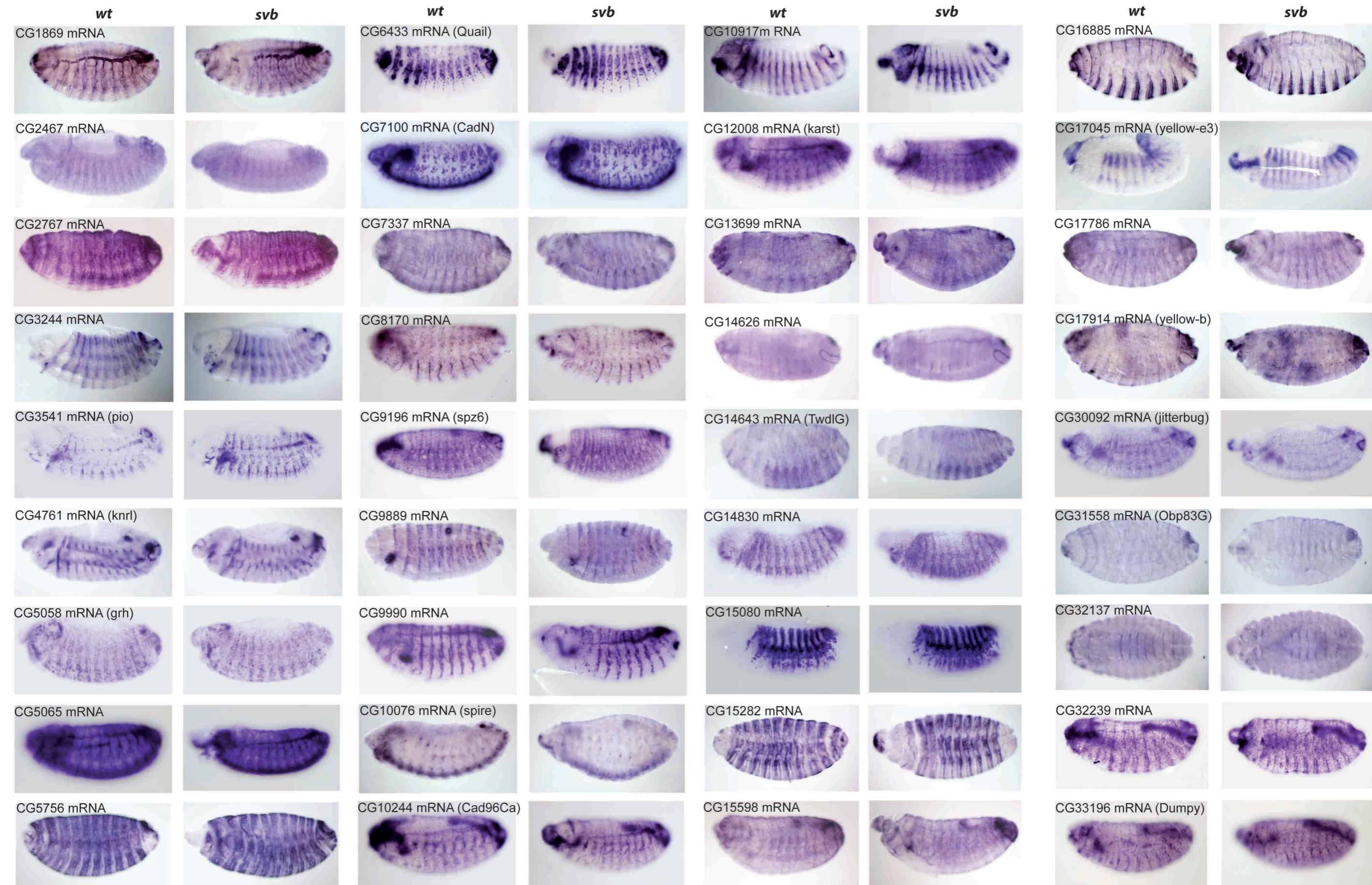


Menoret et al.; Figure S1A



Menoret et al.; Figure S1B

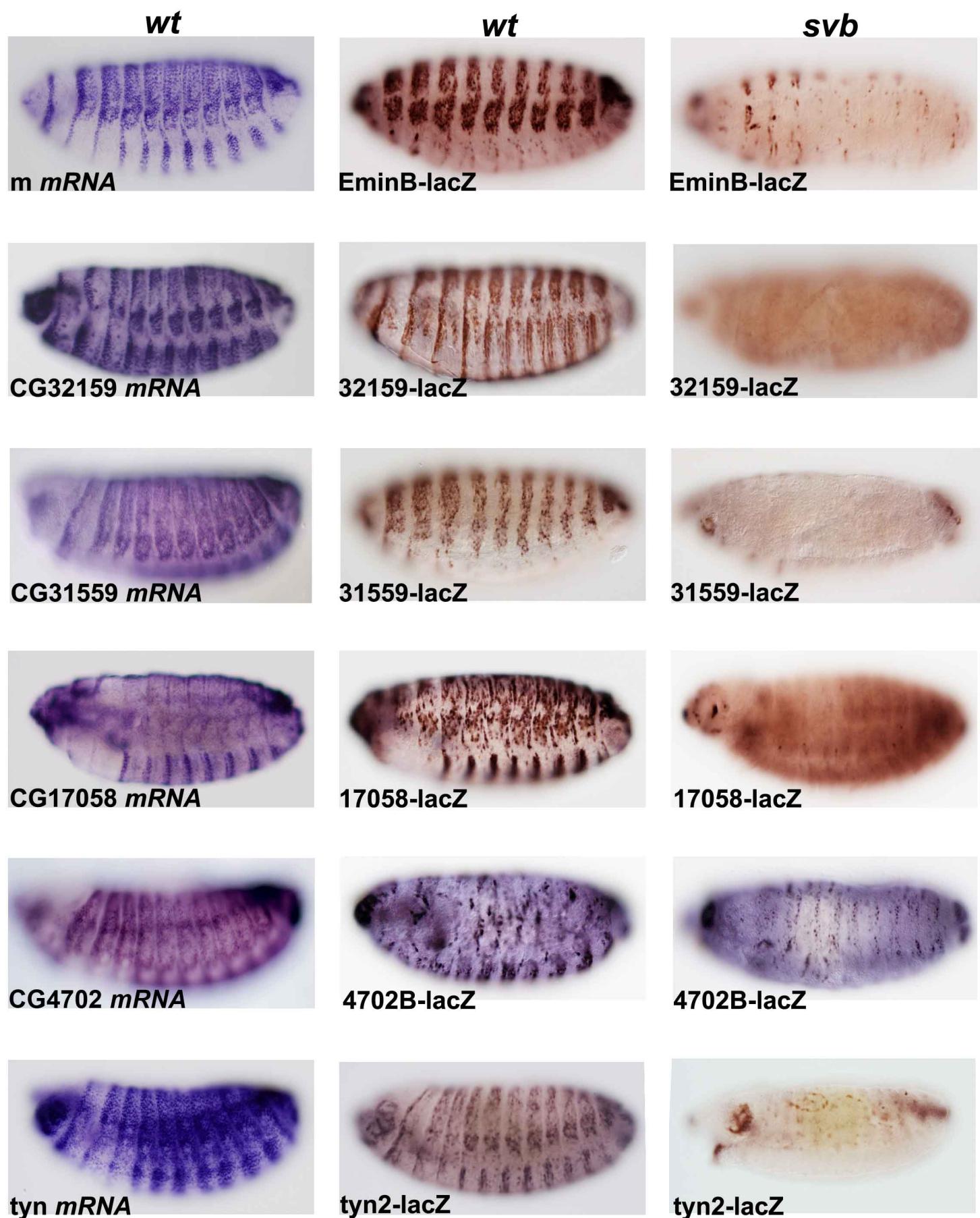
# CisTargetX results for 39 Svb downstream genes

