Supplement to:

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

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Running Title: Targeted RNAseq assay for stress-signaling

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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^{TREX} cells expressing dox-inducible cHSF1⁸, or HEK293^{DAX} cells expressing TMP-inducible ATF6 and dox-inducible XBP1s¹⁵
- **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 Targted RNAseq assay showing the log2 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 R² values from correlations of three technical replicates (calculated as in Fig. S1D) for each treatment condition used in our Targted 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. Log₂ normalized aligned transcript counts for HEK293^{TREX} 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^{TREX} 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.</p>
- C. Residual values per target gene from whole-transcriptome RNAseq data (x-axis){Ryno, 2014 #73} vs. Targeted RNAseq (y-axis) in HEK293^{TREX} cells expressing dox-inducible cHSF1 following 16 h treatment with dox (2.25µM doxycycline).

Figure S3 (Supplement to Fig. 3)

- A. Log₂ normalized aligned transcript counts for HEK293^{DAX} 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^{DAX} 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.</p>
- C. Residual values per target gene from whole-transcriptome RNAseq data (x-axis){Shoulders, 2013 #7} vs. Targeted RNAseq (y-axis) for HEK293^{DAX} 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^{DAX} cells following treatment with doxycycline (1µg/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^{DAX} cells following treatment with both trimethoprim (10 μM, 4 h; activates DHFR.ATF6) and doxycycline (1μg/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 log₂ fold change normalized counts of the HSR target gene BAG3 in HEK293T cells treated with bardoxolone (1 μM; 24 h) or CBR-470-1 (10 μM; 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 log₂ fold change normalized counts of the UPR (ATF6) target gene *BIP* in HEK293T cells treated with bardoxolone (1 μM; 24 h) or CBR-470-1 (10 μM; 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 log₂ fold change normalized counts of the OSR target gene *HMOX1* in HEK293T cells treated with bardoxolone (1 μM; 24 h) or CBR-470-1 (10 μM; 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 µM, 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.</p>
- C. Plot showing residuals calculated by comparing the expression of our stress-responsive gene panel between HEK293T cells treated with compound C1 (10 μM, 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.</p>

- D. Plot showing residuals calculated by comparing the expression of our stress-responsive gene panel between HEK293T cells treated with compound D1 (10 μM, 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.</p>
- E. Plot showing residuals calculated by comparing the expression of our stress-responsive gene panel between HEK293T cells treated with compound F1 (10 μM, 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.</p>
- 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 μM, 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.</p>
- B. Plot showing residuals calculated by comparing the expression of our stress-responsive gene panel between MEF cells treated with compound Tg (1 µM, 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.</p>





FIGURE S3











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	1	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	_ F	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	0.9097	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	****	<0.0001		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	0.8/22		XBP1s vs. HSR	1.343	***	<0.0001
XBP1s vs. OSR	-0.14/5	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
XBPTs Vs. Other	2.641	****	<0.0001	XBP Is vs. Other	0.2062	DE	0.7370	XBP1s vs. Other	0.1916	ns	0.0117		XBPTS VS. Other	0.1029	D5	0.0001
PERK/ISR VS. FISR	-0.1007	ns	0.9968	PERK/ISR VS. FISR	0.3002	ns	0.5805	PERK/ISR VS. HSR	0.05415	113	0.9996		PERK/ISR VS. FISR	0.1038	ns	0.9997
PERK/ISB vs. Other	0.1196	ns	0.9982	PERK/ISR vs. Other	0.1697	ns	0.9128	PERK/ISR vs. Osh	0.1732	ns	>0.9999		PERK/ISB vs. Other	-0.07768	ns	0.9991
HSR vs. OSR	3 44 2	****	<0.0001	HSR vs. OSR	0.1022	ns	0.9988	LICE VIC OCE	0.01982	ns	0.9961		HSR ve 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 (III)					Oligomycin				Paraquat				Thapsigargin			
