

Supporting Information

[Figure S1.](#)

HRE-luciferase reporter induction in cells exposed to hypoxia or DFO. (A) Schematic representation of the HIF-responsive firefly luciferase reporter element used in this study (HRE-Luc). A dimerized regulatory sequence derived from the murine lactate dehydrogenase enhancer was cloned upstream of a firefly luciferase gene in a pGL3 plasmid bearing a fly hsp70 minimal promoter. Each 51 bp sequence contains two HIF responsive elements (HREs) and one cyclic AMP responsive element (CRE). (B) S2-HRE-luc cells were seeded in 96-wells tissue culture plates (1×10^4 cells per well), grown for 3 days, and stimulated with DFO (100 μ M), or exposed to hypoxia (1% O₂) for 20 hours. Strong induction of luciferase activity was observed in cells stimulated with DFO or hypoxia. Results are expressed as fold induction of luciferase activity respect to normoxic untreated cells. (C) Scatter plot of the duplicate results (Z-scores; see [Materials and Methods](#)) of the primary screen, showing the overall reproducibility of the data.

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(0.03 MB PDF)

[Figure S2.](#)

miRNAs and the response to hypoxia. (A) Upper panel, schematic representation of the miRNA reporter CG10011-luc; the *miR-12* miRNA binds to the 3' UTR of the *luciferase* mRNA, thereby inhibiting translation. Over-expression of miR-12 is therefore expected to provoke strong inhibition of translation. Lower panel, S2 cells were co-transfected with the CG10011-luc reporter and the pAC-miR-12 over-expression plasmid, or with an empty vector (pAC) as a control, and exposed to *ago1* or *gfp* dsRNA treatments during 4 days. miR-12 over-expression inhibits 80% of luciferase expression in the control cells treated with *gfp* dsRNA, whereas in cells depleted from *ago1* (*ago1.1* or *ago1.2* dsRNAs) miR-12 over-expression failed to inhibit luciferase expression to a large extent. (B) S2-HRE-luc cells were treated with dsRNA against *gfp* (control), *sima*, *ago1*, *ago2*, *piwi*, or *dicer-2*, grown during 4-8 days, and stimulated with DFO (100 μ M). Cells depleted from *ago1* or *sima* showed strong reduction of reporter activity, whereas cells depleted from *ago2*, *dicer-2*, or *piwi* exhibited normal induction of the reporter upon DFO exposure.

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(0.01 MB PDF)

[Figure S3.](#)

Regulation of Sima subcellular localization is not affected in Ago1 homozygous mutant embryos. We have analyzed Sima subcellular localization in en-Gal4/UAS-sima transgenic embryos carrying a homozygous mutation in the Ago1 locus (*ago1*^{ko208}), and compared with Sima localization in en-Gal4/UAS-sima wild type individuals. The analysis was carried out as we reported previously (Dekanty et al., 2005) [15]. Three categories of Sima subcellular localization were defined for quantitative purposes: "Nuclear" (black color), "Ubiquitous" (grey) and "Cytoplasmic" (white). The Ago1 mutation does not impinge on Sima subcellular localization neither in normoxia nor in hypoxia.

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(0.01 MB PDF)

[Table S1.](#)

Summary of the three phases of the overall screen for genes required for HIF activity.

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(0.04 MB PDF)

[Table S2.](#)

Results of the primary screen carried out in cells exposed to DFO are shown. The screen was performed in duplicate; genes in which at least one of the two Z scores values was below -2.5 are depicted in the table. Under this criterion, 603 genes scored as positives in this initial phase of the screen.

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(0.43 MB PDF)

Table S3.

The data obtained at the primary screen ([Table S2](#)) were filtered against the results of a cell viability screen previously carried out at the DRSC (Boutros et al. 2004) [[23](#)]. Sequences from the “Sanger collection” were also eliminated from the study; the 225 genes that remained as positive hits of the primary screen are depicted.

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(0.27 MB PDF)

Table S4.

The secondary screen was also carried out in cells exposed to DFO. A second-generation library (DRSC 2.0 library) was used, in which most genes are represented by more than one dsRNA. Normalized luciferase activity (*firefly/renilla* luciferase activity ratio) for each well was calculated and expressed as a percentage of the inhibition respect to control cells treated with dsRNA against GFP that were exposed to DFO. The screen was carried out in duplicate and the mean percentage of inhibition is depicted.

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(0.26 MB PDF)

Table S4. Secondary screen.

Secondary screen				
Gene	Amplicon 1	Inhibition(%)	Amplicon 2	Inhibition(%)
GROUP A: Inhibition of the DFO response > 75%				
sima	DRSC33101	96,8 +/- 1,0	DRSC33100	96,4 +/- 0,5
tango	DRSC37262	95,9 +/- 0,6		
brahma	DRSC30902	89,0 +/- 4,1	DRSC30901	85,0 +/- 2,4
Trip1	DRSC32225	87,4 +/- 9,5	DRSC32224	87,3 +/- 0,7
CG14641	DRSC31837	85,7 +/- 0,2	DRSC31836	80,2 +/- 1,0
Ef2b	DRSC32107	85,6 +/- 2,7	DRSC32106	77,4 +/- 7,4
CG7065	DRSC35474	85,2 +/- 2,0		
tango7	DRSC31146	85,1 +/- 3,9	DRSC31145	86,0 +/- 0,0
Spt6	DRSC31075	83,4 +/- 0,0	DRSC31074	69,1 +/- 6,8
AGO1	DRSC30762	83,2 +/- 3,0	DRSC30761	79,7 +/- 2,8
pixie	DRSC32078	81,8 +/- 1,4	DRSC32077	80,6 +/- 7,4
moira	DRSC32754	78,6 +/- 3,9	DRSC32753	83,1 +/- 1,2
Snr1	DRSC32770	78,4 +/- 6,7	DRSC32769	56,4 +/- 5,1
Symplekin	DRSC32363	78,2 +/- 10,7	DRSC32362	81,9 +/- 5,8
CG4849	DRSC31791	76,5 +/- 17,3	DRSC31790	75,3 +/- 8,2
TER94	DRSC32221	75,9 +/- 3,2	DRSC32220	76,5 +/- 11,9
reptin	DRSC32532	75,5 +/- 15,2	DRSC32531	77,7 +/- 5,3
MBD-R2	DRSC32495	75,2 +/- 0,8	DRSC32494	73,4 +/- 7,9
NSL1	DRSC31789	74,5 +/- 2,8	DRSC31788	84,4 +/- 4,7
prp8	DRSC31801	74,3 +/- 2,8	DRSC31800	85,3 +/- 6,9
peanuts	DRSC31799	68,3 +/- 8,4	DRSC31798	80,9 +/- 6,9
CG9769	DRSC32096	66,7 +/- 9,3	DRSC32095	81,2 +/- 16,3
CG2446	DRSC32889	62,2 +/- 1,5	DRSC32888	81,0 +/- 1,3
GROUP B: Inhibition of the DFO response 50 - 75%				
Helicase at 25E	DRSC30680	72,7 +/- 3,0	DRSC30679	61,4 +/- 21,0
tango4	DRSC31783	70,8 +/- 3,4	DRSC31782	43,4 +/- 2,3
pontin	DRSC31863	70,7 +/- 2,2	DRSC31862	72,4 +/- 1,6

CG5931	DRSC32420	70,4 +/- 18,2	DRSC32419	58,8 +/- 1,8
CG32000	DRSC32056	70,2 +/- 12,7	DRSC32055	60,7 +/- 1,6
U2af38	DRSC28068	70,1 +/- 15,6		
CSN3	DRSC32998	69,4 +/- 8,6	DRSC32997	71,9 +/- 2,6
CSN6	DRSC35658	68,8 +/- 19,6		
cropped	DRSC30708	66,0 +/- 9,0		
CG9253	DRSC37278	65,8 +/- 7,1		
CG18591	DRSC31785	65,7 +/- 23,6	DRSC31784	22 +/- 28,7
CG14543	DRSC26647	64,1 +/- 4,5		
U2af50	DRSC37266	64,0 +/- 2,5		
CG7757	DRSC30869	63,1 +/- 18,6	DRSC30868	63,4 +/- 1,4
Gbp	DRSC34548	62,7 +/- 3,5	DRSC34547	51,0 +/- 2,5
dalao	DRSC35681	60,3 +/- 41,0		
crooked-neck	DRSC31853	60,0 +/- 41,1	DRSC31852	64,1 +/- 10,2
Rrp6	DRSC32601	59,5 +/- 41,2	DRSC32600	40,0 +/- 22,0
Tor	DRSC30664	59,4 +/- 41,3	DRSC30663	39,5 +/- 12,5
CG10754	DRSC33610	59,3 +/- 41,4		
CG11583	DRSC32312	58,5 +/- 41,5	DRSC32311	52,0 +/- 7,9
CG6509	DRSC37258	58,3 +/- 41,6		
Sec61alpha	DRSC31246	58,3 +/- 41,7	DRSC31245	12,4 +/- 3,8
lethal(1)10Bb	DRSC31944	58,1 +/- 41,8	DRSC31943	49,2 +/- 52,6
Su(var)3-9	DRSC27837	58,0 +/- 41,9		
CG6197	DRSC31706	57,5 +/- 41,10	DRSC31705	47,2 +/- 44,0
SmD3	DRSC32012	57,4 +/- 41,11		
Dim1	DRSC33266	56,6 +/- 41,12	DRSC33265	55,5 +/- 7,9
TweedleN	DRSC25037	56,4 +/- 41,13		
squid	DRSC32626	55,7 +/- 41,14	DRSC32625	22,3 +/- 26,9
Bap60	DRSC32657	55,5 +/- 41,15	DRSC32656	46,4 +/- 11,1
raptor	DRSC31050	55,2 +/- 41,16	DRSC31049	63,5 +/- 0,9
clipper	DRSC37267	54,1 +/- 41,17		
CG13779	DRSC30654	53,9 +/- 41,18	DRSC30653	70,2 +/- 9,2
lethal(2)35Df	DRSC32489	52,9 +/- 41,19	DRSC32488	38,9 +/- 22,5
Mlf	DRSC35853	52,6 +/- 41,20		
Rbp2	DRSC37291	50,5 +/- 41,21		
cryptocephal	DRSC37279	49,9 +/- 41,22		
Spt5	DRSC31820	48,1 +/- 41,23	DRSC31819	52,2 +/- 1,3
pUf68	DRSC31973	42,3 +/- 41,24	DRSC31972	62,2 +/- 16,8
Nup98	DRSC31804	40,9 +/- 41,25	DRSC31803	59,6 +/- 11,1
CG3605	DRSC31847	40,7 +/- 41,26	DRSC31846	57,8 +/- 15,6
PDK1	DRSC30826	36,1 +/- 41,27	DRSC30825	51,0 +/- 29,6
Inhibition of the DFO response < 50%				
hyrax	DRSC30952	49,3 +/- 0,4	DRSC30951	33,0 +/- 24,6
Hsp83	DRSC33050	48,2 +/- 9,9	DRSC33049	45,4 +/- 12,5
Pvf2	DRSC35971	47,7 +/- 47,4		
SF2	DRSC32605	47,4 +/- 27,0	DRSC32604	51,8 +/- 4,1
CG5525	DRSC35379	47,0 +/- 17,0		
bhringi	DRSC32022	46,9 +/- 3,3	DRSC32021	20,6 +/- 13,8
Rtf1	DRSC30728	46,8 +/- 14,7	DRSC30727	37,5 +/- 8,5
DebB	DRSC31802	46,6 +/- 34,2		

