

**Supplement to:**

**Deconvoluting Stress-Responsive Proteostasis Signaling Pathways for Pharmacologic Activation  
using Targeted RNA-sequencing**

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## SUPPLEMENTAL FIGURE LEGENDS

### Figure S1 (Supplement to Fig. 1)

- A. Percentage of total aligned reads reporting on the selected 150 target genes of interest for Targeted RNAseq, or whole-transcriptome RNAseq from HEK293<sup>TREX</sup> cells expressing dox-inducible cHSF1<sup>8</sup>, or HEK293<sup>DAX</sup> cells expressing TMP-inducible ATF6 and dox-inducible XBP1s<sup>15</sup>
- B. Average reads per individual gene in our Targeted RNAseq assay across all treatment conditions.
- C. Total reads per individual gene in our Targeted RNAseq assay across all treatment conditions.
- D. Example correlation analysis from our Targeted RNAseq assay showing the log<sub>2</sub> normalized aligned counts from two replicates of DMSO-treated HEK293T cells. The tight correlation demonstrates the reproducibility of this assay across individual replicates.
- E. Average R<sup>2</sup> values from correlations of three technical replicates (calculated as in **Fig. S1D**) for each treatment condition used in our Targeted RNAseq assay (see **Table 2** and **Table S1**).
- F. Heat map of relative gene expression values across the Targeted RNAseq panel of 150 genes (y-axis) Versus a total of 19 treatment conditions (including vehicle controls per cell type).

### Figure S2 (Supplement to Fig. 2)

- A. Log<sub>2</sub> normalized aligned transcript counts for HEK293<sup>TREX</sup> cells expressing doxycycline (dox)-inducible cHSF1 treated with 2.25 μM dox (y-axis) or vehicle (x-axis) for 16 h. Aligned transcript counts represent averages from three independent replicates quantified from published whole transcriptome RNAseq {Ryno, 2014 #73}. All identified genes are HSR target genes.
- B. Plot showing residuals calculated by comparing the expression of our panel of stress-responsive genes between HEK293<sup>TREX</sup> cells expressing dox-inducible cHSF1 following 16 h treatment with dox (2.25 μM) or vehicle. Calculation of residuals was performed as described in **Fig. 2A**. Statistics were calculated using one-way ANOVA. Significance shown reflects comparison to “Other” target transcript set. \*\*\*\*p<0.0001. See **Table S3** for full ANOVA table.
- C. Residual values per target gene from whole-transcriptome RNAseq data (x-axis){Ryno, 2014 #73} vs. Targeted RNAseq (y-axis) in HEK293<sup>TREX</sup> cells expressing dox-inducible cHSF1 following 16 h treatment with dox (2.25μM doxycycline).

### Figure S3 (Supplement to Fig. 3)

- A.** Log<sub>2</sub> normalized aligned transcript counts for HEK293<sup>DAX</sup> cells treated with 1 μM Thapsigargin (y-axis) or vehicle (x-axis) for 4 h. Aligned transcript counts represent averages from three independent replicates quantified from our targeted RNAseq data. All identified genes are UPR target genes.
- B.** Plot showing residuals calculated by comparing the expression of our panel of stress-responsive genes between HEK293<sup>DAX</sup> cells following 4 h treatment with Tg (1 μM; induces UPR) and vehicle. Calculation of residuals was performed as described in **Fig. 2A**. Statistics were calculated using one-way ANOVA. Significance shown reflects comparison to “Other” target transcript set. \*\*\*\*p<0.0001. See **Table S3** for full ANOVA table.
- C.** Residual values per target gene from whole-transcriptome RNAseq data (x-axis){Shoulders, 2013 #7} vs. Targeted RNAseq (y-axis) for HEK293<sup>DAX</sup> cells following treatment with trimethoprim (10 μM, 4 h; activates DHFR.ATF6).
- D.** Residual values per target gene from whole-transcriptome RNAseq data (x-axis){Shoulders, 2013 #7} vs. Targeted RNAseq (y-axis) for HEK293<sup>DAX</sup> cells following treatment with doxycycline (1 μg/mL μM, 4 h; activates dox-inducible XBP1s).
- E.** Residual values per target gene from whole-transcriptome RNAseq data (x-axis){Shoulders, 2013 #7} vs. Targeted RNAseq (y-axis) for HEK293<sup>DAX</sup> cells following treatment with both trimethoprim (10 μM, 4 h; activates DHFR.ATF6) and doxycycline (1 μg/mL μM, 4 h; activates dox-inducible XBP1s).

### Figure S4 (Supplement to Fig. 4)

Plot showing residuals calculated by comparing the expression of our stress-responsive gene panel between HEK293T cells following treatment with paraquat (PQ; 400 μM, 24 h) or vehicle. Calculation of residuals was performed as described in **Fig. 2A**. Genes are grouped by target stress-responsive signaling pathway. Statistics were calculated using one-way ANOVA, significance shown reflects comparison to “Other” target transcript set. See **Table S3** for full ANOVA table.

**Figure S5 (Supplement to Fig 5).**

- A.** Structures of the putative NRF2 activating compounds bardoxolone and CBR-470-1.
- B.** Graph showing  $\log_2$  fold change normalized counts of the HSR target gene *BAG3* in HEK293T cells treated with bardoxolone (1  $\mu$ M; 24 h) or CBR-470-1 (10  $\mu$ M; 24 h), as calculated from our targeted RNAseq assay. Error bars show SEM for n=3 independent experiments. P-values calculated using one-tailed Student's t-test.
- C.** Graph showing  $\log_2$  fold change normalized counts of the UPR (ATF6) target gene *BIP* in HEK293T cells treated with bardoxolone (1  $\mu$ M; 24 h) or CBR-470-1 (10  $\mu$ M; 24 h), as calculated from our targeted RNAseq assay. Error bars show SEM for n=3 independent experiments. P-values calculated using one-tailed Student's t-test.
- D.** Graph showing  $\log_2$  fold change normalized counts of the OSR target gene *HMOX1* in HEK293T cells treated with bardoxolone (1  $\mu$ M; 24 h) or CBR-470-1 (10  $\mu$ M; 24 h), as calculated from our targeted RNAseq assay. Error bars show SEM for n=3 independent experiments. P-values calculated using one-tailed Student's t-test.