	Motif	Enrichment score	Logo	ROC	Candidate targets	All genes in top 1000
ACCGTTA	ACCGTTA	7.24081479205049	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
ATMYB77_01	M00968-P-ATMYB77_01	5.23848854240618	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
	M00993-V-TAL1_Q6	5.12497547192746	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
	M01101-I-OVO_Q6	5.00878737312752	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
	M00227-V-VMYB_02	4.97374180007091	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
OVO_Q6	GATCTGC	4.06844736700277	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
	AWNTGGGTCA	4.05223507414695	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
	M00117-V-CEPB_02	3.76311585155174	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
	Hr46	3.74149946107736	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
	AATTAGCA	3.56316423966349	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
	CTTGCAGCA	3.43892403541185	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
CMYB_01	M00004-V-CMYB_01	3.43343887632895	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
	PF0085	3.42806179919847	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
	TTNNRCAATM-slow	3.36051057896594	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
	M01006-P-AGP1_01	3.32270891612382	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
	M00164-I-HSF_03	3.31995282633831	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
	TIFDMEM0000036	3.30919867207731	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
	M00085-V-ZID_01	3.30914463110114	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
OVO	M00190-V-CEBP_Q2	3.30106550516132	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
	ovo	3.29571544851888	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
	M00461-I-OVO_01	3.25783272421251	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
	TCGTCCA	3.24156639038053	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
OVO_01	MA0054	3.15512784897098	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
	M00104-V-CDPCR1_01	3.13894257660326	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>

## CisTargetX results for 36 epidermal Svb independent genes

Motif	Enrichment score	Logo	ROC	Candidate targets	All genes in top 1000
TIFDMEM0000099	4.51171012170964	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
SelexConsensus_grh	4.32098633351667	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
M00117-V-CEPB_02	4.26834490169103	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
badis_Isgf3g_primary	4.20474107256725	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
M00109-V-CEPB_01	4.11706381897675	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
MA0050	3.98553697619372	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
AATTWNAYGCR	3.9350880238277	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
GCANTTGYNWYAATT	3.38916063838056	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
badis_Sry_secondary	3.33871168601454	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
PF0001	3.30801697357978	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
badis_Irf4_primary	3.26638178864145	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
M00276-F-MAT1MC_02	3.18304564438102	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
pros	3.14138853464811	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
ATAATTGC	3.09975334970978	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
badis_Irf6_primary	3.04489751362992	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
MA0051	3.00324040389701	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
PF0085	2.87609852003322	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
RWWNTNRCACYT-brachyenteron	2.85193739638815	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
CTTGACC	2.82567149246181	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
AAGCGCA	2.79938366374089	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
PF0146	2.75777040359717	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
AGGTGAA	2.74018671833095	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
Hr46	2.73135102610866	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
badis_Irf5_primary	2.72920239623823	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
badis_Irf3_primary	2.72700991677858	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
PF0032	2.69410080008959	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
PF0168	2.67004930041748	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
MA0054	2.65246561515126	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
AAAAGCT	2.53404979953681	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
badis_Esrra_secondary	2.5252579569037	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
ACACGTCA	2.52313125182788	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
ATTATGCAA	2.52091684757365	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
TTATGCAA	2.5099544502755	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>
YAATTWNRYGC	2.50559141615085	LOGO	ROC	<a href="#">link</a>	<a href="#">link</a>

Menoret et al.; Figure S1D



Menoret et al.; Figure S2A

Name	Pos/ Neg	svbF7	blue motif	TTATGGAA
dyl2	+	3	3	0
15589	+	3	0	0
32159	+	2	5	1
sha3	+	2	1	1
cyrA	+	2	0	0
Emin	+	1	1	0
sha1	+	1	0	0
nyo1	+	1	0	1
snE1	+	1	1	0
tyn2	+	1	0	0
4702B	+	0	4	0
EminB	+	0	1	0
17058	+	0	0	1
31559	+	0	0	0
nyo3	-	2	0	1
32356	-	1	0	1
12063	-	1	0	0
f4	-	1	0	0
snB2	-	1	0	0
1499-1	-	1	0	0
sn-enh1	-	0	2	0
dyl1	-	0	1	0
f5	-	0	0	0
f3	-	0	0	0
sha2	-	0	0	0
nyo2	-	0	0	2
tyn1	-	0	0	0
sox21b	-	0	0	0
snP	-	0	0	0
4702	-	0	0	0
f2	-	0	0	0
f1	-	0	0	0
dyl3	-	0	0	0
cyrB	-	0	0	0
snE5	-	0	0	0
snH5	-	0	0	0
15013-2	-	0	0	0
15013-1	-	0	0	0
snE4	-	0	0	0

conserved motifs

Name	Pos/Neg	svbF7	blue motif	TTATGGAA
dyl2	+	3	3	0
15589	+	4	1	0
32159	+	3	5	1
sha3	+	2	1	1
cyrA	+	2	0	0
Emin	+	1	1	1
sha1	+	1	0	0
nyo1	+	1	1	1
snE1	+	1	1	1
tyn2	+	1	0	1
4702B	+	1	5	0
EminB	+	1	2	0
17058	+	1	0	1
31559	+	0	0	0
nyo3	-	2	0	1
32356	-	2	0	1
12063	-	1	0	0
f4	-	1	0	1
snB2	-	1	0	1
1499-1	-	1	0	0
sn-enh1	-	1	3	0
dyl1	-	1	2	0
f5	-	0	0	0
f3	-	0	0	1
sha2	-	0	0	0
nyo2	-	0	0	2
tyn1	-	0	0	0
sox21b	-	0	0	0
snP	-	1	0	0
4702	-	0	0	0
f2	-	0	0	0
f1	-	0	0	0
dyl3	-	0	0	0
cyrB	-	0	0	1
snE5	-	0	0	1
snH5	-	0	0	0
15013-2	-	0	0	0
15013-1	-	0	0	0
snE4	-	1	1	0