Comparison	Mean Diff.	Summary	Adjusted P Value	Comparison	Mean Diff.	Summary	Adjusted P Value	Comparison	Mean Diff.	Summary	Adjusted P Value	- 1	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	0.9965	- 1	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	- 1	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	- 1	ATF6 vs. HSR	1.7	****	< 0.0001
AFF6 vs. OSR	-2.288		0.0001	ATF6 vs. OSR	-0.633	ns	0.7940	ATF6 vs. OSR	-0.3808	ns	0.0450		ATE6 vs. OSR	1.507	****	<0.0001
AIF6 vs. Other	-0.4811	ns	0.7045	All-6 vs. Other	-0.1927	ns	0.9928	AIF6 vs. Other	-0.0626/	115	0.99991		AIFO VS. Other	0.2200	DE	0.0522
ABP IS VS. PERK/ISR	1 -1.17	*	0.0395	XBP IS VS. PERK/ISR	-0.0370	**	0.0067	XBP IS VS. PERK/ISR	-0.3075	115	0.0306		ADP 15 VS. PERK/ISK	1 1 3 5	***	0.0006
XBP1s VS. HSK	-1.445	*	0.0112	XBP1s VS. HSR	0.225	ns	0.0007	XBP1s VS. HSR	-0.2797	ns	0.9900	- 1	XDP15 VS. FISR	0.0410		0.0284
XBP1s vs. OSh	01123	ns	0.9994	VBP1s vs. Osh	0.6653	ns	0.3185	XBP1s vs. Osh	0.03845	ns	>0.9999	- 1	XBP1s vs. Other	0.9107	***	0.0002
PERK/ISB vs HSB	-0.2728	ns	0.9886	PERK/ISR vs. HSR	2.159	****	<0.0001	PERK/ISB vs HSB	0.3952	ns	0.4470	- 1	PERK/ISR vs. HSR	1.356	****	< 0.0001
PERK/ISB vs. OSB	-0.5245	ns	0.8993	PERK/ISB vs. OSB	0.8626	ns	0.4800	PERK/ISB vs. OSB	0.02784	ns	>0.9999	- 1	PERK/ISR vs. OSR	1.163	**	0.0027
PERK/ISR vs. Other	r 1.283	**	0.0026	PERK/ISR vs. Other	1.303	**	0.0013	PERK/ISR vs. Other	0.346	ns	0.2766	- 1	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	- 1	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	- 1	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	- 1	OSR vs. Other	-0.03122	ns	>0.9999
	Tuni	connucin			CDD	470.1			Danda							
	Tunio	camycin			CBR	-470-1			Bardo	xolone						
Comparison	Tunio Mean Diff.	camycin ^{Summary}	Adjusted P Value	Comparison	CBR Mean Diff.	-470-1 Summary	Adjusted P Value	Comparison	Bardo: Mean Diff.	xolone _{Summary}	Adjusted P Value	-				
Comparison ATF6 vs. XBP1s	Tunio Mean Diff. 0.7554	camycin Summary ns	Adjusted P Value	Comparison ATF6 vs. XBP1s	CBR Mean Diff. -0.06403	-470-1 Summary ns	Adjusted P Value	Comparison ATF6 vs. XBP1s	Bardo: Mean Diff. 0.0134	xolone Summary ns	Adjusted P Value >0.9999	-				
Comparison ATF6 vs. XBP1s ATF6 vs. PERK/ISR	Tunic Mean Diff. 0.7554 0.4121 2.000	camycin Summary ns ns ****	Adjusted P Value 0.0861 0.6888	Comparison ATF6 vs. XBP1s ATF6 vs. PERK/ISR	CBR Mean Diff. -0.06403 0.1011	-470-1 Summary ns ns	Adjusted P Value 0.9998 0.9981	Comparison ATF6 vs. XBP1s ATF6 vs. PERK/ISR	Bardo: Mean Diff. 0.0134 -1.012	xolone Summary ns ns	Adjusted P Value >0.9999 0.2481	-				
Comparison ATF6 vs. XBP1s ATF6 vs. PERK/ISR ATF6 vs. HSR ATF6 vs. HSR	Tunic Mean Diff. 0.7554 0.4121 2.009 1.315	Camycin Summary ns ns ****	Adjusted P Value 0.0861 0.6888 <0.0001 0.0020	Comparison ATF6 vs. XBP1s ATF6 vs. PERK/ISR ATF6 vs. HSR ATF6 vs. PSR	CBR Mean Diff. -0.06403 0.1011 -0.5881 1.102	-470-1 Summary ns ns ns	Adjusted P Value 0.9998 0.9981 0.1928 0.0033	Comparison ATF6 vs. XBP1s ATF6 vs. PERK/ISR ATF6 vs. HSR	Bardo: Mean Diff. 0.0134 -1.012 -2.319	xolone Summary ns ns ****	Adjusted P Value >0.9999 0.2481 <0.0001	-				
Comparison ATF6 vs. XBP1s ATF6 vs. PERK/ISR ATF6 vs. HSR ATF6 vs. OSR ATF6 vs. OTher	Tunio Mean Diff. 0.7554 0.4121 2.009 1.315 1.396	Summary ns ns *****	Adjusted P Value 0.0861 0.6888 <0.0001 0.0020 <0.0001	Comparison ATF6 vs. XBP1s ATF6 vs. PERK/ISR ATF6 vs. HSR ATF6 vs. OSR ATF6 vs. OSR	CBR Mean Diff. -0.06403 0.1011 -0.5881 -1.102 0.232	-470-1 <u>Summary</u> ns ns **	Adjusted P Value 0.9998 0.9981 0.1928 0.0023 0.8402	Comparison ATF6 vs. XBP1s ATF6 vs. PERK/ISR ATF6 vs. HSR ATF6 vs. OSR ATF6 vs. OSR	Bardo: Mean Diff. 0.0134 -1.012 -2.319 -0.4154 0.3515	summary ns ns ***** ns	Adjusted P Value >0.9999 0.2481 <0.0001 0.9751 0.928	-				
Comparison ATF6 vs. XBP1s ATF6 vs. PERK/ISR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. Other XPP1c vs. PERK/GS	Tunio Mean Diff. 0.7554 0.4121 2.009 1.315 1.396 3 -0.3433	camycin Summary ns ns **** ** ** ns	Adjusted P Value 0.0861 0.6888 <0.0001 0.0020 <0.0001 0.8096	Comparison ATF6 vs. XBP1s ATF6 vs. PERK/ISR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. Other YBP15 vs. PERK/ISP	CBR <u>Mean Diff.</u> -0.06403 0.1011 -0.5881 -1.102 -0.233 0.1651	-470-1 <u>Summary</u> ns ns ** ns ns	Adjusted P Value 0.9998 0.9981 0.1928 0.0023 0.8402 0.9701	Comparison ATF6 vs. XBP1s ATF6 vs. PERK/ISR ATF6 vs. HSR ATF6 vs. OSR ATF6 vs. Other XPR0 see DEPK (#60	Bardo: Mean Diff. 0.0134 -1.012 -2.319 -0.4154 0.3515 1.026	Summary ns ns **** ns ns ns	Adjusted P Value >0.9999 0.2481 <0.0001 0.9751 0.9368 0.2213	-				