**Figure S6 (Supplement to Fig. 6)**

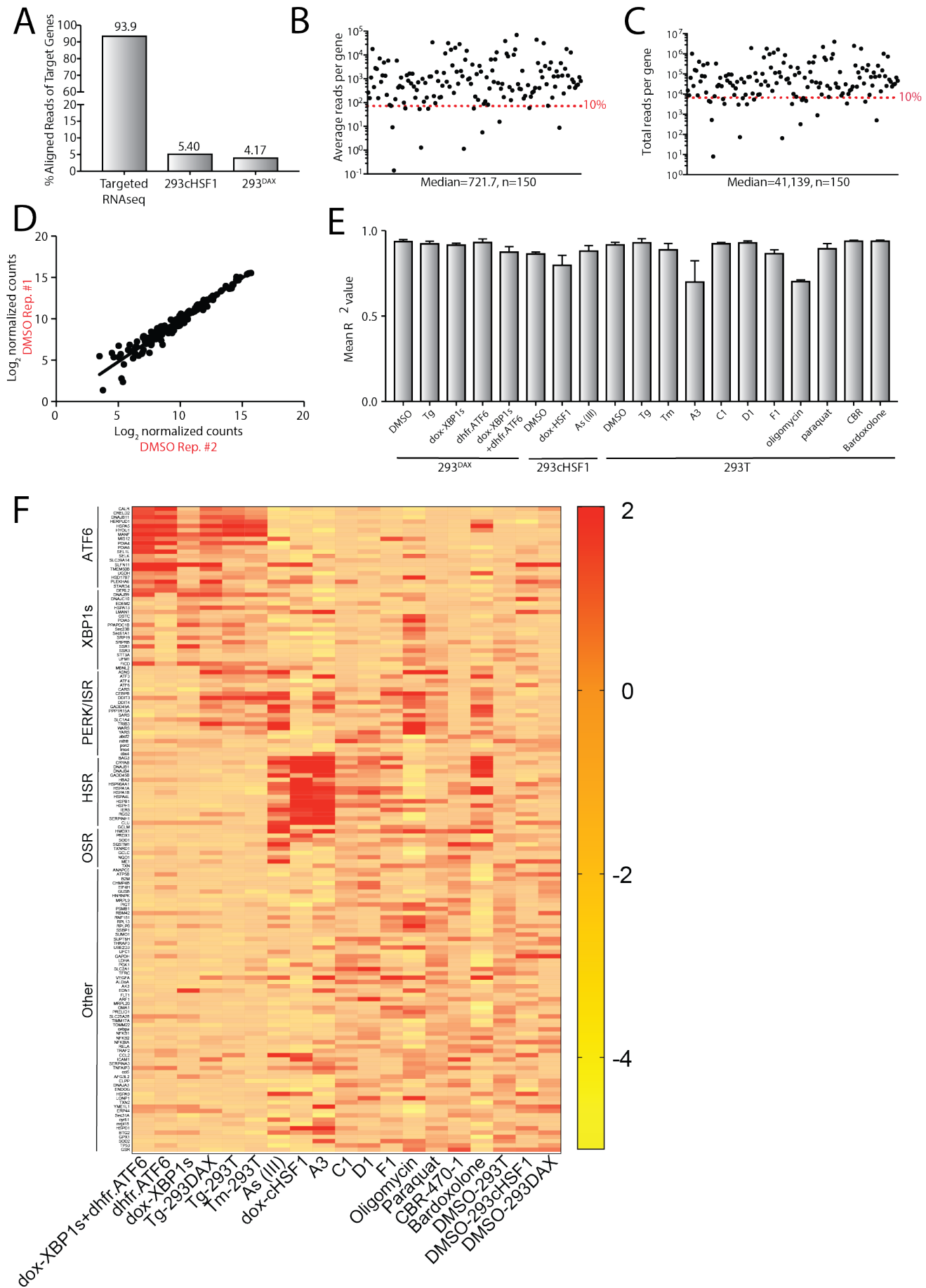
- A.** Structures of the four putative HSF1 activating compounds A3, C1, D1, and F1.
- B.** Plot showing residuals calculated by comparing the expression of our stress-responsive gene panel between HEK293T cells treated with compound A3 (10  $\mu$ M, 4 h) or vehicle from whole-transcriptome RNAseq. Calculation of residuals was performed as described in **Fig. 2A**. Genes are grouped by target stress-responsive signaling pathway. Statistics were calculated using one-way ANOVA. Significance shown reflects comparison to "Other" target transcript set. \*\*\*\*p<0.0001.
- C.** Plot showing residuals calculated by comparing the expression of our stress-responsive gene panel between HEK293T cells treated with compound C1 (10  $\mu$ M, 4 h) or vehicle from whole-transcriptome RNAseq. Calculation of residuals was performed as described in **Fig. 2A**. Genes are grouped by target stress-responsive signaling pathway. Statistics were calculated using one-way ANOVA. Significance shown reflects comparison to "Other" target transcript set. \*\*\*\*p<0.0001.