*D. mel* motifs

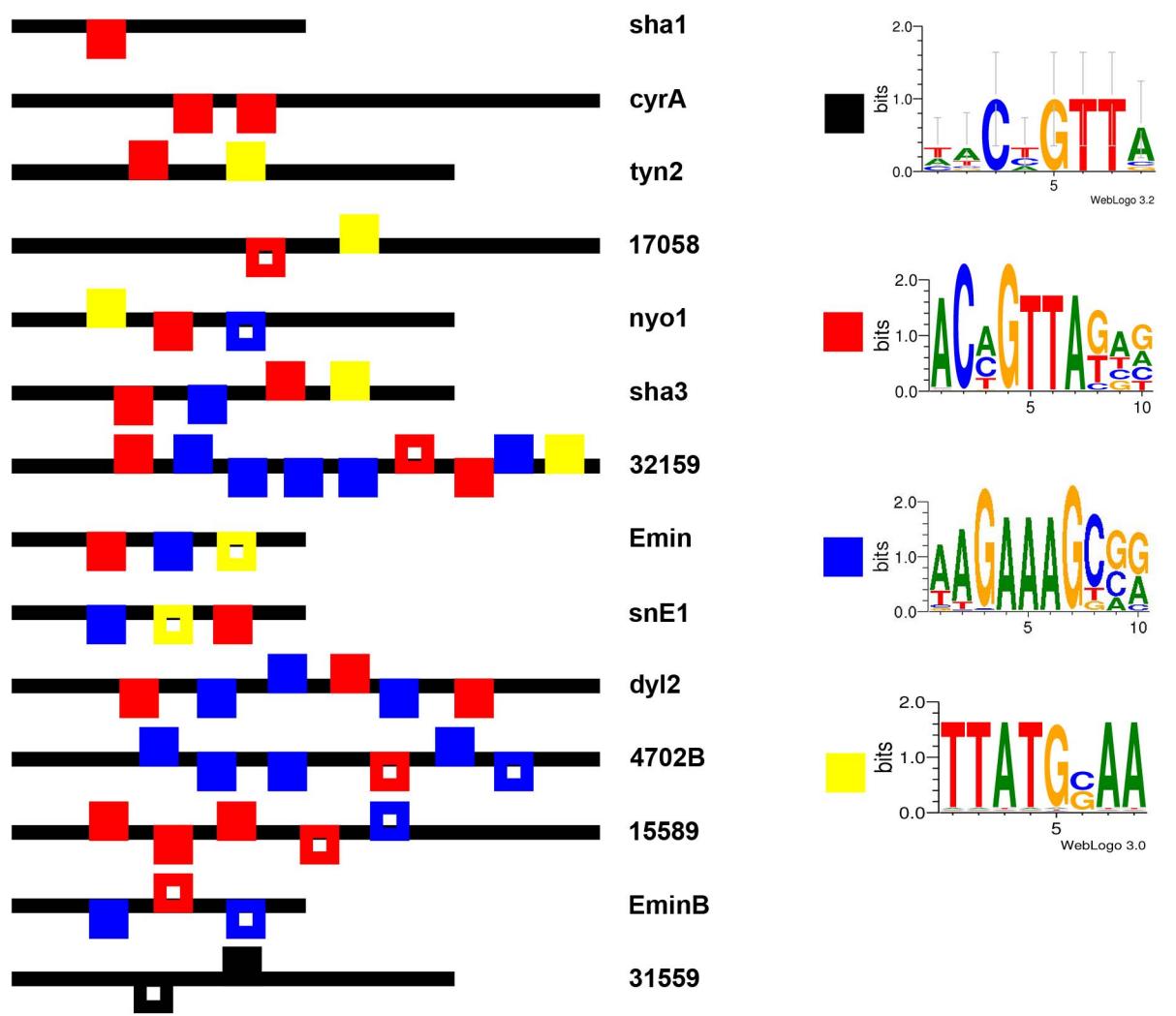
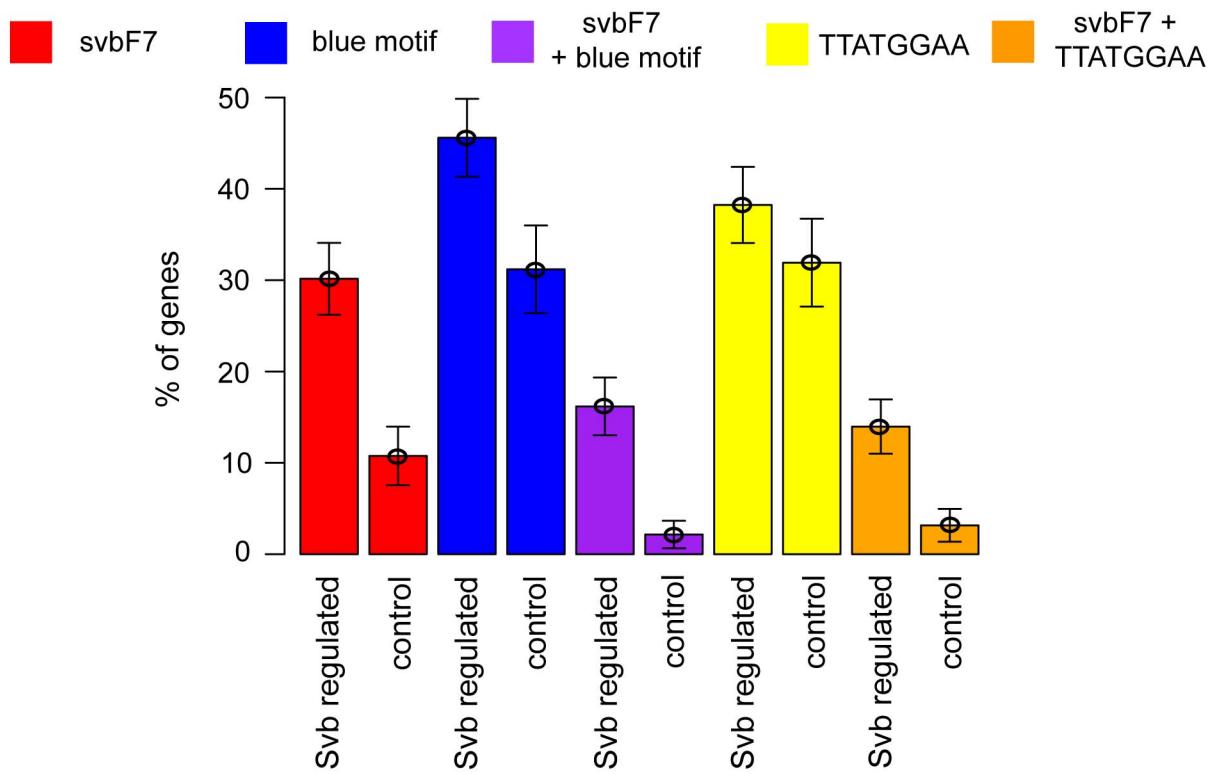
### CisTargetX results on the 39 Svb downstream genes with SvbF7

Motif	Enrichment score	Logo	ROC	Candidate targets	All genes in top 1000
SvbF7	7.00488224690521	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
ACCGTTA	6.61159001238553	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
Bleu motif	4.82608364297727	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
nAACwGTw	4.70815627341058	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
AATTAGCA	4.52720147022047	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
MA0054	4.17331449058271	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
M00968-P-ATMYB77_01	4.07885199335089	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
M01101-I-OVO_Q6	4.01595564839969	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
AWNTGGGTCA	3.99760323428303	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
ovo	3.81405287538217	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
M00117-V-CEBPB_02	3.75113031269652	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
M00227-V-VMYB_02	3.39459534187904	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
M00218-P-MYBPH3_01	3.38670380380889	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
PF0139	3.26342801641395	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
PF0105	3.17174459903407	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
M00630-V-FOXM1_01	3.13239177962111	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
Hr46	3.11663492121525	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
CAGNNGCA	3.05636034970929	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
ATCGATC	3.05379101173296	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
CGCAAGC	3.04852124710804	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
PF0083	2.98289825777381	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
GATCTGC	2.93838054467373	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
CAATTAG	2.88859306694872	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
CGCATGCGC	2.8465660386216	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
SelexConsensus_pros	2.80207454325597	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
CTTGGCCA	2.76799148846791	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
PF0146	2.74182618948447	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
M00104-V-CDPCR1_01	2.72604311334416	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>

### CisTargetX CRMs predictions using SvbF7

	15589	cyrA	nyo3	sha2	dy11	dy12	pmin	32159	Emin	sha3	sne1	sne5	EminB	snB2	nyo1	sn_enh1
RANK	1	2	7	10	11	15	21	24	26	34	38	52	55	58	97	104
ACTIVITY	+	+	-	-	-	+	-	+	+	+	+	-	+	-	+	-