CG11985	DRSC31771	45,5 +/- 1,0	DRSC31770	49,7 +/- 6,0
Slu7	DRSC31779	44,3 +/- 35,0	DRSC31778	23,6 +/- 61,8
p130CAS	DRSC34850	43,1 +/- 9,9		
Su(var)205	DRSC37257	42,3 +/- 10,8		
CG14180	DRSC32333	40,3 +/- 42,3	DRSC32332	20,3 +/- 19,1
bunched	DRSC32803	39,1 +/- 15,4		
SmG	DRSC35622	38,7 +/- 10,4	DRSC35621	37,4 +/- 3,9
CG15278	DRSC37276	38,1 +/- 6,2		
CG4959	DRSC37273	37,9 +/- 10,9		
Rheb	DRSC30920	37,8 +/- 9,8	DRSC30919	46,6 +/- 21,3
CG6962	DRSC32278	36,3 +/- 18,1	DRSC32277	16 +/- 30,2
CG31461	DRSC35138	36,2 +/- 16,3	DRSC35137	19,7 +/- 17,3
CG2685	DRSC32365	36,1 +/- 34,0	DRSC32364	45,4 +/- 52,8
Su(Tpl)	DRSC36037	34,2 +/- 15,5		
Tcp1-like	DRSC34599	33,1 +/- 9,3	DRSC34598	22,5 +/- 6,2
snRNP2	DRSC31833	32,7 +/- 0,7	DRSC31832	25,1 +/- 26,4
CG14995	DRSC31557	32,6 +/- 17,2		
cut	DRSC25100	31,2 +/- 14,6		
CG6015	DRSC32424	31,1 +/- 38,9	DRSC32423	43,3 +/- 20,8
CG9777	DRSC35623	30,5 +/- 0,3		
fruitless	DRSC31020	30,3 +/- 26,5		
CG8929	DRSC34413	30,1 +/- 29,5	DRSC34412	47,6 +/- 5,2
MED22	DRSC35840	29,7 +/- 30,2		
CG3983	DRSC37285	29,2 +/- 3,9		
Rtc1	DRSC35998	28,6 +/- 3,8		
CG9948	DRSC37281	28,6 +/- 9,7		
small bristles	DRSC33352	28,3 +/- 21,5	DRSC33351	32,4 +/- 7,2
CG18131	DRSC31565	28 +/- 15,4	DRSC31564	28,1 +/- 10,8
CG30349	DRSC33264	27,6 +/- 21,2	DRSC33263	22 +/- 9,7
CG14107	DRSC32857	27,3 +/- 16,8		
Neosin	DRSC35885	26,9 +/- 25,1		
Sox100B	DRSC32624	25,9 +/- 11,7		
Cdc42	DRSC31437	25,9 +/- 21,0	DRSC31436	29,1 +/- 29,5
Ef1alpha48D	DRSC32105	25,7 +/- 2,1		
CG14210	DRSC29021	25,4 +/- 25,4		
Rbm13	DRSC33595	25,3 +/- 3,9		
CG32245	DRSC31575	25,2 +/- 2,6	DRSC31574	29,8 +/- 24,0
dre4	DRSC33008	24,6 +/- 4,6	DRSC33007	14,8 +/- 2,5
bric a brac 1	DRSC32796	24,6 +/- 19,4		
CG34159	DRSC31584	24,5 +/- 6,9		
CG9300	DRSC32094	24,4 +/- 20,3	DRSC32093	7,2 +/- 25,6
rab3-GEF	DRSC31094	24,2 +/- 3,1	DRSC31093	44,2 +/- 0,0
SmB	DRSC31869	23,9 +/- 11,4	DRSC31868	18,7 +/- 36,2
CG31179	DRSC35106	23,7 +/- 9,1		
Hsp70Bb	DRSC34562	23,6 +/- 25,6		
Hsp70Ab	DRSC29327	23,3 +/- 35,3		
no hitter	DRSC35889	22,5 +/- 16,4		
CG3436	DRSC32274	22,5 +/- 1,5	DRSC32273	13,1 +/- 9,8
tektin-C	DRSC32219	22,3 +/- 22,1	DRSC32218	59,4 +/- 15,6
Cct5	DRSC32024	22,0 +/- 27,6	DRSC32023	25,1 +/- 10,1
CG31705	DRSC30648	21,5 +/- 9,4		

camta	DRSC26757	21,5 +/- 39,1		
Tie	DRSC30830	21,3 +/- 17,4	DRSC30829	42,3 +/- 8,9
lethal(2)k09022	DRSC32028	20,1 +/- 4,2	DRSC32027	18,4 +/- 11,2
CG6937	DRSC32426	19,6 +/- 3,4	DRSC32425	12,2 +/- 23,8
CG42243	DRSC25912	19,5 +/- 10,9		
stam	DRSC37259	19,4 +/- 13,7		
hook	DRSC31032	19,1 +/- 0,0	DRSC31031	11,6 +/- 0,0
CG17329	DRSC28365	18,8 +/- 16,1		
CG34113	DRSC24955	18,6 +/- 7,3		
CG4218	DRSC27814	18,3 +/- 5,6		
CG31847	DRSC35170	18,3 +/- 9,1		
furin 1	DRSC35749	18,2 +/- 29,9		
CG4174	DRSC37283	17,6 +/- 25,3		
CG13298	DRSC30848	17,3 +/- 9,5		
CG4587	DRSC37274	16,7 +/- 3,7		
CG12484	DRSC28353	16,6 +/- 9,3		
CG10660	DRSC33244	16,5 +/- 12,4		
CG13278	DRSC37275	16,0 +/- 6,3		
Ef1alpha100E	DRSC32104	15,6 +/- 25,0	DRSC32103	24,7 +/- 40,7
minibrain	DRSC24961	15,1 +/- 0,1		
CG15097	DRSC37260	14,7 +/- 9,5		
fasciclin 2	DRSC35731	13,4 +/- 20,7		
Rrp45	DRSC29319	12,5 +/- 6,9		
Mystery 45A	DRSC32156	12,4 +/- 22,2	DRSC32155	14,3 +/- 33,8
CG5732	DRSC31849	12,2 +/- 27,9	DRSC31848	12,2 +/- 16,3
Cbp20	DRSC32000	11,9 +/- 15,3	DRSC31999	15,3 +/- 8,2
CG32335	DRSC25511	10,8 +/- 28,2		
beadex	DRSC33491	10,6 +/- 14,2		
CG9164	DRSC37295	10,4 +/- 39,5		
CG9119	DRSC35587	10,3 +/- 26,8		
Tim9b	DRSC32272	10,1 +/- 50,9		
CG8636	DRSC32088	9,9 +/- 16,6	DRSC32087	90,4 +/- 0,7
calx	DRSC36151	9,3 +/- 14,2		
Ef1gamma	DRSC35716	9,0 +/- 5,0		
ph-d	DRSC32519	8,8 +/- 4,8	DRSC32518	6,2 +/- 7,0
CG9134	DRSC23750	8,6 +/- 23,3		
ascutex	DRSC31953	7,3 +/- 27,2	DRSC31952	6,2 +/- 10,4
lethal(3)03670	DRSC26451	7,3 +/- 1,7		
CG34422	DRSC35485	6,9 +/- 0,4		
CG5446	DRSC36259	6,5 +/- 2,9		
Klp61F	DRSC30824	6,2 +/- 60,4	DRSC30823	31,8 +/- 10,6
CG30127	DRSC37293	6,0 +/- 23,2		
CG4570	DRSC37284	5,0 +/- 5,6		
CG15450	DRSC37292	5,0 +/- 11,5		

Table S3. Filtered results of the primary screen.