Comparison ATF6 vs. XBP1s ATF6 vs. PERK/ISR ATF6 vs. HSR ATF6 vs. OSR ATF6 vs. Other XBP1s vs. PERK/ISR XBP1s vs. HSR	Tunio Mean Diff. 0.7554 0.4121 2.009 1.315 1.396 3 -0.3433 1.253	camycin Summary ns s**** ** **** ns ***	Adjusted P Value 0.0861 0.6888 <0.0001 0.0020 <0.0001 0.8096 0.0005	Comparison ATF6 vs. XBP1s ATF6 vs. PERK/ISR ATF6 vs. DERK/ISR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. Other XBP1s vs. PERK/ISR XBP1s vs. HSR	CBR -0.06403 0.1011 -0.5881 -1.102 -0.233 0.1651 -0.5241	-470-1 Summary ns ns ns ** ns ns ns ns	Adjusted P Value 0.9998 0.9981 0.1928 0.0023 0.8402 0.9791 0.2826	Comparison ATF6 vs. XBP1s ATF6 vs. PERK/ISR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. Other XBP1s vs. PERK/ISR	Bardo: Mean Diff. 0.0134 -1.012 -2.319 -0.4154 0.3515 -1.026 -2.333	Summary ns ns **** ns ns ns ****	Adjusted P Value >0.9999 0.2481 <0.0001 0.9751 0.9368 0.2213 <0.0001	-				
Comparison ATF6 vs. XBP1s ATF6 vs. PERK/ISR ATF6 vs. HSR ATF6 vs. OSR ATF6 vs. Other XBP1s vs. PERK/ISR XBP1s vs. HSR XBP1s vs. OSR	Tunic 0.7554 0.4121 2.009 1.315 1.396 8 -0.3433 1.253 0.5599	camycin Summary ns s**** ** ns **** ns *** ns	Adjusted P Value 0.0861 0.6888 <0.0001 0.0020 <0.0001 0.8096 0.0005 0.5359	Comparison ATF6 vs. XBP1s ATF6 vs. PERK/ISR ATF6 vs. HSR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. Other XBP1s vs. PERK/ISR XBP1s vs. PSR XBP1s vs. OSR	CBR -0.06403 0.1011 -0.5881 -1.102 -0.233 0.1651 -0.5241 -1.037	-470-1 <u>Summary</u> ns ns ns ** ns ns ns **	Adjusted P Value 0.9998 0.9981 0.1928 0.0023 0.8402 0.9791 0.2826 0.0040	Comparison ATF6 vs. X8P1s ATF6 vs. PERK/ISR ATF6 vs. HSR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. Other XBP1s vs. PERK/ISR XBP1s vs. HSR XBP1s vs. OSR	Bardo: Mean Diff. 0.0134 -1.012 -2.319 -0.4154 0.3515 -1.026 -2.333 -0.4288	xolone Summary ns ns ***** ns ns ns ***** ns	Adjusted P Value >0.9999 0.2481 <0.0001 0.9751 0.9368 0.2213 <0.0001 0.9702	-				
Comparison ATF6 vs. XBP1s ATF6 vs. PERK/JSR ATF6 vs. HSR ATF6 vs. OSR XBP1s vs. DSR XBP1s vs. DSR XBP1s vs. OSR XBP1s vs. Other	Tunic Mean Diff. 0.7554 0.4121 2.009 1.315 1.396 3 -0.3433 1.253 0.5599 0.641	camycin Summary ns ns **** ** ** ns ns ns ns	Adjusted P Value 0.0861 0.6888 <.0.0001 0.0020 <.0.0001 0.8096 0.0005 0.5359 0.0510	Comparison ATF6 vs. XBP1s ATF6 vs. PERK/JSR ATF6 vs. HSR ATF6 vs. OSR ATF6 vs. OSR XBP1s vs. PERK/JSR XBP1s vs. DSR XBP1s vs. OSR	CBR -0.06403 0.1011 -0.5881 -1.102 -0.233 0.1651 -0.5241 -1.037 -0.1689	-470-1 Summary ns ns ** ns ns ns ** ns ns ** ns ns s **	Adjusted P Value 0.9998 0.9981 0.0128 0.0023 0.8402 0.9791 0.2826 0.0040 0.09453	Comparison ATF6 vs. XBP1s ATF6 vs. PERK/ISR ATF6 vs. PERK/ISR ATF6 vs. OSR ATF6 vs. Other XBP1s vs. PERK/ISR XBP1s vs. HSR XBP1s vs. OSR XBP1s vs. OSR	Bardox Mean Diff. 0.0134 -1.012 -2.319 -0.4154 0.3515 -1.026 -2.333 -0.4288 0.3381	summary ns ns ns ns ns ns ns ns ns ns ns ns ns	Adjusted P Value >0.9999 0.2481 <0.0001 0.9751 0.9368 0.2213 <0.0001 0.9702 0.9413	-				
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Comparison ATF6 vs. XP1s ATF6 vs. PERKISR ATF6 vs. PERKISR ATF6 vs. PSR ATF6 vs. OSR ATF6 vs. OSR XBP1 svs. Cher XBP1 svs. Cher XBP1 svs. Cher PERKISR vs. OSR PERKISR vs. OSR PERKISR vs. Other OSR vs. Other Comparison ATF6 vs. XBP1s ATF6 vs. XBP1s ATF6 vs. XBP1s ATF6 vs. XBP1s ATF6 vs. XBP1s	Tunic Mean Diff. 0.7554 0.4121 2.009 1.315 1.233 0.5599 0.641 1.597 0.9943 0.6936 -0.6936 -0.6936 -0.6936 -0.6125 0.08112 A Mean Diff. 0.126	Camycin Summary ns ns ns ns ns ns ns ns ns ns	Adjusted P Value 0.0861 0.0861 0.0868 0.0001 0.0000 0.0000 0.3559 0.0510 0.0001 0.0003 0.0001 0.0003 0.0001 0.0003 0.0003 0.0003 0.0003 0.0003 0.0003 0.0003 0.0003 0.0003 0.0003 0.0003 0.0003 0.0003 0.0003 0.0003 0.0005 0.00	Comparison ATE6 vs. XBP1s ATE6 vs. PERK/SR ATE6 vs. DERK/SR ATE6 vs. Other XBP1s vs. DERK/SR XBP1s vs. USR XBP1s vs. OSR YBP1s vs. OSR PERK/SR vs. OSR PERK/SR vs. Other OSR vs. Other Comparison ATE6 vs. XBP1s ATE6 vs. XBP1s	CBR Mean Diff. -0.06403 0.1011 -0.5881 -1.102 -0.233 0.1651 -0.5241 -0.6592 -0.6892 -0.6892 -0.6892 -0.6892 -0.6394 0.3341 0.3552 0.8685 C Mean Diff. 0.112 -0.111 -0.11	-470-1 Summary ns ns ns ns ns ns ns ns ns ns	Adjusted P Value 0.9998 0.9998 0.0928 0.023 0.8402 0.9791 0.2826 0.0004 0.9453 0.0601 0.0004 0.4567 0.4565 0.4565 0.0065 Adjusted P Value 0.9895	Comparison ATF6 vs. XBP1s ATF6 vs. PERK/JSR ATF6 vs. UHSR ATF6 vs. OSR ATF6 vs. OSR XBP1s vs. HSR XBP1s vs. OSR XBP1s vs. OSR PERK/JSR vs. OSR PERK/JSR vs. Other OSR vs. Other Comparison ATF6 vs. XBP1s	Bardo: Mean Diff. 0.0134 -1.012 -2.319 -0.4154 -1.026 -2.333 -0.4288 0.3381 -1.307 0.5971 1.364 2.671 0.04288 D Mean Diff. 0.2399 0.008736	xolone Summary ns ns ns ns ns ns ns ns ns ns	Adjusted P Value >0.9999 0.2481 <0.0001 0.9751 0.9368 0.2213 <0.0001 0.9702 0.9413 0.0828 0.8852 0.00041 0.0143 <0.0001 0.5983 Adjusted P Value 0.9403 >10.9909	F	Comparison ATFoux XBP1s ATFoux PERK MEN	F1 <u>Mean Diff.