- D. Plot showing residuals calculated by comparing the expression of our stress-responsive gene panel between HEK293T cells treated with compound D1 (10  $\mu$ M, 4 h) or vehicle from whole-transcriptome RNAseq. Calculation of residuals was performed as described in **Fig. 2A**. Genes are grouped by target stress-responsive signaling pathway. Statistics were calculated using one-way ANOVA. Significance shown reflects comparison to “Other” target transcript set. \*\*\*\* $p < 0.0001$ .
- E. Plot showing residuals calculated by comparing the expression of our stress-responsive gene panel between HEK293T cells treated with compound F1 (10  $\mu$ M, 4 h) or vehicle from whole-transcriptome RNAseq. Calculation of residuals was performed as described in **Fig. 2A**. Genes are grouped by target stress-responsive signaling pathway. Statistics were calculated using one-way ANOVA. Significance shown reflects comparison to “Other” target transcript set. \*\*\*\* $p < 0.0001$ .
- F. One-way ANOVA statistical analysis for grouped residual values in (**Fig. S6B**).
- G. One-way ANOVA statistical analysis for grouped residual values in (**Fig. S6C**).
- H. One-way ANOVA statistical analysis for grouped residual values in (**Fig. S6D**).
- I. One-way ANOVA statistical analysis for grouped residual values in (**Fig. S6E**).

#### **Figure S7 (Supplement to Concluding Remarks)**

- A. Plot showing residuals calculated by comparing the expression of our stress-responsive gene panel between MEF cells treated with compound As (III) (25  $\mu$ M, 6h) or vehicle from whole-transcriptome RNAseq. Calculation of residuals was performed as described in **Fig. 2A**. Genes are grouped by target stress-responsive signaling pathway. Statistics were calculated using one-way ANOVA. Significance shown reflects comparison to “Other” target transcript set. \*\*\*\* $p < 0.0001$ .
- B. Plot showing residuals calculated by comparing the expression of our stress-responsive gene panel between MEF cells treated with compound Tg (1  $\mu$ M, 6h) or vehicle from whole-transcriptome RNAseq. Calculation of residuals was performed as described in **Fig. 2A**. Genes are grouped by target stress-responsive signaling pathway. Statistics were calculated using one-way ANOVA. Significance shown reflects comparison to “Other” target transcript set. \* $p < 0.05$ , \*\*\*\* $p < 0.0001$ .