Primary screen (filtered)				
Gene	Amplicon	- Z1	- Z2	Average -Z
no hitter	DRSC01976	9.3		9.3
brahma	DRSC11330	7.8	9.1	8.5
CG10660	DRSC09769	7.3	8.6	8.0
cyclophilin-33	DRSC07600	6.3	9.3	7.8
CG4174	DRSC10406	7.7		7.7
CG4587	DRSC01956	7.4		7.4
CG11985	DRSC14460	5.8	8.0	6.9
CG9119	DRSC08620	6.5	7.2	6.9
CG15278	DRSC02481	6.5		6.5
CG32000	DRSC17103	5.7	7.2	6.5
sima	DRSC17055	7.0	5.8	6.4
CG9134	DRSC07954	6.3		6.3
Trip1	DRSC03464	6.1	6.5	6.3
CG3605	DRSC00619	5.8	6.6	6.2
CG18591	DRSC02680	5.6	6.8	6.2
pixie	DRSC10533	5.7	6.4	6.1
CG8636	DRSC18427	5.5	6.4	6.0
Hsc70-4	DRSC16711	5.9	5.9	5.9
Ef2b	DRSC03737	5.2	6.5	5.9
CG15494	DRSC02502	5.7		5.7
SmB	DRSC03437	5.9	5.3	5.6
CG9769	DRSC12328	5.4	5.1	5.3
moira	DRSC15378	5.2	5.3	5.3
p130CAS	DRSC08257	5.5	4.9	5.2
NSL1	DRSC15625	4.8	5.6	5.2
Helicase at 25E	DRSC03342	5.1	5.1	5.1
CG15097	DRSC06526	5.1	5.0	5.1
ran	DRSC20364	4.2	5.8	5.0
DebB	DRSC07397	5.0	4.8	4.9
Rrp6	DRSC16223	4.2	5.6	4.9
CG5931	DRSC10559	4.1	5.6	4.9
SmD3	DRSC07553	3.9	5.8	4.9
squid	DRSC17066	4.8		4.8
raptor	DRSC18359	4.7		4.7

CG42342	DRSC14378	4.2	5.2	4.7
prp8	DRSC07293	5.3	4.1	4.7
CG7065	DRSC18420	3.6	5.7	4.7
Tango7	DRSC07142	5.2	3.8	4.5
CG5482	DRSC06936	6.1	2.8	4.5
CG8929	DRSC07298	3.8	5.1	4.5
CG4849	DRSC15662	5.0	3.8	4.4
CG17304	DRSC15222	4.7	4.1	4.4
CG15450	DRSC20522	4.6	4.2	4.4
Spt6	DRSC18836	4.0	4.8	4.4
AGO1	DRSC05912	6.1	2.6	4.4
chinmo	DRSC00509	3.6	5.1	4.4
SF2	DRSC16845	3.2	5.4	4.3
CSN6	DRSC16593	4.3		4.3
Jon99Ciii	DRSC16859	4.3		4.3
AdoR	DRSC16556	4.3		4.3
crooked-neck	DRSC18755	3.9	4.7	4.3
Patj	DRSC08712	4.0	4.5	4.3
Suv4-20	DRSC18482	3.9	4.6	4.3
snRNP69D	DRSC09800	5.7	2.7	4.2
TER94	DRSC07560	4.5	3.9	4.2
pontin	DRSC17029	4.5	3.9	4.2
ascutex	DRSC05924	2.7	5.7	4.2
reptin	DRSC11388	5.1	3.2	4.2
small bristles	DRSC20368	4.2	4.1	4.2
CG7757	DRSC10912	5.1	3.2	4.2
tango	DRSC17077	3.3	4.8	4.1
Bap60	DRSC19337	3.8	4.4	4.1
Slu7	DRSC14729	3.7	4.5	4.1
Tango4	DRSC19786	3.9	4.3	4.1
CG13298	DRSC09972	3.3	4.9	4.1
CG7918	DRSC16345	5.9	2.2	4.1
Trn-SR	DRSC00546	3.7	4.4	4.1
Su(var)3-9	DRSC13081	4.0	4.1	4.1
ph-d	DRSC18819	4.0		4.0
CG14641	DRSC12227	3.1	4.9	4.0
CG14180	DRSC10179	4.0	3.9	4.0
CG6197	DRSC06967	4.1	3.8	4.0
Pvf2	DRSC00968	2.6	5.2	3.9
Calx	DRSC13457	3.9		3.9
Neosin	DRSC11235	3.5	4.3	3.9
Ef1alpha48D	DRSC07421	3.5	4.3	3.9
Rheb	DRSC12148	3.0	4.7	3.9
CG14995	DRSC08452	4.6	3.1	3.9
CG12499	DRSC14521	3.8		3.8
Chrac-16	DRSC20343	3.8		3.8
U2af50	DRSC20297	3.5	4.0	3.8
bric a brac 1	DRSC08379	3.0	4.4	3.7
minibrain	DRSC20058	2.7	4.7	3.7
Ef1gamma	DRSC16659	2.8	4.5	3.7
I(3)03670	DRSC16981	3.6		3.6

stumps	DRSC15332	5.3	1.9	3.6
Rtf1	DRSC04085	3.8	3.4	3.6
Tcp1-like	DRSC16877	4.5	2.6	3.6
CG32335	DRSC07948	4.5	2.6	3.6
rab3-GEF	DRSC19956	3.5		3.5
hook	DRSC18674	3.5		3.5
l(1)10Bb	DRSC20346	3.8	3.1	3.5
CG9164	DRSC19087	3.2	3.7	3.5
CG34422	DRSC20029	3.2	3.7	3.5
Camta	DRSC06441	4.2	2.6	3.4
CG10927	DRSC06014	3.2	3.6	3.4
fruitless	DRSC16951	3.4		3.4
CG31179	DRSC13494	3.4		3.4
CG12470	DRSC18620	3.4		3.4
CG12484	DRSC05883	3.0	3.8	3.4
CG9253	DRSC03171	4.2	2.5	3.4
CG17329	DRSC01926	3.3		3.3
Furin 1	DRSC13707	3.2	3.4	3.3
Tektin-C	DRSC09741	3.0	3.6	3.3
CG4570	DRSC15602	4.1	2.4	3.3
Snr1	DRSC12369	3.2	3.3	3.3
Sox100B	DRSC15090	3.2		3.2
Rrp45	DRSC20198	3.2		3.2
CG11138	DRSC19385	3.2		3.2
bhringi	DRSC11000	3.1	3.3	3.2
CG3436	DRSC00605	4.2	2.1	3.2
CG3983	DRSC15529	5.0	1.3	3.2
thisbe	DRSC06153	4.6	1.7	3.2
CG31461	DRSC13113	2.5	3.8	3.2
CG14543	DRSC14887	3.1		3.1
RnrL	DRSC03413	2.7	3.5	3.1
CG6937	DRSC16140	3.4	2.8	3.1
CG31847	DRSC02535	2.9	3.3	3.1
D19A	DRSC11133	3.5	2.6	3.1
U2af38	DRSC00796	3.2	2.9	3.1
cropped	DRSC03515	2.7	3.4	3.1
CG2446	DRSC19847	3.0		3.0
CG2685	DRSC18463	3.0		3.0
CG9777	DRSC20208	3.0		3.0
Rbm13	DRSC17749	3.0		3.0
Cbp20	DRSC16601	3.0		3.0
snRNP2	DRSC12536	2.8	3.2	3.0
CG15630	DRSC00465	3.7	2.2	3.0
l(2)35Df	DRSC03560	3.6	2.3	3.0
roadkill	DRSC14526	3.4	2.5	3.0
Clipper	DRSC00746	2.9	3.0	3.0
CG10754	DRSC09801	2.7	3.2	3.0
Sec61alpha	DRSC03256	3.7	2.1	2.9
Spt5	DRSC07556	3.6	2.2	2.9
TweedleN	DRSC15813	2.9		2.9
CG4218	DRSC01939	2.9		2.9