Menoret et al., Fig.S2B

**A****B**

Menoret et al.; Figure S2C

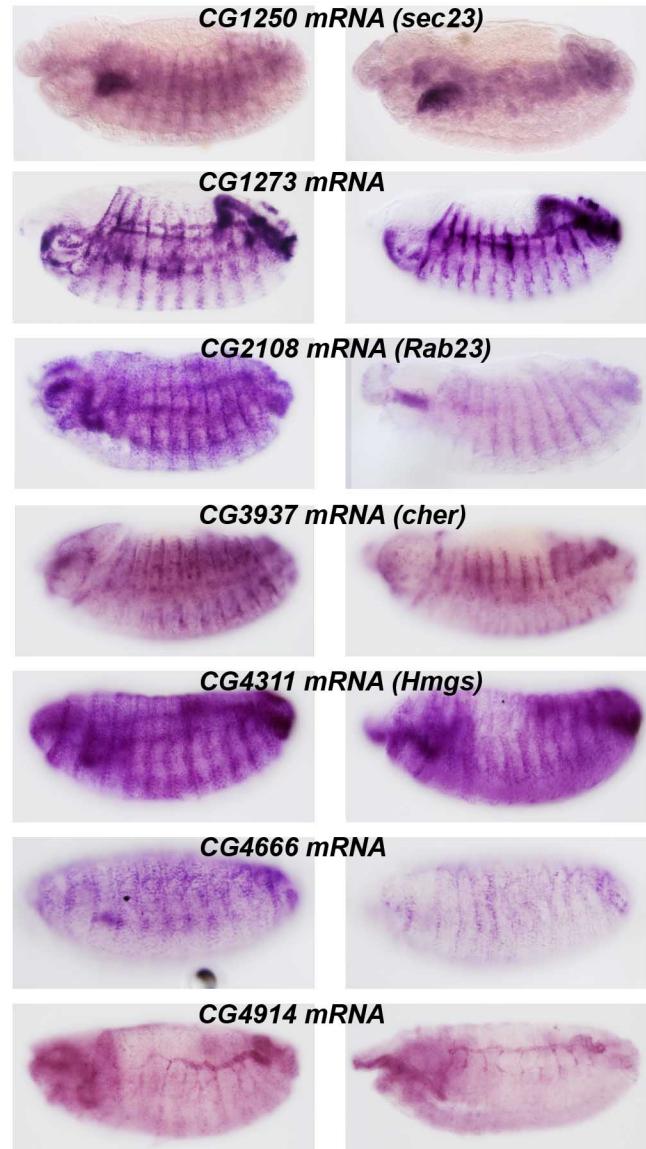
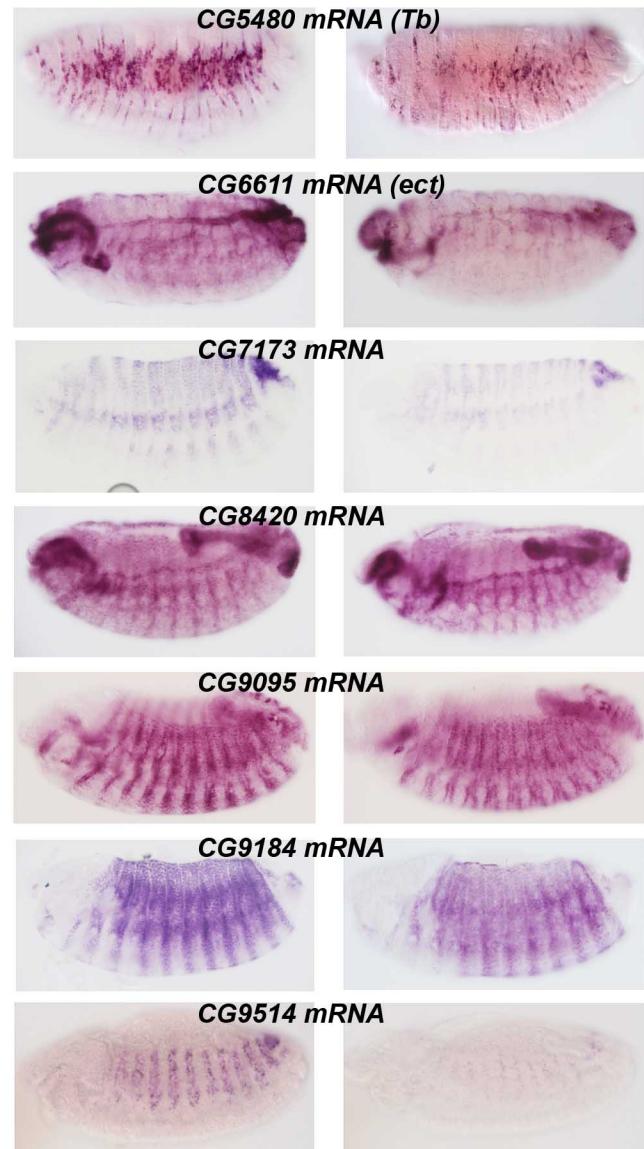
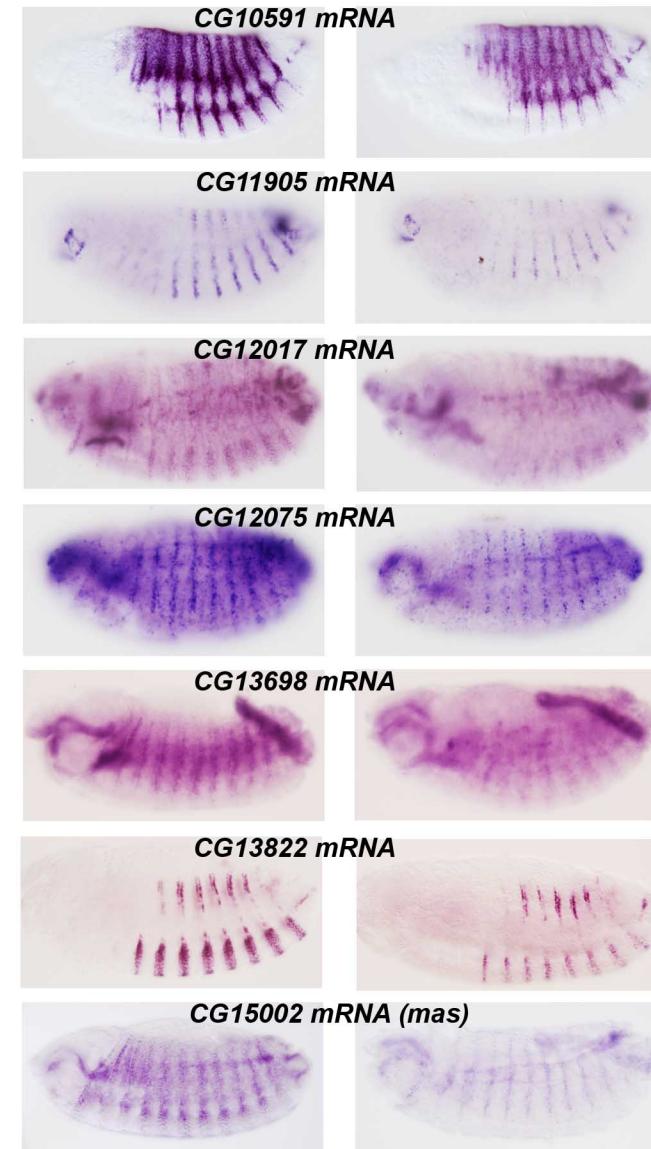
Gene symbol	Representative Public ID	putative function / features	epidermal expression	additional expression #	svb mutant microarrays (% of wt)	pri mutant microarrays (% of wt)	validated in svb mutant (in situ)	validated in svb ectopic (in situ)	svbF7	blue motif	ChIP peaks in 5kb (12-14h)	ChIP peaks in 5kb (8-10h)	reference
CG15370	CG15370	unknown	no	ubiquitous	13,1	2,1	no	ND	no	yes	yes	yes	this work
sha	CG13209	cuticle pattern formation & epidermal cell differentiation	stripes		24,6	6,6	yes	yes	yes	yes	yes	yes	ref 1
CG14395	CG14395	unknown	stripes		41,2	3,0	yes	yes	yes	yes	yes	yes	this work, FigS1
CG4386	CG4386	proteolysis	no	trachea	43,5	11,3	no	ND	no	yes	no	no	this work
CG15818	CG15818	unknown	no	midgut	47,9	17,8	no	ND	no	yes	no	yes	this work
m	CG9369	actin filament organization & epidermal cell differentiation	stripes		48,5	6,2	yes	yes	yes	yes	yes	yes	ref 1
CG32159	CG32159	chitin-based cuticle development	stripes		50,1	12,6	yes	yes	yes	yes	yes	yes	ref 2
nyo	CG1499	regulation of embryonic cell shape	stripes	all gut	54,7	15,3	yes	yes	yes	yes	yes	yes	ref 1
CG4914	CG4914	proteolysis	stripes	hindgut	55,9	21,7	yes	ND	yes	yes	yes	yes	this work, FigS4
neyo	CG7802	regulation of embryonic cell shape	stripes	all gut	56,1	17,3	yes	yes	no	yes	yes	yes	ref 1
mey	CG12063	regulation of embryonic cell shape	stripes		57,1	7,8	yes	yes	yes	yes	yes	yes	ref 1
CG16798	CG16798	Extracellular matrix component	stripes		57,1	18,4	yes	yes	no	yes	yes	yes	ref 1
CHOp24	CG3564	protein secretion	stripes	salivary gland	59,0	27,0	ND	ND	no	yes	no	yes	
CG11905	CG11905	Microtubule associated complex	stripes	trachea	59,3	20,1	yes	no	yes	yes	no	yes	this work, FigS4
CG14356	CG14356	unknown	no	foregut	60,3	27,1	ND	ND	yes	no	no	no	
CG17211	CG17211	unknown	ND	ND	60,5	26,4	ND	ND	no	yes	yes	yes	
CG17780	CG17781	unknown	no	hindgut & anal pad	61,0	27,1	no	ND	no	yes	no	no	this work
mwh	CG13913	actin filament polarization & planar polarity	stripes		61,1	25,6	yes	yes	no	no	yes	yes	ref 1
CG30283	CG30283	proteolysis	stripes	atrium & adult eve PR	62,0	18,3	ND	ND	no	yes	no	yes	
CG4500	CG4500	mesoderm development	ND	ND	65,2	30,3	ND	ND	no	no	yes	yes	
spz6	CG9196	Toll signalling pathway	stripes		66,9	16,5	no	no	no	yes	no	yes	this work, FigS1
CG1273	CG1273	unknown	stripes	all gut & trachea	67,2	20,8	yes	yes	yes	yes	yes	yes	this work, FigS4
CG6785	CG6785	unknown	ND	ND	67,7	21,4	ND	ND	no	no	yes	yes	
CG10591	CG10591	unknown	stripes		67,8	21,7	yes	yes	yes	no	yes	yes	this work, FigS4
CG13698	CG13698	unknown	stripes	gut & salivary gland	68,4	29,3	yes	yes	yes	yes	yes	yes	this work, FigS4
CG9514	CG9514	oxidation reduction process	stripes		69,0	22,4	yes	yes	yes	yes	yes	no	this work, FigS4
CG17562	CG17562	oxidation-reduction process	no	oenocytes	69,2	25,3	no	ND	no	no	no	no	this work
f	CG5424	actin filament assembly & epidermal cell differentiation	stripes		70,3	26,0	yes	yes	yes	yes	yes	yes	ref 1
CG9184	CG9184	unknown	stripes	corpus cardiacum	70,9	15,7	yes	yes	yes	yes	yes	yes	this work, FigS4
CG12075	CG12075	Pleckstrin Homology-like domain	stripes	gut & salivary gland	71,5	33,4	yes	yes	yes	yes	yes	yes	this work, FigS4
tyn	CG17131	actin filament organization & cell matrix adhesion	stripes		72,9	22,2	yes	yes	yes	yes	yes	yes	ref 1
CG4678	CG4678	proteolysis	no	foregut & anal pad	73,4	36,3	ND	ND	yes	no	yes	yes	
CG13616	CG13616	unknown	no	intestine & anal pad	73,4	12,7	ND	ND	no	yes	no	no	
CG14756	CG14756	unknown	no	salivary gland	74,0	12,3	ND	ND	no	yes	no	no	
CG4666	CG4666	unknown	stripes	post spiracle	76,5	24,5	yes	yes	no	yes	yes	yes	this work, FigS4
CG4686	CG4686	unknown	ND	ND	77,0	33,7	ND	ND	no	no	no	no	
CG13082	CG13082	unknown	stripes	all gut	77,7	20,7	ND	ND	yes	yes	no	yes	
CG7173	CG7173	unknown	stripes		77,8	11,6	yes	yes	no	no	yes	yes	this work, FigS4
CG1632	CG1632	proteolysis	ND	ND	78,0	18,9	ND	ND	no	no	yes	yes	
Orct	CG6331	transmembrane transport	no	midgut & fat body	78,1	35,5	ND	ND	no	no	yes	no	
mas	CG15002	proteolysis	stripes	foregut & hindgut & trachea	78,1	31,7	yes	yes	no	yes	yes	yes	this work, FigS4
CG5039	CG5039	unknown	ND	ND	78,6	12,6	ND	ND	no	yes	yes	yes	
CG12017	CG12017	putative thioesterase	stripes		78,6	18,0	yes	yes	yes	yes	yes	yes	this work, FigS4
CG5873	CG5873	oxidation-reduction process	stripes	all gut & trachea	78,7	36,1	ND	ND	yes	yes	yes	yes	
CG8420	CG8420	endoplasmic reticulum	stripes		79,3	15,0	yes	no	yes	yes	yes	yes	this work, FigS4
CG11200	CG11200	metabolic process	stripes	trachea	79,8	32,0	ND	ND	no	no	yes	yes	
Cyp301a1	CG8587	oxidation-reduction process	stripes	trachea	80,3	34,3	ND	ND	yes	no	no	no	
CG42331	CG6879	oxidation-reduction process	ND	ND	80,4	9,8	ND	ND	yes	yes	yes	yes	
CG13822	CG13822	unknown	stripes	lymph gland	80,8	34,3	yes	yes	yes	no	yes	yes	this work, FigS4
CG12009	CG12009	chitin metabolic process	no	trachea	82,4	17,3	ND	ND	yes	yes	yes	yes	