</u> -0.1053	Summary ns	Adjusted P Value 0.9987 0.0013
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Comparison ATF6 vs. XPI s ATF6 vs. XPI s ATF6 vs. PERK/SR ATF6 vs. HSR ATF6 vs. OSR ATF6 vs. OSR XBP1 svs. CHR XBP1 svs. CHR PERK/SR vs. OSR PERK/SR vs. OSR PERK/SR vs. OTher OSR vs. OTher Comparison ATF6 vs. HSR ATF6 vs. HSR ATF6 vs. HSR ATF6 vs. HSR ATF6 vs. HSR	Tunic Mean Diff. 0.7554 0.4121 2.009 1.315 1.396 1.337 1.233 0.5599 0.641 1.597 0.9032 0.9032 0.9032 0.00812 0.00912 0.009 0.00912 0.0092 0.0082 0.0092 0.0082 0.0092 0.0082 0.00	Camycin Summary ns ns ns ns ns ns ns ns ns ns	Adjusted P Value 0.0861 0.0861 0.0888 <-0.0001 0.0000 0.0000 0.0005 0.03510 -0.0001 0.0745 0.0003 0.0745 0.0003 0.3409 0.1277 0.9998 Adjusted P Value >0.0999 0.0587 -0.0001 0.5256	Comparison ATE6 vs. SRP1s ATE6 vs. PERK/SR ATE6 vs. USA ATE6 vs. USA ATE6 vs. OSA ATE6 vs. OSA XBP1s vs. DERK/SR XBP1s vs. OSA PERK/SR vs. OSA PERK/SR vs. OSA PERK/SR vs. OSA DERK/SR vs. Other OSR vs. Other Comparison ATE6 vs. PERK/SR ATE6 vs. PERK/SR	CBR Mean Diff. -0.06403 0.1011 -0.5881 -1.102 -0.233 0.01651 -0.5241 -0.689 -0.689 -0.689 -0.689 -0.689 -0.689 -0.5134 0.3552 0.8685 C Mean Diff 0.112 -0.1011 -0.8171 -0.2562	-470-1 <u>Summary</u> ns ns ns ns ns ns ns ns ns ns	Adjusted P Value 0.9998 0.9998 0.9998 0.028 0.023 0.8402 0.9791 0.2826 0.0404 0.9453 0.0601 0.0004 0.4567 0.4565 0.0456 0.0515 0.0065 Adjusted P Value 0.9897 0.9990 0.9905 0.9900 0.9905 0.0001 0.8243 0.9804 0.9804 0.9805 0.9905 0.9905 0.0001 0.8243 0.9804 0.9804 0.9805 0.9905 0.9905 0.9905 0.0001 0.8243 0.9804 0.9804 0.9805 0.9905 0.9905 0.0001 0.8043 0.8001 0.8043 0.9804 0.9905 0.0001 0.9805 0.9001 0.9805 0.9905 0.0001 0.8004 0.9805 0.0001 0.8004 0.8004 0.9805 0.0001 0.8004 0.8005 0.8005 0.9905 0.0001 0.8004 0.8005 0.8005 0.9905 0.0001 0.8004 0.8005 0.9005 0.0001 0.8004 0.8005 0.0001 0.8005 0.0001 0.8005 0.0001 0.8005 0.0001 0.8005 0.0001 0.8005 0.0001 0.8005 0.0001 0.8005 0.0001 0.8005 0.0001 0.00	Comparison ATF6 vs. XBP1s ATF6 vs. PERK/JSR ATF6 vs. VHSR ATF6 vs. OSR ATF6 vs. OSR XBP1s vs. DHsr XBP1s vs. OSR YBP1s vs. OSR PERK/JSR vs. OSR PERK/JSR vs. Other OSR vs. Other OSR vs. Other Comparison ATF6 vs. NBP1s ATF6 vs. HSR ATF6 vs. NSR	Bardo: Mean Diff. 0.0134 -1.012 -2.319 -0.4154 0.3515 -1.026 -2.333 -1.307 0.5971 1.364 1.904 2.6716 0.5971 1.364 1.904 2.6716 D Mean Diff. 0.2399 -0.008735 -1.127 -0.1254	xolone Summary ns ns ns ns ns ns ns ns ns ns	Adjusted P Value >0.9999 0.2481 <0.0001 0.9751 0.9368 0.2213 <0.0001 0.9702 0.9413 0.0628 0.0041 0.0143 <0.0001 0.5983 Adjusted P Value 0.9403 >0.9999 0.0010		Comparison ATF6 vs. XBP1s ATF6 vs. PERK/SR ATF6 vs. HSR	F1 Mean Diff. -0.1053 -0.6955 -0.8594 -0.577	Summary ns s	Adjusted P Value 0.9987 0.0913 0.0322 0.4599
Comparison ATF6 vs. XBP1s ATF6 vs. PERK/JSR ATF6 vs. PERK/JSR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. OSR XBP1 vs. PERK/JSR vs. OSR XBP1 vs. Vs. PERK/JSR vs. OSR PERK/JSR vs. OSR PERK/JSR vs. OSR HSR vs. Other OSR vs. Other Comparison ATF6 vs. XBP1s ATF6 vs. VSR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. OSR	Tunia Mean Diff. 0.7554 0.4121 2.009 1.315 1.396 1.333 1.253 0.5599 0.641 1.597 0.9843 -0.6125 0.08112 0.08112 Mean Diff. 0.04237 -1.146 -4.115 -0.84284 -0.4475	camycin Summary ns ns ns ns ns ns ns ns ns ns	Adjusted P Value 0.0961 0.0961 0.0070 0.0070 0.0070 0.0005 0.0005 0.0005 0.0055 0.005510 0.0745 0.0001 0.0745 0.0001 0.0745 0.09998 Adjusted P Value 5.0.9999 0.0587 -0.0001 0.5256 0.7581	Comparison ATF6 vs. XBP1s ATF6 vs. PERK/ISR ATF6 vs. HSR ATF6 vs. OSR ATF6 vs. OSR XBP1s vs. DSR XBP1s vs. DSR XBP1s vs. OSR XBP1s vs. OSR PERK/ISR vs. OSR HSR vs. OSR ATF6 vs. KBP1s ATF6 vs. USR ATF6 vs. OSR ATF6 vs. OSR	CBR Mean Diff. -0.06403 0.1011 -0.5881 -1.102 -0.5241 -0.1689 -0.6892 -0.6892 -0.6892 -0.6892 -0.6892 -0.6892 -0.6892 -0.6892 -0.6892 -0.5134 -0.5134 -0.5134 -0.5134 -0.5126 -0.05106 -0.8717 -0.2562 -0.05506	-470-1 Summary ns ns ns ns ns ns ns ns ns ns	Adjusted P Value 0.9998 0.9998 0.0998 0.023 0.023 0.024 0.024 0.0040 0.0040 0.0601 0.0004 0.4567 0.4567 0.04563 0.5156 0.0065 0.0055 Adjusted P Value 0.9857 0.9905 <.0.001 0.8943 0.9991 1.02843 0.9991 0.9	Comparison ATF6 vs. X8P1s ATF6 vs. DSR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. OSR XBP1s vs. DSR XBP1s vs. DSR XBP1s vs. OSR YBP1s vs. OSR PERK/ISR vs. OSR HSR vs. OSR HSR vs. OSR HSR vs. OSR HSR vs. OSR HSR vs. OSR ATF6 vs. XBP1s ATF6 vs. HSR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. OSR	Bardoo Mean Diff. 0.0134 -1.012 -2.319 -0.4154 0.33815 -1.026 -2.333 -0.4288 0.3381 -1.307 0.5971 1.364 1.904 2.671 0.7668 D D Mean Diff. 0.2399 -0.008735 -1.127 -0.1254 -0.2551	xolone Summary ns ns ns ns ns ns ns ns ns ns	Adjusted P Value >0.9999 0.2481 0.9751 0.9368 0.2213 <0.0001 0.9702 0.9403 0.0828 0.0828 0.0844 0.0143 <0.0001 0.5983 Adjusted P Value 0.9403 >0.9999 0.0010 0.9998 6.09998 0.0010 0.09988 0.0010 0.09988 0.0010 0.09988 0.0010 0.09988 0.0010 0.09988 0.0010 0.09998 0.0010 0.0010 0.0010 0.0010 0.0010 0.0010 0.0010 0.0010 0.0010 0.0010 0.0010 0.0021 0.0010 0.0010 0.0021 0.	ľ	Comparison ATF6 vs. XBP1s ATF6 vs. PERK/SR ATF6 vs. HSR ATF6 vs. OSR ATF6 vs. OSR	F1 Mean Diff. -0.1053 -0.6955 -0.8594 -0.577 -0.09598	Summary DS NS * NS	Adjusted P Value 0.9987 0.0913 0.0322 0.4599 0.9978
Comparison ATF6 vs. XPI s ATF6 vs. VSPI s ATF6 vs. PERK/SR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. OSR VBP1 sv. CSR VBP1 sv. CSR TF6 vs. CSR ATF6 vs. CSR	Tunia Mean Diff. 0.7554 0.4121 2.009 1.315 1.336 1.233 0.5599 0.641 1.597 0.9032 0.9043 1.597 0.9032 0.08112 0.08112 0.08112 0.08112 0.08112 0.04237 -1.146 -0.4237 -1.146 -0.4247 -0.4247 -0.4247 -0.42475 -0.4245	Camycin Summary ns ns ns ns ns ns ns ns ns ns	Adjusted P Value 0.0861 0.0861 0.0868 <0.0001 0.0000 0.0000 0.0000 0.03510 0.0001 0.0745 0.0001 0.0745 0.0003 0.1277 0.3909 0.1277 0.3909 Adjusted P Value 5.0.5959 0.0587 <0.0001 0.5256 0.7581 0.0351 0.0351 0.0351 0.0351 0.0351 0.0351 0.0525 0.0351 0.0351 0.0351 0.0351 0.0525 0.0351 0.0351 0.0351 0.0525 0.0351 0.0351 0.0351 0.0351 0.0351 0.0351 0.0351 0.0581 0.0587 0.0051 0.0587 0.0558 0.0058 0.0558 0.0058 0.0558 0.0558 0.0058 0.0058 0.0558 0.0058 0.0058 0.0558 0.0058 0.0558 0.0058 0.0558 0.0058 0.0558 0.0058 0.0058 0.0558 0.0058 0.0558 0.0058 0.0558 0.0058 0.0558 0.0058 0.0558 0.0058 0.0558 0.0058 0.055	Comparison ATF6 vs. X8P1s ATF6 vs. PERK/JSR ATF6 vs. USHSR ATF6 vs. USHSR ATF6 vs. OSH XBP1s vs. OSH XBP1s vs. OSH YBP1s vs. OSH PERK/JSR vs. USHer PERK/JSR vs. OSH HSR vs. OSR HSR vs. OSH ATF6 vs. NEHR/JSR ATF6 vs. OSH ATF6 vs. OSH ATF6 vs. OSH	CBR Mean Diff. -0.06403 0.1011 -0.5881 -1.102 -0.233 -0.3681 -0.5241 -1.037 -0.1689 -0.6892 -0.6892 -0.5134 0.3552 0.05134 0.35552 0.05885 C Mean Diff. -0.2131 -0.25066 -0.2131	-470-1 <u>Summary</u> ns ns ns ns ns ns ns ns ns ns	Adjusted P Value 0.9998 0.9998 0.9998 0.0928 0.0023 0.8402 0.02826 0.0040 0.9453 0.0601 0.0004 0.4567 0.0004 0.4567 0.0005 0.0055 0.0055 0.0055 0.0055 0.09857 0.09905 0.99905 0.0001 0.09905 0.09905 0.09905 0.09905 0.0001 0.09905 0.09905 0.0001 0.09905 0.09905 0.0001 0.09905 0.0905 0.0001 0.09905 0.0001 0.09905 0.0001 0.09905 0.0001 0.09905 0.0001 0.09905 0.0001 0.09905 0.0001 0.0005 0.0005 0.0001 0.0005 0.0001 0.0005 0.0001 0.0005 0.0005 0.0005 0.0005 0.0005 0.0005 0.0001 0.0005 0.0	Comparison ATFG vs. XBP1s ATFG vs. PERK/SR ATFG vs. VHSR ATFG vs. OSR ATFG vs. OSR XBP1s vs. OSR VBP1s vs. OSR VBP1s vs. OSR PERK/ISR vs. OSR PERK/ISR vs. OSR HSR vs. OSR ATFG vs. XBP1s ATFG vs. SCher OSR vs. Other Comparison ATFG vs. HSR ATFG vs. OSR ATFG vs. OSR ATFG vs. OSR	Bardo: Mean Diff. 0.0134 -1.012 -2.319 -0.4154 0.3515 -1.026 -2.333 -0.4288 0.3381 -1.307 0.4288 0.5971 1.364 2.6716 0.2399 D Mean Diff. 0.2399 -0.008735 -1.127 -0.008735 -1.127 -0.2389 -0.1254 -0.52619 -0.2487	xolone Summary ns ns ns ns ns ns ns ns ns ns	Adjusted P Value >0.9999 0.2481 <0.0001 0.9751 0.9368 0.2213 <0.0001 0.9702 0.9413 0.0828 0.0041 0.0143 0.08452 0.0041 0.0143 0.0041 0.5983 Adjusted P Value 0.9403 0.5989 0.0010 0.9999 0.0010 0.9998 0.9998		Comparison ATF6 vs. XBP1s ATF6 vs. PERK/SR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. OSR	F1 Mean Diff. -0.0553 -0.6955 -0.8594 -0.5577 -0.09598 -0.5592	Summary ns ns ns ns ns ns	Adjusted P Value 0.9987 0.0913 0.0322 0.4599 0.9978 0.2073
