Induction of Apoptosis in Triple Negative Breast Cancer Cells
Background

• Cancer cells utilize the adaptive branch of the UPR pathway to survive and progress in a stressful microenvironment

• The endoplasmic reticulum (ER) is the major cellular organelle responsible for protein folding

• Disturbance in the ER leads to the accumulation of misfolded or unfolded proteins in the ER, a condition termed ER stress

• Failure of UPR adaptive responses to re-establish homeostasis induces cell death
Solution

**Problem**

- Triple Negative Breast Cancer (TNBC) Cells
- Homeostasis of Unfolding Protein Response (UPR)
- Regulation of protein folding, secretion, calcium homeostasis, and lipid biogenesis
- TNBC expansion

**OMRF’s Solution**

- 5-Nitrofuran-2-Amide Derivative
- Activation of CHOP
- Activation of UPR
- Induction of TNBC apoptosis
- Apoptosis
Figure 1. Derivative induces apoptosis of HCC-1806 cells. (A) Cells were treated with derivative (10 μM) for the indicated times, and cleavage of caspase-3 was determined by Western blotting. (B, C) Cells were treated with DMSO (B) or derivative (10 μM) (C) for 24 h, and live-cell phase-contrast images were acquired (magnification 10×).
Figure 2. Cells were treated with derivative at the indicated concentrations for 8 h, and CHOP mRNA and protein levels were analyzed by qRT-PCR (A) and by Western blotting (B). Cells were treated with derivative (10 μM) for the indicated times, and ATF4 mRNA levels were analyzed by qRT-PCR (C) and ATF4 and p-eIF2α protein levels were analyzed by Western blotting (D).
Summary

• Weidong Wang has identified a series of 5-Nitrofuran-2-Amide derivatives that activate CHOP expression via the PERK–eIF2α–ATF4 branch of the UPR.

• These compounds represent first-in-class CHOP activators which induce apoptosis in Triple Negative Breast Cancer Cells.
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