CG8239	CG8239	isoprenoid biosynthesis	stripes	hindgut & anal pad	82,9	12,7	no	ND	no	no	no	no	this work
snRNP-U1	CG5454	mRNA splicing	no	ubiquitous	83,2	38,9	ND	ND	no	yes	no	yes	
CG1140	CG1140	ketone body catabolism	no	midgut & fat body	83,4	39,7	ND	ND	no	no	yes	no	
dyl	CG15013	actin filament organization & cell matrix adhesion	stripes	foregut & hindgut	85,3	16,1	yes	yes	yes	yes	yes	yes	ref 1
Hr46	CG33183	metamorphosis	no	ubiquitous	85,5	39,9	ND	ND	yes	yes	yes	yes	
vri	CG14029	tracheal system development	stripes	hindgut	85,6	30,5	ND	ND	yes	yes	yes	yes	
wus	CG9089	tracheal system development & extracellular matrix organization	stripes	all gut & trachea	86,1	12,6	no	ND	no	no	yes	yes	this work
ImpE1	CG32356	intrinsic to membrane, imaginal disc eversion	stripes	all gut	86,3	14,8	yes	yes	yes	yes	yes	yes	this work, FigS1
Plip	CG10371	protein dephosphorylation	ubiquitous	midgut & hindgut	86,7	32,5	ND	ND	no	no	yes	yes	
CG17672	CG11271	translation	no	ubiquitous	86,7	22,3	ND	ND	no	no	yes	yes	
CG32354	CG32354	unknown	stripes	all gut	86,8	42,3	ND	ND	no	yes	no	yes	
CG8306	CG8306	oxidation-reduction process	stripes	foregut & hindgut	86,8	41,3	ND	ND	no	no	no	yes	
CG10585	CG10585	unknown	stripes	all gut	87,1	27,3	ND	ND	no	yes	no	yes	
fw	CG1500	wing imaginal disc morphogenesis & cell adhesion	no		87,2	30,5	ND	ND	no	yes	yes	yes	
Obp99c	CG7584	sensory perception of chemical stimulus	no	fat body & amnioserosa	87,3	27,4	ND	ND	no	yes	no	yes	
CG5525	CG5525	mitotic spindle organization & microtubule organization	no	muscle system & hindgut	87,4	31,5	ND	ND	no	yes	no	no	
CG34007	Dm.2L.4959.0	unknown	ND	ND	87,5	25,6	ND	ND	no	no	yes	yes	
CG14470	CG14470	unknown	no	hindgut	87,5	39,1	ND	ND	no	no	no	no	
CG18249	CG18249	unknown	no	midgut & amnioserosa	87,6	28,4	ND	ND	no	no	yes	yes	
CG8386	CG8386	lateral inhibition	ubiquitous	salivary gland	87,9	41,5	ND	ND	no	no	no	no	
pwn	CG11101	EGF-like calcium binding, chaeta morphogenesis	ND	ND	88,0	29,8	ND	ND	no	yes	yes	yes	
PH4alpha SG1	CG31014	oxidation-reduction process & salivary gland development	no	salivary gland	88,1	39,7	ND	ND	no	no	no	no	
CG6415	CG6415	glycine catabolic process	no	fat body	88,2	37,1	ND	ND	no	yes	yes	yes	
cher	CG3937	actin binding	stripes	muscle system	88,3	40,5	yes	no	yes	yes	no	yes	this work, FigS4
CG2016	CG2016	unknown	stripes	all gut & trachea	88,4	22,9	ND	ND	no	yes	no	no	
Tb	CG5480	chitin-based cuticle development	stripes		88,6	21,5	yes	yes	no	yes	yes	no	this work, FigS4
CG10932	CG10932	mitotic spindle organization	no	midgut	88,8	34,6	ND	ND	no	no	no	yes	
scu	CG7113	ecdysone metabolism	no	midgut	89,1	39,8	ND	ND	no	no	no	no	
CG7860	CG7860	salivary gland autophagic cell death	no	midgut & crystal cells	89,7	15,8	ND	ND	no	yes	no	yes	
CG9356	CG9356	unknown	no		89,7	39,8	ND	ND	no	no	no	yes	
Hmgs	CG4311	hydroxymethylglutaryl-CoA synthase	stripes	foregut & hindgut	90,0	28,7	yes	no	no	no	yes	yes	this work, FigS4
CG11836	CG11836	proteolysis	ubiquitous		90,3	32,3	ND	ND	no	no	yes	no	
CG9503	CG9503	oxidation reduction process	no	dorsal trunk	90,4	22,4	ND	ND	no	no	yes	yes	
CG1837	CG1837	apoptotic cell clearance	no	ubiquitous	90,4	39,5	ND	ND	yes	no	yes	yes	
tw	CG12311	somatic muscle development	ND	ND	90,5	38,0	ND	ND	no	no	no	yes	
PH4alpha EFB	CG31022	oxidation reduction process	stripes	muscle system & plasmacytocytes	90,6	40,5	yes	yes	yes	yes	yes	yes	this work, FigS1
amd	CG10501	chitin-based cuticle development	ND	ND	90,6	38,1	ND	ND	yes	no	yes	yes	
Rab23	CG2108	GTPase, morphogenesis of a polarized epithelium	stripes	foregut	91,5	31,9	yes	yes	no	yes	yes	yes	this work, FigS4
Smn	CG16725	neuromuscular junction development	no	gonad	91,5	37,6	ND	ND	no	no	no	yes	
Pros28.1	CG3422	ubiquitin dependent proteolysis	no	ubiquitous	91,6	28,1	ND	ND	yes	no	yes	yes	
CG9175	CG9175	cell morphogenesis & protein secretion	no	midgut & hindgut& salivary gland	91,6	40,9	ND	ND	no	no	no	yes	
Rlc1	CG9378	translation	ND	ND	91,8	45,2	ND	ND	no	yes	no	yes	
Lip4	CG6113	lipide metabolism	no	amnioserosa	91,9	44,5	ND	ND	no	no	yes	no	
CG7840	CG7840	lipide metabolism	no		91,9	35,2	ND	ND	yes	no	no	no	
Gtp-bp	CG2522	protein secretion	stripes	midgut & hindgut& salivary gland	92,1	39,0	ND	ND	no	no	no	yes	
CG32250	CG32250	transport	ND	ND	92,2	41,7	ND	ND	no	no	no	no	
CG15506	CG15506	unknown	ND	ND	92,2	13,6	ND	ND	yes	yes	yes	yes	
TRAM	CG11642	protein targeting to membrane	stripes	salivary gland	92,3	36,0	ND	ND	yes	no	no	yes	
CG6704	CG6704	unknown	no	yolk nuclei	92,5	16,3	ND	ND	no	yes	no	no	
CG17218	CG17218	tracheal system development	stripes	all gut & anal pad	92,5	40,8	ND	ND	no	no	no	no	
CG4065	CG4065	unknown	no	midgut & muscle system	92,6	46,3	ND	ND	no	no	yes	yes	
mRpL46	CG13922	unknown	no	midgut & muscle system	92,7	42,8	ND	ND	no	no	no	no	