Ef1alpha100E	DRSC16658	2.9		2.9
Fasciclin 2	DRSC17308	2.9		2.9
CG12278	DRSC14494	2.9		2.9
Cdc42	DRSC20228	3.3	2.4	2.9
CG6509	DRSC02964	2.8	2.9	2.9
Nup98	DRSC14209	3.6	2.0	2.8
peanuts	DRSC07120	3.2	2.4	2.8
blue cheese	DRSC02333	3.2	2.4	2.8
Dim1	DRSC00563	3.0	2.6	2.8
beat-IIb	DRSC13219	2.8		2.8
MED28	DRSC15721	2.8		2.8
Cpr66D	DRSC10646	3.9	1.6	2.8
CG9426	DRSC03219	3.6	1.9	2.8
MBD-R2	DRSC14180	3.1	2.4	2.8
Beadex	DRSC19350	2.6	2.9	2.8
CSN3	DRSC11859	3.4	2.0	2.7
Tim9b	DRSC19566	3.1	2.3	2.7
MED22	DRSC18175	2.7		2.7
Tim17b2	DRSC03457	2.7		2.7
Nepriylsin 1	DRSC18389	2.7		2.7
CG31229	DRSC13309	2.9	2.2	2.6
dalao	DRSC18419	2.9	2.2	2.6
CG18375	DRSC04305	2.7	2.5	2.6
CG4959	DRSC01938	2.6		2.6
CG5732	DRSC15863	2.6		2.6
CG30127	DRSC05786	2.6		2.6
vrille	DRSC03633	4.6	0.6	2.6
Symplekin	DRSC12301	2.8	2.4	2.6
CG5739	DRSC02885	3.1	2.0	2.6
CG4830	DRSC15657	3.1	2.0	2.6
spn-F	DRSC14475	2.8	2.3	2.6
Rbp2	DRSC20276	2.9	2.2	2.6
cut	DRSC18757	2.8	2.1	2.5
I(2)k09022	DRSC02108	3.8	1.2	2.5
Su(Tpl)	DRSC10954	2.8	2.2	2.5
CG8885	DRSC03117	2.8	2.2	2.5
CG13278	DRSC02252	2.5		2.5
CG7532	DRSC01910	2.5		2.5
Hsp83	DRSC08664	2.7	2.2	2.5
CG7597	DRSC11836	2.5	2.4	2.5
CG2865	DRSC18528	2.8	2.1	2.5
SmG	DRSC20207	2.9	2.0	2.5
Stam	DRSC03444	2.6	2.2	2.4
pUf68	DRSC08731	3.4	1.4	2.4
Tor	DRSC02811	2.8	2.0	2.4
CG4615	DRSC18376	3.0	1.7	2.4
Hsp70Ab	DRSC15380	2.9	1.8	2.4
hyrax	DRSC14462	2.7	2.0	2.4
Fatty acid synthetase	DRSC00268	2.6	2.0	2.3
Neurocalcin	DRSC07022	2.5	2.1	2.3
PDK1	DRSC08682	3.0	1.5	2.3

CG31705	DRSC01991	2.9	1.6	2.3
bunched	DRSC03500	2.7	1.8	2.3
Klp61F	DRSC08671	2.7	1.8	2.3
pgant6	DRSC08552	2.7	1.8	2.3
CSN7	DRSC06807	2.5	2.0	2.3
dre4	DRSC08714	3.7	0.7	2.2
CG13779	DRSC02282	3.1	1.3	2.2
CG34113	DRSC12263	3.1	1.3	2.2
Hexokinase C	DRSC07079	2.8	1.6	2.2
CG6015	DRSC15948	2.7	1.7	2.2
Hsp70Bb	DRSC21248	2.7	1.7	2.2
Cct5	DRSC07357	3.5	0.8	2.2
muscleblind	DRSC07651	2.9	1.4	2.2
Mlf	DRSC07472	3.4	0.7	2.1
Tie	DRSC08702	2.8	1.3	2.1
CG5446	DRSC02862	3.0	1.0	2.0
hook-like	DRSC02062	2.8	1.2	2.0
bubblegum	DRSC03495	3.2	0.7	2.0
CG6854	DRSC10729	2.7	1.2	2.0
cryptocephal	DRSC03513	2.9	1.0	2.0
Nnp-1	DRSC02165	3.7	0.1	1.9
Gbp	DRSC07434	2.5	1.2	1.9
CG32245	DRSC08327	3.8	-0.1	1.9
CG30349	DRSC06421	3.5	0.1	1.8
Rtc1	DRSC20285	3.0	0.5	1.8
CG6962	DRSC16153	2.7	0.7	1.7
CG4585	DRSC04475	3.1	0.3	1.7
CG11583	DRSC08202	2.8	0.6	1.7
Vps4	DRSC19338	2.5	0.8	1.7
CG5525	DRSC02865	2.6	0.6	1.6
CG18131	DRSC00517	2.5	0.7	1.6
CG14107	DRSC10110	3.2	-0.1	1.6
CG9300	DRSC11064	2.9	0.2	1.6
Mystery 45A	DRSC07067	2.6	0.5	1.6
Su(var)205	DRSC03446	2.6	0.4	1.5
pasilla	DRSC16388	2.6	0.1	1.4
CG9948	DRSC09690	2.7	-0.2	1.3
CG12880	DRSC14568	2.6	-0.2	1.2

Table S2. Primary screen.

Primary screen				
Gene	Amplicon	-Z1	-Z2	Average - Z
HDC05561 ('+' in Hild et al)	DRSC05209	13.3	12.4	12.9
RpL15	DRSC20963	12.7	9.7	11.2
HDC06418 ('+' in Hild et al)	DRSC05498	9.2	11.2	10.2
no hitter	DRSC01976	9.3		9.3
HDC17524 ('+' in Hild et al)	DRSC17394	9.4	8.8	9.1
RpL19	DRSC04649	7.9	10.1	9.0
HDC07108 ('+' in Stolc / Hild et al)	DRSC05715	8.5	9.3	8.9
HDC07858 ('+' in Hild et al)	DRSC07932	6.7	10.9	8.8
Pdp1	DRSC08897	8.6		8.6
brahma	DRSC11330	7.8	9.1	8.5
RpS26	DRSC03420	6.0	10.5	8.3
HDC14318 ('+' in Hild et al)	DRSC13298	11.4	5	8.2
Pomp	DRSC03201	6.7	9.5	8.1
RpL21	DRSC03704	6.6	9.3	8.0
CG10660	DRSC09769	7.3	8.6	8.0
cyclophilin-33	DRSC07600	6.3	9.3	7.8
hoi-polloi	DRSC03546	6.4	9.1	7.8
RpL12	DRSC04344	6.3	9.2	7.8
CG4174	DRSC10406	7.7		7.7
HDC18812 ('+' in Hild et al)	DRSC18999	7.7	7.6	7.7
HDC15690 ('+' in Hild et al)	DRSC13740	8.7	6.3	7.5
RpL18	DRSC11016	5.1	9.9	7.5
RpS12	DRSC11270	6.4	8.4	7.4
MED11	DRSC10739	8.1	6.7	7.4
CG4587	DRSC01956	7.4		7.4
RpL26	DRSC10726	7.2	7.3	7.3
RpL35A	DRSC12302	7.1	7.4	7.3
RpL7	DRSC03417	6.4	8	7.2
RpL23	DRSC04648	6.5	7.9	7.2

CG2807	DRSC00535	7.2	7.1	7.2
RpS19a	DRSC20281	5.4	8.9	7.2
Tbp-1	DRSC16842	5.7	8.5	7.1
RpL8	DRSC08695	6.8	7.4	7.1
RpL14	DRSC11269	6.0	8.2	7.1
HDC12613 ('+' in Hild et al)	DRSC12723	5.0	9	7.0
Pros26.4	DRSC16799	5.8	8.1	7.0
HDC17815 ('+' in Hild et al)	DRSC17506	6.8	7.1	7.0
eIF-4G	DRSC17218	6.0	7.8	6.9
Rpn11	DRSC03422	6.6	7.2	6.9
CG11985	DRSC14460	5.8	8	6.9
RpL32	DRSC16835	5.6	8.2	6.9
CG9119	DRSC08620	6.5	7.2	6.9
RpL8	DRSC08532	6.2	7.5	6.9
RpS9	DRSC11273	5.8	7.8	6.8
eIF-4a	DRSC03526	5.0	8.6	6.8
RpL10Ab	DRSC10798	7.1	6.5	6.8
RpL22	DRSC18707	5.4	8	6.7
quemao	DRSC11947	6.2	7.1	6.7
RpS13	DRSC03419	5.4	7.8	6.6
RpL38	DRSC07818	5.6	7.6	6.6
Rpn7	DRSC16841	5.5	7.6	6.6
RpL39	DRSC04651	7.0	6	6.5
HDC12958	DRSC12832	7.2	5.8	6.5
CG15278	DRSC02481	6.5		6.5
RpS18	DRSC07540	5.1	7.8	6.5
RpS4	DRSC11272	5.2	7.7	6.5
RpS14b	DRSC18711	4.4	8.5	6.5
RpS15Ab, RpS15Aa	DRSC19831	4.2	8.7	6.5
Dsp1	DRSC20315	5.8	7.1	6.5
CG32000	DRSC17103	5.7	7.2	6.5
RpL5	DRSC03801	5.4	7.4	6.4
eIF3-S10	DRSC12339	5.4	7.4	6.4
sima	DRSC17055	7.0	5.8	6.4
RpL13	DRSC03416	4.0	8.8	6.4
RpL27	DRSC15638	6.9	5.8	6.4
CG9134	DRSC07954	6.3		6.3
Trip1	DRSC03464	6.1	6.5	6.3
RpL27A	DRSC00781	6.5	6.1	6.3
CG3605	DRSC00619	5.8	6.6	6.2
RpL4	DRSC16833	5.8	6.6	6.2
CG18591	DRSC02680	5.6	6.8	6.2
RpL3	DRSC16834	5.4	7	6.2

