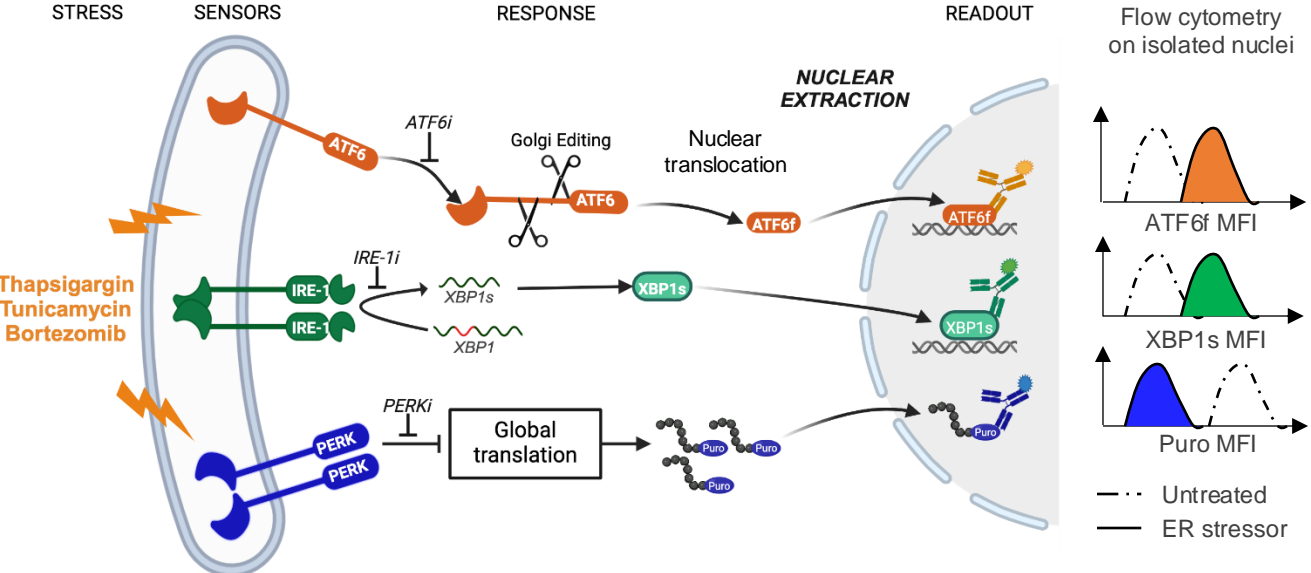
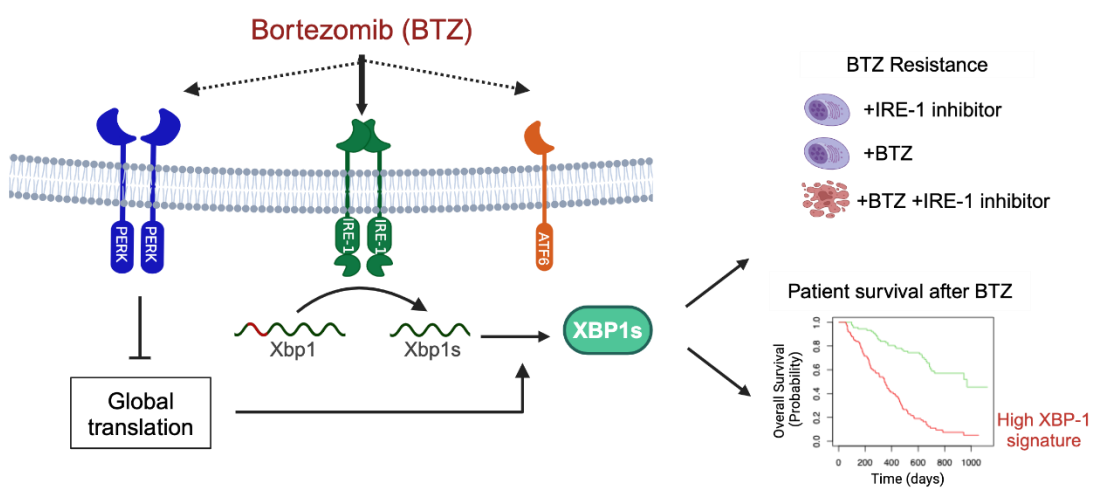


# SNUPR

Simultaneous profiling of PERK, IRE-1 and ATF6 activation with single-cell resolution.



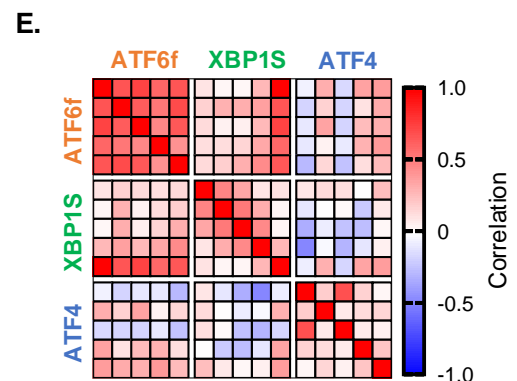
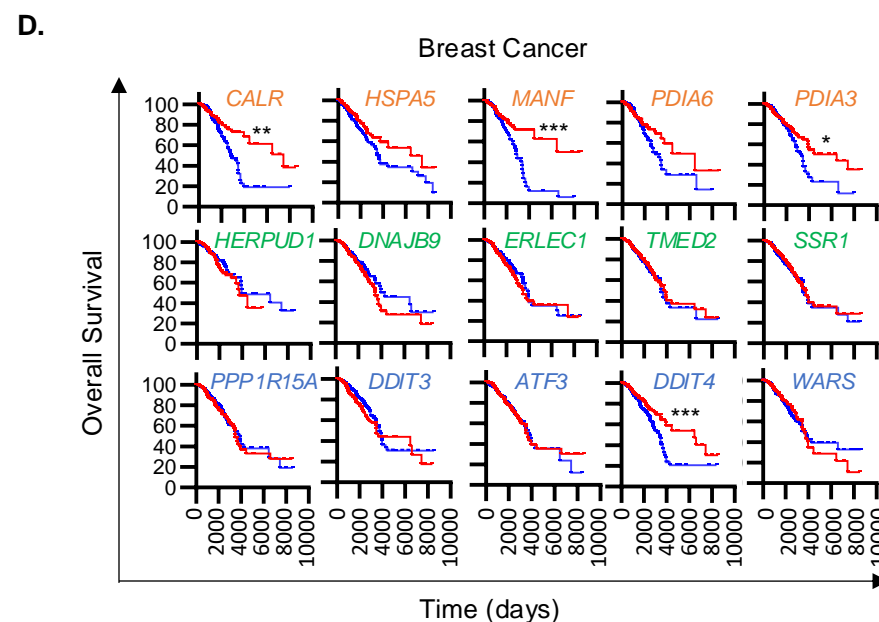
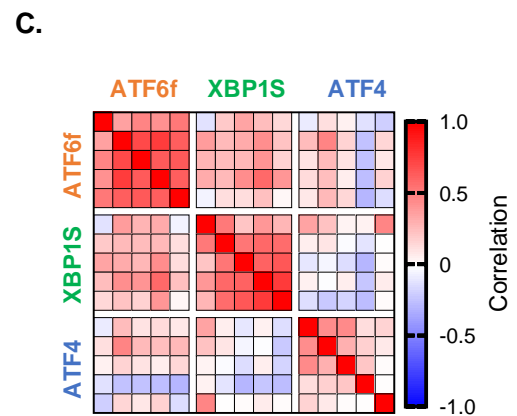
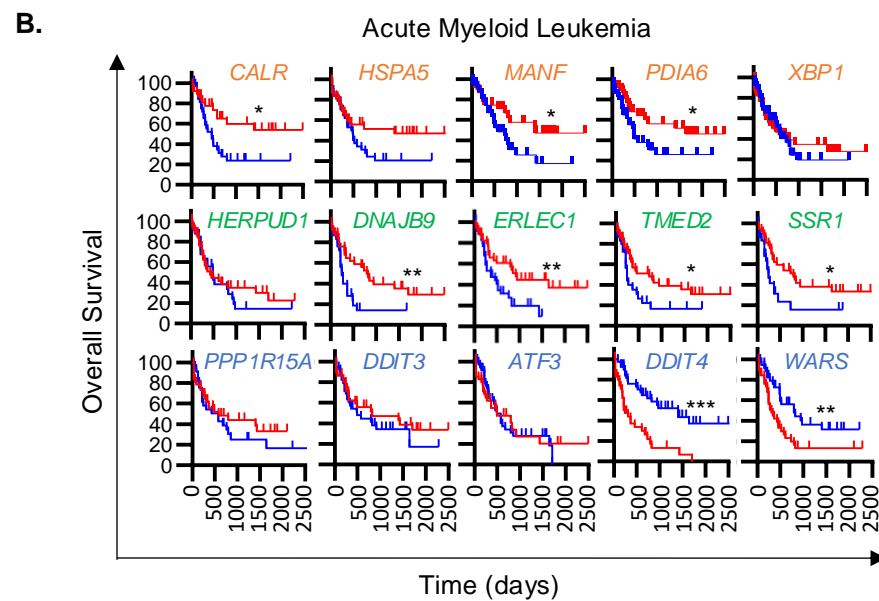
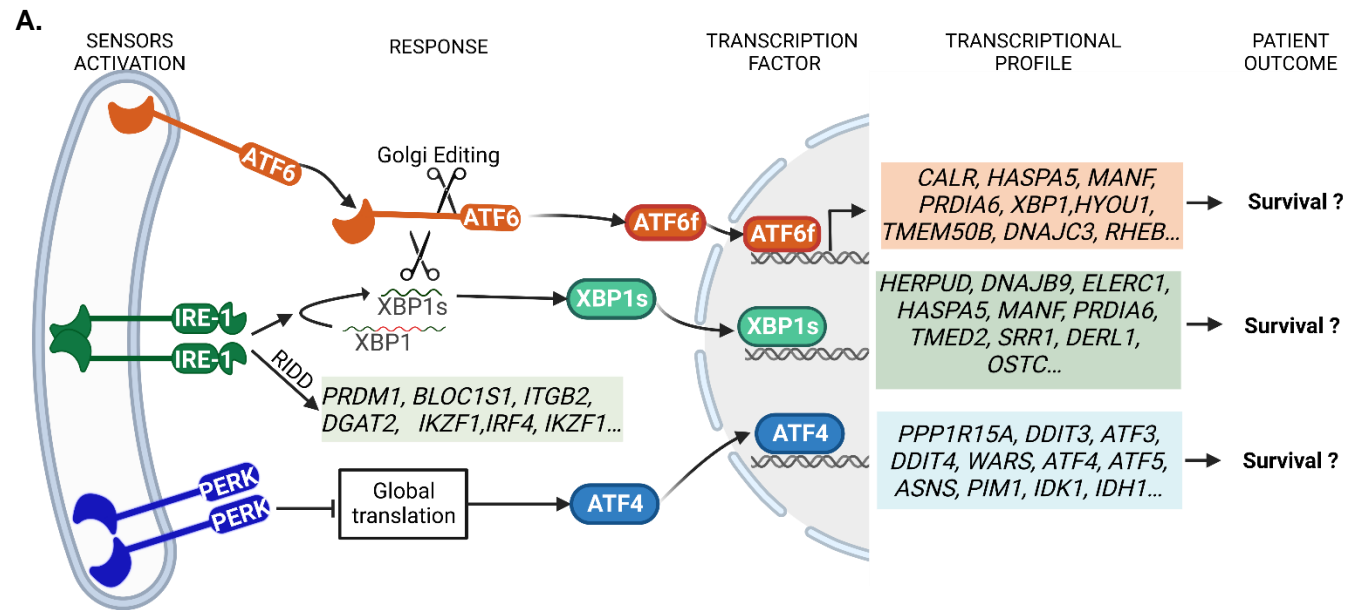
# Multiple Myeloma