**FIGURE S1**



**FIGURE S2**

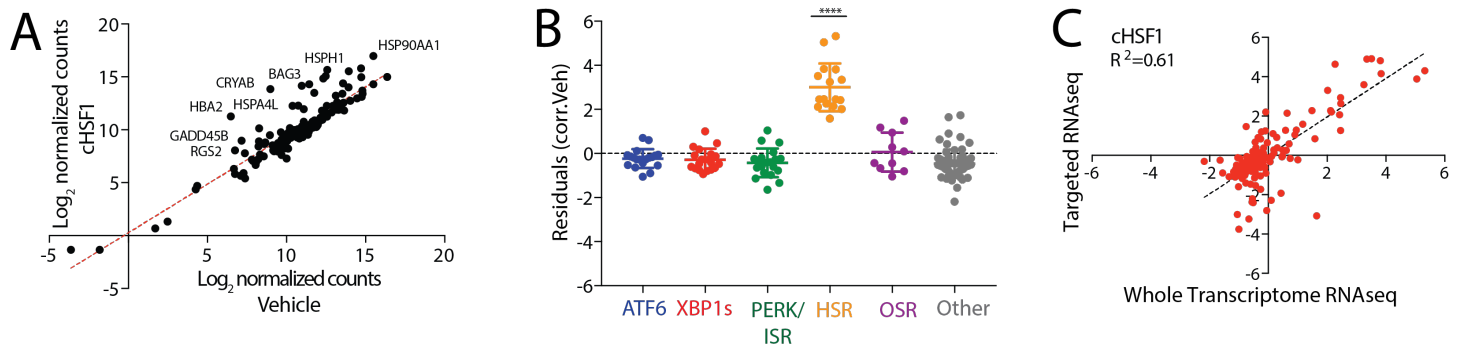


FIGURE S3

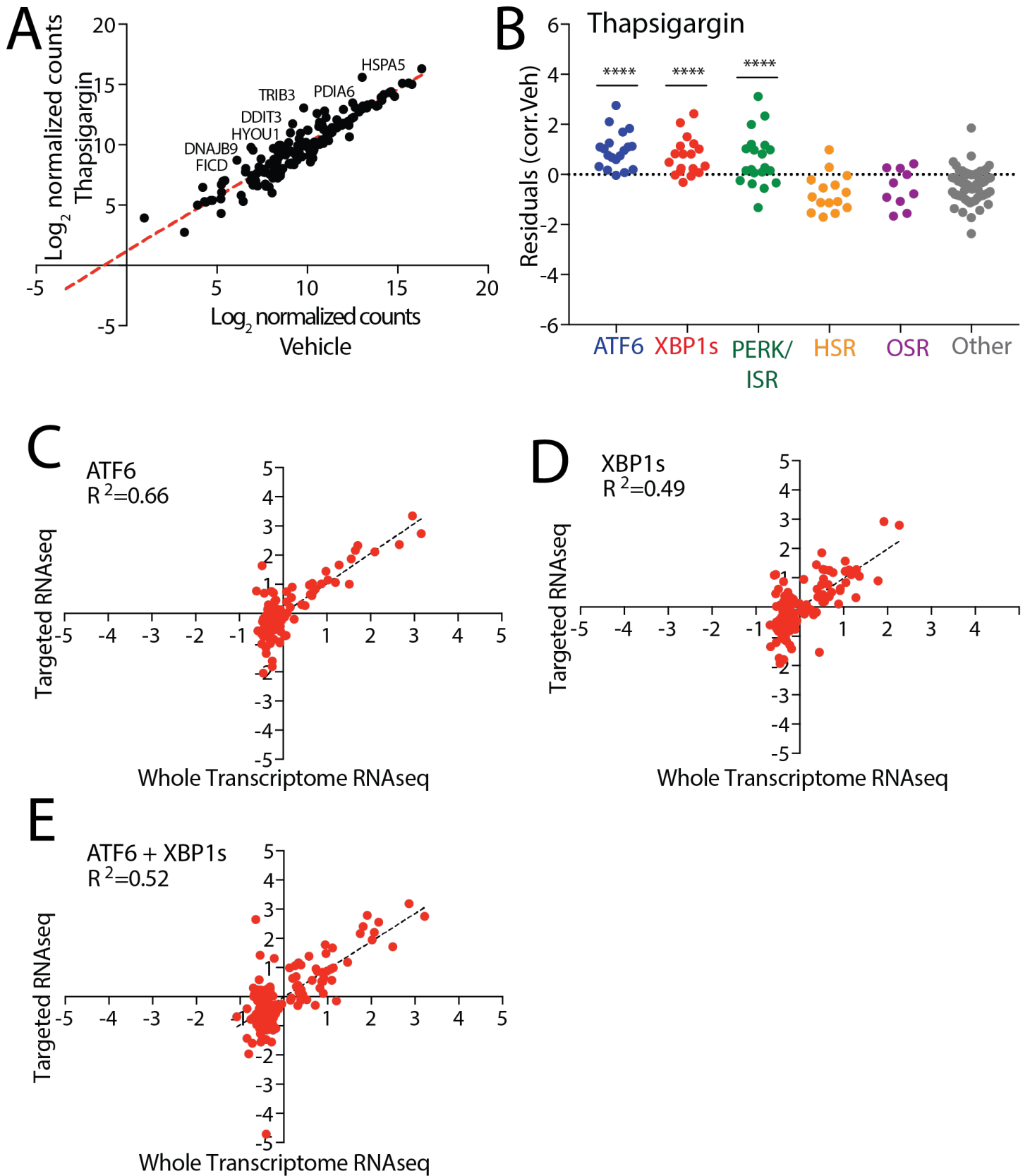




FIGURE S4

