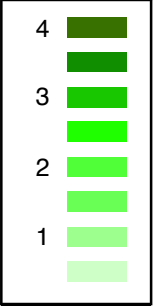


Supplementary Figure 1

Group I

Group II

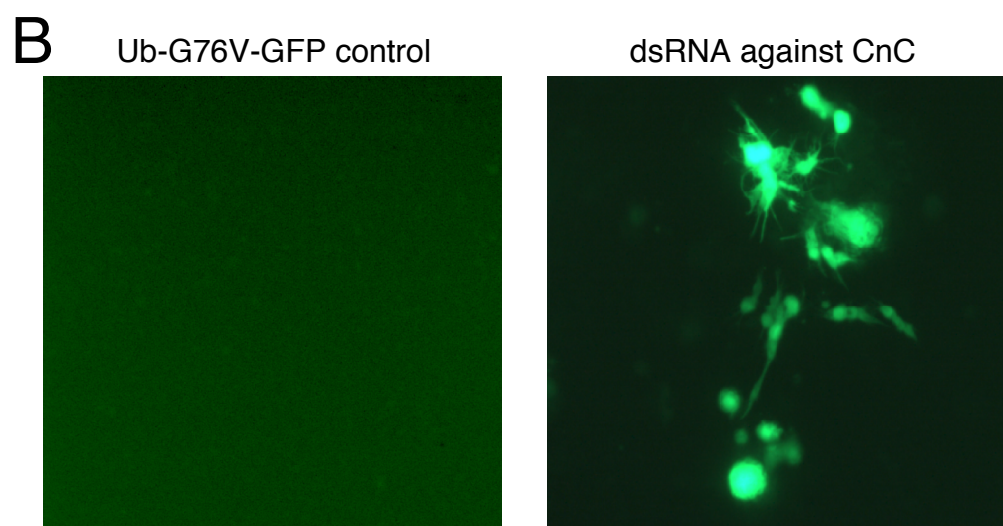
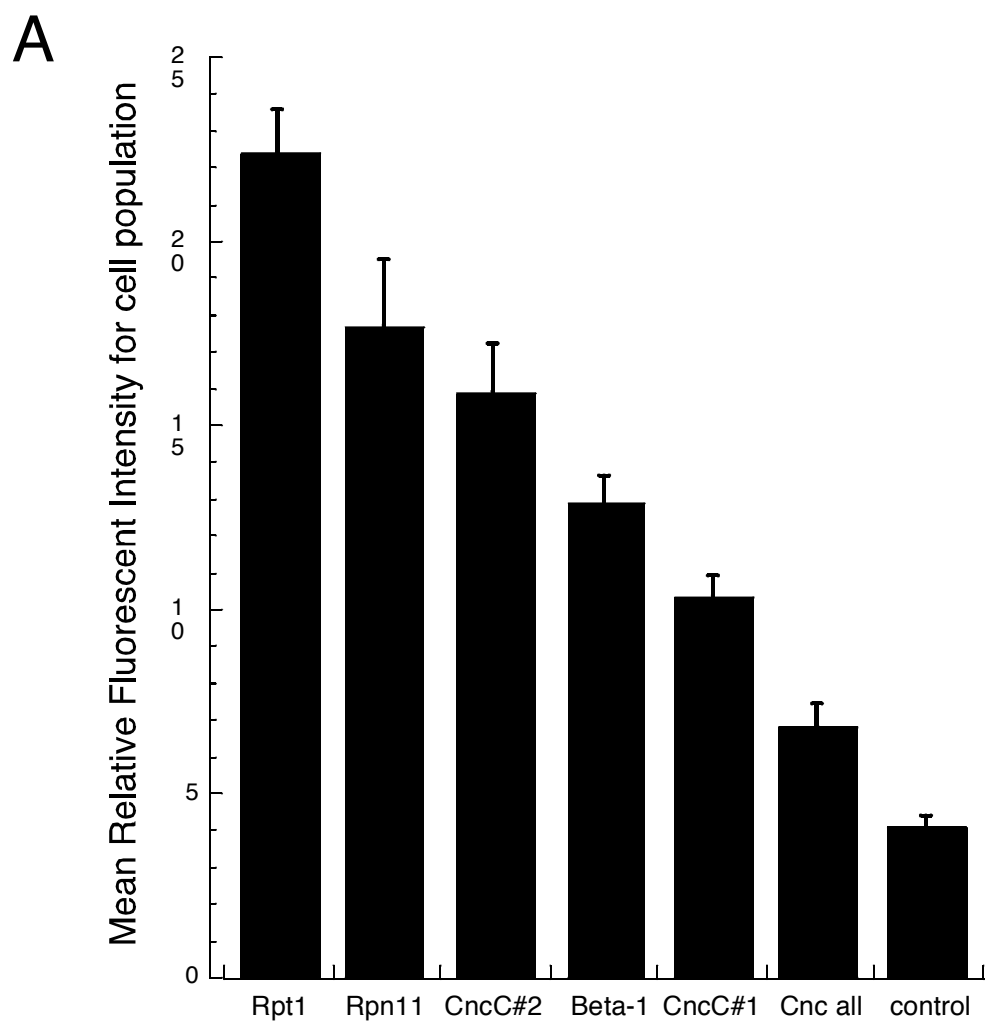
Score Ub-GFP stabilization



