Supplemental Table 1. HNE-responsive transcription factors and their target genes

OverRep FDR: False Discovery Rate in the hypergeometric test for over-representation analysis
log FC: log fold change (HNE treatment vs control)
DiffExp FDR: False Discovery Rate in moderated *t*-test for differential gene expression analysis

Transcription Factor	**Target genes**		
	Name	**log FC**	**DiffExp_FDR**
Name: CREB1 **OverRep FDR: 3.83E-06** **log FC: -0.066** **DiffExp FDR: 0.8**	ATF3	1.23	2.45E-04
	CAMK2D	0.48	5.22E-03
	CHAC1	0.68	8.41E-03
	CHD2	0.49	3.51E-03
	CLCN3	0.72	7.25E-04
	DNAJB2	1.25	9.99E-05
	DNAJB5	0.51	8.37E-03
	EGR2	0.66	9.86E-04
	EGR3	0.85	5.69E-03
	FOS	1.53	3.01E-05
	FOSB	1.33	9.99E-05
	GADD45B	1.82	9.99E-05
	GEM	1.60	1.55E-05
	HERPUD1	2.05	3.21E-04
	ING3	0.74	2.92E-03
	KLHL12	0.63	1.37E-03
	MAFF	1.44	5.77E-05
	MBNL2	0.66	4.05E-04
	MXD1	1.09	3.99E-04
	PPP1R15A	1.66	6.52E-05
	SERTAD1	0.75	4.12E-03
	SLC38A2	1.11	3.81E-04
	SMAD1	0.48	9.16E-03
	TM2D2	0.46	3.52E-03
	UBE2H	0.42	8.81E-03
	VEGFA	0.86	2.28E-03
	WBP5	0.65	8.08E-03
	ZBTB20	0.99	1.88E-04
	ZNF184	0.53	7.00E-03
	ZNF23	0.72	7.17E-03
Name: ATF2 **OverRep FDR: 4.76e-5** **log FC: 0.34** **DiffExp FDR: 0.04**	ARRDC3	1.94	8.72E-04
	ATF3	1.23	2.45E-04
	C17orf91	0.66	3.51E-03
	CAMK2D	0.48	5.22E-03
	CLCN3	0.72	7.25E-04
	CREB5	0.76	2.22E-03
	EGR2	0.66	9.86E-04
	EGR3	0.85	5.69E-03
	FOS	1.53	3.01E-05
	FOSB	1.33	9.99E-05
	GEM	1.60	1.55E-05
	HERPUD1	2.05	3.21E-04
	ING3	0.74	2.92E-03

	JMJD1C	1.04	1.78E-04
	MAFF	1.44	5.77E-05
	MBNL2	0.66	4.05E-04
	PPP1R15A	1.66	6.52E-05
	SLC38A2	1.11	3.81E-04
	SMAD1	0.48	9.16E-03
	TM2D2	0.46	3.52E-03
	UBE2H	0.42	8.81E-03
	WBP5	0.65	8.08E-03
	WEE1	0.76	1.34E-03
	ZFYVE9	0.42	8.19E-03
	ZNF184	0.53	7.00E-03
Name: CDC5L **OverRep FDR: 8.47e-5** **log FC: -0.15** **DiffExp FDR: 0.56**	ARRDC3	1.94	8.72E-04
	BAMBI	1.24	9.99E-05
	CDC42EP3	0.92	1.04E-03
	CDKN2C	1.46	5.11E-05
	CHD2	0.49	3.51E-03
	CHRNA5	0.88	9.71E-04
	CPEB4	1.36	6.64E-04
	CREB5	0.76	2.22E-03
	EGR2	0.66	9.86E-04
	GOLPH3L	0.81	5.74E-04
	ING3	0.74	2.92E-03
	PDGFA	0.40	7.27E-03
	PURA	1.42	2.10E-03
	SAT1	0.46	6.78E-03
	VEGFA	0.86	2.28E-03
	ZBTB20	0.99	1.88E-04
Name: HSF1 **OverRep FDR: 1.65e-4** **log FC: -0.24** **DiffExp FDR: 0.27**	ADM	1.63	3.81E-04
	ALKBH6	0.50	7.98E-03
	ASNS	0.78	5.06E-04
	CHD2	0.49	3.51E-03
	DMTF1	0.60	6.56E-03
	DNAJB1	1.52	9.99E-05
	DNAJB5	0.51	8.37E-03
	EGR3	0.85	5.69E-03
	FOS	1.53	3.01E-05
	HSPA1A	2.25	8.85E-05
	HSPA1B	0.65	2.30E-03
	HSPB1	0.63	2.71E-03
	HSPH1	2.22	5.42E-07
	MBNL2	0.66	4.05E-04
	MORF4L2	0.94	1.68E-04
	PLOD1	0.52	8.44E-03
	PURA	1.42	2.10E-03
	SERPINH1	0.88	8.29E-03
	SMAD1	0.48	9.16E-03
	XPO1	1.15	9.99E-05
	ZBTB20	0.99	1.88E-04