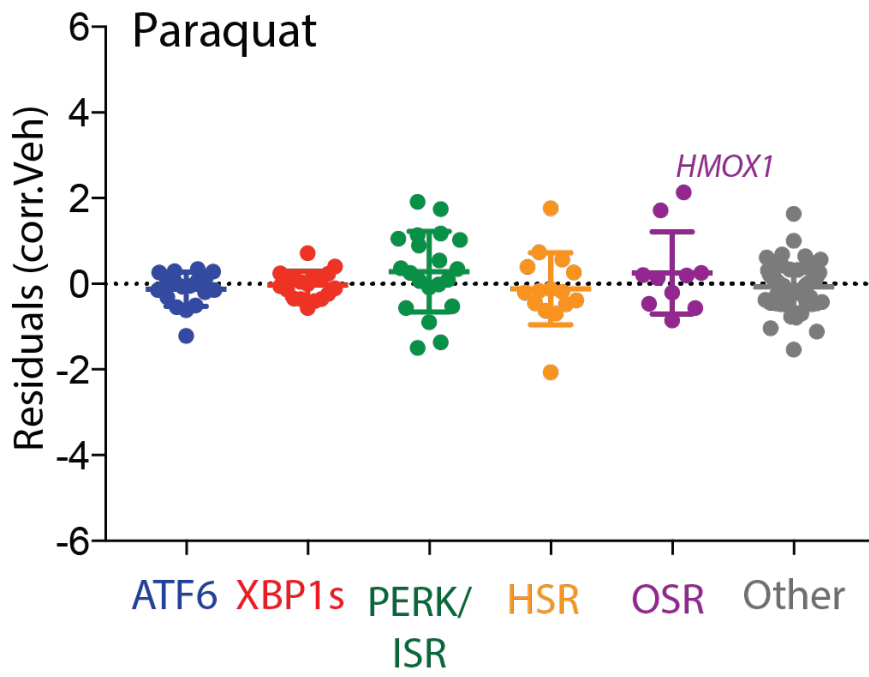
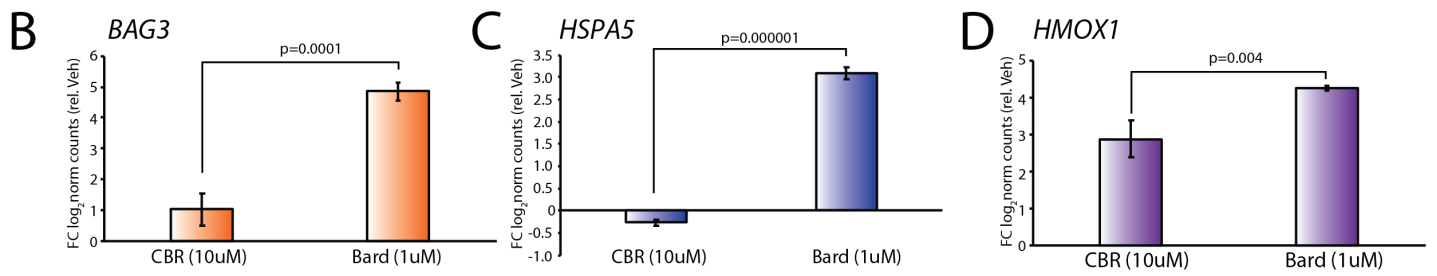
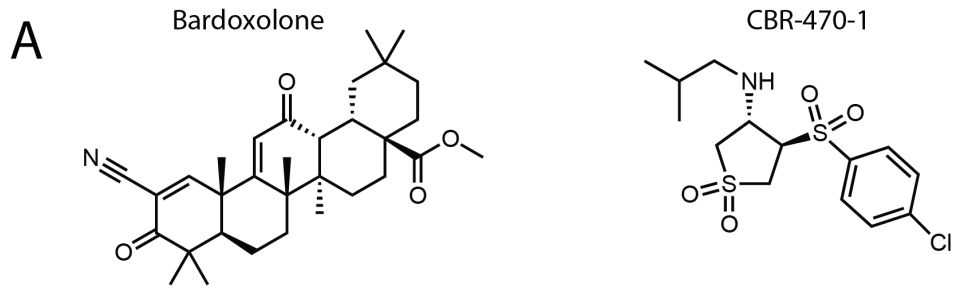
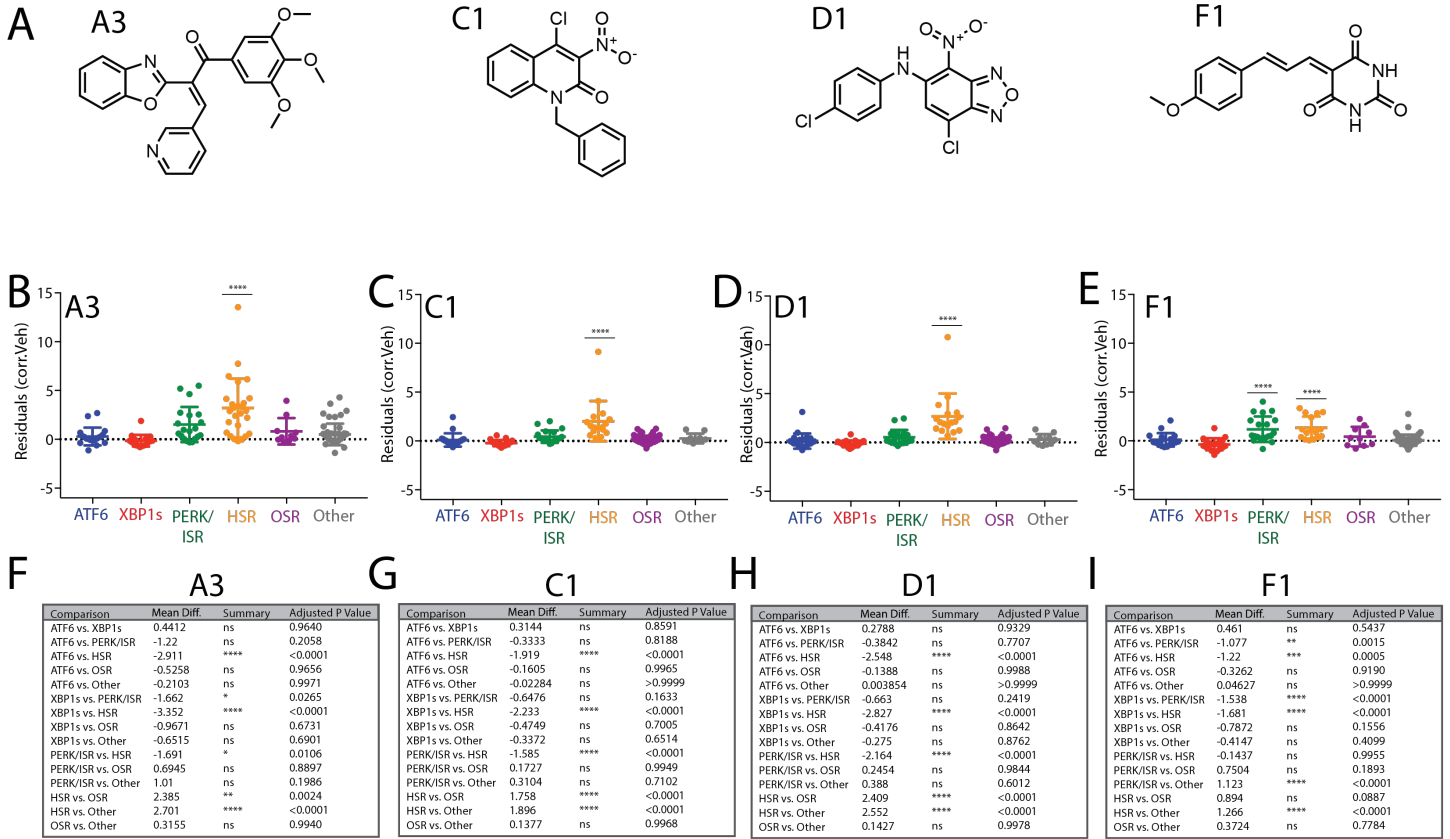