CG6180	CG6180	unknown	no	midgut	92,7	44,0	ND	ND	no	yes	no	yes	
T-cp1	CG5374	protein folding & mitotic spindle organization	no	ubiquitous	92,9	41,1	ND	ND	yes	no	yes	no	
CG13585	CG13585	unknown	no	garland cell	93,0	45,3	ND	ND	no	no	no	no	
nimb3	Dm.2L.8912.0	unknown	ND	ND	93,6	29,5	ND	ND	no	no	no	no	
CG2663	CG2663	transport	head	post spiracle	93,7	41,8	ND	ND	no	yes	yes	yes	
CG11786	CG11786	unknown	no	dorsal trunk	93,8	27,0	ND	ND	no	no	yes	no	
rt	CG6097	somatic muscle development & synaptic activity	ND	ND	94,0	25,7	ND	ND	no	yes	yes	yes	
CG13627	CG13627	unknown	no	trachea	94,2	16,2	ND	ND	no	yes	no	no	
Gmap	CG33206	protein targeting to Golgi	ND	ND	94,3	41,8	ND	ND	no	no	no	yes	
Rlc1	CG9378	translation	ND	ND	94,3	40,5	ND	ND	no	yes	no	yes	
CG6672	CG6672	transmembrane transport	ND	ND	94,4	42,0	ND	ND	no	yes	no	yes	
CG4702	CG4702	unknown	stripes	all gut	94,5	16,9	yes	yes	no	yes	yes	yes	ref 1
CG3831	CG3831	unknown	no	corpus allatum	94,5	37,3	ND	ND	yes	no	no	yes	
sec23	CG1250	chitin-based cuticle development, cell polarity & transport	stripes	salivary gland	94,5	41,8	yes	ND	no	no	yes	yes	this work, FigS4
CG31559	CG31559	redox homeostasis	stripes	foregut	94,8	14,3	yes	yes	no	yes	yes	yes	this work, FigS1
CG11771	CG11771	proteolysis	no	all gut & muscle system	95,0	45,4	ND	ND	yes	no	no	yes	
CG9095	CG9095	cell adhesion	stripes		95,4	36,9	yes	yes	yes	yes	yes	yes	this work, FigS4
--	GM01028	unknown	ND	ND	95,6	42,4	ND	ND	no	no	yes	no	
CG32039	CG32039	unknown	no		95,7	26,7	ND	ND	no	no	yes	yes	
CG1753	CG1753	cystein biosynthesis	no	midgut	96,0	26,3	ND	ND	no	yes	yes	yes	
CG4822	CG4822	unknown	ND	ND	96,3	43,6	ND	ND	yes	yes	yes	no	
CG8112	CG8112	unknown	no	yolk nuclei	96,8	30,2	ND	ND	no	yes	yes	yes	
ect	CG6611	tube development	stripes	oesophagus & anal pad	96,9	19,7	yes	no	yes	yes	yes	yes	this work, FigS4
CG15239	CG15239	unknown	stripes	salivary gland	97,0	19,4	ND	ND	yes	yes	yes	yes	
CG9689	CG9689	unknown	stripes	oesophagus & post spiracle	97,1	43,7	ND	ND	no	yes	no	yes	
mRpL45	CG6949	translation & transport	no	ubiquitous	97,2	22,6	ND	ND	no	no	no	yes	
CG8213	CG8213	proteolysis	ND		97,3	13,7	ND	ND	yes	yes	no	yes	
CG2263	CG2263	phenylalanyl-tRNA aminoacylation	no	ubiquitous	97,4	46,9	ND	ND	no	yes	yes	yes	
Rpb8	CG11246	transcription	no	midgut	97,8	45,1	ND	ND	no	no	yes	yes	
qua	CG6433	actin filament organization	stripes	all gut & lymph gland	97,8	43,1	no	no	yes	yes	no	yes	this work, FigS1
CG11227	CG13630	proteolysis	ND	ND	97,8	47,0	ND	ND	yes	no	no	no	
CG9205	CG9205	unknown	ND	ND	98,0	44,9	ND	ND	no	yes	no	yes	
Nf-YA	CG3891	transcription & phagocytosis	no	ubiquitous	98,3	39,6	ND	ND	no	yes	yes	yes	
kar	CG12286	transmembrane transport	no	midgut & amnioserosa	98,3	42,8	ND	ND	no	no	no	yes	
CG31717	CG31717	unknown	ND	ND	98,4	45,2	ND	ND	yes	yes	no	no	
Past1	CG6148	endocytosis	no	midgut & salivary gland	98,4	46,6	ND	ND	no	yes	yes	yes	
bw	CG17632	transport & eye pigment biosynthesis	no	malpighian tubule & fat body	98,4	37,4	ND	ND	no	yes	no	yes	
mRpL51	CG13098	translation	no	midgut & muscle system	98,5	39,3	ND	ND	no	no	no	yes	
pk	CG11084	planar polarity	no	ubiquitous	98,6	45,5	ND	ND	yes	yes	yes	yes	
CG5171	CG5171	trehalose biosynthesis	no	amnioserosa & yolk nuclei	98,9	37,8	ND	ND	no	yes	yes	yes	
CG13365	CG13365	unknown	no		98,9	43,2	ND	ND	no	yes	yes	yes	
CG5742	CG5742	neurogenesis	no	ubiquitous	98,9	43,8	ND	ND	no	no	no	yes	
KD	CG7125	protein phosphorylation & intracellular signal transduction	ND	ND	99,0	46,5	ND	ND	no	yes	yes	yes	
CG11127	CG11127	unknown	no		99,1	47,2	ND	ND	no	yes	no	yes	
Fib	CG9888	centrosome organization & RNA processing	no	ubiquitous	99,1	49,2	ND	ND	no	no	no	yes	
CG30423	CG30423	unknown	ND	ND	99,1	43,0	ND	ND	yes	yes	no	no	
CG3842	CG3842	oxidation reduction process	stripes	foregut & anal pad	99,2	14,1	ND	ND	no	no	yes	yes	
CG15743	CG15743	phosphatidylinositol phosphorylation	no	salivary gland	99,9	44,9	ND	ND	no	no	no	yes	