	ZNF212	0.61	1.27E-03
Name: HSF2 **OverRep FDR: 1.93e-4** **log FC: -0.38** **DiffExp FDR: 0.02**	ALKBH6	0.50	7.98E-03
	DNAJB1	1.52	9.99E-05
	DNAJB5	0.51	8.37E-03
	EGR3	0.85	5.69E-03
	FOS	1.53	3.01E-05
	HSPA1A	2.25	8.85E-05
	HSPA1B	0.65	2.30E-03
	HSPH1	2.22	5.42E-07
	MBNL2	0.66	4.05E-04
	MORF4L2	0.94	1.68E-04
	PLOD1	0.52	8.44E-03
	SERPINH1	0.88	8.29E-03
	SMAD1	0.48	9.16E-03
	ZBTB20	0.99	1.88E-04
	ZNF212	0.61	1.27E-03
Name: NFYB **OverRep FDR: 2.17e-4** **log FC: -0.18** **DiffExp FDR: 0.5**	ANKRD49	0.50	4.51E-03
	ARRDC3	1.94	8.72E-04
	ARRDC4	0.57	4.84E-03
	ASB7	0.41	9.72E-03
	C17orf91	0.66	3.51E-03
	CCNG2	1.29	2.13E-04
	CHAC1	0.68	8.41E-03
	CPEB4	1.36	6.64E-04
	CREB5	0.76	2.22E-03
	CYP39A1	1.35	1.03E-03
	DDIT3	1.73	5.86E-06
	DNAJB1	1.52	9.99E-05
	DNAJB5	0.51	8.37E-03
	EIF2AK3	0.91	2.79E-03
	FICD	0.54	4.35E-03
	FOSB	1.33	9.99E-05
	GLA	0.53	4.12E-03
	GOLPH3L	0.81	5.74E-04
	GOT1	0.43	7.09E-03
	HERPUD1	2.05	3.21E-04
	HMGCS1	1.01	2.10E-03
	HSPA1A	2.25	8.85E-05
	HSPA1B	0.65	2.30E-03
	IER5	1.69	1.10E-04
	INSIG1	1.24	1.18E-04
	MBNL2	0.66	4.05E-04
	RP5-1022P6.2	0.54	5.01E-03
	SERTAD1	0.75	4.12E-03
	SESN2	2.21	2.74E-05
	SLC7A11	2.54	6.76E-05
	STARD4	0.46	8.60E-03
	STAT2	0.41	8.26E-03
	THAP9	0.75	2.28E-03

