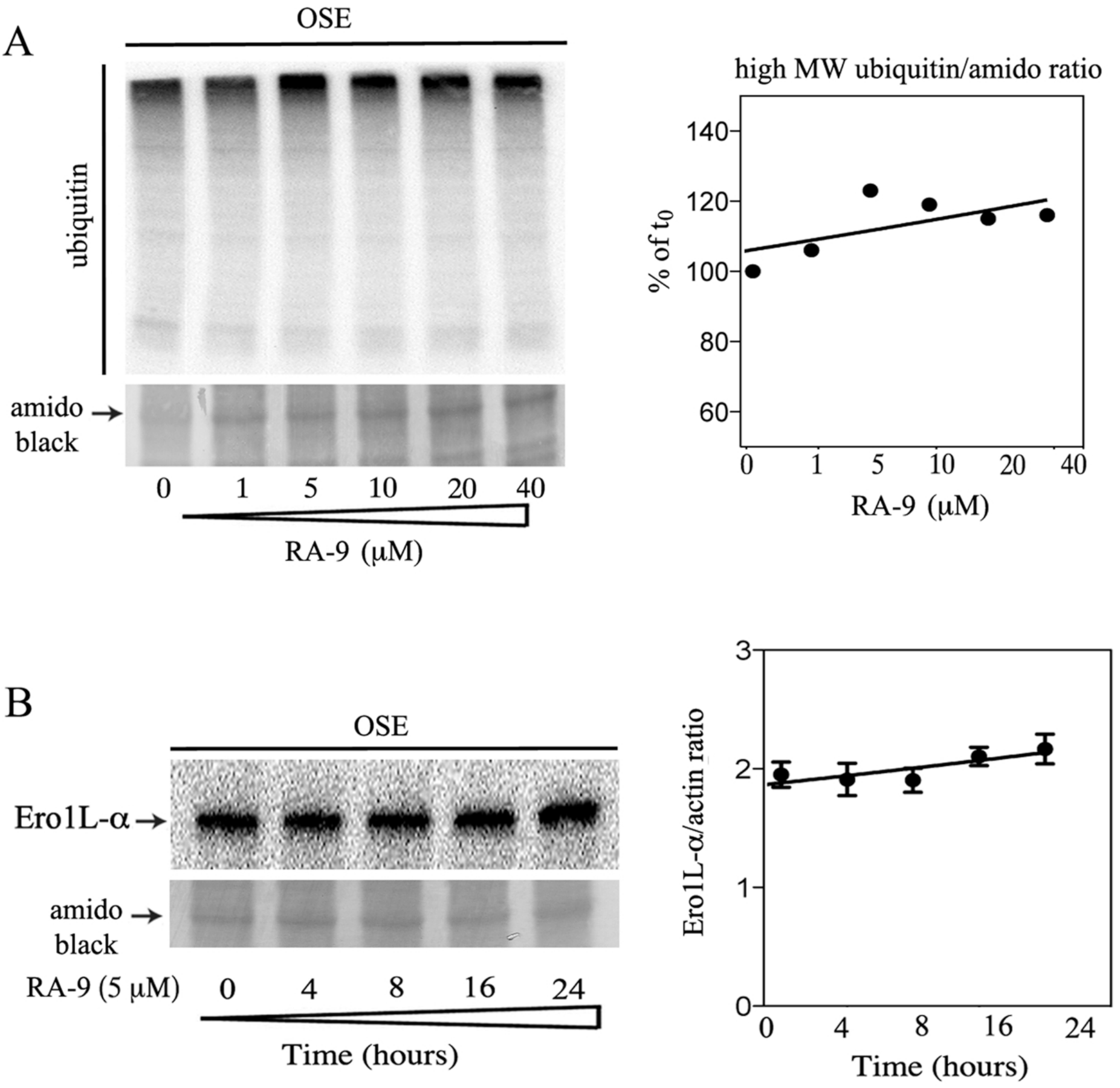




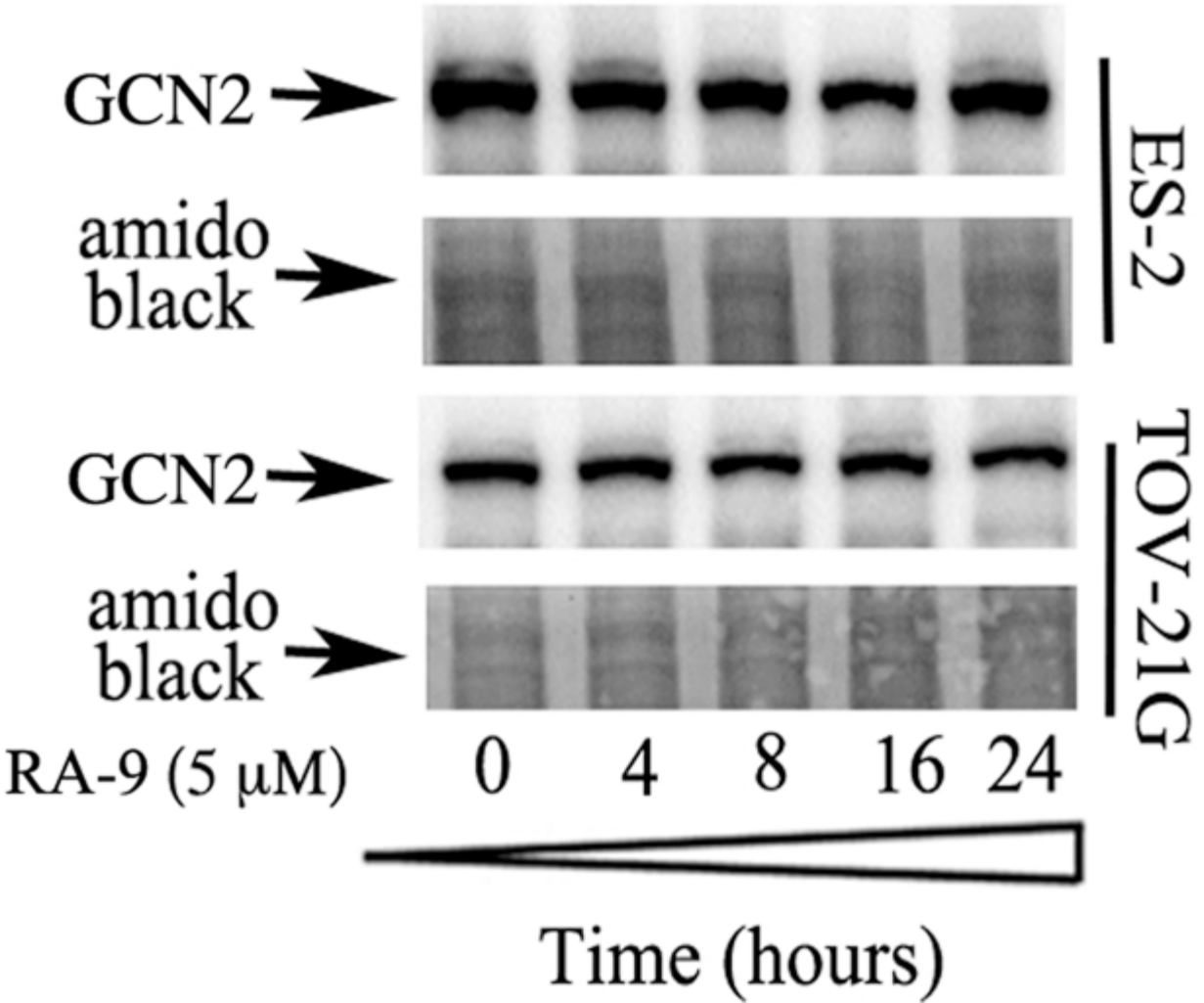
Supplementary Figure 2