RpL18A	DRSC07538	5.9	6.4	6.2
HDC18154 ('+' in Hild et al)	DRSC17612	5.4	6.9	6.2
RpL24	DRSC03185	5.1	7.1	6.1
combgap	DRSC07650	7.1	5.1	6.1
HDC07436 ('+' in Hild et al)	DRSC05853	5.7	6.5	6.1
Mov34	DRSC04624	6.5	5.6	6.1
pixie	DRSC10533	5.7	6.4	6.1
Pros25	DRSC16798	4.7	7.4	6.1
sop	DRSC03614	6.8	5.2	6.0
arrest	DRSC01234	4.7	7.3	6.0
CG8636	DRSC18427	5.5	6.4	6.0
Rpn2	DRSC16839	5.8	6.1	6.0
RpS7	DRSC15394	6.9	5	6.0
Hsc70-4	DRSC16711	5.9	5.9	5.9
RpL32	DRSC16835	6.6	5.2	5.9
nucampholin	DRSC02179	7.9	3.8	5.9
RpS5a	DRSC20282	4.7	7	5.9
Ef2b	DRSC03737	5.2	6.5	5.9
Rpn12	DRSC11275	4.6	7.1	5.9
eIF3-p48/Int6	DRSC11199	5.3	6.4	5.9
Pros26	DRSC11256	5.3	6.3	5.8
RpL17	DRSC18293	4.6	7	5.8
eIF3-S8	DRSC06905	6.4	5.2	5.8
RpS17	DRSC11271	5.6	6	5.8
Rpt1	DRSC07542	6.4	5.1	5.8
RpS6	DRSC18712	4.1	7.4	5.8
RpS29	DRSC16433	5.2	6.3	5.8
RpS3	DRSC16838	6.2	5.3	5.8
Pros35	DRSC03401	6.1	5.3	5.7
Prosbeta5	DRSC07517	5.2	6.2	5.7
CG6694	DRSC10696	4.9	6.5	5.7
RpS30	DRSC15119	7.6	3.8	5.7
BarH2	DRSC19335	6.1	5.3	5.7
nAcRalpha-96Aa	DRSC13670	8.1	3.3	5.7
CG15494	DRSC02502	5.7		5.7
RpS15	DRSC07151	4.4	6.9	5.7
RpLP2	DRSC07539	6.2	5.1	5.7
RpS3A	DRSC17168	6.9	4.4	5.7
SmB	DRSC03437	5.9	5.3	5.6
RpS8	DRSC16318	6.2	5	5.6
Prosalpha7	DRSC07516	5.8	5.3	5.6
eIF-4E	DRSC11342	3.7	7.3	5.5
CG30089	DRSC06127	4.7	6.3	5.5

RpL36	DRSC18708	5.8	5.2	5.5
Rpn1	DRSC11274	5.0	5.8	5.4
RpL32	DRSC16835	5.2	5.6	5.4
Prosbeta3	DRSC16801	4.6	6.1	5.4
CG1161	DRSC12180	5.5	5.2	5.4
RpL7A	DRSC18709	4.2	6.5	5.4
Ataxin-2	DRSC15727	5.4	5.2	5.3
CG13235	DRSC06355	5.6	5	5.3
Rpt3	DRSC20283	4.1	6.5	5.3
CG9769	DRSC12328	5.4	5.1	5.3
moira	DRSC15378	5.2	5.3	5.3
HDC17859 ('+' in Hild et al)	DRSC17532	6.8	3.7	5.3
CG42400	DRSC02458	4.3	6.2	5.3
p130CAS	DRSC08257	5.5	4.9	5.2
NSL1	DRSC15625	4.8	5.6	5.2
seven up	DRSC15311	6.0	4.4	5.2
Dox-A2	DRSC03318	4.6	5.7	5.2
RpL35	DRSC18347	3.9	6.4	5.2
Helicase at 25E	DRSC03342	5.1	5.1	5.1
RpL9	DRSC03418	5.7	4.5	5.1
RpS14a	DRSC18710	4.6	5.6	5.1
CG15097	DRSC06526	5.1	5	5.1
Prosbeta2	DRSC11257	4.3	5.8	5.1
RpS15Ab, RpS15Aa	DRSC06129	3.3	6.8	5.1
RpL31	DRSC06716	4.8	5.3	5.1
RpL18	DRSC12366	5.5	4.6	5.1
eIF3-S9	DRSC06900	5.1	4.9	5.0
ran	DRSC20364	4.2	5.8	5.0
HDC09524 ('+' in Hild et al)	DRSC09077	4.4	5.6	5.0
HDC17206 ('+' in Stolc / Hild et al)	DRSC17248	6.0	4	5.0
oho23B	DRSC00833	4.6	5.4	5.0
RpL40	DRSC00782	5.0	4.9	5.0
eIF-3p66	DRSC16938	5.1	4.8	5.0
DebB	DRSC07397	5.0	4.8	4.9
Rrp6	DRSC16223	4.2	5.6	4.9
Cyclin E	DRSC03296	4.4	5.4	4.9
Rpb5	DRSC06100	4.0	5.8	4.9
Rpt4	DRSC18713	4.9	4.9	4.9
CG5931	DRSC10559	4.1	5.6	4.9
thread	DRSC11404	4.9	4.8	4.9
SmD3	DRSC07553	3.9	5.8	4.9
dos	DRSC07992	5.3	4.4	4.9
abdominal A	DRSC16897	5.0	4.6	4.8

RpS20	DRSC16836	5.8	3.8	4.8
HDC02682 ('+' in Hild et al)	DRSC01481	6.1	3.5	4.8
squid	DRSC17066	4.8		4.8
CG13550	DRSC04191	4.5	5	4.8
CG14459	DRSC11719	5.3	4.2	4.8
raptor	DRSC18359	4.7		4.7
double parked	DRSC07088	4.9	4.5	4.7
CG42342	DRSC14378	4.2	5.2	4.7
prp8	DRSC07293	5.3	4.1	4.7
CG7065	DRSC18420	3.6	5.7	4.7
eIF-5A	DRSC04681	4.5	4.8	4.7
RpL28	DRSC08293	4.8	4.5	4.7
RpS28b	DRSC18258	4.6	4.6	4.6
CG12912	DRSC06227	4.5	4.7	4.6
HDC16553 ('+' in Hild et al)	DRSC14046	4.6	4.6	4.6
CG16941	DRSC15166	3.7	5.4	4.6
murashka	DRSC16484	4.2	4.9	4.6
Tango7	DRSC07142	5.2	3.8	4.5
Rpn6	DRSC07541	4.0	5	4.5
lethal(2)05070	DRSC07159	5.4	3.6	4.5
CG17331	DRSC02603	4.6	4.4	4.5
CG17836	DRSC15282	4.9	4.1	4.5
HDC09397 ('+' in Stolc / Hild et al)	DRSC09009	6.6	2.4	4.5
CG5482	DRSC06936	6.1	2.8	4.5
CG8929	DRSC07298	3.8	5.1	4.5
Prosbeta4	DRSC12186	4.5	4.4	4.5
Ken and Barbie	DRSC04696	5.8	3	4.4
CG4849	DRSC15662	5.0	3.8	4.4
CG17304	DRSC15222	4.7	4.1	4.4
CG15450	DRSC20522	4.6	4.2	4.4
Spt6	DRSC18836	4.0	4.8	4.4
HDC07396 ('+' in Hild et al)	DRSC05818	3.4	5.4	4.4
AGO1	DRSC05912	6.1	2.6	4.4
RpII215	DRSC20280	3.5	5.2	4.4
chinmo	DRSC00509	3.6	5.1	4.4
Nup98	DRSC14210	4.1	4.6	4.4
CG30382	DRSC07515	4.2	4.4	4.3
RpS16	DRSC04442	4.5	4.1	4.3
CG12897	DRSC06212	3.4	5.2	4.3
SF2	DRSC16845	3.2	5.4	4.3
HDC01261 ('+' in Stolc / Hild et al)	DRSC00977	2.9	5.7	4.3
HDC02560 ('+' in Hild et al)	DRSC01970	3.6	5	4.3
CSN6	DRSC16593	4.3		4.3

Jon99Ciii	DRSC16859	4.3		4.3
AdoR	DRSC16556	4.3		4.3
crooked-neck	DRSC18755	3.9	4.7	4.3
cdc2	DRSC03504	4.0	4.5	4.3
Patj	DRSC08712	4.0	4.5	4.3
Suv4-20	DRSC18482	3.9	4.6	4.3
snRNP69D	DRSC09800	5.7	2.7	4.2
TER94	DRSC07560	4.5	3.9	4.2
Bx42	DRSC17743	4.9	3.5	4.2
Nup153	DRSC19904	2.9	5.5	4.2
CG32365	DRSC10041	3.7	4.7	4.2
CG4328	DRSC10410	4.6	3.8	4.2
pontin	DRSC17029	4.5	3.9	4.2
ascutex	DRSC05924	2.7	5.7	4.2
HDC19639 ('+' in Stolc / Hild et al)	DRSC19272	3.1	5.3	4.2
orb	DRSC17021	4.5	3.8	4.2
Nup153	DRSC19904	5.5	2.8	4.2
RpL30	DRSC02087	3.7	4.6	4.2
reptin	DRSC11388	5.1	3.2	4.2
small bristles	DRSC20368	4.2	4.1	4.2
CG7757	DRSC10912	5.1	3.2	4.2
CG33967	DRSC16257	4.7	3.6	4.2
HDC13910	DRSC13145	4.1	4.2	4.2
HDC15172 ('+' in Hild et al)	DRSC13607	6.3	2.0	4.2
CG32606	DRSC19001	6.4	1.9	4.2
tango	DRSC17077	3.3	4.8	4.1
Bap60	DRSC19337	3.8	4.4	4.1
Slu7	DRSC14729	3.7	4.5	4.1
CG4266	DRSC04456	4.1	4.1	4.1
Tango4	DRSC19786	3.9	4.3	4.1
CG13298	DRSC09972	3.3	4.9	4.1
CG7918	DRSC16345	5.9	2.2	4.1
HDC03687 ('+' in Hild et al)	DRSC03744	5.3	2.9	4.1
Trn-SR	DRSC00546	3.7	4.4	4.1
CG17742	DRSC10285	5.3	2.8	4.1
Su(var)3-9	DRSC13081	4.0	4.1	4.1
eIF-1A	DRSC16937	4.7	3.4	4.1
His3:CG31613	DRSC21267	5.9	2.2	4.1
starry night	DRSC05234	4.1	4	4.1
ph-d	DRSC18819	4.0		4.0
CG14641	DRSC12227	3.1	4.9	4.0
RpLP1	DRSC00783	4.8	3.2	4.0
CG13165	DRSC06292	4.2	3.8	4.0