	WEE1	0.76	1.34E-03
	XBP1	0.71	5.29E-03
	XPO1	1.15	9.99E-05
	YPEL5	0.54	2.24E-03
	ZBTB20	0.99	1.88E-04
	ZNF14	0.39	9.19E-03
	ZNF436	0.82	3.00E-03
Name: CEBPA **OverRep FDR: 0.0010** **log FC: -0.12** **DiffExp FDR: 0.55**	ADM	1.63	3.81E-04
	ARHGAP5	0.84	7.27E-03
	ARRDC3	1.94	8.72E-04
	ARRDC4	0.57	4.84E-03
	ATF3	1.23	2.45E-04
	C17orf91	0.66	3.51E-03
	CHAC1	0.68	8.41E-03
	CHD2	0.49	3.51E-03
	CLIC4	0.48	4.19E-03
	CLU	1.23	2.58E-05
	CPEB4	1.36	6.64E-04
	CREB5	0.76	2.22E-03
	CTGF	1.69	1.78E-04
	DDIT3	1.73	5.86E-06
	DUSP2	1.53	4.76E-04
	EGR2	0.66	9.86E-04
	FOSB	1.33	9.99E-05
	GARS	0.47	2.78E-03
	GOT1	0.43	7.09E-03
	HERPUD1	2.05	3.21E-04
	ING3	0.74	2.92E-03
	JMJD1C	1.04	1.78E-04
	KIAA0355	0.49	7.60E-03
	MBNL2	0.66	4.05E-04
	MOAP1	0.53	7.60E-03
	NSMCE2	0.53	4.83E-03
	PURA	1.42	2.10E-03
	SAT1	0.46	6.78E-03
	SESN2	2.21	2.74E-05
	SLC38A2	1.11	3.81E-04
	TM2D2	0.46	3.52E-03
	VEGFA	0.86	2.28E-03
	WEE1	0.76	1.34E-03
	ZBTB20	0.99	1.88E-04
	ZNF436	0.82	3.00E-03
Name: E4F1 **OverRep FDR: 0.0015** **log FC: -0.43** **DiffExp FDR: 0.02**	C17orf91	0.66	3.51E-03
	DMTF1	0.60	6.56E-03
	DNAJA4	1.49	4.78E-05
	DNAJB4	2.51	2.09E-04
	EGR2	0.66	9.86E-04
	EGR3	0.85	5.69E-03
	FBXO8	0.78	3.82E-03

	FOSB	1.33	9.99E-05
	GEM	1.60	1.55E-05
	GOLGA5	0.43	9.19E-03
	HIST1H4H	0.51	9.62E-03
	KLHL12	0.63	1.37E-03
	MAFF	1.44	5.77E-05
	MORF4L2	0.94	1.68E-04
	NIT1	0.41	7.58E-03
	PKIB	0.47	9.85E-03
	PNPLA8	1.10	6.33E-05
	PPP1R15A	1.66	6.52E-05
	SELK	0.58	5.22E-03
	SLC38A2	1.11	3.81E-04
	UBE2H	0.42	8.81E-03
	WBP5	0.65	8.08E-03
	XBP1	0.71	5.29E-03
	ZBTB20	0.99	1.88E-04
	ZNF184	0.53	7.00E-03
	ZNF23	0.72	7.17E-03
Name: SREBF1 **OverRep FDR: 0.0023** **log FC: -0.20** **DiffExp FDR: 0.17**	ATP6V1C1	0.56	8.99E-03
	CAMK2D	0.48	5.22E-03
	CHD2	0.49	3.51E-03
	CLN3	0.53	2.20E-03
	DDIT3	1.73	5.86E-06
	GEM	1.60	1.55E-05
	GLA	0.53	4.12E-03
	HMOX1	2.93	5.42E-07
	KLHL24	1.03	4.09E-03
	MAFF	1.44	5.77E-05
	MBNL2	0.66	4.05E-04
	MORF4L2	0.94	1.68E-04
	NSMCE2	0.53	4.83E-03
	PURA	1.42	2.10E-03
	RNF185	0.51	5.71E-03
	RRAGC	0.74	4.86E-04
	SLC3A2	1.12	9.99E-05
	SNX16	1.04	3.15E-03
	TPP1	0.69	8.62E-04
	WBP5	0.65	8.08E-03
	XPO1	1.15	9.99E-05
	ZFYVE1	0.42	6.90E-03
Name: USF1 **OverRep FDR: 0.0039** **log FC: -0.30** **DiffExp FDR: 0.1**	ARRDC3	1.94	8.72E-04
	ATP6V1C1	0.56	8.99E-03
	CDKN2C	1.46	5.11E-05
	CHAC1	0.68	8.41E-03
	CLN3	0.53	2.20E-03
	CPEB4	1.36	6.64E-04
	CREB5	0.76	2.22E-03
	DDIT3	1.73	5.86E-06

