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Simvastatin Induces Unfolded Protein Response and Enhances Temozolomide-Induced Cell Death in Glioblastoma Cells.

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Correction

Correction: Dastghaib et al. Simvastatin Induces Unfolded Protein Response and Enhances Temozolomide-Induced Cell Death in Glioblastoma Cells. *Cells* 2020, 9, 2339

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In the original publication [1], there was a mistake in Figures 4A, 6A, 7A and 9A as published. The protein loading controls (GAPDH) were the same. The corrected Figures 4A, 6A, 7A and 9A appear below. The authors state that the scientific conclusions are unaffected. This correction was approved by the Academic Editor. The original publication has also been updated.

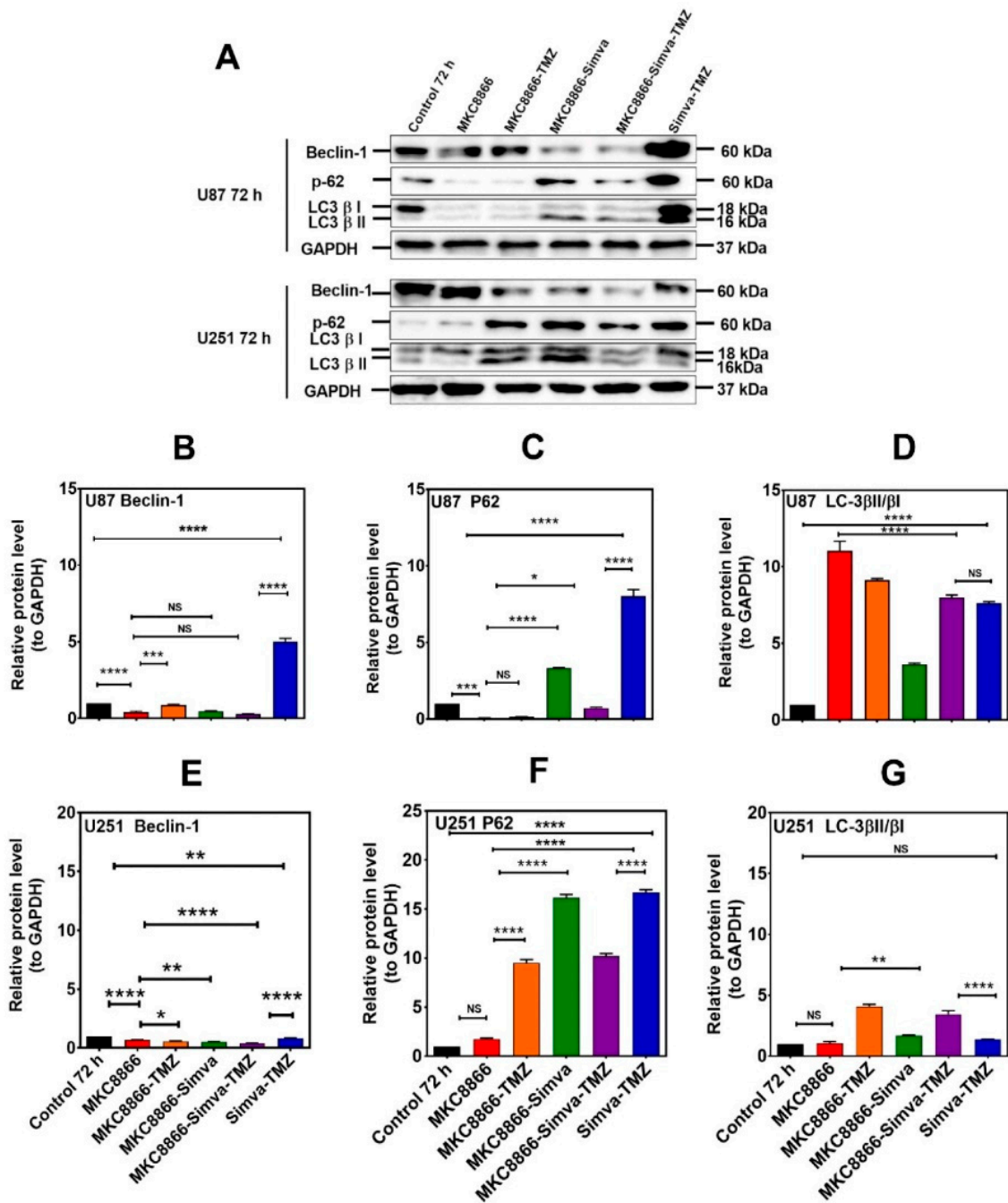