# : from BDGP and experimental approaches

Menoret et al.; Figure S3

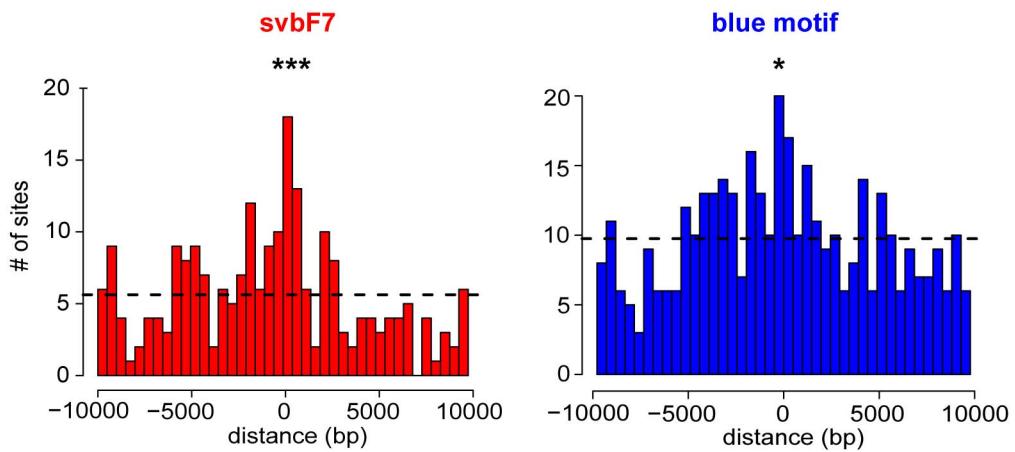
*wt**svb**wt**svb**wt**svb*

Menoret et al.; Figure S4A

**CisTargetX results for 150 Svb regulated genes**

Motif	Enrichment score	Logo	ROC	Candidate targets	All genes in top 1000
<a href="#">ken_SANGER_10_FBgn0011236</a>	7.37531372161641	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
ACCGTTA	6.84383162504572	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
ovo_SOLEXA_5_FBgn0003028	6.63292929690881	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">ken_SOLEXA_5_FBgn0011236</a>	6.42715336468385	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
→ <b>blue motif</b>	6.25223867875159	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
→ <b>svbF7</b>	5.65047866631769	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">M01101-I-OVO_Q6</a>	5.06408069648283	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">M00972-V-IRF_Q6_01</a>	5.05374217897479	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">AAAGTGANA</a>	5.0160914584977	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">Hr46_FlyReg_FBgn0000448</a>	4.85317836834593	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">Hr46</a>	4.85317836834593	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">Motif_1_f55t8-1x2</a>	4.49654237716018	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">M01138-V-RORA_Q4</a>	4.46741278968724	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">MA0389.1-SRD1</a>	4.46228639377529	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">M01126-P-BPC1_Q2</a>	4.43823176680381	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">M00028-I-HSF_01</a>	4.37308024685257	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">M00157-V-RORA2_01</a>	4.32682266768719	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">AWNTGGGTCA</a>	4.31307226795011	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">M00063-V-IRF2_01</a>	4.27540440233619	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">MA0050.1-IRF1</a>	4.24622337945276	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">MA0072.1-RORA_2</a>	4.17594546358957	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">RAGTGAAGT</a>	4.12277839428199	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">MA0302.1-GAT4</a>	3.91703675233069	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">M00029-F-HSF_01</a>	3.87588842394043	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">kni_NAR_FBgn0001320</a>	3.87240796116408	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">M00767-V-FXR_IR1_Q6</a>	3.8106854685787	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>
<a href="#">nAACwGTw</a>	3.75928434836453	<a href="#">LOGO</a>	<a href="#">ROC</a>	<a href="#">link</a>	<a href="#">link</a>

# Cross-correlation between conserved svbF7 or blue motif instances and ChIP peaks within Svb-regulated genes

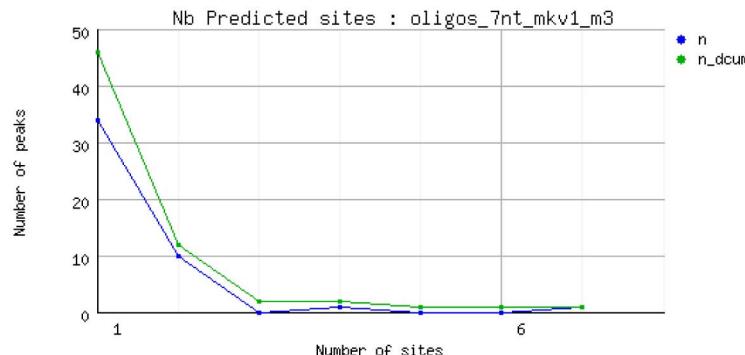
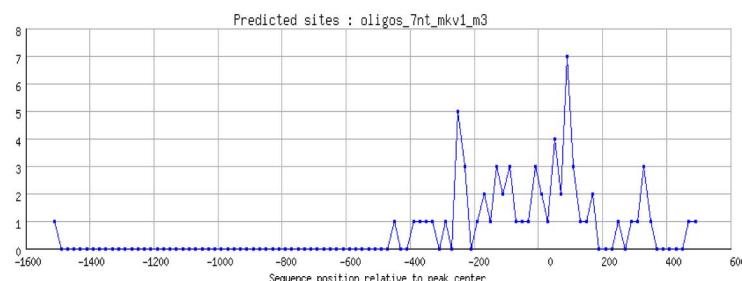
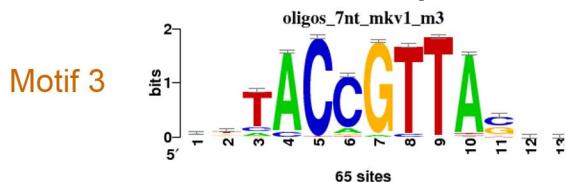


## RSA tools "peak-motifs" results from microarrays Svb regulated genes

### All discovered motifs

Motif 1	aCrCACACaCaC	Motif 6	wrCCGGwTAhv
Motif 2	atAwatAhATATdTatwtat	Motif 7	yaaATATAwATATAtat
Motif 3	rktACC GTTAsck	Motif 8	caYaCACACACACAc
Motif 4	srAGGCATGrg	Motif 9	wgCTTTTCasy
Motif 5	rgGGACTACwa		

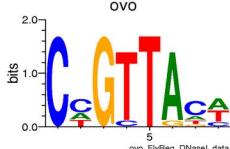
### Discovered motifs with motif comparison



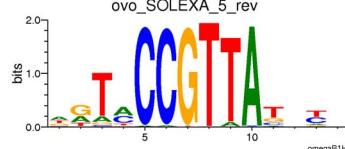
► jaspar\_core\_vertebrates : no matches