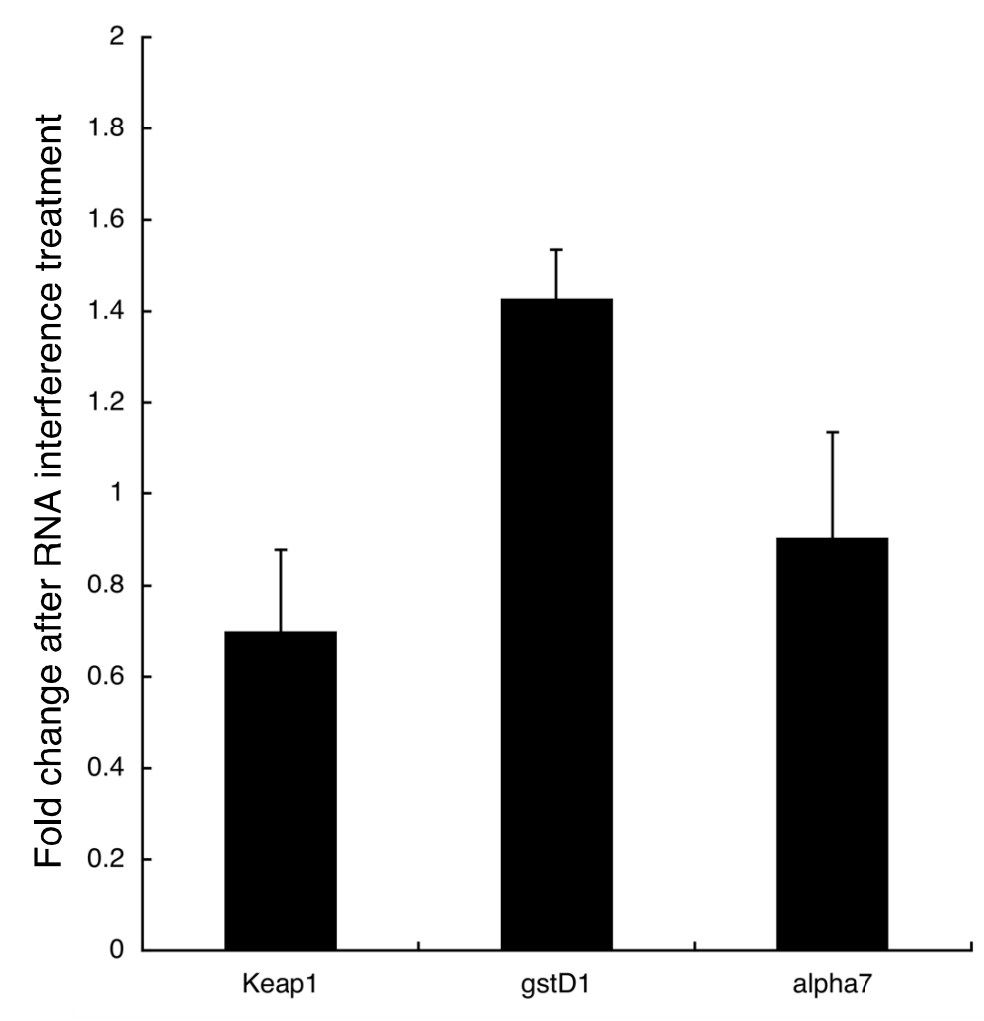
Group III

		Day 2	Day 3	Day 4
Group I	cnc			
	spen			
	spen			
	cnc			
	Kr-h1			
	Ssrp			
	maf-S			
	ken			
	sd			
	Taf12			
	CG2875			
	CG4557			
	e(r)			
	Cenp-C			
	jumu			
Group II	lin-28			
	lola			
	sv			
	Spt3			
	CG17257			
	CG5708			
	Cenp-C			
	Sox15			
	gsb-n			
	CG11971			
	HLH106			
	l(1)10Bb			
	HP1b			
	foxo			
	CG13176			
Group III	vri			
	corto			
	CG11294			
	DIP1			
	jing			
	CG15105			
	Jra			
	CG33097			
	foxo			
	king-tubby			
	Tip60			
	Nipped-A			
	Lim1			
	CG34406			
	bip2			
Group III	CG4914			
	Sox14			
	CG5366			
	ush			
	Hr39			
	rgr			
	Z4			
	exex			
	MED26			
	AP-2			
	CG4374			
	pros			
	bl			
	CG17803			
	CG34406			
Group III	Xbp1			
	usp			
	Doc2			
	CG32006			
	nub			
	run			
	knrl			
	CG14216			
	Met			
	CG11762			
	CG11906			
	Trf2			
	CG12769			
	oc			
	CG5366			
Group III	MED15			
	ftz-f1			
	Hcf			
	stc			
	az2			
	crol			
	Snr1			
	CG34346			
	E(bx)			
	Qm			
	Su(var)2-10			
	GABA-B-R3			
	CG17385			
	Scr			
	CG5147			
Group III	CG11695			
	Pcl			
	La			
	CG32264			
	Thd1			
	prd			