Figure 4. Simva–TMZ modulates the autophagy machinery via the IRE-1 pathway. (A) After pretreatment with MKC8866 (30 μ M, 4 h), U87 and U251 cells were co-treated with TMZ, Simva, or Simva–TMZ for 72 h. The protein levels of Beclin-1, p62, LC3 β -II, and LC3 β -I were determined by immunoblotting. Simva–TMZ induced an inhibition of autophagy flux (accumulation of p62 and LC3 β -II) in GBM cells. In Simva–TMZ-treated cells, MKC8866 increased p62 and Beclin-1 degradation, while it differentially affected the LC3 β -II/LC3 β -I ratio; GAPDH was used as loading control. Densitometric analysis of the Western blot bands confirmed that Simva–TMZ significantly induced Beclin-1 and p62 accumulation in both U87 and U251 cells ($p < 0.0001$), which was markedly prevented in the presence of MKC8866 (B,C,E,F). In addition, MKC8866 increased the LC3 β -II/LC3 β -I ratio in Simva–TMZ-treated U251 cells ($p < 0.0001$) (G), whereas it did not change LC3 β -II/LC3 β -I in U87 cells ($p < 0.0001$) (D). The data are shown as the mean \pm SD from three independent experiments (* $p < 0.05$; ** $p < 0.01$, *** $p < 0.001$; **** $p < 0.0001$).