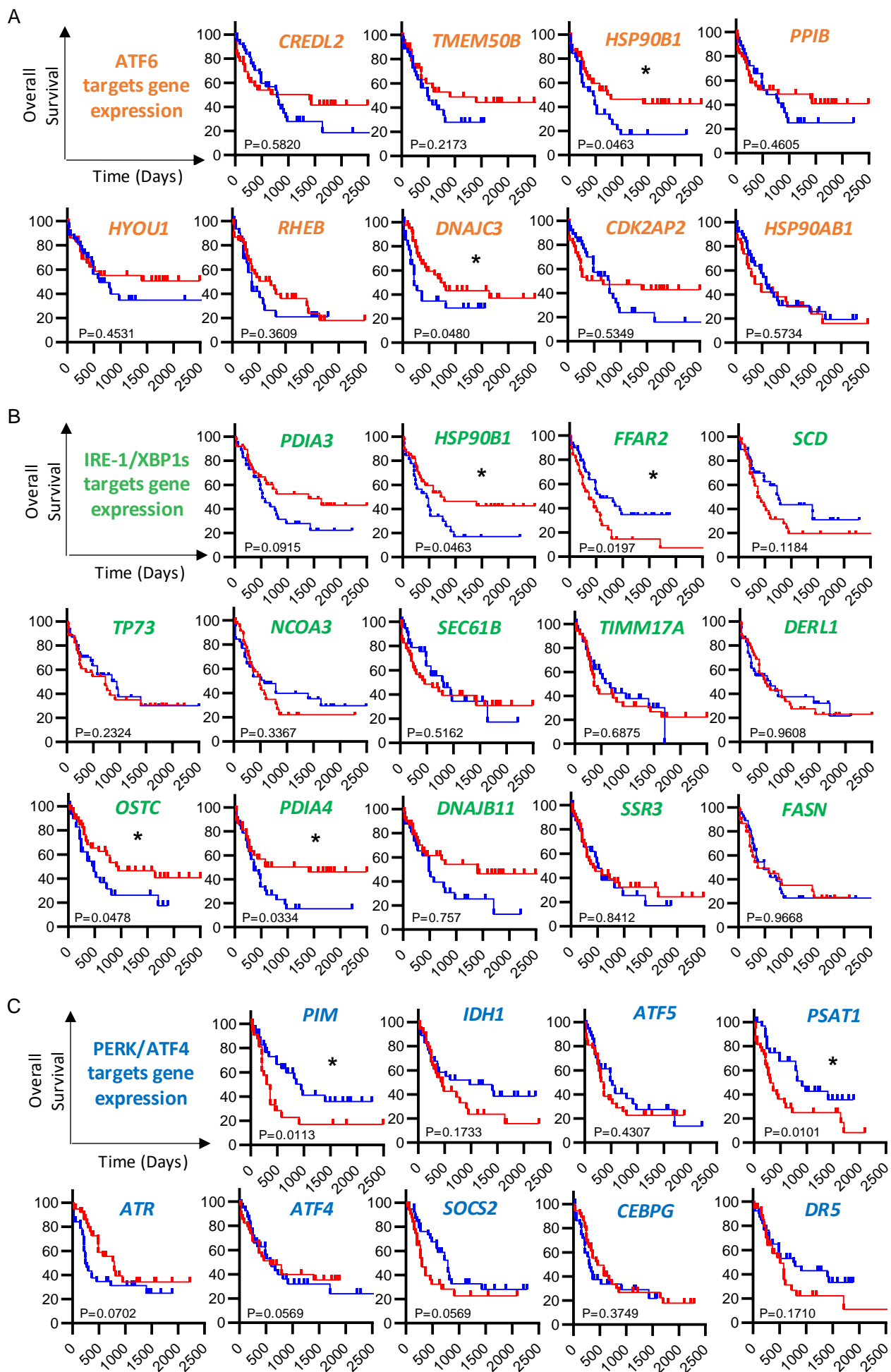
Inhibition of protein synthesis via PERK control the activation levels of the IRE-1/XBP1s and ATF6 pathway.

IRE-1 inhibitor kills bortezomib resistant cells and and XBP-1 associated transcriptional signatures predict the outcome of patients with multiple myeloma treated with Bortezomib.

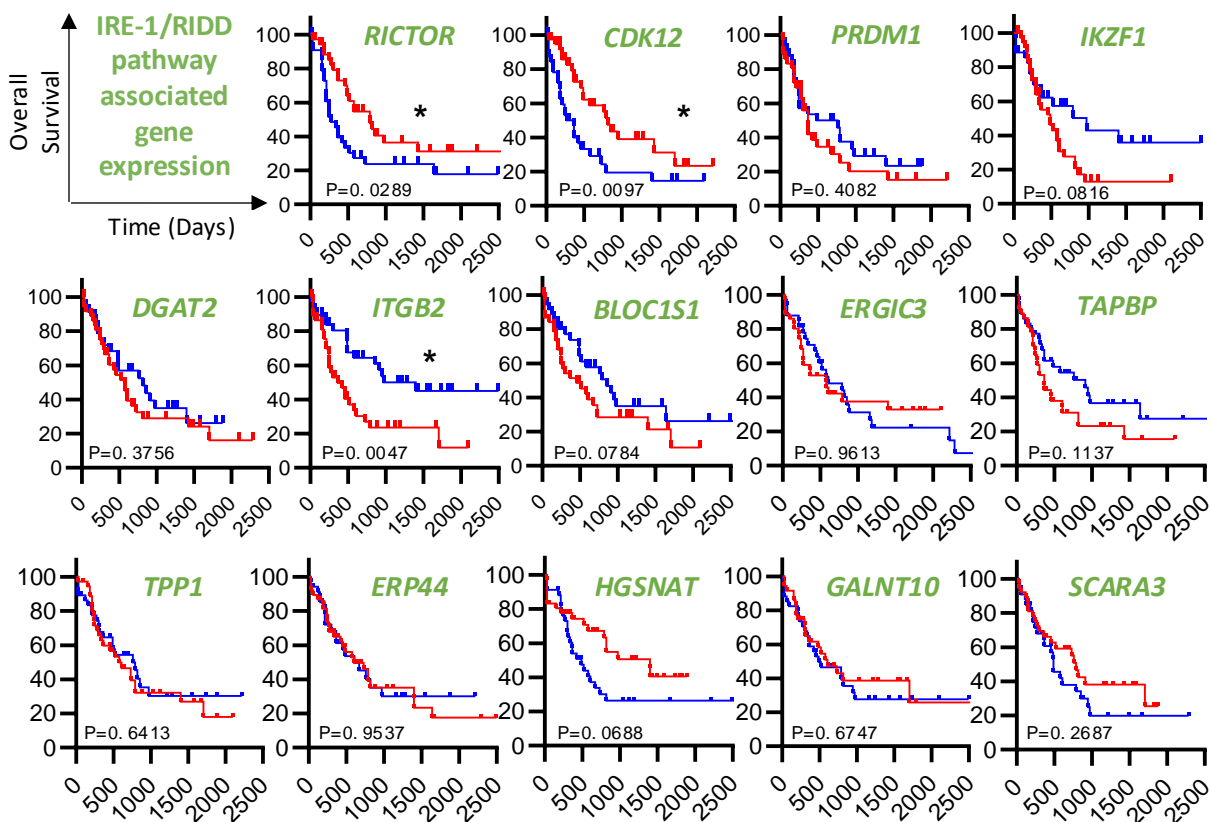
**Figure 1: UPR signatures correlate with survival prognosis of AML and breast cancer patients.**



**supplemental Figure 1.** Branch-specific UPR signatures correlate with survival prognosis of patients with Acute Myeloid Leukemia.

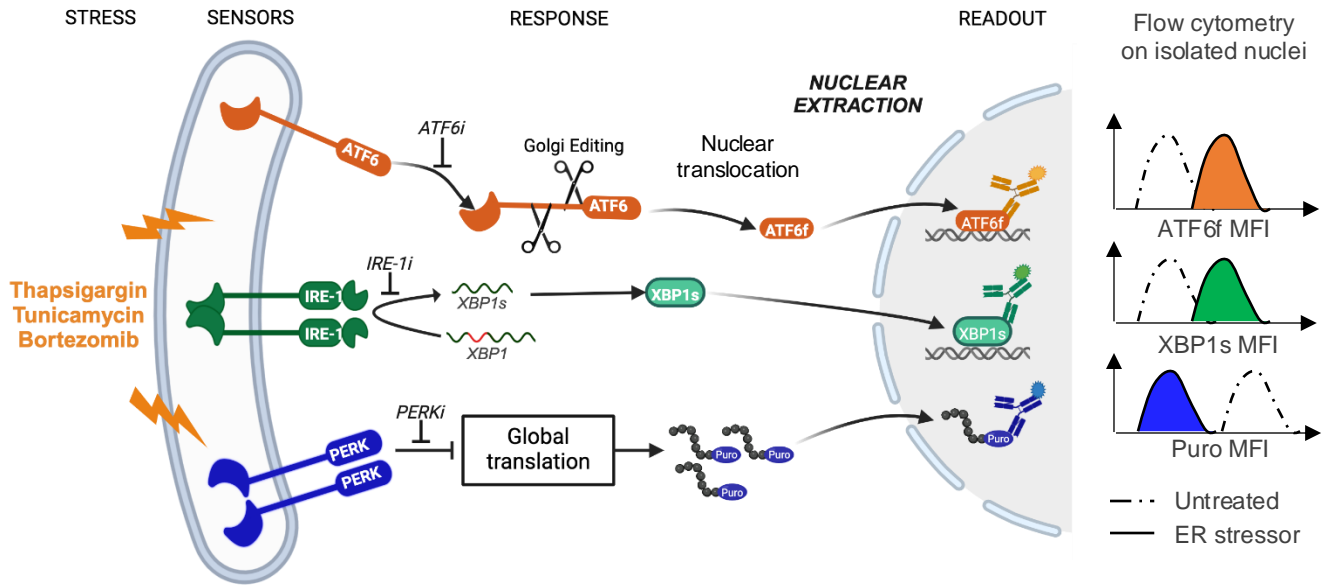


supplemental Figure 2. RIDD targets expression correlate with survival prognosis of AML patients.