Comparison ATF6 vs. XBP1s ATF6 vs. PERK/ISR ATF6 vs. PERK/ISR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. OSR XBP1 svs. PERK/ISR vs. OSR XBP1 svs. PERK/ISR vs. OSR PERK/ISR vs. OSR PERK/ISR vs. OSR HSR vs. OSR HSR vs. Other OSR vs. Other Comparison ATF6 vs. XBP1s ATF6 vs. USR ATF6 vs. OSR ATF6 vs. OSR	Mean Diff. 0.7554 0.4121 2.009 1.315 1.315 1.315 1.315 0.5599 0.641 1.597 0.9032 0.6412 0.6125 0.6125 0.612 0.04237 -1.146 -4.115 -0.8284 -0.4475 -1.189	camycin Summary ns ns ns ns ns ns ns ns ns ns	Adjusted P Value 0.0261 0.0261 0.0201 0.0201 0.0001 0.0005 0.00	Comparison ATE6 vs. XBP1s ATE6 vs. PERK/ISR ATE6 vs. HSR ATE6 vs. OSR ATE6 vs. OSR XBP1s vs. DSR XBP1s vs. HSR XBP1s vs. OSR PERK/ISR vs. OSR PERK/ISR vs. OSR HSR vs. OSR ATE6 vs. NBP1s ATE6 vs. DERK/ISR ATE6 vs. OSR ATE6 vs. OSR ATE6 vs. OSR ATE6 vs. OSR ATE6 vs. OSR ATE6 vs. OSR ATE6 vs. OSR	CBR Mean Diff. -0.06403 -0.1021 -0.2331 0.1651 -0.52411 -1.037 -0.6892 -0.6892 -0.6892 -0.6892 -0.3341 -0.5134 0.3552 0.8685 C Mean Diff. -0.5262 -0.05006 -0.2131 -0.59837 -0.59837 -0.59826 -0.59837 -0.59826 -0.59837 -0.59827 -0.59826 -0.59827 -0	-470-1 Summary ns ns ns ns ns ns ns ns ns ns	Adjusted P Value 0.9998 0.9998 0.0998 0.023 0.8402 0.023 0.8402 0.024 0.024 0.0040 0.0040 0.0601 0.0004 0.4567 0.4567 0.4565 0.0065 Xadjusted P Value 0.9857 0.9857 0.9905 Adjusted P Value 0.9857 0.9905 0.9905 0.9905 0.0004 0.9857 0.9905 0.0004 0.9857 0.9905 0.0001 0.0004 0.9857 0.9905 0.0001 0.9991 0.7880	Comparison ATT6 vs. XBP1s ATT6 vs. PERK/JSR ATT6 vs. OSR ATT6 vs. OSR TF6 vs. Other XBP1s vs. DFRK/JSR XBP1s vs. OSR YBP1s vs. OSR PERK/JSR vs. OSR PERK/JSR vs. Other Comparison ATT6 vs. XBP1s ATT6 vs. OSR ATT6 vs. OSR ATT6 vs. OSR ATT6 vs. OSR ATT6 vs. Other XBP1s vs. Other	Bardo: Mean Diff. 0.0134 -1.012 -2.319 -0.4154 0.3515 -1.026 -2.333 -0.4288 0.3381 -1.307 0.5971 1.364 1.364 1.364 1.364 0.2691 0.2399 -0.02895 -0.02895 -0.02895 -0.02591 0.02594 -0.05619 -0.05619 -0.2564 -0.25	xolone Summary ns ns ns ns ns ns ns ns ns ns	Adjusted P Value >0.9999 0.2481 <0.0001 0.9751 0.9368 0.2213 <0.0001 0.9702 0.9403 0.0828 0.8852 0.00041 0.0143 <0.0001 0.5983 Adjusted P Value 0.9403 >0.9999 0.0010 0.9998 0.9187 <0.0001		Comparison ATF6 vs. XBP1s ATF6 vs. PERK/ISA ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. OSR	F1 Mean Diff. -0.1053 -0.6955 -0.8594 -0.5775 -0.5902 -0.7541	Summary ns ns ns ns ns ns ns	Adjusted P Value 0.9987 0.0913 0.0322 0.4599 0.2073 0.2073
Comparison ATFG vs. XPI s ATFG vs. PERK/SR ATFG vs. PERK/SR ATFG vs. OSR ATFG vs. OSR ATFG vs. OSR XBP1 sv. CHer PERK/SR vs. OSR PERK/SR vs. OSR PERK/SR vs. OSR PERK/SR vs. OSR PERK/SR vs. OSR ATFG vs. Other Comparison ATFG vs. PERK/SR ATFG vs. OSR ATFG vs. OSR ATFG vs. OSR ATFG vs. OSR ATFG vs. OSR ATFG vs. OSR ATFG vs. OSR	Mean Diff. 0.7554 0.4121 2.009 1.336 1.336 1.336 1.336 0.5554 0.4111 0.537 0.641 0.9032 0.643 0.9032 0.643 0.9032 0.643 0.9032 0.643 0.9032 0.643 0.9032 0.643 0.9043 -0.6125 0.8044 0.4125 0.4115 0.8284 -0.4145 + 1.184 -0.8704	Campan Summary ns ns ns ns ns ns ns ns ns ns	Adjusted P Value 0.0861 0.0861 0.0888 <0.0001 0.0000 0.0000 0.0300 0.0310 0.0001 0.0745 0.0003 0.0745 0.0003 0.0745 0.0003 0.1277 0.3909 Adjusted P Value >0.0587 <0.0001 0.0557 <0.0001 0.0557 <0.0001 0.0557 <0.0001 0.0557 <0.0001 0.0557 <0.0001 0.0558 <0.0051 <0.0001 0.0558 <0.0557 <0.0001 0.0558 <0.0051 <0.0001 0.0557 <0.0001 0.0557 <0.0001 0.0557 <0.0001 0.0557 <0.0001 0.0557 <0.0001 0.0557 <0.0001 0.0557 <0.0001 0.0557 <0.0001 0.0557 <0.0001 0.0558 <0.0001 0.0557 <0.0001 0.0558 <0.0001 0.0557 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0558 <0.0001 0.0458 0.04	Comparison ATE6 vs. XBP1s ATE6 vs. PERK/JSR ATE6 vs. BHSR ATE6 vs. USHSR ATE6 vs. OSH XBP1s vs. OSH XBP1s vs. OSH YBP1s vs. OSH PERK/JSR vs. OSH PERK/JSR vs. OSH PERK/JSR vs. OSH HSR vs. OSH HSR vs. OSH ATE6 vs. NEHR/JSR ATE6 vs. OSH ATE6 vs. OSH	CBR Mean Diff. -0.06403 0.1011 -0.5881 -1.102 -0.233 -0.35241 -1.037 -0.6892 -0.6892 -0.3341 -0.3341 -0.35134 -0.3552 0.8685 C Mean Diff. -0.2101 -0.2562 -0.2131 -0.3837 -0.3683 -0.3683 -0.3683 -0.2131 -0.8683 -0.2131 -0.8685 -0.2131 -0.8685 -0.2131 -0.8685 -0.2131 -0.8685 -0.2131 -0.8685 -0.2131 -0.2562 -0.2134 -0.21552 -0.21552 -0.2562 -0.21552 -0.2562 -0.21552 -0.2562 -0.2552	-470-1 Summary ns	Adjusted P Value 0.9998 0.9998 0.9998 0.028 0.023 0.8402 0.9791 0.2826 0.0044 0.9453 0.0004 0.4963 0.0004 0.4963 0.0005 0.0005 0.0005 0.0005 0.09857 0.09905 0.0001 0.08043 0.09910 0.07880 0.07880 0.07880 0.07880 0.07880 0.07880 0.04481 0.04481 