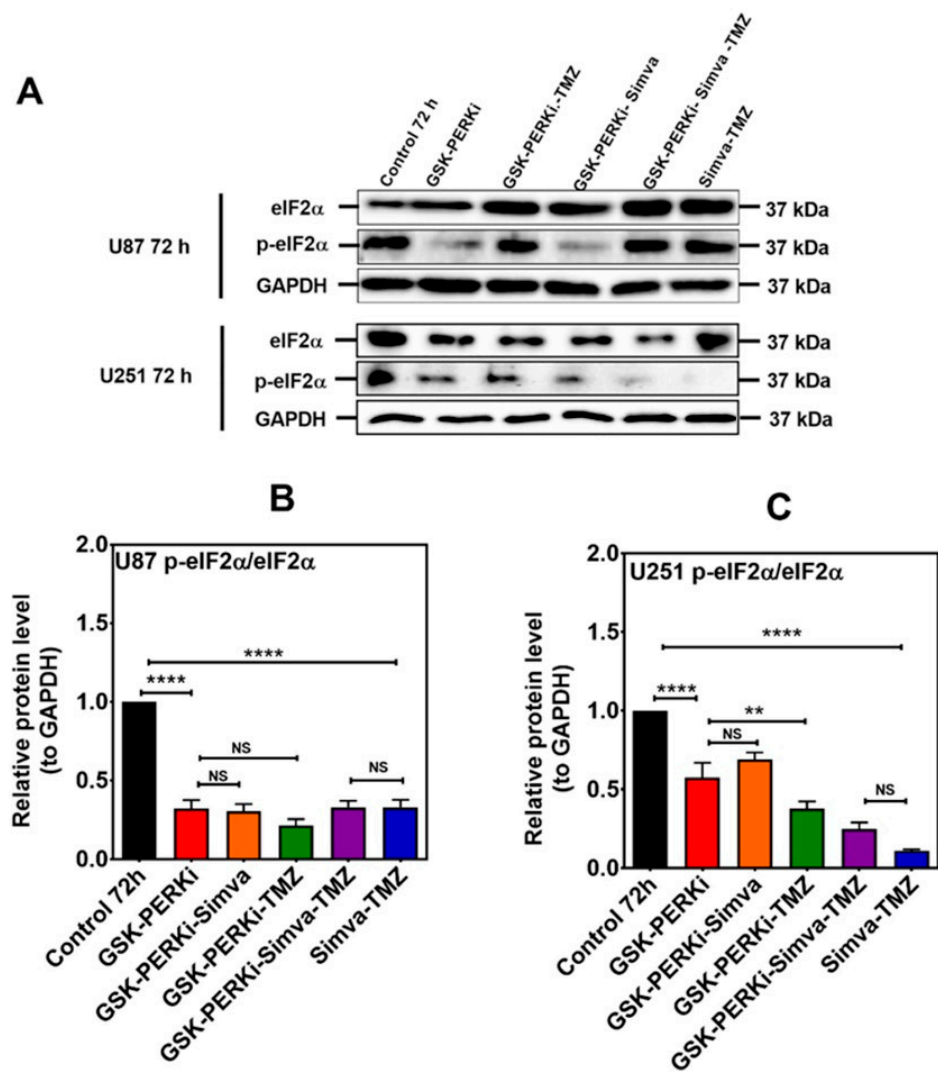


Figure 6. PERK inhibition does not change the p-eIF2 α /eIF2 α ratio in Simva-TMZ-treated cells. (A) U87 and U251 were pretreated with PERKi (5 μ M, 30 min) and then co-treated with Simva-TMZ for 72 h. The protein levels of eIF2 α and p-eIF2 α were determined using immunoblotting; GAPDH was used as a loading control. (B,C) Densitometric analysis of the immunoblots showed that Simva-TMZ by itself significantly reduced the p-eIF2 α /eIF2 α ratio, which was not further decreased by the PERKi in either cell line. Of note, control levels of p-eIF2 α were significantly decreased by the PERKi as well. The data are expressed as the means \pm SD of three independent experiments (** $p < 0.01$; **** $p < 0.0001$).