CG13675	DRSC10034	4.1	3.9	4.0
RpII15	DRSC16832	3.7	4.3	4.0
CG4325	DRSC18516	4.3	3.7	4.0
CG14180	DRSC10179	4.0	3.9	4.0
CG34139	DRSC15701	4.0		4.0
CG6197	DRSC06967	4.1	3.8	4.0
CG1542	DRSC15035	4.8	3.2	4.0
Nup153	DRSC19904	2.8	5.1	4.0
Pvf2	DRSC00968	2.6	5.2	3.9
Calx	DRSC13457	3.9		3.9
Neosin	DRSC11235	3.5	4.3	3.9
RpL36A	DRSC03055	4.3	3.5	3.9
Ef1alpha48D	DRSC07421	3.5	4.3	3.9
CG14952	DRSC08412	3.9	3.9	3.9
HDC03105 ('+' in Hild et al)	DRSC01651	3.9		3.9
ind	DRSC11355	3.0	4.8	3.9
Rheb	DRSC12148	3.0	4.7	3.9
CG14995	DRSC08452	4.6	3.1	3.9
MED25	DRSC14483	4.4	3.3	3.9
HDC05695	DRSC06151	3.9	3.8	3.9
Cpr47Ee	DRSC06343	5.1	2.6	3.9
unc-13-4A	DRSC10203	4.0	3.7	3.9
stubarista	DRSC18838	3.8	3.9	3.9
CG30126	DRSC05769	3.6	4.1	3.9
HDC11530	DRSC11566	4.9	2.8	3.9
smt3	DRSC03611	4.5	3.1	3.8
Fs(2)Ket	DRSC03328	3.9	3.7	3.8
gawky	DRSC17160	4.8	2.8	3.8
CR11700	DRSC17794	3.9	3.7	3.8
CG8179	DRSC07091	4.8	2.8	3.8
CG12499	DRSC14521	3.8		3.8
Chrac-16	DRSC20343	3.8		3.8
U2af50	DRSC20297	3.5	4	3.8
HDC05705 ('+' in Stolc / Hild et al)	DRSC06353	3.7	3.8	3.8
diminutive	DRSC18762	4.7	2.8	3.8
HDC10026	DRSC09271	2.8	4.7	3.8
HDC14006	DRSC13177	4.3	3.2	3.8
Rdh	DRSC08434	5.0	2.5	3.8
HDC12966 ('+' in Hild et al)	DRSC14922	3.8	3.7	3.8
Pvr	DRSC03080	2.9	4.5	3.7
bruno-2	DRSC02557	2.8	4.6	3.7
bric a brac 1	DRSC08379	3.0	4.4	3.7
minibrain	DRSC20058	2.7	4.7	3.7

blistered	DRSC04676	4.4	3	3.7
HDC02560 ('+' in Hild et al)	DRSC01970	3.7	3.6	3.7
Pros29	DRSC04644	4.0	3.3	3.7
RpS24	DRSC04414	5.9	1.4	3.7
Ef1gamma	DRSC16659	2.8	4.5	3.7
l(3)03670	DRSC16981	3.6		3.6
stumps	DRSC15332	5.3	1.9	3.6
Rtf1	DRSC04085	3.8	3.4	3.6
HDC05705 ('+' in Stolc / Hild et al)	DRSC06353	3.5	3.7	3.6
split thorax	DRSC18720	2.6	4.6	3.6
HDC07387 ('+' in Hild et al)	DRSC05810	4.3	2.9	3.6
HDC09490 ('+' in Hild et al)	DRSC09057	5.1	2.1	3.6
CG31395	DRSC12788	6.6	0.6	3.6
RpS10b	DRSC19561	5.1	2.1	3.6
CG32772	DRSC18052	4.6	2.6	3.6
Cyclin T	DRSC11124	4.2	2.9	3.6
His4r	DRSC16703	3.3	3.8	3.6
Tcp1-like	DRSC16877	4.5	2.6	3.6
CG32335	DRSC07948	4.5	2.6	3.6
rab3-GEF	DRSC19956	3.5		3.5
hook	DRSC18674	3.5		3.5
l(1)10Bb	DRSC20346	3.8	3.1	3.5
RpL13A	DRSC12265	3.5	3.5	3.5
E2f	DRSC16655	4.1	2.9	3.5
E23	DRSC00425	4.0	2.9	3.5
Pabp2	DRSC07501	2.5	4.4	3.5
CG9164	DRSC19087	3.2	3.7	3.5
CG34422	DRSC20029	3.2	3.7	3.5
Camta	DRSC06441	4.2	2.6	3.4
CG10927	DRSC06014	3.2	3.6	3.4
RpS23	DRSC07169	3.3	3.5	3.4
fru	DRSC16951	3.4		3.4
RpL37A	DRSC02899	4.2	2.6	3.4
luna	DRSC06663	3.7	3.1	3.4
scruff	DRSC12604	4.8	2.0	3.4
CG31179	DRSC13494	3.4		3.4
CG12470	DRSC18620	3.4		3.4
CG42389	DRSC02245	3.9	2.9	3.4
CG12484	DRSC05883	3.0	3.8	3.4
CG32062	DRSC10157	5.0	1.8	3.4
RpS27A	DRSC03421	3.0	3.7	3.4
Proctolin	DRSC03009	5.1	1.6	3.4
CG9253	DRSC03171	4.2	2.5	3.4

RpS27	DRSC14244	5.1	1.6	3.4
A3-3	DRSC17225	3.5	3.2	3.4
HDC10243 ('+' in Hild et al)	DRSC09354	3.2	3.5	3.4
RpII33	DRSC03415	3.0	3.6	3.3
homeobrain	DRSC04082	4.0	2.6	3.3
CG30460	DRSC06560	4.2	2.4	3.3
CG17329	DRSC01926	3.3		3.3
Furin 1	DRSC13707	3.2	3.4	3.3
Tektin-C	DRSC09741	3.0	3.6	3.3
HDC09523 ('+' in Stolc / Hild et al)	DRSC09076	4.5	2.1	3.3
CG4570	DRSC15602	4.1	2.4	3.3
Alhambra	DRSC12447	3.3		3.3
CG9007	DRSC11051	3.8	2.7	3.3
Snr1	DRSC12369	3.2	3.3	3.3
noisette	DRSC12383	3.2	3.3	3.3
CG32776	DRSC18119	4.6	1.9	3.3
rutabaga	DRSC20367	4.4	2.1	3.3
Sox100B	DRSC15090	3.2		3.2
Rrp45	DRSC20198	3.2		3.2
CG11138	DRSC19385	3.2		3.2
Cdc27	DRSC11112	2.8	3.6	3.2
mei-P26	DRSC17735	3.8	2.6	3.2
Hey	DRSC07440	5.2	1.2	3.2
CG32306	DRSC08333	4.2	2.2	3.2
msopa	DRSC11895	4.5	1.9	3.2
RpL6	DRSC14323	4.2	2.2	3.2
HDC17386	DRSC17342	3.4	3	3.2
bhringi	DRSC11000	3.1	3.3	3.2
CG3436	DRSC00605	4.2	2.1	3.2
CG3983	DRSC15529	5.0	1.3	3.2
shrub	DRSC07061	3.4	2.9	3.2
RpII140	DRSC16831	3.3	3	3.2
canoe	DRSC12374	4.6	1.7	3.2
thisbe	DRSC06153	4.6	1.7	3.2
alphaTub85E	DRSC16899	3.5	2.8	3.2
HDC08349 ('+' in Hild et al)	DRSC08080	4.2	2.1	3.2
HDC09253 ('+' in Hild et al)	DRSC08978	2.8	3.5	3.2
CG31461	DRSC13113	2.5	3.8	3.2
CG14543	DRSC14887	3.1		3.1
RnrL	DRSC03413	2.7	3.5	3.1
antimeros	DRSC12310	3.8	2.4	3.1
CG6937	DRSC16140	3.4	2.8	3.1
Rpb7	DRSC16068	2.7	3.5	3.1