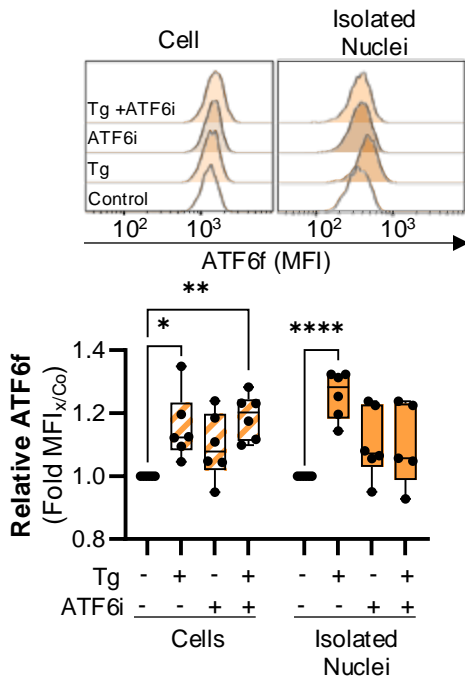
**Figure 2.** SNUPR, a method to profile UPR sensors activation during ER stress

**A.**



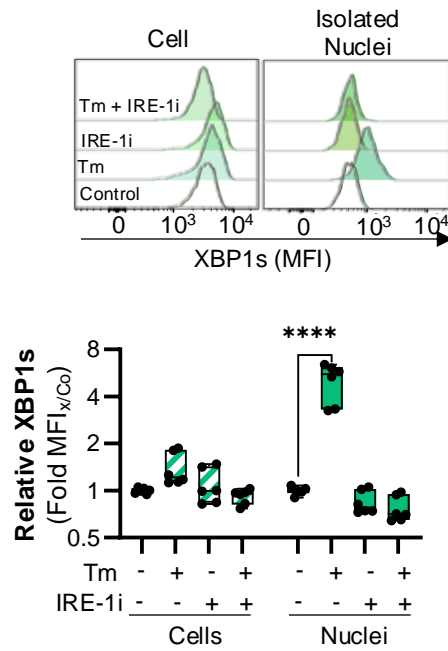
**B.**

**ATF6 branch**



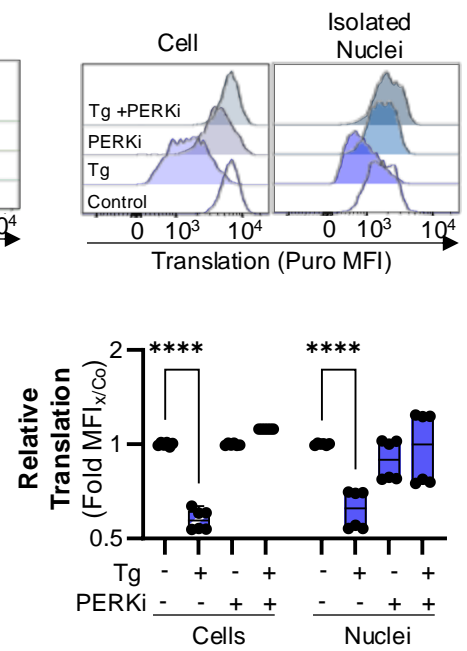
**C.**

**IRE-1 branch**



**D.**

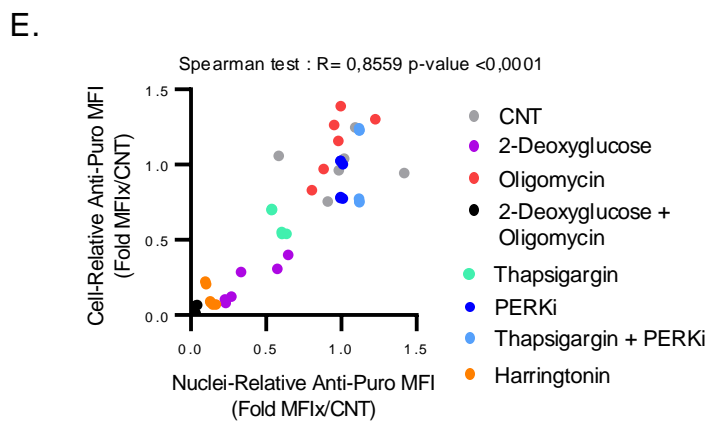
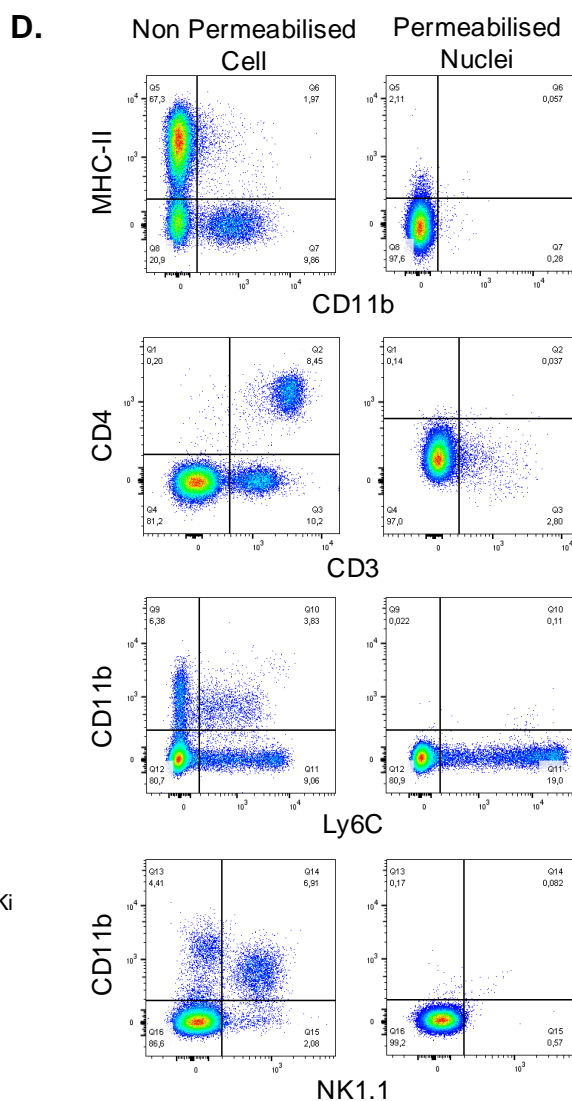
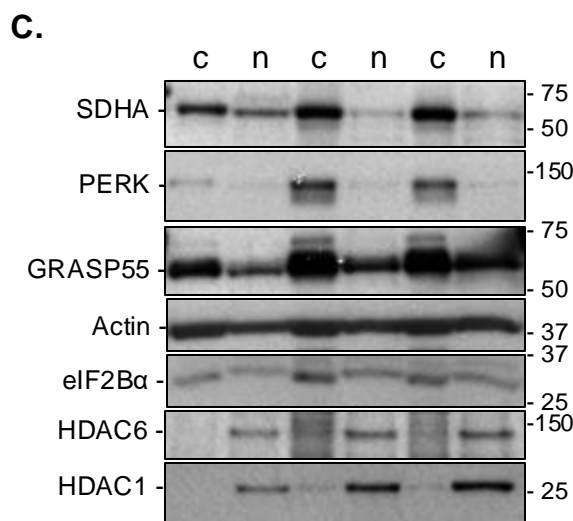
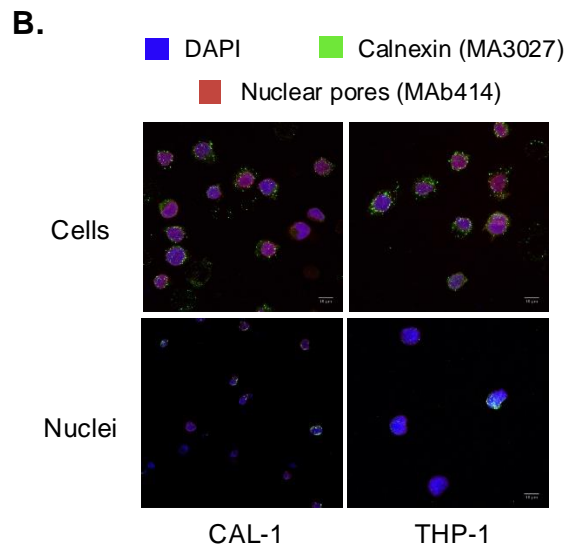
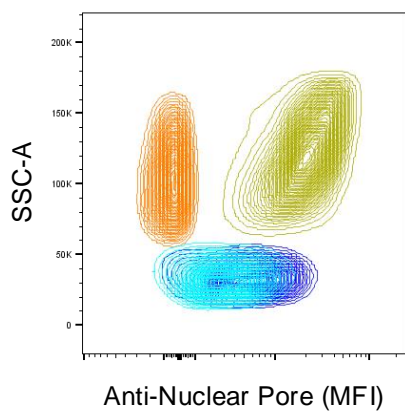
**PERK branch**