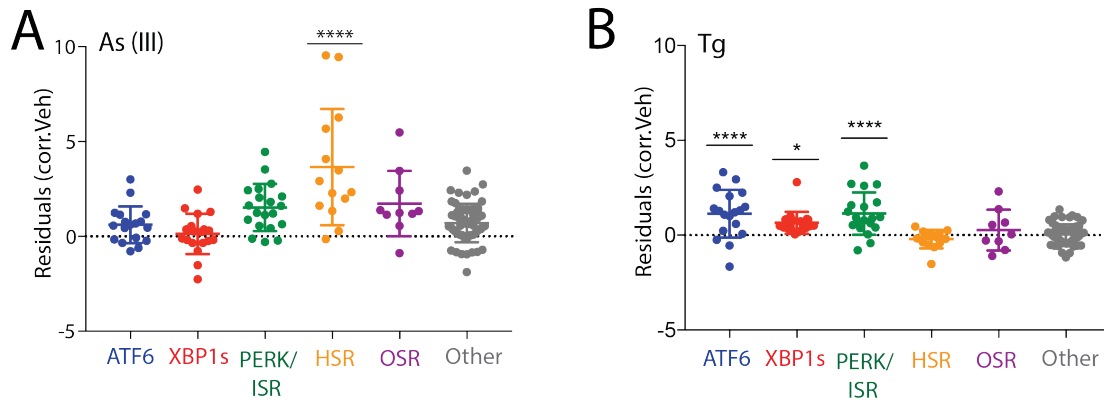
FIGURE S5



**FIGURE S6**



**FIGURE S7**



**Table S1. Treatment conditions for Targeted RNAseq with concentrations and treatment durations (see Excel Spreadsheet)**

**Table S2 Aligned counts from Targeted RNAseq (see Excel Spreadsheet)**

**Table S3. ANOVA Statistical Analysis from Targeted RNAseq**

HSF1				XBP1s				ATF6				XBP1s+ATF6			
Comparison	Mean Diff.	Summary	Adjusted P Value	Comparison	Mean Diff.	Summary	Adjusted P Value	Comparison	Mean Diff.	Summary	Adjusted P Value	Comparison	Mean Diff.	Summary	Adjusted P Value
ATF6 vs. XBP1s	-0.2735	ns	0.9671	ATF6 vs. XBP1s	-0.5015	ns	0.1807	ATF6 vs. XBP1s	1.546	****	<0.0001	ATF6 vs. XBP1s	0.6466	ns	0.1510
ATF6 vs. PERK/ISR	-0.2218	ns	0.9878	ATF6 vs. PERK/ISR	0.7097	*	0.0123	ATF6 vs. PERK/ISR	1.717	****	<0.0001	ATF6 vs. PERK/ISR	1.886	****	<0.0001
ATF6 vs. HSR	-3.863	****	<0.0001	ATF6 vs. HSR	1.016	***	0.0002	ATF6 vs. HSR	1.772	****	<0.0001	ATF6 vs. HSR	1.989	****	<0.0001
ATF6 vs. OSR	-0.421	ns	0.9057	ATF6 vs. OSR	1.119	****	0.0003	ATF6 vs. OSR	1.891	****	<0.0001	ATF6 vs. OSR	2.09	****	<0.0001
ATF6 vs. Other	-0.1022	ns	0.9991	ATF6 vs. Other	0.8789	****	<0.0001	ATF6 vs. Other	1.737	ns	0.9961	ATF6 vs. Other	1.808	****	<0.0001
XBP1s vs. PERK/ISR	0.05166	ns	>0.9999	XBP1s vs. PERK/ISR	1.211	****	<0.0001	XBP1s vs. PERK/ISR	0.1717	ns	0.9412	XBP1s vs. PERK/ISR	1.239	****	<0.0001
XBP1s vs. HSR	-3.59	****	<0.0001	XBP1s vs. HSR	1.517	****	<0.0001	XBP1s vs. HSR	0.2259	ns	0.8722	XBP1s vs. HSR	1.343	****	<0.0001
XBP1s vs. OSR	-0.1475	ns	0.9992	XBP1s vs. OSR	1.62	****	<0.0001	XBP1s vs. OSR	0.3449	ns	0.6569	XBP1s vs. OSR	1.444	****	0.0002
XBP1s vs. Other	0.1712	ns	0.9894	XBP1s vs. Other	1.38	****	<0.0001	XBP1s vs. Other	0.1916	ns	0.8117	XBP1s vs. Other	1.161	****	<0.0001
PERK/ISR vs. HSR	-3.641	****	<0.0001	PERK/ISR vs. HSR	0.3062	ns	0.7370	PERK/ISR vs. HSR	0.05413	ns	0.9998	PERK/ISR vs. HSR	0.1038	ns	0.9991
PERK/ISR vs. OSR	-0.1992	ns	0.9968	PERK/ISR vs. OSR	0.4091	ns	0.5805	PERK/ISR vs. OSR	0.1732	ns	0.9727	PERK/ISR vs. OSR	0.2048	ns	0.9872
PERK/ISR vs. Other	0.1196	ns	0.9982	PERK/ISR vs. Other	0.1692	ns	0.9128	PERK/ISR vs. Other	0.01982	ns	>0.9999	PERK/ISR vs. Other	-0.07768	ns	0.9991
HSR vs. OSR	3.442	****	<0.0001	HSR vs. OSR	0.1029	ns	0.9988	HSR vs. OSR	0.119	ns	0.9961	HSR vs. OSR	0.101	ns	0.9997
HSR vs. Other	3.761	****	<0.0001	HSR vs. Other	-0.137	ns	0.9775	HSR vs. Other	-0.03431	ns	>0.9999	HSR vs. Other	-0.1815	ns	0.9723
OSR vs. Other	0.3187	ns	0.9490	OSR vs. Other	-0.2399	ns	0.8867	OSR vs. Other	-0.1534	ns	0.9721	OSR vs. Other	-0.2825	ns	0.9135

