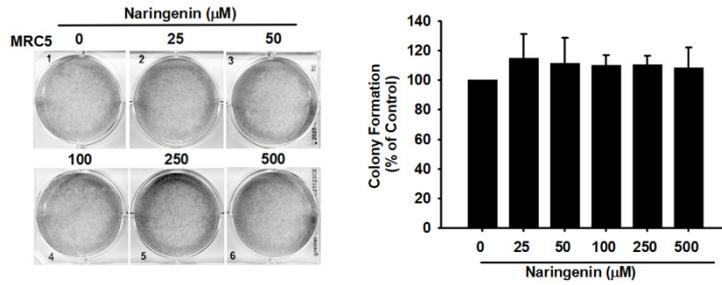


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### Supplemental figures and legends



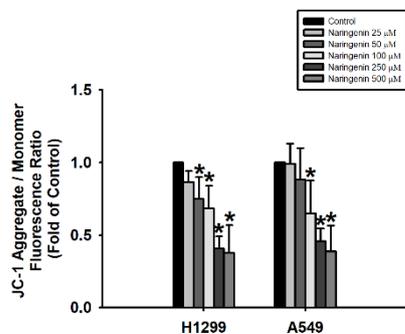
**Figure S1. Cytotoxic effect of naringenin in normal cells.** MRC5 cells were treated with naringenin (25-500 μM) for 6 h and then incubated for a further 14 days in naringenin-free medium. Cell reproductive viability was assessed by colony formation assay (n=4). Untreated cells were used as control. Results are shown as means ± SD.

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36 **Figure S2. Naringenin promoted perturbations in mitochondrial membrane**  
37 **potential in non-small cell lung cancer cells.** H1299 and A549 cells were treated with  
38 naringenin (25-500 μM) for 24 h and then incubated with JC-1 for 30 min; fluorescence  
39 intensity was measured by a fluorescence plate reader (n=4). Untreated cells were used  
40 as control. Results are shown as means ± SD. \* $p < 0.05$  compared with untreated control.

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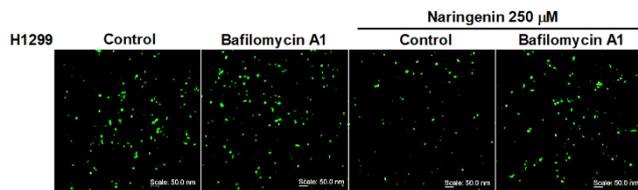
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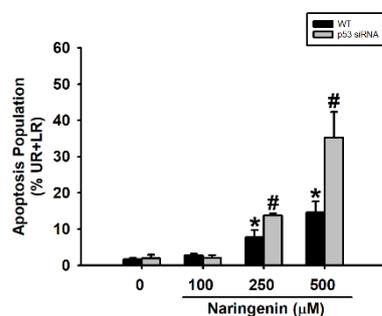
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**Figure S3. Naringenin promoted autophagic flux in non-small cell lung cancer cells.**

GFP-LC3-transfected H1299 cells were pretreated with autophagy inhibitor bafilomycin A1 (100 nM) for 1 h, followed by treatment with naringenin (250 μM) for 6 h. Autophagic flux was assessed by fluorescent microscopy (n=4). Scale bar = 50 nm. Untreated cells were used as control.

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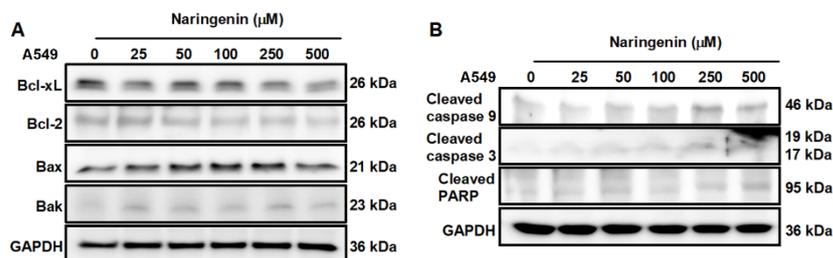
**Figure S4. Transfection of p53 siRNA increased naringenin-induced apoptosis in A549 cells.** WT and p53 siRNA-transfected A549 cells were treated with naringenin (100-500 µM) for 24 h. Apoptosis was assessed by Annexin V/PI assay (n=4). Untreated cells were used as controls. Results are shown as means ± SD. \* $p < 0.05$  compared with untreated control. # $p < 0.05$  compared with WT cells.