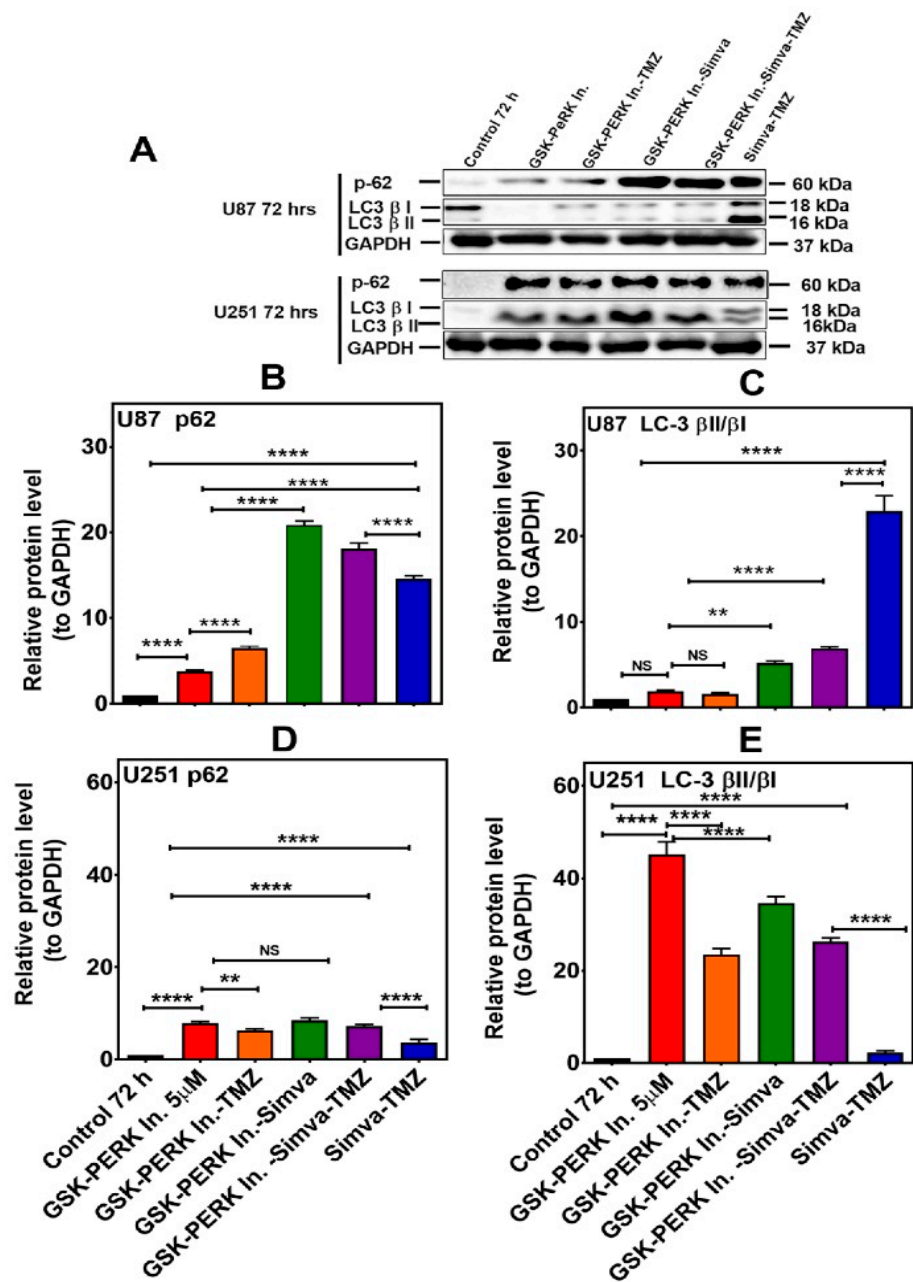


Figure 7. PERK inhibition differentially affects autophagy flux in U87 and U251 cells treated with Simva-TMZ. (A) U87 and U251 cells were pretreated GSK PERK inhibitor (5 μ M, 30 min) and then co-treated with Simva-TMZ as described for 72 h. The protein levels of p62, LC3 β -II, and LC β -I were determined by immunoblotting. Simva-TMZ induced an inhibition of autophagy flux (accumulation of p62 and LC3 β -II) in GBM cells. The PERKi decreased p62 degradation (autophagosome degradation) in both U87 and U251 cells, while it increased the LC3 β -II/LC3 β -I ratio in U251 cells and decreased it in U87 cells. GAPDH was used as a loading control. (B–E) Densitometric analysis of the Western blot bands to quantify p62 and LC3 β -II/LC3 β -I protein amount. Data are expressed as the mean \pm SD of three independent experiments (** $p < 0.01$; **** $p < 0.0001$).