	DNAJB5	0.51	8.37E-03
	EGR2	0.66	9.86E-04
	GLA	0.53	4.12E-03
	HERPUD1	2.05	3.21E-04
	HMOX1	2.93	5.42E-07
	HSPA4	0.70	1.53E-03
	HSPH1	2.22	5.42E-07
	KIAA0355	0.49	7.60E-03
	MORF4L2	0.94	1.68E-04
	MYCL1	0.68	1.37E-03
	NIT1	0.41	7.58E-03
	PURA	1.42	2.10E-03
	SLC38A2	1.11	3.81E-04
	SNX16	1.04	3.15E-03
	WEE1	0.76	1.34E-03
	XPO1	1.15	9.99E-05
	YPEL5	0.54	2.24E-03
Name: CEBPD **OverRep FDR: 0.0047** **log FC: -0.18** **DiffExp FDR: 0.23**	ARRDC3	1.94	8.72E-04
	ATF3	1.23	2.45E-04
	CHD2	0.49	3.51E-03
	CREB5	0.76	2.22E-03
	FOS	1.53	3.01E-05
	FOSB	1.33	9.99E-05
	GLA	0.53	4.12E-03
	MBNL2	0.66	4.05E-04
	NSMCE2	0.53	4.83E-03
	SLC7A11	2.54	6.76E-05
	SMAD1	0.48	9.16E-03
	ZFYVE9	0.42	8.19E-03
Name: ATF4 **OverRep FDR: 0.0073** **log FC: 0.32** **DiffExp FDR: 0.1**	CHAC1	0.68	8.41E-03
	CHD2	0.49	3.51E-03
	FOS	1.53	3.01E-05
	FOSB	1.33	9.99E-05
	GEM	1.60	1.55E-05
	MBNL2	0.66	4.05E-04
	PPP1R15A	1.66	6.52E-05
	SLC38A2	1.11	3.81E-04
	SMAD1	0.48	9.16E-03
	UBE2H	0.42	8.81E-03
	XPO1	1.15	9.99E-05
	ZBTB20	0.99	1.88E-04
Name: ATF3 **OverRep FDR: 0.0084** **log FC: 1.23** **DiffExp FDR: 2.45e-4**	ATF3	1.23	2.45E-04
	CAMK2D	0.48	5.22E-03
	CREB5	0.76	2.22E-03
	DNAJB4	2.51	2.09E-04
	DNAJB5	0.51	8.37E-03
	FOS	1.53	3.01E-05
	FOSB	1.33	9.99E-05
	GABARAPL1	0.85	5.06E-04

	GEM	1.60	1.55E-05
	MAFF	1.44	5.77E-05
	MBNL2	0.66	4.05E-04
	MXD1	1.09	3.99E-04
	PAPD5	0.85	6.09E-03
	PDGFA	0.40	7.27E-03
	PPP1R15A	1.66	6.52E-05
	SIPA1L2	0.76	1.13E-03
	SLC3A2	1.12	9.99E-05
	SNX16	1.04	3.15E-03
	UBE2H	0.42	8.81E-03
	ZNF184	0.53	7.00E-03
Name: FOXO1 **OverRep FDR: 0.0090** **log FC: -0.11** **DiffExp FDR: 0.87**	ASB7	0.41	9.72E-03
	AZI2	1.08	3.91E-04
	CCNG2	1.29	2.13E-04
	CHD2	0.49	3.51E-03
	DDIT4	1.48	8.74E-04
	EXT1	0.48	6.72E-03
	FOSL2	0.66	9.76E-04
	INSIG1	1.24	1.18E-04
	MAFF	1.44	5.77E-05
	PDGFA	0.40	7.27E-03
	PURA	1.42	2.10E-03
	SLC38A2	1.11	3.81E-04
	SLU7	0.63	7.58E-03
	SMAD1	0.48	9.16E-03
	UBE2H	0.42	8.81E-03
	ZFYVE1	0.42	6.90E-03
Name: MYC **OverRep FDR: 5.03e-5** **log FC: -0.60** **DiffExp FDR: 0.1**	ABCE1	-0.59	4.88E-03
	AKAP1	-0.84	8.92E-04
	AMD1	-1.22	1.10E-04
	CCDC41	-0.94	2.64E-03
	CCND1	-0.81	6.78E-03
	CD3EAP	-0.80	3.81E-04
	CIRH1A	-0.50	6.12E-03
	DCUN1D4	-0.46	3.34E-03
	DUSP7	-0.91	1.68E-04
	E2F8	-1.54	3.66E-06
	EIF4E	-0.84	3.15E-03
	FEN1	-0.59	2.22E-03
	GEMIN4	-1.06	1.12E-04
	GNL3	-0.68	3.38E-03
	IPO7	-0.69	4.60E-04
	IVNS1ABP	-0.49	5.04E-03
	JPH1	-0.40	8.64E-03
	KIAA1737	-0.94	1.65E-03
	LMNB1	-0.89	6.77E-03
	LRFN4	-0.69	1.37E-03
	LYAR	-0.58	8.42E-03