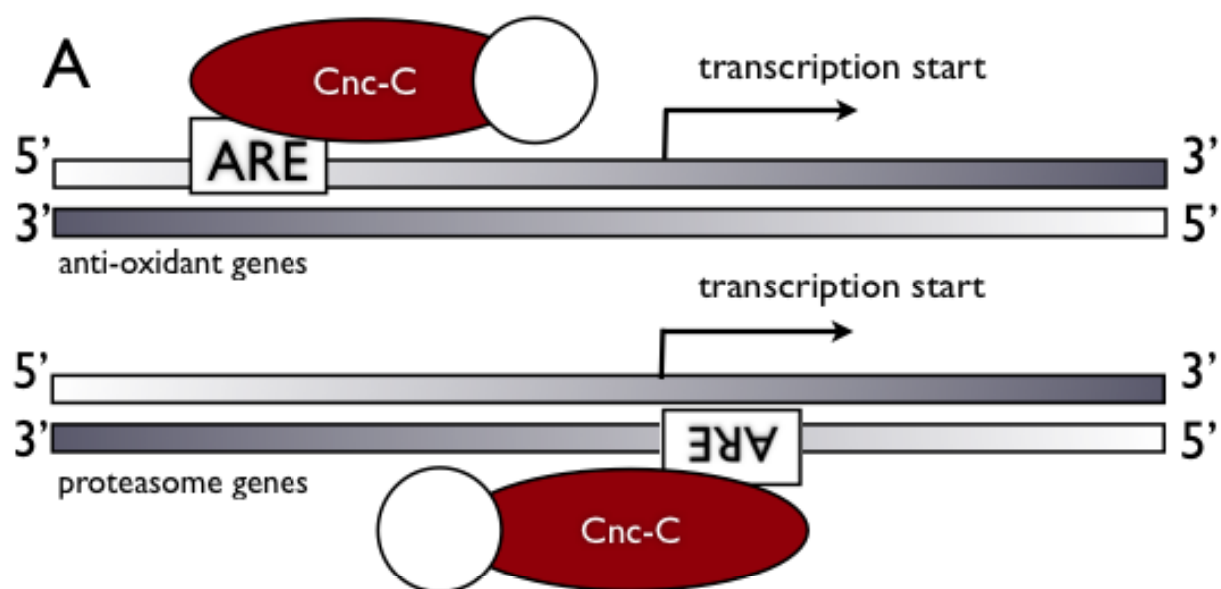
Supplementary Figure 2



Supplementary Figure 3



Supplementary Figure 4



B

gstD **TGCCCGGTCATGCTGA**
rpn1(S2) **CGCGCGGTCACACTGC**

alpha-2 TGCTGT**GTCAT**TTTTTG
alpha-5 CCGCAA**GTCAT**TTTCAG
alpha-6 CTACTT**GTCAT**CATTG
beta-1 AAGCCA**GTCAT**TTTCGT
beta-2 TTGTTT**GTCAT**CGCGC
beta-3 CAAAA**GTCAT**CTTCC
beta-4 TTGCTT**GTCAT**CGCAT
beta-5 TTGTTT**GTCAT**CGGCA
beta-7 GTGCCC**GTCAT**TCTCC

examples 20S proteasome
start sites

gstD **TGCCCGGTCATGCTGA**
rpt1 TGTTC**AGTCAT**TCTCG
rpt3 TGACGA**AGTCAT**TTTGG
rpt5 TTACA**AGTCAT**CGACA
rpt6 GCATGT**GTCAT**CTCGA
rpn5 TGCCTC**GTCAT**ATCGG
rpn9 GAATGA**GTCAT**CGAGT
rpn8 CTGCTT**GTCAT**TTTGG
rpn11 CAAATC**GTCAT**TCTCT

examples 19S regulator complex
start sites

Supplementary Table 1.

<u>Species, class</u>	<u>Accession</u>
<i>Aedes aegypti</i> CnC	XP 001650316
<i>Apis mellifera</i> CnC	XP 001120971
<i>Tribolium castaneum</i> CnC	XP 968642
<i>Pediculus humanus corporis</i> hypothetical	XP 002431112
<i>Anopheles gambiae</i> str. PEST	XP 309091
<i>Mus musculus</i> Nrf1	NP 001123925
<i>Gallus gallus</i> Nrf1	NP 001025927
<i>Monodelphis domestica</i> MA1 1	XP 001366904
<i>Homo sapiens</i> Nrf1	NP 003195
<i>Taeniopygia guttata</i> Nrf1	XP 002193524
<i>Canis familiaris</i> Nrf1	XP 864626
<i>Nasonia vitripennis</i> CnC	XP 001603983
<i>Homo sapiens</i> Nrf3	NP 004280
<i>Ornithorhynchus anatinus</i> NFE2L1	XP 001513064
<i>Xenopus laevis</i> hypothetical	NP 001080013
<i>Canis familiaris</i> Nrf3	XP 539481
<i>Bos taurus</i> Nrf3	NP 001071367
<i>Acyrtosiphon pisum</i> CnC	XP 001942705