**supplemental Figure 3. Quality control of nuclear extraction for SNUPR profiling**

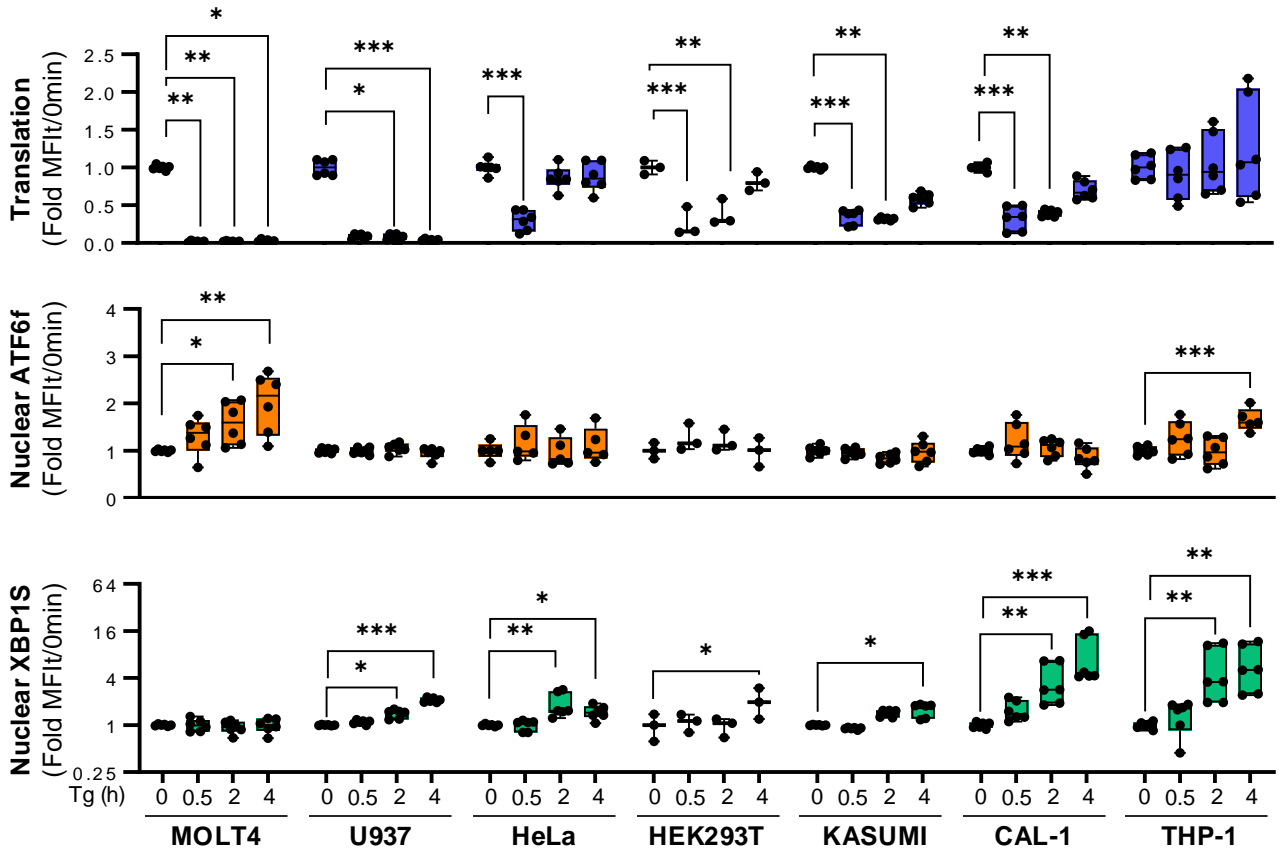
**A.**

- Non-permeabilized cells
- Permeabilized cells
- Non-permeabilized nuclei
- Permeabilized nuclei

