**Supplemental Figure Legends**

**Supplemental Figure 1. Model ranges, their range, and description.** The descriptions and variables used in the Fig. 5 models are listed in supplementary figure 1. Because of the phenomenological nature of the model, we do not use reaction rate equations to model the evolution of the components, but rather adopt an approach based on soft-Heaviside functions.

**Supplemental Figure 2. Nuclear IRF1 is induced following ATG7 and BECN1 knockdown.**

Western blot images of indicated proteins in LCC1 and LCC9 cytoplasmic and nuclear fractions following ATG7 and BECN1 knockdown. Cells were transfected with siRNA for 48 hours before nuclear isolation; β-actin and histone 1 served as the loading controls; *n* = 3 independent experiments.

**Supplemental Figure 3. Silencing ATG7 and BECN1 induces IRF1 expression independently of ROS.** A, LCC1 cells transfected with Ctrl or ATG7 siRNA were treated with 100 nM ICI for 48 hours. Total ROS production was quantified using flow cytometry. Data are presented as total ROS-stained cells (green fluorescence) relative to vehicle control and represent the mean ± SEM for ≥ 3 independent experiments. B, LCC1 and LCC9 cells were transfected with Ctrl or ATG7 siRNA and treated with 5 mM of the ROS inhibitor, N-acetyl-L-cysteine (NAC) for 48 hours. Protein homogenates were collected and probed for the indicated proteins. β-actin served as the loading control. *n* = 3 independent experiments.

**Supplemental Figure 4. Knockdown of IRF1 alters BECN1 and IGF1R/mTOR expression.** A, Western blot images of LCC1 and LCC9 cells transfected with IRF1 or Ctrl siRNA and treated with vehicle or 100 nM ICI for 48 hours. β-actin served as the loading control. B-C, Densitometric analysis from (B). *n* = 3 independent experiments; \**P* *<* 0.05 versus control/vehicle experiment.

**Supplementary Figure 5. dnIRF1 blocks ICI sensitivity in LCC1 cells.** A,LCC1 cells transfected with dnIRF1 or Ctrl cDNA were treated with vehicle control, 10 nM, 100 nM, or 1000 nM ICI for 6 days and cell density measured by crystal violet. B, Western blot analysis confirmed knockdown of IRF1. n=3 independent experiments; \*\*\**P* *<* 0.001 versus indicated groups.

**Supplemental Figure 6. Efficient knockdown of IRF1 using siRNA.** A, IRF1 was effectively knocked down in LCC1 cells using increasing concentrations of IRF1 siRNA (10-30 nM). Knockdown of IRF1 protein was confirmed by Western blotting using β-actin as a loading control. Image is representative of three independent experiments. B, Transfection with IRF1 siRNA had no effect on cell density as measured by crystal violet staining. n=3 independent experiments.