0.04481 0.04481 0.09915 0.07880 0.0001 0.07880 0.07880 0.07880 0.07880 0.07880 0.07880 0.0001 0.07880 0.04481	Comparison ATFG vs. XBP1s ATFG vs. PERK/SR ATFG vs. VHSR ATFG vs. OSR ATFG vs. OSR XBP1s vs. OSR VBP1s vs. OSR VBP1s vs. OSR PERK/ISR vs. OSR PERK/ISR vs. OSR PERK/ISR vs. OSR ATFG vs. XBP1s ATFG vs. PERK/ISR ATFG vs. Uther OSR vs. OSR ATFG vs. OSR ATFG vs. OSR ATFG vs. OSR ATFG vs. OSR ATFG vs. OSR	Bardo: Mean Diff. 0.0134 -1.012 -2.319 -0.4154 0.3515 -1.026 -2.333 -0.4288 -0.3381 -1.307 0.5971 0.3381 -1.307 0.3381 -1.307 0.3381 -1.307 0.3381 -1.307 0.3381 -1.307 0.3381 -1.254 0.008735 -1.127 -0.1254 0.05819 -1.254 0.3551 -1.254 -0.3553 -1.254 -0.3553 -1.254 -0.3553 -1.254 -0.3555 -1.254 -0.3555 -1.254 -0.3555 -1.254 -0.3555 -1.254 -0.3555 -1.254 -0.3555 -1.254 -0.3555 -1.254 -0.3555 -1.254 -0.3555 -1.254 -0.3555 -1.254 -0.3555 -1.254 -0.3555 -1.254 -0.3555 -1.254 -0.3555 -1.254 -0.3555 -1.254 -0.3555 -1.254 -0.3555 -1.254 -0.3555 -0.254 -0.3555 -0.254 -0.3555 -0.2	xolone Summary ns	Adjusted P Value >0.9999 0.2481 <0.0001 0.9751 0.9368 0.2213 <0.0001 0.9702 0.9413 0.08852 0.0041 0.0413 0.0433 0.0413 0.0433 0.0001 0.5983 Adjusted P Value 0.9403 0.9099 0.0010 0.9998 0.9998 0.9998 0.9998 0.9998 0.9917 <0.0001		Comparison ATF6 vs. XBP1s ATF6 vs. PERK/SR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. OSR XBP1 svs. PERK/SR XBP1 svs. OSR	F1 Mean Diff. -0.1053 -0.6955 -0.8594 -0.5577 -0.09598 -0.5574 -0.5592	Summary ns ns ns ns ns ns ns ns ns	Adjusted P Value 0.9987 0.0913 0.0322 0.4599 0.9978 0.2073 0.0801 0.6664
Comparison ATF6 vs. XPI1s ATF6 vs. PERK/ISR ATF6 vs. Other ATF6 vs. Other ATF6 vs. Other XBP1 svs. FERK/ISR XBP1 svs. FERK/ISR vs. Other PERK/ISR vs. Other PERK/ISR vs. Other Comparison ATF6 vs. XBP1 s ATF6 vs. SOR ATF6 vs. SOR ATF6 vs. Other Comparison ATF6 vs. Other XBP1 svs. Other X	Mean Diff. 0.7554 0.4121 2.009 1.336 1.335 1.336 1.353 0.55599 0.6411 1.597 0.9032 0.9041 1.597 0.0932 0.6125 0.6125 0.6125 0.04237 -1.146 -4.115 -0.4875 -1.189 -4.158 -0.438707 -0.4899	Carmycin Summary ns ns ns ns ns ns ns ns ns ns	Adjusted P Value 0.0261 0.0261 0.0201 0.0200 0.0001 0.0005 0.0005 0.0001 0.0745 0.0001 0.0003 0.0003 0.0003 0.0003 0.0003 0.0003 0.0003 0.0277 0.9998 0.0587 < 0.0001 0.5256 0.0587 < 0.0001 0.5256 0.0587 < 0.0001 0.0585 < 0.0001 0.0585 < 0.0001 0.0585 0.0581 0.0585 < 0.0001 0.0585 0.0581 0.0585	Comparison ATE6 vs. XBP1s ATE6 vs. PERKJSR ATE6 vs. DERKJSR ATE6 vs. OFR XBP1s vs. DERKJSR XBP1s vs. DFR XBP1s vs. OFR PERKJSR vs. OSR PERKJSR vs. OSR HSR vs. OSR HSR vs. OSR HSR vs. OTher OSR vs. Other Comparison ATE6 vs. NERS ATE6 vs. DERKJSR ATE6 vs. DERKJSR ATE6 vs. SHSR ATE6 vs. OSR ATE6 vs. SHSR ATE6 vs. OTHER XBP1s vs. OSR XBP1s vs. OSR XBP1s vs. OSR XBP1s vs. OSR XBP1s vs. OSR	CBR Mean Diff. -0.06403 -0.06403 -0.05403 -0.5881 -0.5881 -0.5241 -1.037 -0.6892 -0.6892 -0.6892 -0.3341 -0.3352 0.8685 C Mean Diff. -0.112 -0.0514 -0.312 -0.0514 -0.312 -0.0514 -0.3552 -0.05262 -0.05262 -0.05206 -0.2131 -0.05881 -0.3881 -0.3681 -0.162	-470-1 Summary ns ns ns ns ns ns ns ns ns ns	Adjusted P Value 0.9998 0.9998 0.0998 0.023 0.8402 0.9791 0.2826 0.0040 0.9453 0.0601 0.0004 0.4557 0.4565 0.0065 0.9857 0.9905 0.9005 0.9005 0.9005 0.9005 0.00001 0.8943 0.9991 0.7880 0.0001 0.4841 0.08341 0.09391	Comparison ATT6 vs. XBP1s ATT6 vs. PERK/JSR ATT6 vs. VHSR ATT6 vs. OSR XBP1s vs. PERK/JSR XBP1s vs. USR XBP1s vs. OSR PERK/JSR vs. OSR PERK/JSR vs. OSR HSR vs. OSR HSR vs. OSR MSR vs. Other Comparison ATT6 vs. XBP1s ATT6 vs. OSR ATT6 vs. VHSR ATT6 vs. OSR ATT6 vs. USR ATT6 vs. OSR ATT6 vs. USR ATT6 vs. OSR ATT6 vs. USR ATT6 vs. USR ATT6 vs. USR ATT6 vs. USR ATT6 vs. VHSR ATT6 vs. VHSR ATT6 vs. USR	Bardo: Mean Diff. 0.0134 -1.012 -2.319 -0.4154 -1.026 -2.333 -1.026 -1.307 0.5971 1.364 1.304 1.304 2.671 0.7668 D D Mean Diff. 0.2399 -0.008735 -1.127 -0.1254 -0.05619 -0.20561 -1.367 -1.367 -1.127 -1.127 -1.127 -1.127 -1.1264 -0.05619 -0.20561 -1.367 -0.3653 -0.2961 -0.2961 -0.2961 -0.2961 -0.2961 -0.2961 -0.2961 -0.2961 -0.2961 -0.2961 -0.2961 -0.2961 -0.2961 -0.2961 -0.2961 -0.2051 -0.	xolone Summary ns ns ns ns ns ns ns ns ns ns	Adjusted P Value >0.9999 0.2481 <0.0001 0.9751 0.9368 0.0213 <0.0001 0.9702 0.9413 0.0828 0.8852 0.0041 0.0143 <0.0001 0.5983 Adjusted P Value 0.9403 >0.9999 0.0010 0.9998 0.9187 <0.0001 0.8956		Comparison ATF6 vs. X8P 1s ATF6 vs. PERK/JSR ATF6 vs. PERK/JSR ATF6 vs. OSR ATF6 vs. OSR ATF6 vs. OSR X8P 1s vs. OSR X8P 1s vs. OSR	F11 Mean Diff. -0.1053 -0.6955 -0.69554 -0.5902 -0.5902 -0.7541 -0.4717 -0.4717	Summary ns ns * ns ns ns ns ns ns ns ns ns	Adjusted P Value 0.9987 0.0913 0.0322 0.45599 0.2073 0.0801 0.6664 >0.9999