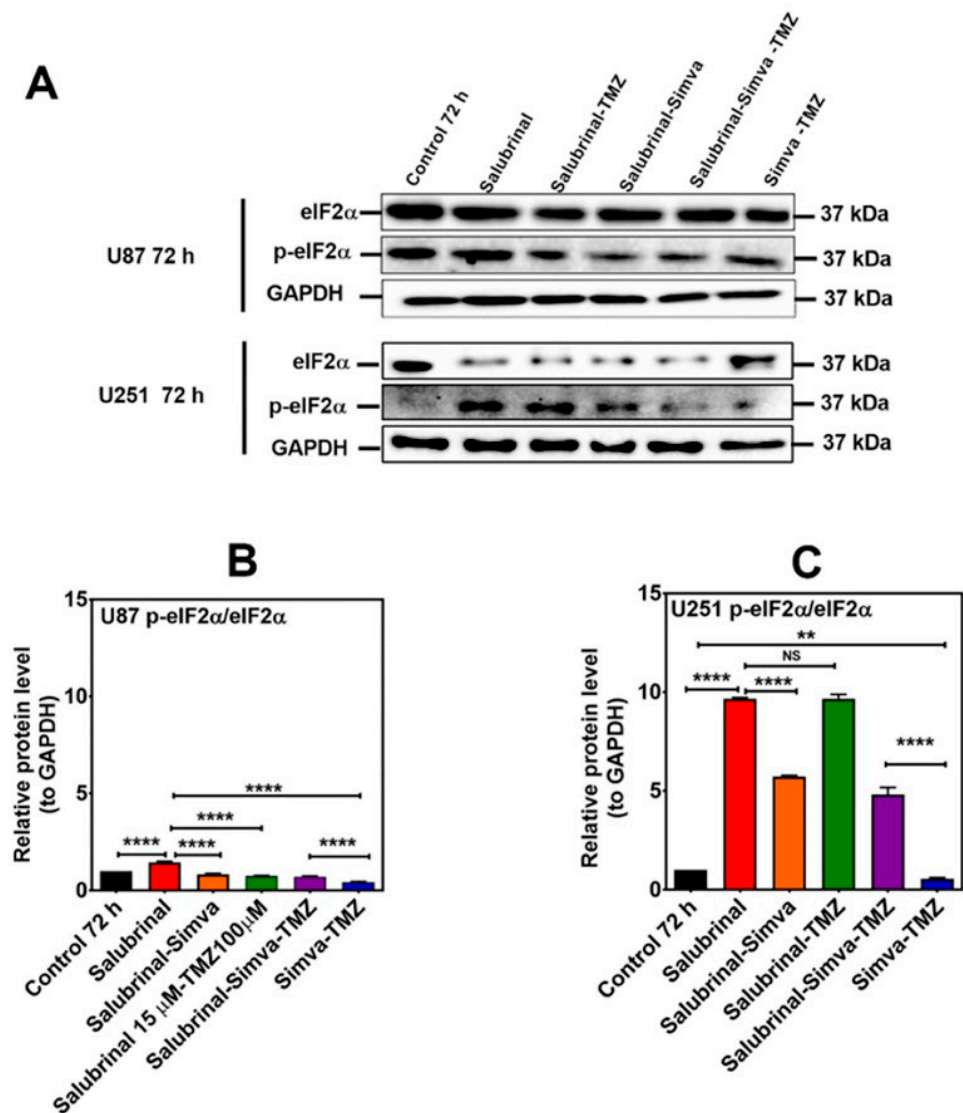


Figure 9. p-eIF2 α phosphatase inhibition increases the p-eIF2 α /eIF2 α ratio in Simva-TMZ treated in GBM cells. **(A)** U87 and U251 cells were pretreated with salubrinal (15 μ M, 30 min) followed by co-treatment with Simva-TMZ for 72 h. Cell lysates were collected, and the p-eIF2 α /eIF2 α protein amount ratios were determined using immunoblotting; GAPDH was used as a loading control. **(B,C)** Densitometric analysis of the Western blot bands shows that salubrinal significantly ($p < 0.0001$) increased the p-eIF2 α /eIF2 α ratio with Simva-TMZ treatment. Data are expressed as the means \pm SD of three independent experiments (** $p < 0.01$, **** $p < 0.0001$).

Reference

1. Dastghaib, S.; Shojaei, S.; Mostafavi-Pour, Z.; Sharma, P.; Patterson, J.B.; Samali, A.; Mokarram, P.; Ghavami, S. Simvastatin Induces Unfolded Protein Response and Enhances Temozolomide-Induced Cell Death in Glioblastoma Cells. *Cells* **2020**, *9*, 2339. [[CrossRef](#)] [[PubMed](#)]

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