CG31847	DRSC02535	2.9	3.3	3.1
Rgk1	DRSC07344	2.7	3.5	3.1
HDC13476 ('+' in Hild et al)	DRSC12996	3.2	3	3.1
D19A	DRSC11133	3.5	2.6	3.1
U2af38	DRSC00796	3.2	2.9	3.1
cropped	DRSC03515	2.7	3.4	3.1
Mrtf	DRSC08263	4.1	2.0	3.1
HDC07103 ('+' in Hild et al)	DRSC05711	4.2	1.9	3.1
CG31353	DRSC13530	5.8	0.3	3.1
translucent	DRSC11308	4.5	1.5	3.0
CG2446	DRSC19847	3.0		3.0
CG2685	DRSC18463	3.0		3.0
CG9777	DRSC20208	3.0		3.0
Rbm13	DRSC17749	3.0		3.0
Cbp20	DRSC16601	3.0		3.0
snRNP2	DRSC12536	2.8	3.2	3.0
His2B:CG17949	DRSC03757	3.3	2.7	3.0
HDC19527 ('+' in Hild et al)	DRSC19637	4.0	2.0	3.0
CG15630	DRSC00465	3.7	2.2	3.0
l(2)35Df	DRSC03560	3.6	2.3	3.0
roadkill	DRSC14526	3.4	2.5	3.0
CG31475	DRSC14762	3.4	2.5	3.0
Clipper	DRSC00746	2.9	3	3.0
CG10754	DRSC09801	2.7	3.2	3.0
His-Psi:CR31615/CR31616	DRSC03760	3.3	2.6	3.0
HDC05639 ('+' in Hild et al)	DRSC05231	3.1	2.8	3.0
HDC07480 ('+' in Stolc / Hild et al)	DRSC05871	5.2	0.7	3.0
Sec61alpha	DRSC03256	3.7	2.1	2.9
Spt5	DRSC07556	3.6	2.2	2.9
TweedleN	DRSC15813	2.9		2.9
CG4218	DRSC01939	2.9		2.9
HLH106	DRSC11182	3.5	2.3	2.9
CG15470	DRSC18053	4.1	1.7	2.9
HDC13798	DRSC13109	3.1	2.7	2.9
RpS11	DRSC07289	3.8	2.0	2.9
sine oculis	DRSC07693	3.1	2.7	2.9
Ef1alpha100E	DRSC16658	2.9		2.9
CG32970	DRSC01375	2.9		2.9
Fasciclin 2	DRSC17308	2.9		2.9
CG12278	DRSC14494	2.9		2.9
Cdc42	DRSC20228	3.3	2.4	2.9
CG6509	DRSC02964	2.8	2.9	2.9
Nup98	DRSC14209	3.6	2.0	2.8

peanuts	DRSC07120	3.2	2.4	2.8
CG32043	DRSC10330	4.3	1.3	2.8
bluecheese	DRSC02333	3.2	2.4	2.8
Dim1	DRSC00563	3.0	2.6	2.8
CG3563	DRSC13053	2.9	2.7	2.8
beat-IIb	DRSC13219	2.8		2.8
MED28	DRSC15721	2.8		2.8
couch potato	DRSC14503	2.8		2.8
anterior open	DRSC00801	4.6	0.9	2.8
Cpr66D	DRSC10646	3.9	1.6	2.8
CG9426	DRSC03219	3.6	1.9	2.8
MBD-R2	DRSC14180	3.1	2.4	2.8
Beadex	DRSC19350	2.6	2.9	2.8
CSN3	DRSC11859	3.4	2.0	2.7
CG31145	DRSC14670	4.6	0.8	2.7
Tim9b	DRSC19566	3.1	2.3	2.7
MED22	DRSC18175	2.7		2.7
CG15365	DRSC18038	4.0	1.4	2.7
Tim17b2	DRSC03457	2.7		2.7
HDC17481 ('+' in Hild et al)	DRSC17379	3.9	1.5	2.7
Nepriylsin 1	DRSC18389	2.7		2.7
warts	DRSC17096	4.3	1.0	2.7
NF-YC-like	DRSC18272	3.9	1.4	2.7
HDC18875 ('+' in Hild et al)	DRSC19029	3.2	2.1	2.7
CG31229	DRSC13309	2.9	2.2	2.6
dalao	DRSC18419	2.9	2.2	2.6
Smrter	DRSC19495	3.8	1.4	2.6
CG18375	DRSC04305	2.7	2.5	2.6
CG4959	DRSC01938	2.6		2.6
CG5732	DRSC15863	2.6		2.6
CG30127	DRSC05786	2.6		2.6
vrille	DRSC03633	4.6	0.6	2.6
mRNA-capping-enzyme	DRSC19789	3.2	2.0	2.6
HDC08744 ('+' in Hild et al)	DRSC08800	3.8	1.4	2.6
Symplekin	DRSC12301	2.8	2.4	2.6
foxo	DRSC13017	3.2	2.0	2.6
HDC17467 ('+' in Hild et al)	DRSC17370	3.1	2.1	2.6
Rpb8	DRSC11642	2.7	2.4	2.6
CG3918	DRSC18331	3.7	1.4	2.6
CG5739	DRSC02885	3.1	2.0	2.6
CG4830	DRSC15657	3.1	2.0	2.6
CG12454	DRSC19458	3.7	1.4	2.6
HDC05227 ('+' in Hild et al)	DRSC05108	2.5	2.6	2.6

HDC08028	DRSC07960	2.9	2.2	2.6
spn-F	DRSC14475	2.8	2.3	2.6
Rbp2	DRSC20276	2.9	2.2	2.6
cut	DRSC18757	2.8	2.1	2.5
l(2)k09022	DRSC02108	3.8	1.2	2.5
CG14023	DRSC02353	2.9	2.1	2.5
Su(Tpl)	DRSC10954	2.8	2.2	2.5
CG8885	DRSC03117	2.8	2.2	2.5
CG13278	DRSC02252	2.5		2.5
CG7532	DRSC01910	2.5		2.5
Su(z)2	DRSC07558	3.0	2.0	2.5
eyegone	DRSC11344	3.3	1.7	2.5
HDC14033	DRSC13200	2.7	2.3	2.5
Hsp83	DRSC08664	2.7	2.2	2.5
CG7597	DRSC11836	2.5	2.4	2.5
CG2865	DRSC18528	2.8	2.1	2.5
smG	DRSC20207	2.9	2.0	2.5
HDC01635	DRSC01082	2.8	2.1	2.5
HDC10238	DRSC09350	2.6	2.3	2.5
HDC12272	DRSC12455	2.6	2.3	2.5
Stam	DRSC03444	2.6	2.2	2.4
pUf68	DRSC08731	3.4	1.4	2.4
CG12054	DRSC14467	2.6	2.2	2.4
Tor	DRSC02811	2.8	2.0	2.4
serpent	DRSC17068	2.7	2.1	2.4
CG4615	DRSC18376	3.0	1.7	2.4
CG5466	DRSC15808	3.7	1.1	2.4
CG15740	DRSC19706	2.8	2.0	2.4
dpr6	DRSC09005	3.9	0.9	2.4
Hsp70Ab	DRSC15380	2.9	1.8	2.4
hyrax	DRSC14462	2.7	2.0	2.4
CG5844	DRSC15890	2.5	2.2	2.4
HDC02165 ('+' in Hild et al)	DRSC01243	3.0	1.7	2.4
HDC02637 ('+' in Hild et al)	DRSC01452	2.7	2.0	2.4
HDC04273 ('+' in Stolc / Hild et al)	DRSC03998	2.7	2.0	2.4
HDC13786	DRSC13099	2.5	2.2	2.4
Fatty acid synthetase	DRSC00268	2.6	2.0	2.3
Neurocalcin	DRSC07022	2.5	2.1	2.3
PDK1	DRSC08682	3.0	1.5	2.3
Eip74EF	DRSC10613	3.3	1.3	2.3
HDC15185	DRSC14674	5.2	-0.6	2.3
CG33110	DRSC14694	3.5	1.1	2.3
HDC14620 ('+' in Stolc / Hild et al)	DRSC13410	5.0	-0.4	2.3

CG12650	DRSC17609	2.8	1.8	2.3
HDC08749 ('+' in Hild et al)	DRSC08805	2.8	1.8	2.3
CG31705	DRSC01991	2.9	1.6	2.3
bunched	DRSC03500	2.7	1.8	2.3
Klp61F	DRSC08671	2.7	1.8	2.3
pgant6	DRSC08552	2.7	1.8	2.3
CSN7	DRSC06807	2.5	2.0	2.3
CG15753	DRSC19718	4.6	-0.1	2.3
CG42270	DRSC19967	2.8	1.7	2.3
HDC09080 ('+' in Hild et al)	DRSC08919	5.6	-1.1	2.3
HDC18214 ('+' in Hild et al)	DRSC17632	2.7	1.8	2.3
dre4	DRSC08714	3.7	0.7	2.2
CG13779	DRSC02282	3.1	1.3	2.2
CG6043	DRSC02922	3.5	0.9	2.2
CG34113	DRSC12263	3.1	1.3	2.2
Hexokinase C	DRSC07079	2.8	1.6	2.2
TORC	DRSC10578	4.1	0.3	2.2
alphaTub84B	DRSC12622	2.8	1.6	2.2
CG6015	DRSC15948	2.7	1.7	2.2
CG34354	DRSC14558	4.3	0.1	2.2
Hsp70Bb	DRSC21248	2.7	1.7	2.2
HDC05820 ('+' in Stolc / Hild et al)	DRSC05297	2.8	1.6	2.2
snRNA:U1:95Cc	DRSC13640	4.2	0.2	2.2
Cct5	DRSC07357	3.5	0.8	2.2
muscleblind	DRSC07651	2.9	1.4	2.2
alphaTub84D	DRSC12623	3.5	0.8	2.2
HDC18498 ('+' in Stolc / Hild et al)	DRSC19661	3.7	0.6	2.2
araucan	DRSC11322	3.0	1.2	2.1
CG30387	DRSC04256	3.3	0.8	2.1
Mlf	DRSC07472	3.4	0.7	2.1
CG14982	DRSC08440	3.2	0.9	2.1
Tie	DRSC08702	2.8	1.3	2.1
CG3982	DRSC10394	2.8	1.3	2.1
HDC18670 ('+' in Hild et al)	DRSC18963	3.2	0.9	2.1
CG5446	DRSC02862	3.0	1.0	2.0
hook-like	DRSC02062	2.8	1.2	2.0
bubblegum	DRSC03495	3.2	0.7	2.0
Tbp	DRSC04662	2.6	1.4	2.0
CG17622	DRSC15247	3.9	0.1	2.0
HDC01575 ('+' in Hild et al)	DRSC01059	2.9	1.1	2.0
par-1	DRSC05792	2.7	1.3	2.0
HDC09511 ('+' in Stolc / Hild et al)	DRSC09067	4.4	-0.4	2.0
CG9817	DRSC18446	3.7	0.3	2.0