	MAT2A	-1.47	6.24E-05
	MID1IP1	-0.77	8.98E-04
	NOL6	-0.47	7.51E-03
	NOLC1	-0.43	6.68E-03
	PATZ1	-0.94	4.35E-04
	PDP2	-0.55	3.15E-03
	POGK	-0.44	8.57E-03
	POP1	-0.68	1.01E-03
	PPAT	-0.62	2.21E-03
	PPRC1	-1.36	4.01E-04
	PRR7	-0.68	3.10E-03
	PUS1	-0.79	1.16E-03
	RCL1	-0.43	8.51E-03
	RRS1	-1.04	3.39E-04
	SC65	-0.60	2.92E-03
	SLC16A1	-0.69	2.25E-03
	SLC25A32	-0.94	8.91E-04
	SLC25A37	-0.61	4.23E-03
	SLC4A11	-0.57	5.29E-03
	SOCS5	-0.70	7.25E-04
	SYNCRIP	-0.52	9.99E-03
	TGIF2	-0.61	3.10E-03
	TIMM8A	-0.41	9.55E-03
	TNFRSF21	-0.61	2.10E-03
	TRIB1	-0.56	3.18E-03
	TSEN2	-1.05	3.00E-04
	TUBA4A	-0.53	9.55E-03
	UMPS	-0.79	1.78E-04
	USP31	-0.75	5.96E-03
	UTP14A	-0.42	9.00E-03
	ZADH2	-0.72	2.11E-03
Name: E2F1 **OverRep FDR: 0.0032** **log FC: 0.04** **DiffExp FDR: 0.87**	ABCE1	-0.59	4.88E-03
	AMD1	-1.22	1.10E-04
	APPL1	-0.62	8.18E-03
	ARHGAP11A	-1.16	5.63E-04
	ARPC5L	-0.50	3.80E-03
	CD3EAP	-0.80	3.81E-04
	CDCA7	-0.74	3.81E-04
	CTCF	-0.57	2.34E-03
	DUSP7	-0.91	1.68E-04
	E2F8	-1.54	3.66E-06
	FBXO5	-1.34	4.35E-03
	GINS3	-0.71	5.21E-04
	GNL3	-0.68	3.38E-03
	IPO7	-0.69	4.60E-04
	JPH1	-0.40	8.64E-03
	MAT2A	-1.47	6.24E-05
	NASP	-0.45	6.58E-03
	NOLC1	-0.43	6.68E-03