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124 **Figure S5. Naringenin promoted apoptosis in A549 cells.** A549 cells were treated

125 with naringenin (25-500  $\mu\text{M}$ ) for 8 h. Expression levels of (A) Bcl-xL, Bcl-2, Bak, and

126 Bax and (B) cleaved caspase 9, cleaved caspase 3, and cleaved PARP were examined

127 by Western blot (n=4). Untreated cells were used as control.

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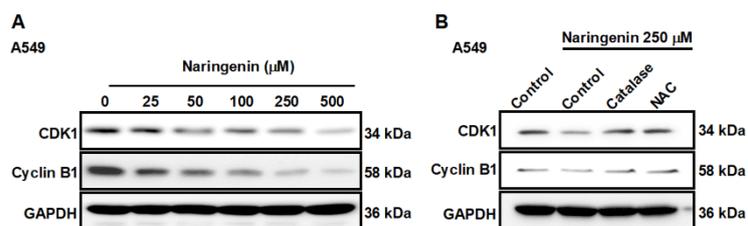
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152 **Figure S6. Naringenin promoted cell cycle arrest through ROS production in A549**

153 **cancer cells. (A)** A549 cells were treated with naringenin (25-500  $\mu\text{M}$ ) for 6 h. CDK1

154 and cyclin B1 protein expression was examined by Western blot (n=4). **(B)** A549 cells

155 were pretreated with ROS scavengers, catalase (50 U/mL) and NAC (1 mM), for 1 h

156 and then treated with naringenin (250  $\mu\text{M}$ ) for 6 h. Protein expression levels of CDK1

157 and cyclin B1 were examined by Western blot (n=4). Untreated cells were used as

158 control.

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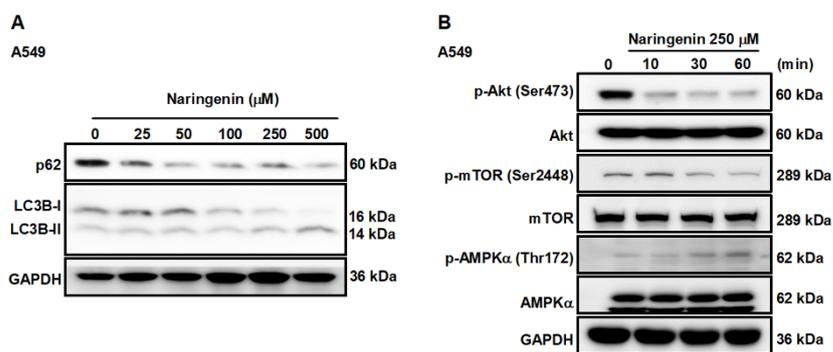
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183 **Figure S7. Naringenin promoted autophagy in A549 cells.** (A) A549 cells were  
184 treated with naringenin (25-500  $\mu\text{M}$ ) for 6 h. Expression of p62 protein and LC3II/LC3I  
185 ratio was examined by Western blot (n=4). (B) A549 cells were treated with naringenin  
186 (250  $\mu\text{M}$ ) for the indicated times, after which phosphorylation of Akt, mTOR, and  
187 AMPK $\alpha$  was examined by Western blot (n=4). Untreated cells were used as control.

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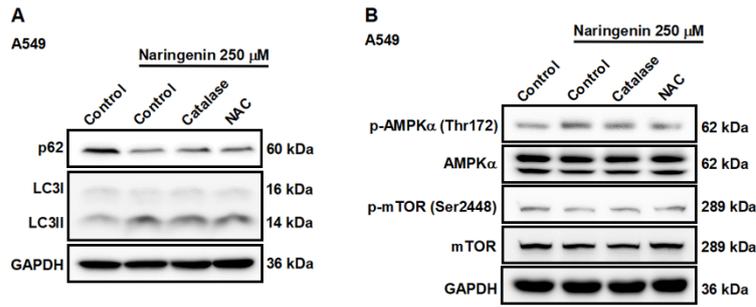
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210 **Figure S8. Naringenin promoted autophagy via ROS production in A549 cells. (A)**

211 A549 cells were pretreated with ROS scavengers, catalase (50 U/mL) or NAC (1 mM),

212 for 1 h and then treated with naringenin (250  $\mu$ M) for 6 h. Expression of p62 protein

213 and LC3II/LC3I ratio was examined by Western blot (n=4). **(B)** A549 cells were

214 pretreated with ROS scavengers for 1 h and then treated with naringenin (250  $\mu$ M) for

215 1 h. Phosphorylation of AMPK $\alpha$  and mTOR was examined by Western blot (n=4).

216 Untreated cells were used as control.

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