As (II)				Oligomycin				Paraquat				Thapsigargin			
Comparison	Mean Diff.	Summary	Adjusted P Value	Comparison	Mean Diff.	Summary	Adjusted P Value	Comparison	Mean Diff.	Summary	Adjusted P Value	Comparison	Mean Diff.	Summary	Adjusted P Value
ATF6 vs. XBP1s	-0.5934	ns	0.7071	ATF6 vs. XBP1s	-0.858	ns	0.3063	ATF6 vs. XBP1s	-0.1011	ns	0.9665	ATF6 vs. XBP1s	0.5652	ns	0.2424
ATF6 vs. PERK/ISR	-1.764	***	0.0005	ATF6 vs. PERK/ISR	-1.496	**	0.0055	ATF6 vs. PERK/ISR	-0.4086	ns	0.3509	ATF6 vs. PERK/ISR	0.3443	ns	0.7605
ATF6 vs. HSR	-2.037	***	<0.0001	ATF6 vs. HSR	0.6632	ns	0.6571	ATF6 vs. HSR	-0.01337	ns	>0.9999	ATF6 vs. HSR	1.7	****	<0.0001
ATF6 vs. OSR	-2.288	****	0.0001	ATF6 vs. OSR	-0.633	ns	0.7940	ATF6 vs. OSR	-0.3808	ns	0.6450	ATF6 vs. OSR	1.507	****	<0.0001
ATF6 vs. Other	-0.4811	ns	0.7045	ATF6 vs. Other	-0.1927	ns	0.9928	ATF6 vs. Other	-0.06267	ns	0.9991	ATF6 vs. Other	1.476	****	<0.0001
XBP1s vs. PERK/ISR	-1.17	ns	0.0593	XBP1s vs. PERK/ISR	-0.6376	ns	0.6083	XBP1s vs. PERK/ISR	-0.3075	ns	0.6508	XBP1s vs. PERK/ISR	-0.2209	ns	0.9522
XBP1s vs. HSR	-1.443	*	0.0138	XBP1s vs. HSR	1.521	**	0.0067	XBP1s vs. HSR	0.08775	ns	0.9986	XBP1s vs. HSR	1.135	****	0.0006
XBP1s vs. OSR	-1.695	*	0.0112	XBP1s vs. OSR	0.225	ns	0.9972	XBP1s vs. OSR	-0.2797	ns	0.8659	XBP1s vs. OSR	0.9419	*	0.0284
XBP1s vs. Other	0.1123	ns	0.9994	XBP1s vs. Other	0.6653	ns	0.3185	XBP1s vs. Other	0.03845	ns	>0.9999	XBP1s vs. Other	0.9107	****	0.0002
PERK/ISR vs. HSR	-0.2728	ns	0.9886	PERK/ISR vs. HSR	2.159	****	<0.0001	PERK/ISR vs. HSR	0.3952	ns	0.4470	PERK/ISR vs. HSR	1.356	****	<0.0001
PERK/ISR vs. OSR	-0.5245	ns	0.8993	PERK/ISR vs. OSR	0.8626	ns	0.4800	PERK/ISR vs. OSR	0.02784	ns	>0.9999	PERK/ISR vs. OSR	1.163	**	0.0027
PERK/ISR vs. Other	1.283	**	0.0026	PERK/ISR vs. Other	1.303	**	0.0013	PERK/ISR vs. Other	0.346	ns	0.2766	PERK/ISR vs. Other	1.132	****	<0.0001
HSR vs. OSR	-0.2517	ns	0.9965	HSR vs. OSR	-1.296	ns	0.1134	HSR vs. OSR	-0.3674	ns	0.7106	HSR vs. OSR	-0.1931	ns	0.9904
HSR vs. Other	1.556	***	0.0004	HSR vs. Other	-0.8559	ns	0.1614	HSR vs. Other	-0.0493	ns	0.9998	HSR vs. Other	-0.2243	ns	0.9167
OSR vs. Other	1.807	***	0.0008	OSR vs. Other	0.4403	ns	0.9019	OSR vs. Other	0.3181	ns	0.6774	OSR vs. Other	-0.03122	ns	>0.9999

Tunicamycin				CBR-470-1				Bardoxolone			
Comparison	Mean Diff.	Summary	Adjusted P Value	Comparison	Mean Diff.	Summary	Adjusted P Value	Comparison	Mean Diff.	Summary	Adjusted P Value
ATF6 vs. XBP1s	0.7554	ns	0.0861	ATF6 vs. XBP1s	-0.06403	ns	0.9998	ATF6 vs. XBP1s	0.0134	ns	>0.9999
ATF6 vs. PERK/ISR	0.4121	ns	0.6888	ATF6 vs. PERK/ISR	0.1011	ns	0.9981	ATF6 vs. PERK/ISR	-1.012	ns	0.2481
ATF6 vs. HSR	2.009	****	<0.0001	ATF6 vs. HSR	-0.5881	ns	0.1928	ATF6 vs. HSR	-2.319	****	<0.0001
ATF6 vs. OSR	1.315	****	0.0020	ATF6 vs. OSR	-1.102	**	0.0023	ATF6 vs. OSR	-0.4154	ns	0.9751
ATF6 vs. Other	1.396	****	<0.0001	ATF6 vs. Other	-0.233	ns	0.8402	ATF6 vs. Other	0.3515	ns	0.9368
XBP1s vs. PERK/ISR	-0.2433	ns	0.8096	XBP1s vs. PERK/ISR	0.1651	ns	0.9791	XBP1s vs. PERK/ISR	-1.026	ns	0.2213
XBP1s vs. HSR	1.253	***	0.0005	XBP1s vs. HSR	-0.5241	ns	0.2826	XBP1s vs. HSR	-2.323	****	<0.0001
XBP1s vs. OSR	0.5599	ns	0.5359	XBP1s vs. OSR	-1.037	**	0.0040	XBP1s vs. OSR	-0.4288	ns	0.9702
XBP1s vs. Other	0.641	ns	0.0510	XBP1s vs. Other	-0.1689	ns	0.9453	XBP1s vs. Other	0.3381	ns	0.9413
PERK/ISR vs. HSR	1.597	****	<0.0001	PERK/ISR vs. HSR	-0.6892	ns	0.0601	PERK/ISR vs. HSR	-1.307	ns	0.0828
PERK/ISR vs. OSR	0.9032	ns	0.0745	PERK/ISR vs. OSR	-1.203	***	0.0004	PERK/ISR vs. OSR	0.5971	ns	0.8852
PERK/ISR vs. Other	0.9843	***	0.0003	PERK/ISR vs. Other	-0.3341	ns	0.4567	PERK/ISR vs. Other	1.364	**	0.0041
HSR vs. OSR	-0.6936	ns	0.3409	HSR vs. OSR	-0.5134	ns	0.4963	HSR vs. OSR	1.904	*	0.0143
HSR vs. Other	0.6125	ns	0.1277	HSR vs. Other	0.3552	ns	0.5156	HSR vs. Other	2.671	****	<0.0001
OSR vs. Other	0.08112	ns	0.9998	OSR vs. Other	0.8685	**	0.0065	OSR vs. Other	0.7668	ns	0.5983