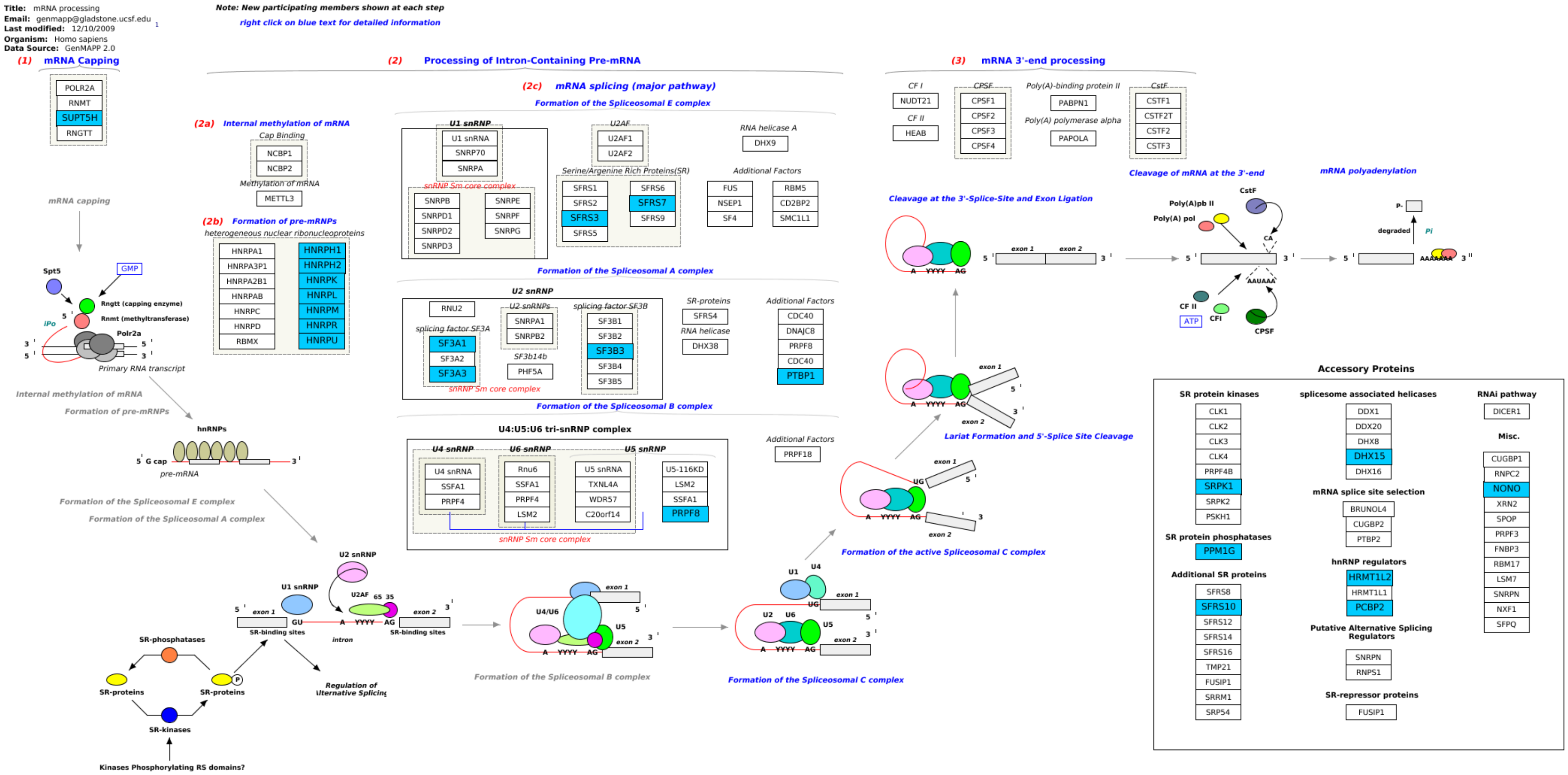
	NR2F2	-0.62	7.47E-03
	NUP62	-0.63	8.19E-03
	PCNA	-0.60	3.30E-03
	PPRC1	-1.36	4.01E-04
	PRPF4B	-0.57	8.11E-03
	RRM2	-0.43	4.40E-03
	SFRS1	-0.44	9.55E-03
	SFRS2	-0.58	2.10E-03
	SLC35D1	-0.50	2.64E-03
	SYNCRIP	-0.52	9.99E-03
Name: E2F3 **OverRep FDR: 0.0032** **log FC: -0.03** **DiffExp FDR: 0.91**	APPL1	-0.62	8.18E-03
	ARHGAP11A	-1.16	5.63E-04
	CD3EAP	-0.80	3.81E-04
	CDCA7	-0.74	3.81E-04
	CTCF	-0.57	2.34E-03
	DUSP7	-0.91	1.68E-04
	E2F8	-1.54	3.66E-06
	EFNA3	-0.54	4.49E-03
	FBXO5	-1.34	4.35E-03
	GINS3	-0.71	5.21E-04
	GNL3	-0.68	3.38E-03
	IPO7	-0.69	4.60E-04
	JPH1	-0.40	8.64E-03
	MAT2A	-1.47	6.24E-05
	NASP	-0.45	6.58E-03
	NOLC1	-0.43	6.68E-03
	NUP62	-0.63	8.19E-03
	PATZ1	-0.94	4.35E-04
	PCNA	-0.60	3.30E-03
	PPRC1	-1.36	4.01E-04
	PRPF4B	-0.57	8.11E-03
	RBPJ	-0.46	9.79E-03
	RRM2	-0.43	4.40E-03
	SFRS1	-0.44	9.55E-03
	SFRS2	-0.58	2.10E-03
	SUV39H2	-0.67	1.22E-03
	SYNCRIP	-0.52	9.99E-03
Name: NRF1 **OverRep FDR: 0.0032** **log FC: -0.33** **DiffExp FDR: 0.03**	ARMC8	-0.65	2.85E-03
	AURKA	-0.85	1.16E-03
	BTBD3	-0.65	2.30E-03
	CCDC12	-0.57	3.36E-03
	CCNA2	-0.77	3.81E-04
	CCNF	-0.97	5.92E-04
	CDV3	-0.40	8.04E-03
	CHCHD4	-0.64	1.91E-03
	CHERP	-0.45	8.19E-03
	CTCF	-0.57	2.34E-03
	EXOSC2	-0.57	5.87E-03
	FADD	-0.56	3.25E-03