<i>Mus musculus</i> Nrf2	NP 035032
<i>Danio rerio</i> Nrf1	XP 001920265
<i>Ornithorhynchus anatinus</i> Nrf3	XP 001509998
<i>Homo sapiens</i> Nrf2	NP 001138885
<i>Mus musculus</i> Nrf3	NP 035033
<i>Canis familiaris</i> Nrf2	XP 862205
<i>Bos taurus</i> Nrf2	NP 001011678
<i>Monodelphis domestica</i> hypothetical	XP 001377155
<i>Gallus gallus</i> Nrf2	NP 990448
<i>Branchiostoma floridae</i> hypothetical	XP 002612697
<i>Bos taurus</i> Nrf	NP 001014923
<i>Homo sapiens</i> Nrf	NP 006154
<i>Rattus norvegicus</i> Nrf	NP 001012224
<i>Canis familiaris</i> P45	XP 543621
<i>Mus musculus</i> Nrf	NP 032711
<i>Taeniopygia guttata</i> Nrf2	XP 002199433
<i>Xenopus Silurana tropicalis</i> hypothetical	NP 001135645
<i>Danio rerio</i> Nrf2	NP 878309
<i>Rattus norvegicus</i> Nrf3	XP 001058195
<i>Xenopus laevis</i> MGC84750	NP 001086307
<i>Salmo salar</i> Nrf2	NP 001133279
<i>Taeniopygia guttata</i> Nrf3	XP 002192143
<i>Xenopus laevis</i> Nrf2	NP 001079522
<i>Ornithorhynchus anatinus</i> Nrf2	XP 001515289
<i>Strongylocentrotus purpuratus</i> Nrf	NP 001123278
<i>Danio rerio</i> Nrf3	NP 998396
<i>Rattus norvegicus</i> Nrf1	NP 001101763
<i>Danio rerio</i> Nrf	NP 778208
<i>Ciona intestinalis</i> TF	NP 001071770
<i>Xenopus Silurana tropicalis</i> Nrf	NP 001123389
<i>Xenopus laevis</i> hypothetical	NP 001088660
<i>Monodelphis domestica</i> hypothetical	XP 001368299
<i>Nemastolella vectensis</i> predicted	XP 001626072
<i>Trichoplax adhaerens</i> predicted	XP 002116568
<i>Caenorhabditis elegans</i> SKiNhead	NP 741406
<i>Caenorhabditis elegans</i> SKiNhead	NP 741404
<i>Caenorhabditis briggsae</i> CBR SKN 1	XP 002633846