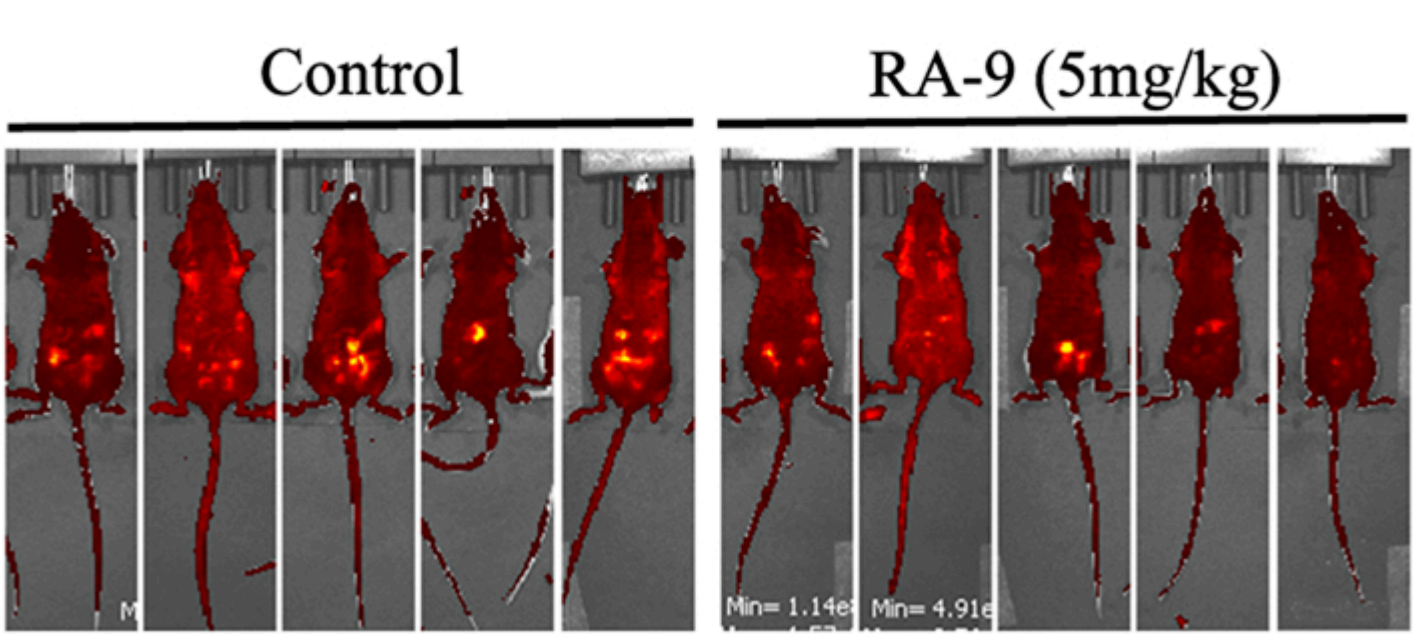
Supplementary Figure 3



Supplementary Figure 4



Supplementary Figure 5



Supplementary Figure 6