	FARSB	-0.60	2.85E-03
	FASTKD2	-0.91	4.67E-04
	FBXO5	-1.34	4.35E-03
	GEMIN4	-1.06	1.12E-04
	KIAA1737	-0.94	1.65E-03
	KIF3A	-0.62	8.81E-03
	MED11	-0.38	9.79E-03
	MRPL14	-0.47	9.72E-03
	MRPL36	-0.50	4.18E-03
	NUP62	-0.63	8.19E-03
	PCNA	-0.60	3.30E-03
	PDCD2L	-0.57	8.81E-03
	POP7	-0.77	4.78E-04
	PRKRIR	-0.61	1.74E-03
	PRRG1	-0.64	2.64E-03
	SART3	-0.53	4.18E-03
	SELT	-0.45	7.07E-03
	SFRS1	-0.44	9.55E-03
	SFRS2	-0.58	2.10E-03
	SLC35D1	-0.50	2.64E-03
	TMEM115	-0.69	1.65E-03
	TSEN2	-1.05	3.00E-04
	TSEN54	-0.41	7.67E-03
	WDR35	-0.52	5.69E-03

Supplemental Table 2. Predicted protein sensors for HNE damage

Protein/gene information			Protein adduction data (Codreanu et al.)											Network analysis	
Gene Symbol	Entrez_ID	Protein Description	Spectral counts									Regression coefficient	Regression p-value	Statistical significance	
			0 μM [HNE]			50 μM [HNE]			100 μM [HNE]					p_l	p_g
			1	2	3	1	2	3	1	2	3				
CCNA2	890	Cyclin-A2 (Cyclin-A)	0	0	0	0	1	2	3	2	2	0.0152	0.0075	0	0.009
EEF1G	1937	Elongation factor 1-gamma	3	3	3	34	24	51	41	56	47	0.0518	0.0039	0.008	0.035
HSPB1	3315	Heat-shock protein beta-1	2	1	2	6	7	12	10	8	7	0.016	0.0233	0.003	0.04
LMNA	4000	Lamin-A/C	0	0	0	6	1	8	7	7	4	0.0243	0.0144	0.018	0.01
PPA1	5464	Inorganic pyrophosphatase	2	0	0	9	2	2	9	12	6	0.025	0.0022	0.011	0.01
PPP2R1A	5518	protein phosphatase 2, regulatory subunit A, alpha	0	0	1	0	1	8	1	25	21	0.0319	0.0149	0.038	0.004
RUVBL2	10856	RuvB-like 2	0	0	1	0	1	2	1	2	3	0.0105	0.0045	0.04	0.015
SF3A1	10291	splicing factor 3a, subunit 1	2	0	0	2	1	5	7	2	4	0.0155	0.0178	0.027	0.025

Electronic Supplementary Material (ESI) for Molecular BioSystems



Supplemental Figure 1. mRNA processing pathways. The pathway map was curated in the WikiPathways database. Cyan nodes represent HNE targets.