Supplementary Figure 1. Complete list of *Drosophila* genes that showed apparent stabilization of the proteasome substrate reporter. Ranking for stabilizing the proteasome reporter Ub^{G76V}GFP from a RNAi genomic wide screening of *Drosophila* transcription factors. The positive hits were ranked in a heat map and grouped into three categories based on the number of days that Ub^{G76V}GFP was observed to be stabilized. Group I represents targets that showed consistent stabilization for all three screening periods. Group II genes stabilized Ub^{G76V}GFP for two consecutive days and group III one day.

Supplementary Figure 2. A, Triplicate RNAi knockdowns on proposed *Drosophila* proteasome transcription factors. Relative fluorescent intensity of Ub^{G76V}GFP stabilization is ranked from highest to lowest. As positive controls, proteasome subunits were also knocked down with double stranded RNAi. B. Representative fluorescence micrograph showing stabilization of Ub^{G76V}-RFP reporter after RNAi depletion of Cnc-C.

Supplementary Figure 3. Quantitative PCR measurements on *Drosophila* S2 cells that have been RNAi treated with dsRNA to the Keap1 gene. Three independent RNAi treatments were carried out and for each treatment triplicate qPCR measurements were carried out. Modest depletion of Keap1 are sufficient to increase the levels of mRNA for the known ARE regulated glutathione S transferase, *gstD*, Student's *t*-test value ($p < 0.022$) for Keap1 mRNAs and for *gstD* ($p < 0.0019$). The Keap1 depleted cells did not show increased mRNA levels for a proteasome gene mRNA alpha 7.

Supplementary Figure 4. A. Antioxidant response elements (ARE) are enhancer sequences that allow Nrf transcription factors to bind at the promoter region of regulated genes. For *Drosophila* Cnc-C an ARE enhancer element has been identified for oxidative stress regulation and Cnc-C binding upstream of the glutathione S transferase gene, *gstD*. This *Drosophila* *gstD* regulatory sequence (TCAGcATGACcggGCAaaaa) shows clear similarity with

the extended consensus of the mammalian ARE sequence motif. B. The gstD regulatory domain is shown as the reverse complement sequence and aligned with *Drosophila* Rpn1 transcription start region. For the proteasome genes the transcriptional start regions may contain ARE-like sequences centered within previously mapped locations essential for induced transcription after proteasome inhibition (29). However, these sequences are directly after the transcription start site, are centered in highly conserved UTR regions and are present on the bottom strand of the DNA.

Supplementary Table 1. List of accession numbers and species used in the phylogenetic analysis.