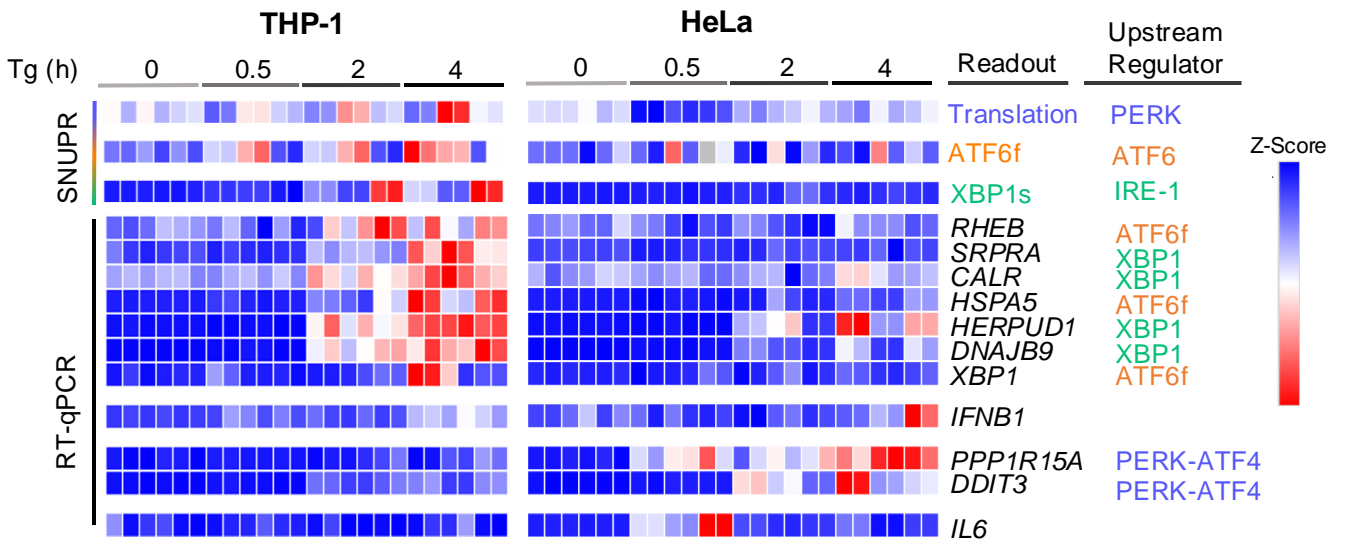


**Figure 3.** Induction of acute ER stress induces different UPR profiles in cell lines

**A.**

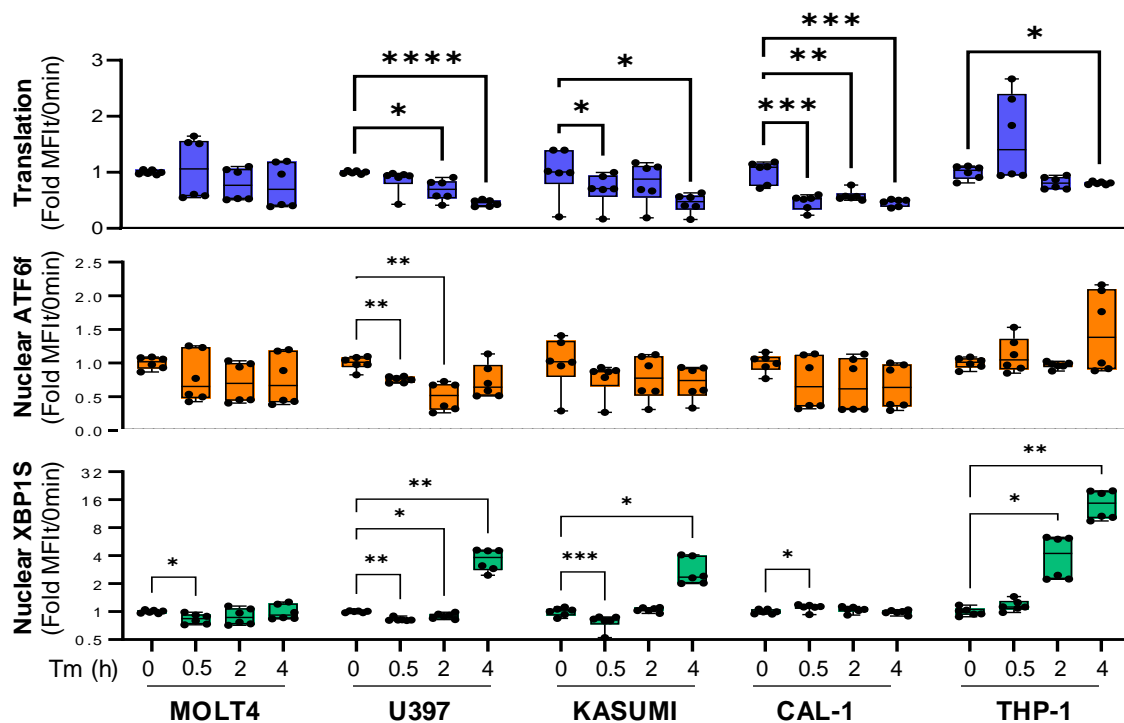


**B.**

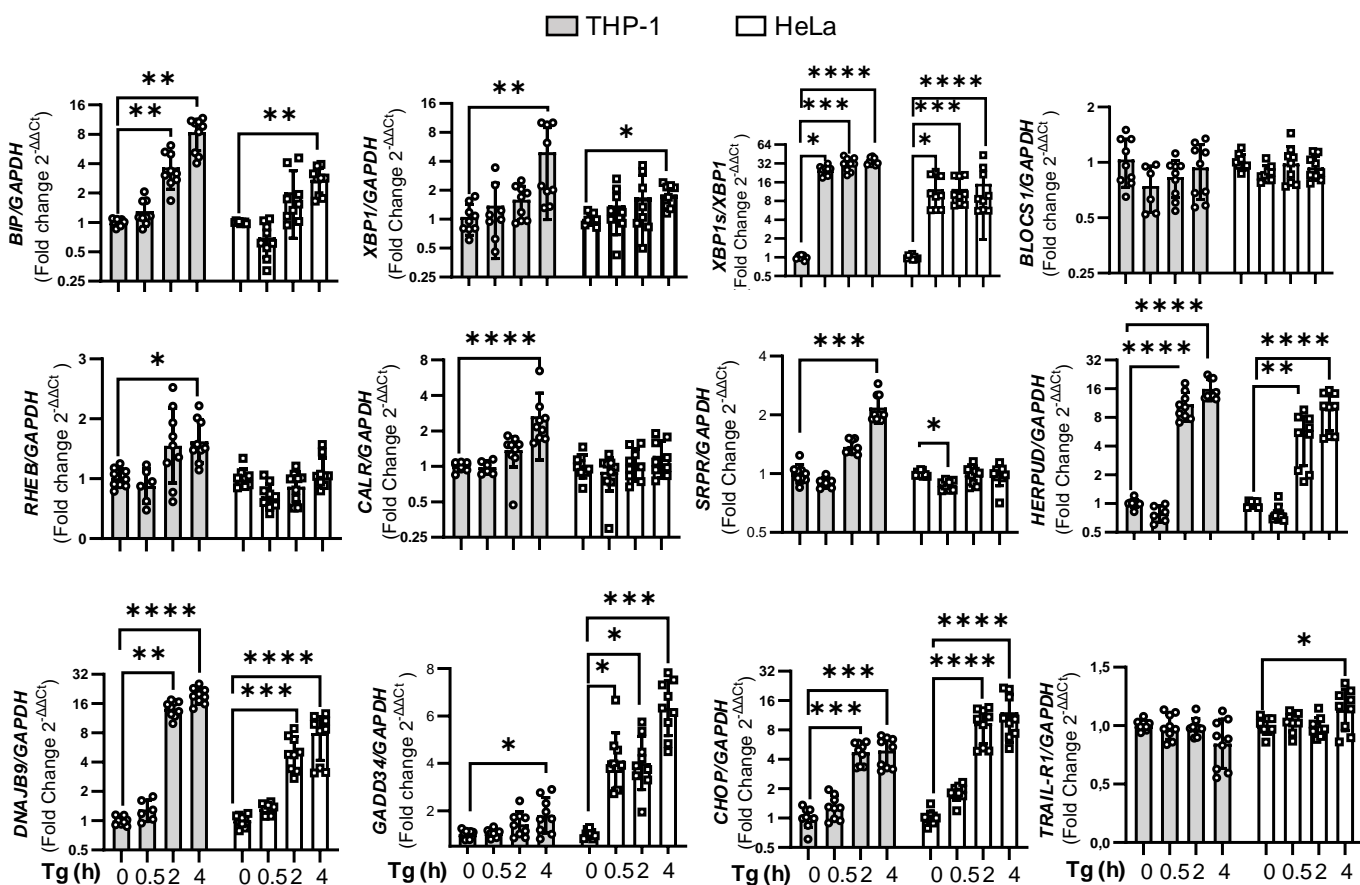


supplemental Figure 4. Rapid and efficient inhibition of protein synthesis modulates UPR activation

A.



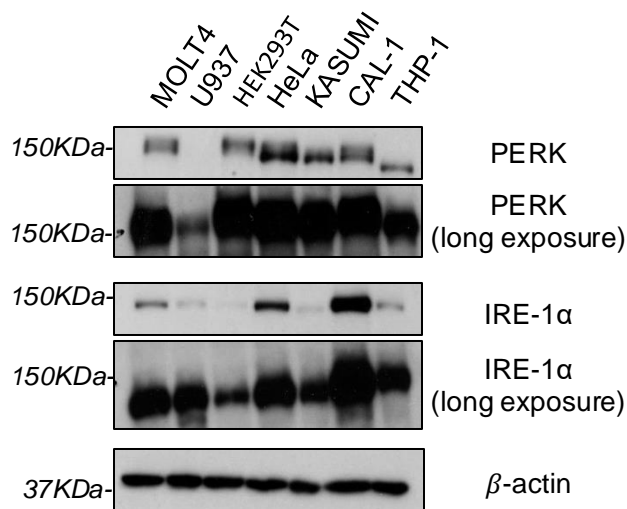
B.



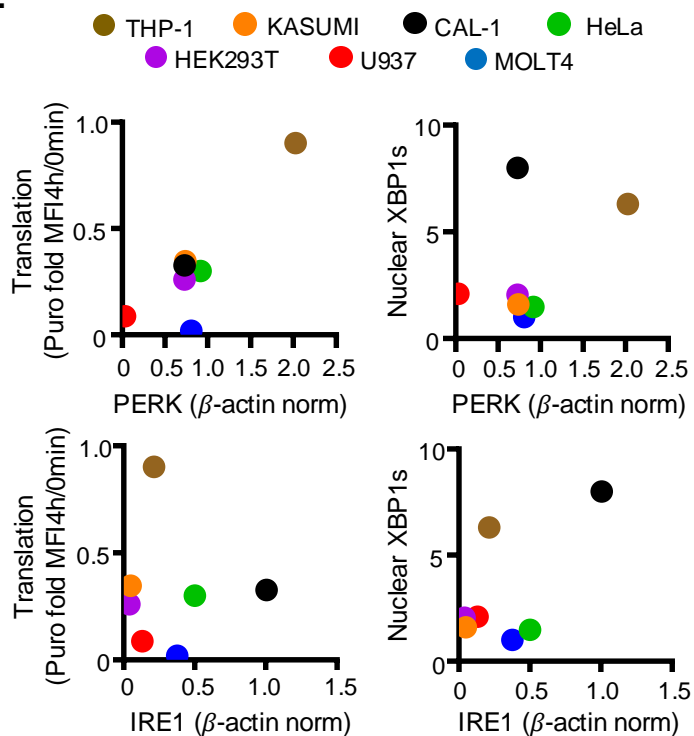


supplemental Figure 5.

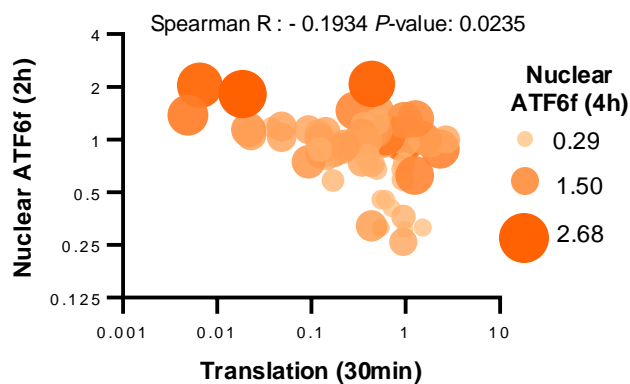
A.



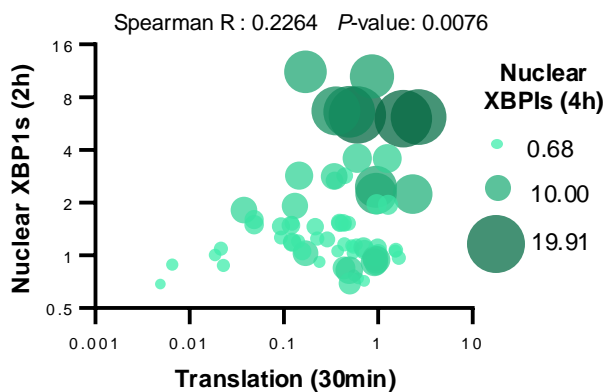
B.



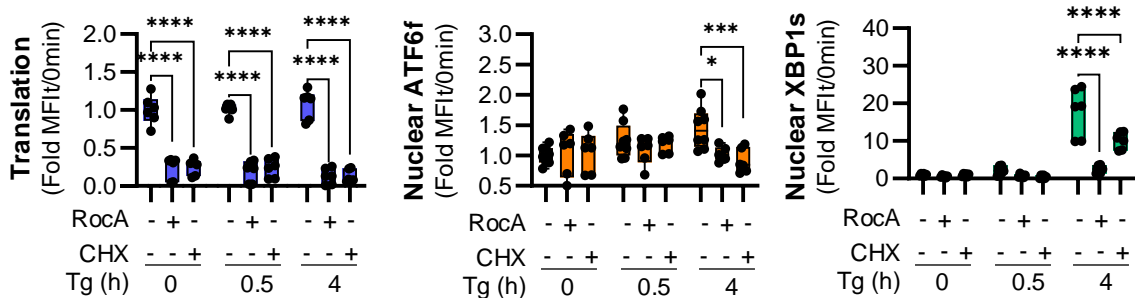
C.



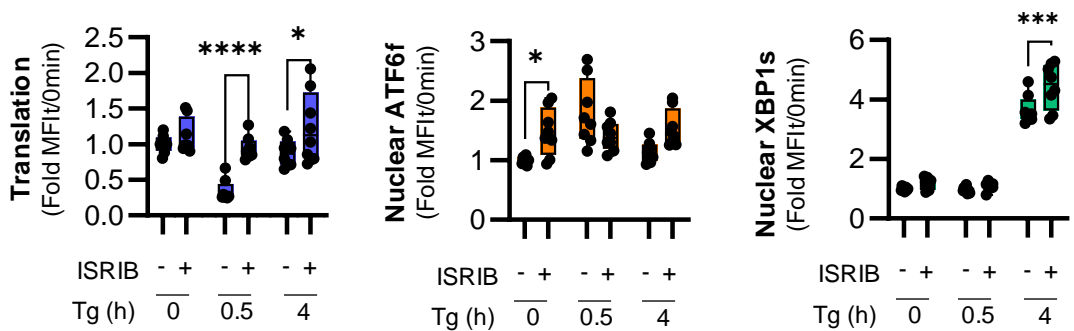
D.