Comparison ATFG vs. XBP15 ATFG vs. PERK/ISR ATFG vs. OSR ATFG vs. OSR ATFG vs. OSR ATFG vs. OSR XBP15 vs. OSR XBP15 vs. OSR VSR VS. Other PERK/ISR vs. OTher PERK/ISR vs. OTher OSR vs. Other OSR vs. Other OSR vs. Other OSR vs. Other ATFG vs. PERK/ISR ATFG vs. PERK/ISR ATFG vs. OSR ATFG vs. OSR	Mean Diff. 0.7554 0.4752 0.4752 0.4752 0.4752 0.4711 1.396 1.396 1.395 0.5599 0.641 1.597 0.9032 0.643 0.6645 0.6636 0.66125 0.0812 0.04237 -1.146 -0.4175 -0.4244 -0.4175 -0.8284 -0.4175 -0.4870 -0.4874 -0.4874 -0.4874 -0.4874 -0.4824 -0.4824 -0.4824 -0.4824 -0.4824 -0.4824 -0.4824 -0.4824 -0.4824 -0.4824 -0.4824 -0.4824 -0.4824 -0.4824 -0.4824 -0.4824 <td>carwycin Summary ns ns ns ns ns ns ns ns ns ns</td> <td>Adjusted P Value 0.0861 0.0861 0.0888 <.0.0001 0.0000 0.0000 0.0000 0.03510 <.0.0001 0.0745 0.0003 0.0745 0.0003 0.0745 0.0003 0.3369 0.1277 0.02998 Adjusted P Value >0.0999 Adjusted P Value >0.05256 0.7581 0.0351 <.0.0001 0.5256 0.7581 0.0351 <.0.0001 0.5256 0.7581 0.0351 <.0.0001 0.5256 0.7581 0.0351 <.0.0001 0.5256 0.7581 0.0351 <.0.0001 0.5256 0.7581 0.0351 <.0.0001 0.5256 0.7581 0.0351 <.0.0001 0.5256 0.7581 0.0351 <.0.0001 0.5256 0.7581 0.0351 <.0.0001 0.5256 0.7581 0.0351 <.0.0001 0.05256 0.0351 <.0.0001 0.05256 0.0351 <.0.0001 0.0531 <.0.0001 0.0526 0.0351 <.0.0001 0.0526 0.0351 <.0.0001 0.0526 0.0351 <.0.0001 0.0526 0.0531 <.0.0001 0.0526 0.0351 <.0.0001 0.0526 0.0351 <.0.0001 0.0526 0.0351 <.0.0001 0.0525 0.0351 <.0.0001 0.0525 0.0351 <.0.0001 0.0525 0.0351 <.0.0001 0.0525 0.0351 <.0.0001 0.0525 0.0001 0.0525 0.0001 0.0351 <.0.0001 0.0525 0.0001 0.0525 0.0001 0.0525 0.0001 0.0533 <.0.0001 0.04458 0.0001 0.04458 0.0001 0.0001 0.00001 0.0001 0.0001 0.00001 0.00001 0.0001 0.00</td> <td>Comparison ATE6 vs. XBP1s ATE6 vs. PERK/JSR ATE6 vs. BHSR ATE6 vs. USA XEF6 vs. OSA ATE6 vs. OSA XBP1s vs. OSA XBP1s vs. OSA PERK/JSR vs. OSA PERK/JSR vs. OSA PERK/JSR vs. OSA ATE6 vs. NBP1 ATE6 vs. NBP1 ATE6 vs. DERK/JSR ATE6 vs. DERK/JSR ATE6 vs. NSA ATE6 vs. VSA ATE6 vs. VSA</td> <td>CBR Mean Diff. -0.06403 -0.06403 -0.05881 -1.102 -0.5281 -1.037 -0.5241 -1.037 -0.5241 -0.6892 -0.6892 -0.6892 -0.6892 -0.6892 -0.6892 -0.5241 -0.35341 -0.5252 0.8685 -0.5134 -0.5134 -0.5134 -0.5134 -0.5134 -0.5134 -0.5262 -0.50066 -0.2131 -0.9837 -0.3681 -0.3681 -0.3681 -0.3681 -0.5262 -0.5261 -0.5262 -0.5383 -0.5262 -0.5383 -0.5262 -0.5383 -0.5383 -0.5262 -0.5362 -0.5762 -0.5762 -0.5762 -0.5762 -0.5762 -0.5762 -0.5762 -0.5762 -0.5777 -0.7777 -0.7777 -0.7777 -0.7777 -0.562 -0.7777 -0.7777 -0.562 -0.7777 -0.7777 -0.562 -0.7777 -0.7777 -0.562 -0.7777 -0.7777 -0.562 -0.7777 -0.7777 -0.562 -0.7777 -0.7777 -0.562 -0.7777 -0.7777 -0.562 -0.5762 -0.5762 -0.5762 -0.7777 -0.7777 -0.7777 -0.7777 -0.5762 -0.5762 -0.7777 -0</td> <td>-470-1 Summary ns ns ns ns ns ns ns ns ns ns</td> <td>Adjusted P Value 0.9998 0.9998 0.9998 0.022 0.022 0.8402 0.9791 0.2826 0.0040 0.9453 0.0004 0.4963 0.0004 0.4963 0.0065 0.0055 0.0055 0.0055 0.9995 0.09905 0.9995 0.09905 0.09905 0.09905 0.09905 0.09905 0.09905 0.09905 0.09905 0.09905 0.09905 0.09905 0.09905 0.09905 0.09905 0.09905 0.09905 0.0001 0.57880 0.7880 0.07880 0.0001 0.4481 0.8341 0.0003 0.0003 0.0003 0.0005 0.0</td> <td>Comparison ATFG vs. XBP1s ATFG vs. PERK/SR ATFG vs. VHSR ATFG vs. OSR XBP1s vs. VHSR XBP1s vs. OSR XBP1s vs. OSR PERK/ISR vs. OSR PERK/ISR vs. OSR PERK/ISR vs. OSR Comparison ATFG vs. XBP1s ATFG vs. VHSR ATFG vs. OSR ATFG vs. OSR ATFG vs. OSR ATFG vs. OSR XBP1s vs. OSR</td> <td>Bardo: Mean DIF. 0.0134 -1.012 -2.319 0.4154 0.3515 -1.026 -2.333 -0.4288 0.3381 -1.307 0.3381 -1.307 0.3381 -1.307 0.3381 -1.307 0.4284 0.008735 -1.1254 0.02845 -1.1187 -0.3653 -0.2684 -0.3655 -0.2684 -0.3655 -0.2684 -0.3685 -0.3685</td> <td>xolone Summary ns ns</td> <td>>djusted P Value >0.9999 0.2481 <0.0001</td> 0.9751 0.9368 0.2133 <0.0001	carwycin Summary ns ns ns ns ns ns ns ns ns ns	Adjusted P Value 0.0861 0.0861 0.0888 <.0.0001 0.0000 0.0000 0.0000 0.03510 <.0.0001 0.0745 0.0003 0.0745 0.0003 0.0745 0.0003 0.3369 0.1277 0.02998 Adjusted P Value >0.0999 Adjusted P Value >0.05256 0.7581 0.0351 <.0.0001 0.5256 0.7581 0.0351 <.0.0001 0.5256 0.7581 0.0351 <.0.0001 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Table S4. Whole transcriptome RNAseq of putative HSF1 activators (see Excel Spreadsheet)

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