A3				C1				D1				F1			
Comparison	Mean Diff.	Summary	Adjusted P Value	Comparison	Mean Diff.	Summary	Adjusted P Value	Comparison	Mean Diff.	Summary	Adjusted P Value	Comparison	Mean Diff.	Summary	Adjusted P Value
ATF6 vs. XBP1s	0.04237	ns	>0.9999	ATF6 vs. XBP1s	0.112	ns	0.9857	ATF6 vs. XBP1s	0.2399	ns	0.9403	ATF6 vs. XBP1s	-0.1053	ns	0.9987
ATF6 vs. PERK/ISR	-1.146	ns	0.0587	ATF6 vs. PERK/ISR	-0.1011	ns	0.9905	ATF6 vs. PERK/ISR	-0.008735	ns	>0.9999	ATF6 vs. PERK/ISR	-0.6955	ns	0.0913
ATF6 vs. HSR	-4.115	****	<0.0001	ATF6 vs. HSR	-0.8717	****	<0.0001	ATF6 vs. HSR	-1.127	**	0.0010	ATF6 vs. HSR	-0.8594	*	0.0322
ATF6 vs. OSR	-0.8284	ns	0.5256	ATF6 vs. OSR	-0.2562	ns	0.8043	ATF6 vs. OSR	-0.1254	ns	0.9986	ATF6 vs. OSR	-0.577	ns	0.4599
ATF6 vs. Other	-0.4475	ns	0.7581	ATF6 vs. Other	-0.05006	ns	0.9991	ATF6 vs. Other	-0.05619	ns	0.9998	ATF6 vs. Other	-0.09598	ns	0.9978
XBP1s vs. PERK/ISR	-1.189	*	0.0351	XBP1s vs. PERK/ISR	-0.2131	ns	0.7880	XBP1s vs. PERK/ISR	-0.2487	ns	0.9187	XBP1s vs. PERK/ISR	-0.5902	ns	0.2073
XBP1s vs. HSR	-4.158	****	<0.0001	XBP1s vs. HSR	-0.9837	****	<0.0001	XBP1s vs. HSR	-1.367	****	<0.0001	XBP1s vs. HSR	-0.7541	ns	0.0801
XBP1s vs. OSR	-0.8707	ns	0.4458	XBP1s vs. OSR	-0.3681	ns	0.4481	XBP1s vs. OSR	-0.3653	ns	0.8364	XBP1s vs. OSR	-0.4717	ns	0.6664
XBP1s vs. Other	-0.4899	ns	0.6393	XBP1s vs. Other	-0.162	ns	0.8341	XBP1s vs. Other	-0.2961	ns	0.6956	XBP1s vs. Other	0.009311	ns	>0.9999
PERK/ISR vs. HSR	-2.969	****	<0.0001	PERK/ISR vs. HSR	-0.7707	***	0.0003	PERK/ISR vs. HSR	-1.118	***	0.0007	PERK/ISR vs. HSR	-0.1639	ns	0.9912
PERK/ISR vs. OSR	0.318	ns	0.9848	PERK/ISR vs. OSR	-0.1551	ns	0.9707	PERK/ISR vs. OSR	-0.1167	ns	0.9989	PERK/ISR vs. OSR	0.1185	ns	0.9990
PERK/ISR vs. Other	0.6989	ns	0.2461	PERK/ISR vs. Other	0.05103	ns	0.9999	PERK/ISR vs. Other	-0.04745	ns	0.9999	PERK/ISR vs. Other	0.5995	ns	0.0506
HSR vs. OSR	3.287	****	<0.0001	HSR vs. OSR	0.6156	*	0.0444	HSR vs. OSR	1.002	ns	0.0242	HSR vs. OSR	0.2824	ns	0.9556
HSR vs. Other	3.668	****	<0.0001	HSR vs. Other	0.8217	****	<0.0001	HSR vs. Other	1.071	****	<0.0001	HSR vs. Other	0.7634	*	0.0160
OSR vs. Other	0.3809	ns	0.9405	OSR vs. Other	0.2061	ns	0.8467	OSR vs. Other	0.06923	ns	0.9998	OSR vs. Other	0.481	ns	0.5023

**Table S4. Whole transcriptome RNAseq of putative HSF1 activators (see Excel Spreadsheet)**

**Table S5. GO analysis of HSF1 activating compound A3 (see Excel Spreadsheet)**