**A.**



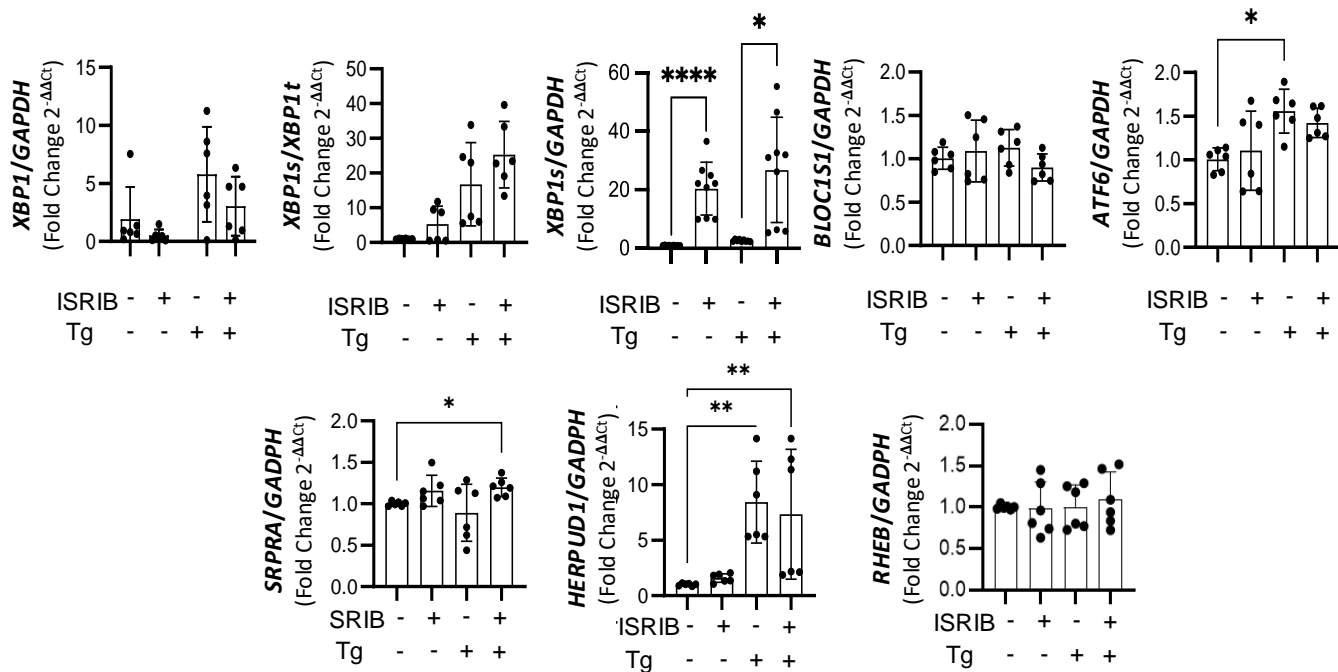
**B.**



**Figure 4.** Translation arrest delays the activation of the IRE1/XBP1s and ATF6 pathways

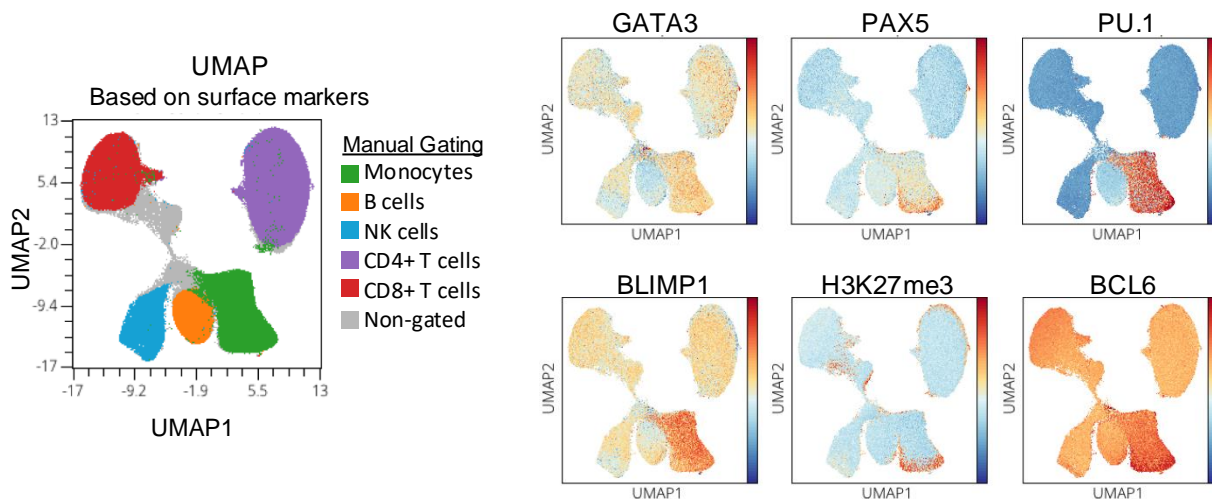
**supplemental Figure 6.** Translation inhibition delays IRE-1/XBP1s axis activation

**A.**

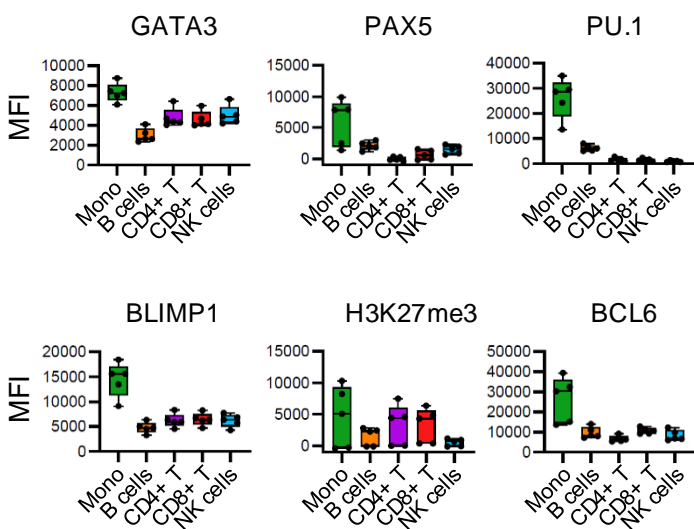


supplemental Figure 7. Lineage-associated transcription factor staining allows SNUPR profiling on specific cell subsets on PBMC.

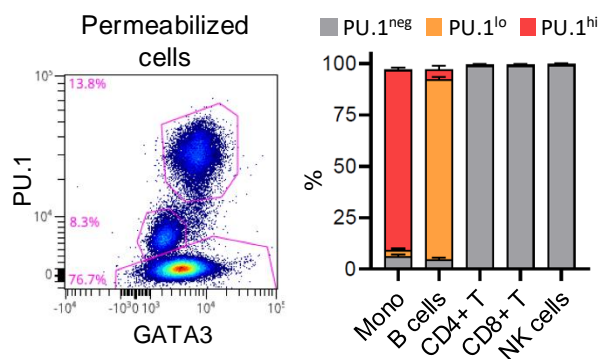
A.



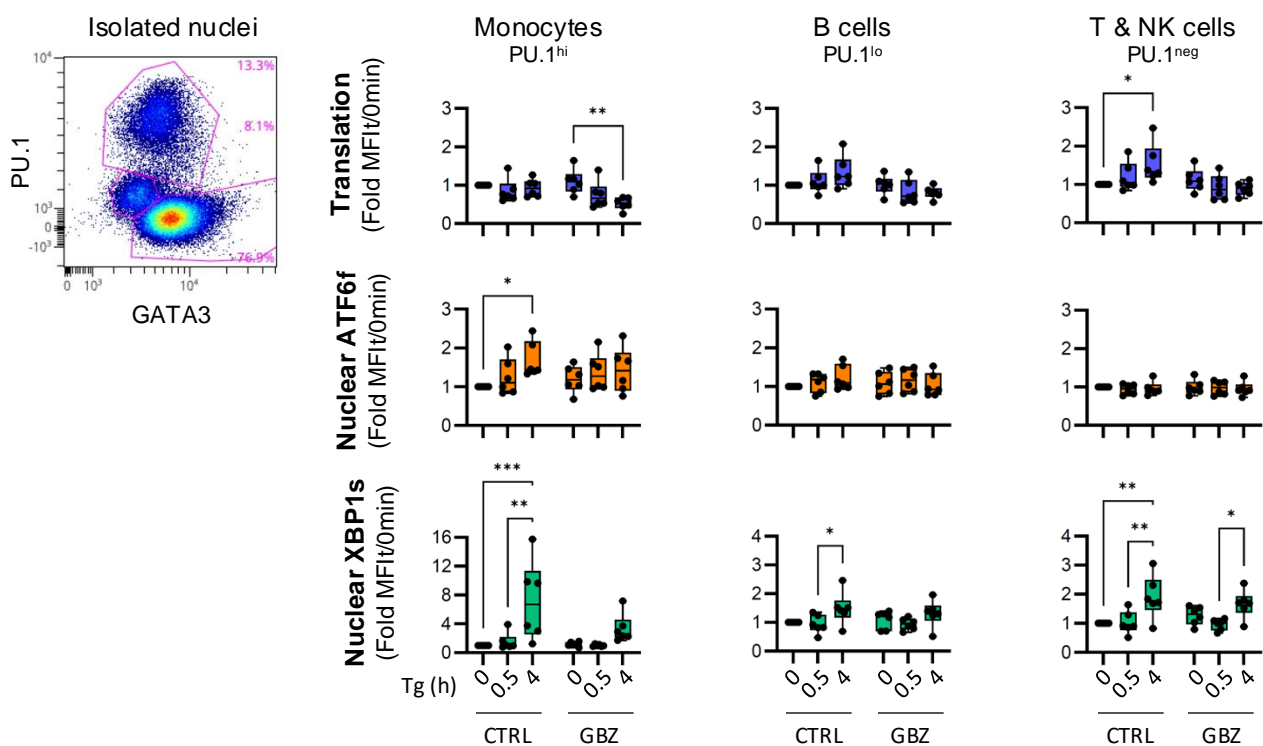
B.



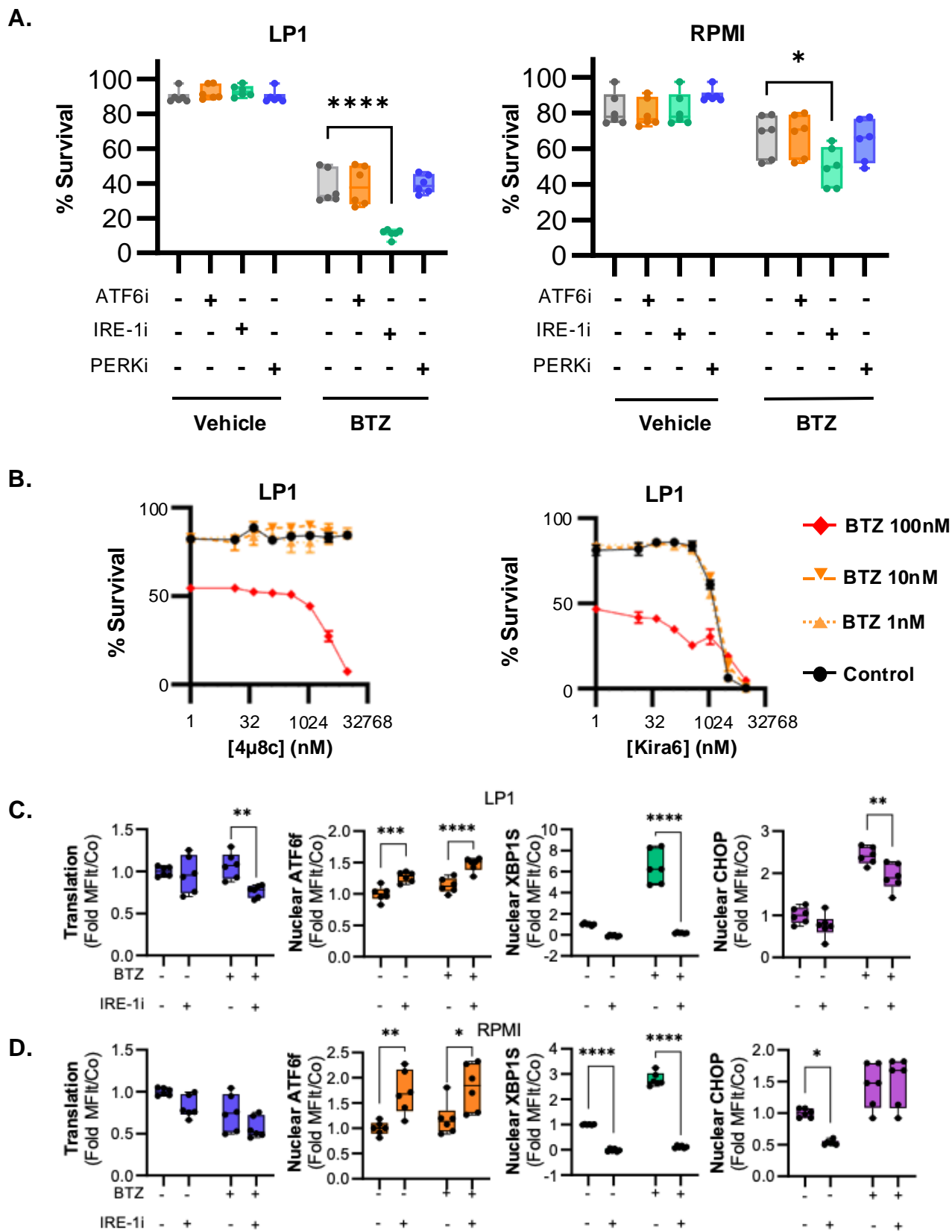
C.