CG6854	DRSC10729	2.7	1.2	2.0
cryptocephal	DRSC03513	2.9	1.0	2.0
CG33558	DRSC05013	2.5	1.4	2.0
sticks and stones	DRSC06423	3.3	0.6	2.0
HDC11218 ('+' in Hild et al)	DRSC11443	2.6	1.3	2.0
HDC12421 ('+' in Hild et al)	DRSC12666	3.8	0.1	2.0
Nnp-1	DRSC02165	3.7	0.1	1.9
HDC09529 ('+' in Hild et al)	DRSC09082	2.9	0.9	1.9
HDC14879 ('+' in Hild et al)	DRSC13509	3.7	0.1	1.9
CG30497	DRSC06425	2.7	1.0	1.9
Gbp	DRSC07434	2.5	1.2	1.9
CG32245	DRSC08327	3.8	-0.1	1.9
PP2A-B'	DRSC16337	3.0	0.7	1.9
HDC07450	DRSC05865	2.5	1.2	1.9
CG33980	DRSC18089	2.9	0.8	1.9
HDC18410 ('+' in Stolc / Hild et al)	DRSC18886	2.9	0.8	1.9
CG30349	DRSC06421	3.5	0.1	1.8
CG5151	DRSC10487	3.4	0.2	1.8
E5	DRSC16585	2.7	0.9	1.8
CG34436	DRSC15165	4.1	-0.5	1.8
Rtc1	DRSC20285	3.0	0.5	1.8
HDC14311 ('+' in Hild et al)	DRSC14786	3.5	0.0	1.8
CG6962	DRSC16153	2.7	0.7	1.7
CG4585	DRSC04475	3.1	0.3	1.7
CG11583	DRSC08202	2.8	0.6	1.7
fizzy	DRSC03534	2.7	0.7	1.7
CG6764	DRSC16111	2.9	0.5	1.7
Ten-a	DRSC19496	2.7	0.7	1.7
Vps4	DRSC19338	2.5	0.8	1.7
CG9836	DRSC16572	2.6	0.7	1.7
CG7031	DRSC16178	3.1	0.2	1.7
CG12071	DRSC14471	2.8	0.5	1.7
Pdp1	DRSC08896	3.7	-0.4	1.7
CG5525	DRSC02865	2.6	0.6	1.6
CG18131	DRSC00517	2.5	0.7	1.6
nop5	DRSC03582	2.6	0.6	1.6
CG14107	DRSC10110	3.2	-0.1	1.6
CG32432	DRSC11703	3.1	0.1	1.6
fd3F	DRSC17843	3.5	-0.3	1.6
HDC14836 ('+' in Hild et al)	DRSC13493	3.1	0.1	1.6
CG9300	DRSC11064	2.9	0.2	1.6
CG30349	DRSC06839	2.9	0.2	1.6
Mystery 45A	DRSC07067	2.6	0.5	1.6

Su(var)205	DRSC03446	2.6	0.4	1.5
HDC08645 ('+' in Stolc / Hild et al)	DRSC08772	2.9	0.1	1.5
HDC14699 ('+' in Stolc / Hild et al)	DRSC13445	3.4	-0.4	1.5
CG42337	DRSC11687	2.6	0.2	1.4
HDC14817 ('+' in Hild et al)	DRSC13481	2.8	0.0	1.4
pasilla	DRSC16388	2.6	0.1	1.4
HDC12808	DRSC12769	2.6	0.0	1.3
HDC15101 ('+' in Stolc / Hild et al)	DRSC13589	2.6	0.0	1.3
CG9948	DRSC09690	2.7	-0.2	1.3
CG12880	DRSC14568	2.6	-0.2	1.2
HDC08562	DRSC08743	2.7	-0.3	1.2
HDC11852 ('+' in Hild et al)	DRSC12050	2.6	-0.2	1.2
HDC14962 ('+' in Hild et al)	DRSC13553	2.7	-0.4	1.2
HDC02648 ('+' in Stolc / Hild et al)	DRSC01457	2.6	-0.4	1.1
HDC14638	DRSC13421	2.5	-0.5	1.0

Table S1. Summary of the three phases of the overall screen for genes required for HIF activity.

Screen	Genes Analyzed	Reporter System	dsRNA library	Stimulus	Hit Selection Criterion	N° of hits
Primary	~22,000 genes (Whole DRSC 1.0 dsRNA library)	HRE- firefly Luc	DRSC 1.0	DFO	Z score \leq -2,5	609
Secondary	225 Primary hits (Total primary hits filtered against cell viability screen and Sanger Collection)	HRE- firefly Luc and Actin- <i>Renilla</i> Luc	DRSC 2.0	DFO	Inhibition of HRE-luc activity \geq 50% (Group A >75% ; Group B 50%-75%)	66
Tertiary	35 Secondary hits (Group A and 12 genes from Group B functionally related to Group A genes)	HRE- firefly Luc and Actin- <i>Renilla</i> Luc	DRSC 2.0	Hypoxia (1% O ₂)	Inhibition of HRE-luc activity \geq 50%	30

Figure S3. Regulation of Sima subcellular localization is not affected in Ago1 homozygous mutant embryos.

A

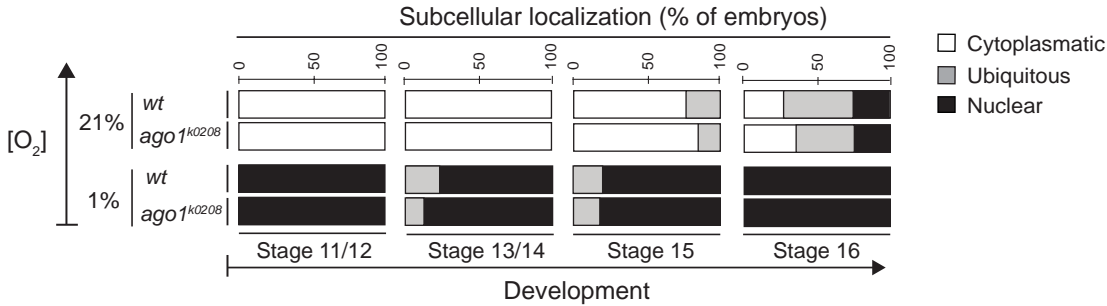


Figure S2. miRNAs and the response to hypoxia.

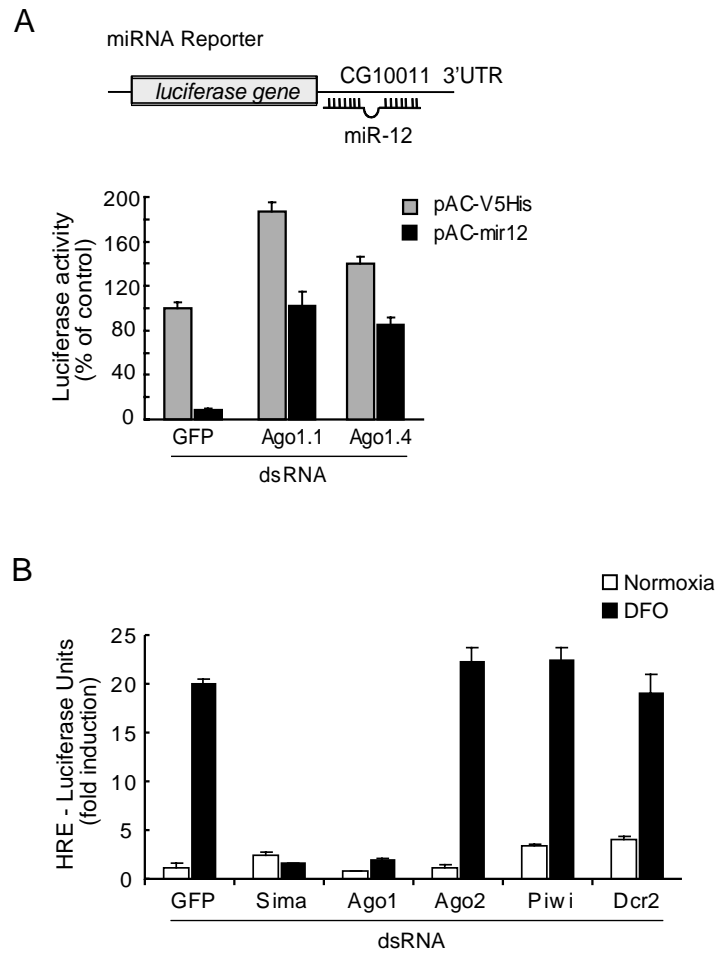
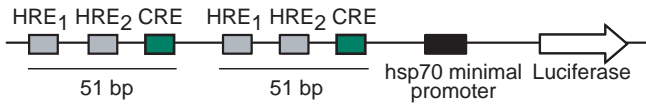


Figure S1. HRE-Luciferase reporter induction in cells exposed to hypoxia or DFO.

A

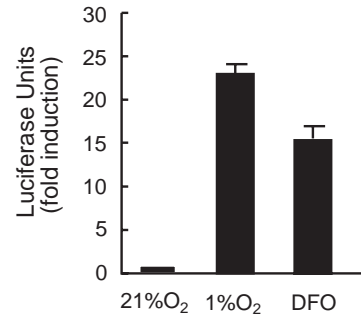


HRE₁ : TACACGTGGGTT

HRE₂ : CCCGCACGTCCG

CRE : CTTGACGTCAGC

B



C