D.

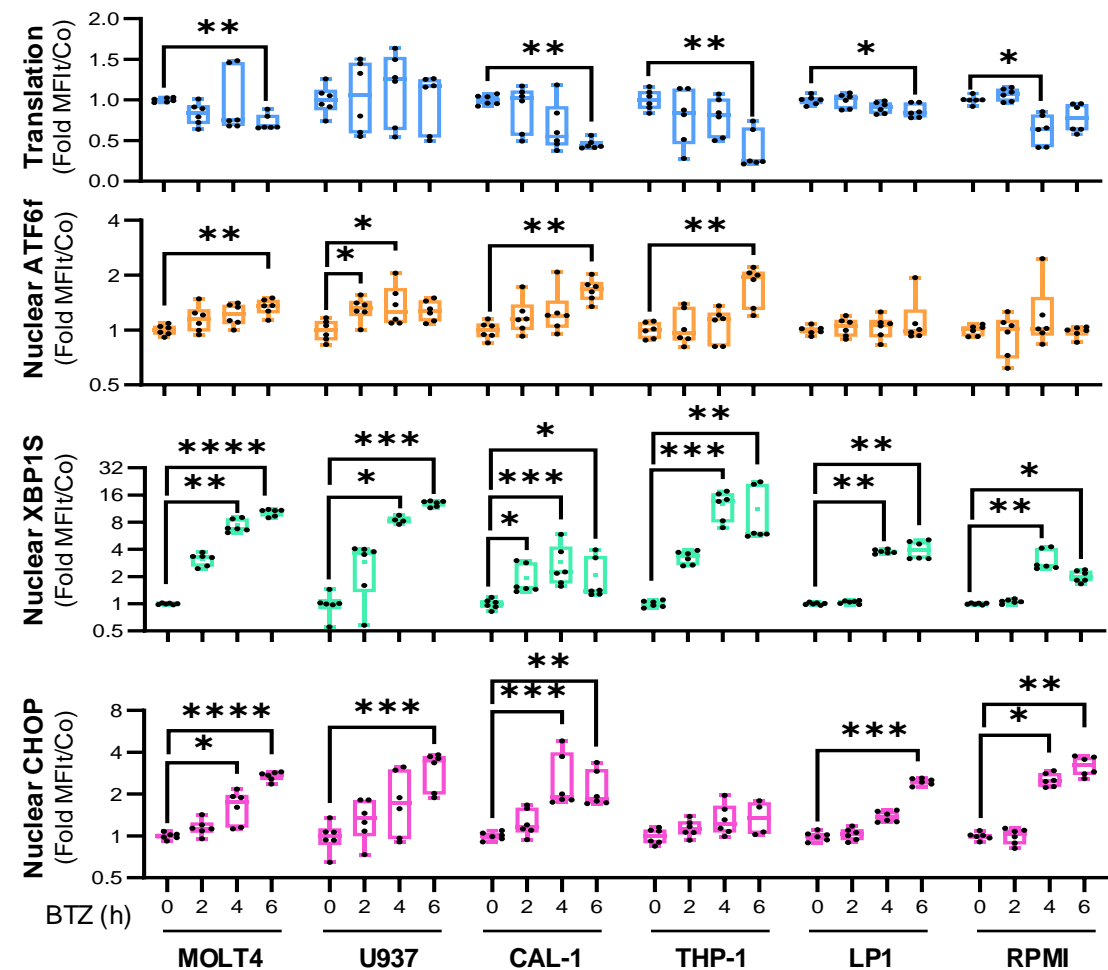


**Figure 5. IRE-1 contributes to bortezomib resistance in multiple myeloma cell lines.**

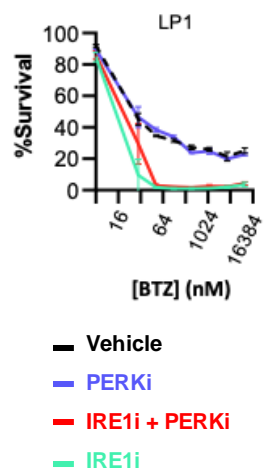


**supplemental Figure 8.** Bortezomib induces UPR activation in leukemic and myeloma cells.

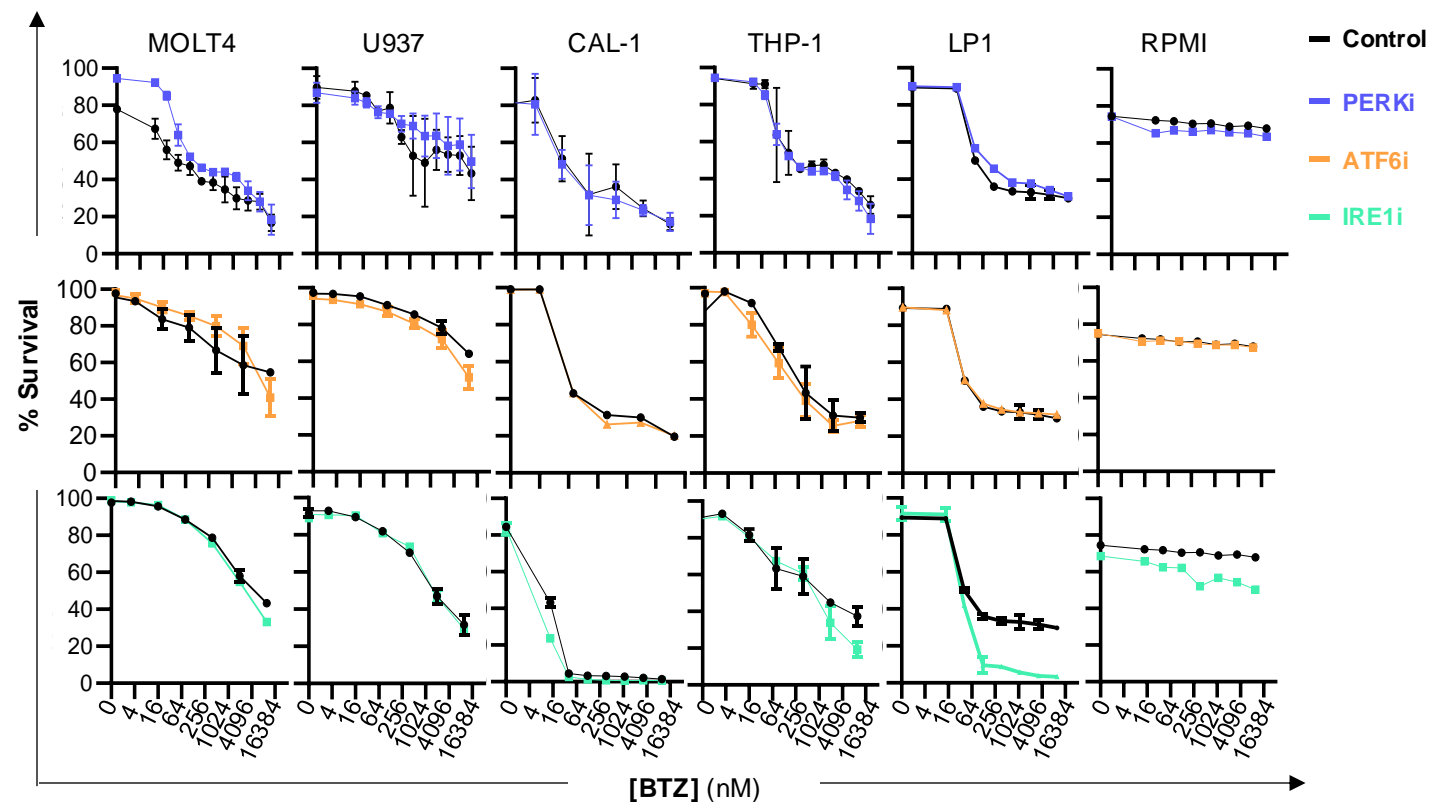
**A.**



**B.**

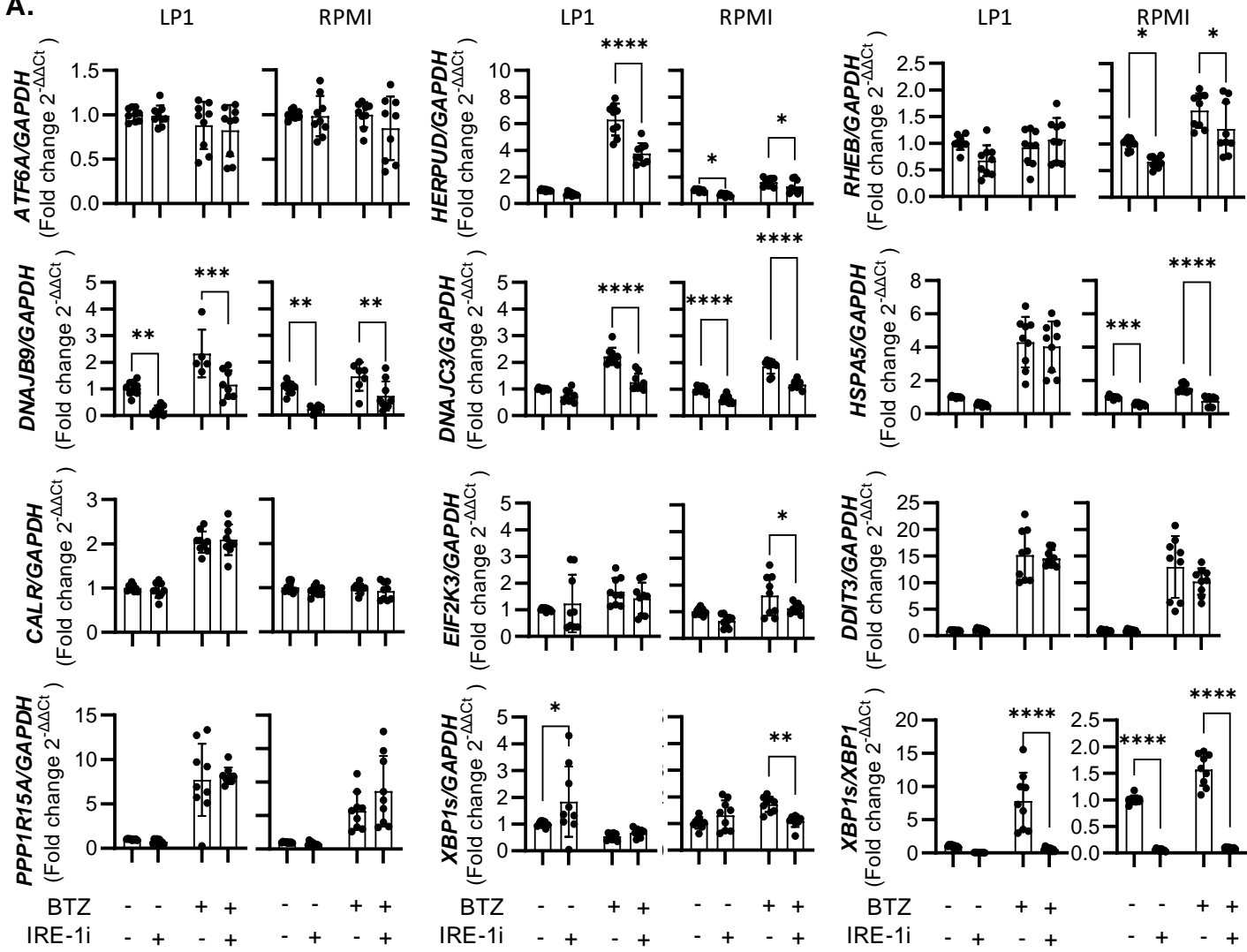


**C.**

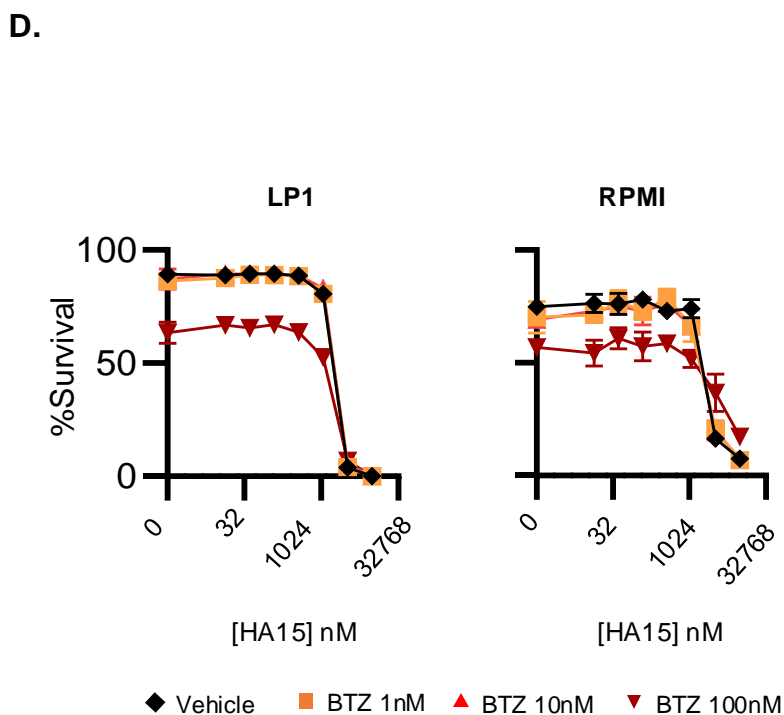
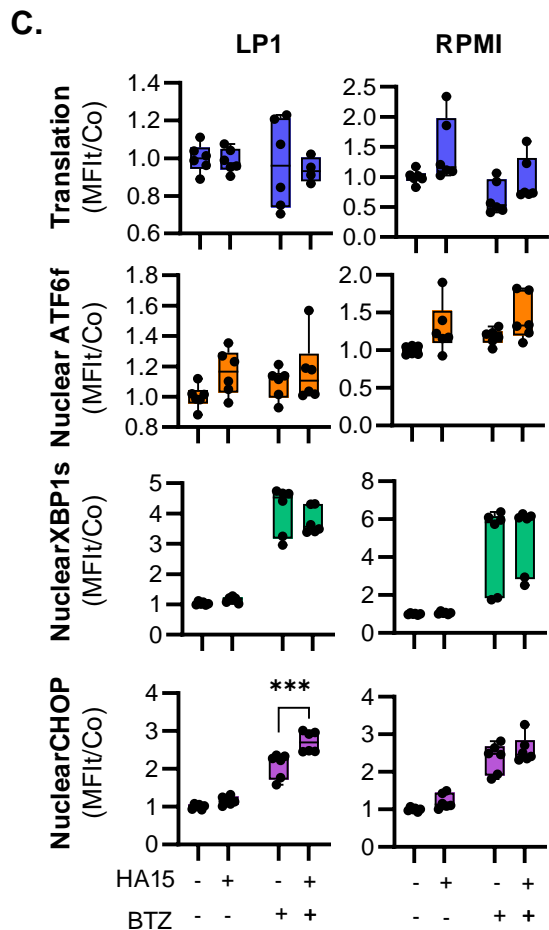
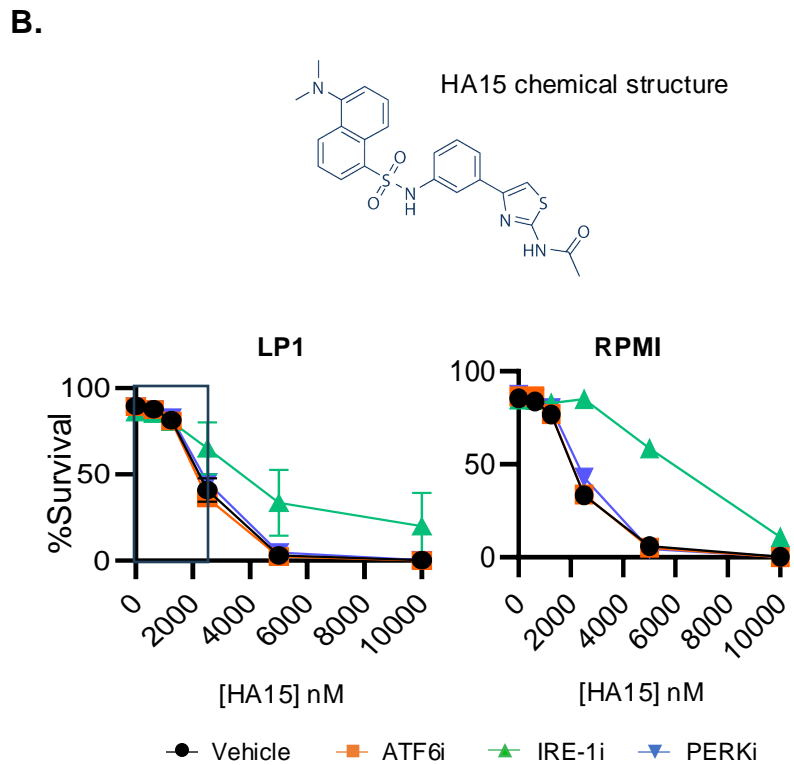
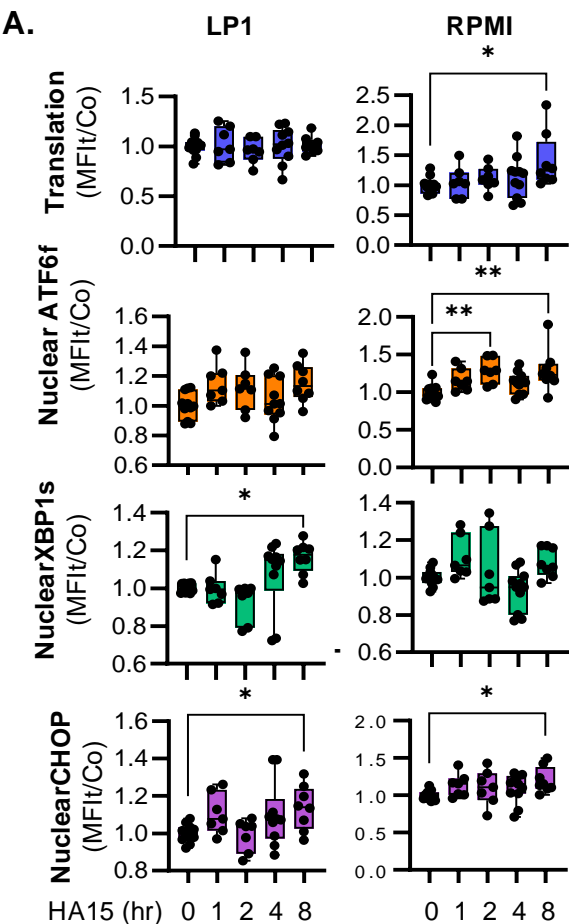


**supplemental Figure 9. IRE-1 inhibition affects ER chaperone expression on MM cells.**

**A.**



**Figure 6.**





**Figure 7. XBP1 gene signature correlates with unfavorable outcome in Multiple Myeloma patients treated with Bortezomib**