► FlyFactorSurvey : 3 matches

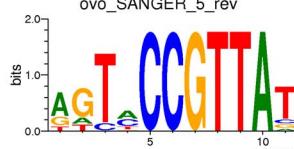
ovo\_FlyReg  
(aligned 6/9 bases)



ovo\_SOLEXA\_5  
(aligned 8/9 bases)



ovo\_SANGER\_5  
(aligned 8/9 bases)

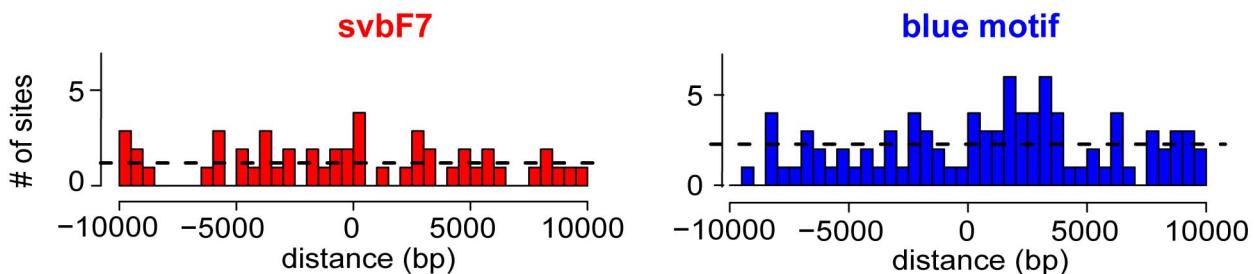


► DMMPMM\_drosophila : 1 match

ovo  
(aligned 5/9 bases)



### Cross-correlation between conserved svbF7 or blue motif instances and ChIP peaks within control genes

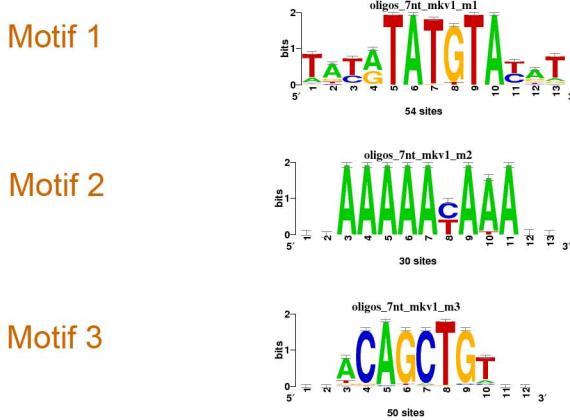


### RSA tools "peak-motifs" results from microarrays control genes

#### All discovered motifs

Motif 1	<b>tayrTATGTAyrt</b>	Motif 6	<b>raCAGCTGTy</b>
Motif 2	<b>rsAAAAAYAAAak</b>	Motif 7	<b>bataTACATAACata</b>
Motif 3	<b>sraCAGCTGTys</b>	Motif 8	<b>mmACAAmAACAAaAcrcA</b>
Motif 4	<b>wwkCTAGTrCCbt</b>		
Motif 5	<b>rcGCGCGCGCgy</b>		

#### Discovered motifs with motif comparison



Menoret et al.; Figure S5B

**Figure S1 : In situ Hybridization of epidermal genes (from BDGP) and motifs predictions candidate genes.**

**A:** identification of 21 additional Svb-dependent genes. Genes having an epidermal expression pattern were chosen from the BDGP expression pattern project and tested in *svb* mutant embryos. Their expression is decreased in *svb* mutants.

**B:** 36 epidermal genes showing no significant decrease of their expression in *svb* mutant embryos.

**C:** Motifs predictions in the set of 39 Svb downstream genes using cisTargetX: predicted motifs are ranked according to their enrichment and conservation. Related motifs are shown using the same color code. Ovo binding sites or motifs related to (CnGTT) are detected on top.

**D:** Motifs Predictions in epidermal control genes using cisTargetX. Motifs enriched in the set of 36 epidermal genes (not Svb-dependent) are ranked. Motifs associated to the epidermal transcription factors (grh, cEBP (vri in drosophila)... ) are found on top of the detected motifs, but not OvoQ6.

**Figure S2 : CRM activity and *de novo* motif discovery.**

Several fragments were selected through different parameters (single, multiple Ovo BS, evolutionary conserved or not) and assayed for *in vivo* CRM activity in transgenic assays.

**A:** expression pattern of 5 CRMs not predicted by cisTargetX on the basis of conserved Ovo clusters. These CRMs contain only a single Ovo binding site (sometimes not conserved) and are able to sustain *svb* dependent epidermal activity

**B:** number of conserved and non-conserved motifs (Dmel) in the various genomic fragment assayed for CRM activity *in vivo*. The numbers of conserved binding sites are listed. Note that svbF7 is more discriminative between positives and negatives, the blue and TTATGCAA motifs being less discriminant. Note that blue and TTATGCAA motifs are frequently located in a mutually exclusive manner. CisTarget prediction using SvbF7: In the set of 39 Svb downstream, SvbF7 PWM becomes the most significant detected motif. CRM prediction leads to the detection of less negative (in comparison with Fig2: not detected are not shown)) and prediction of few new positives (Emin, EminB, 32159)

**C:** on top, schematic representation of CRM architecture (binding sites location and orientation). Open boxes indicate non-conserved sites. Note that several grammars are found (variation in the type, number, orientation of the binding sites). Bottom: svbF7+blue or svbF7+TTATGCAA motifs combinations perform equally to predict TGs.

**Figure S3 : High confidence list of genes regulated by Svb from microarrays experiments.**

From microarrays analysis, genes are selected according to a significant level of expression in wild type condition. From this set of 5000 genes, 150 of them display a decrease of expression in *svb* mutant and *pri* mutant embryos. Genes are ranked according to their respective level of expression in *svb* mutant embryos compared to the wild type. % of residual expression relative to wt is indicated in *pri* and *svb* mutants. Putative gene function is indicated. Validation of downregulated genes by In Situ Hybridization is performed in *svb* mutants and in ectopic *svb* expression. For each gene, expression pattern, predictions for svbF7 and blue motifs, and ChIP peak in a 5kb window are mentioned. Expression pattern is indicated when existing. Co-occurrence of in silico prediction and ChIP are shown, giving rise to high confident *svb* direct target genes. In green are summarized the *svb*-regulated genes. In grey color bacground, genes tested but not *svb*)dependent.

**Figure S4 : In situ Hybridization and motifs predictions in svb downstream set defined from genome wide approach.**

**A:** validation of new Svb downstream genes by In situ Hybridization experiments of microarrays. 21 genes downregulated in *svb* and *pri* mutants from microarrays were assayed in wild type embryos (left panels) and tested for residual expression in *svb* mutant embryos (right panels).

**B:** cisTargetX predicted motifs. svbF7 and blue motif are highly ranked using this set of downstream gene.

**Figure S5 : Motif analysis of svb ChIP peaks associated of Svb regulated (A) and non-regulated genes (microarrays) (B).**

On top : cross-correlation between conserved svbF7 or blue motif instances and Svb ChIP-Seq peaks among Svb-regulated (A) and control set (B) of genes

Bottom: Sequences of peaks associated to Svb regulated genes and non-regulated genes (5kb upstream and downstream + introns) are subjected to a de novo motif discovery approach using the RSAT “peak motif” software. Discovered motifs are listed and subjected to motif comparison.

**A:** For peaks associated to *svb* regulated genes, Motif 3 is clearly related to svbF7 and to the Ovo PWM previously reported. The distributions of the predicted sites respective to the peak of the ChIP fragments are shown (left graph). The number of sites (clusters) found in ChIP fragments is also indicated (right graph). Motif9 appears related to the blue motif. Bottom: Logos of PWM for known TFs. Note that all are Ovo “signature”

**B:** For peaks associated to *svb* non regulated genes, we cannot find a motif that corresponds to svbF7 motif, indicating that svbF7 is specific of Svb bound fragments.

## **SUPPLEMENTARY METHOD**

### **De novo motif generation**

We used the phylogeny-based *de novo* motif generation algorithm described in [Rouault et al. 2011], available on the website (<https://github.com/hrouault/Imogene/>). The 14 positive CRM (Fig.S2) were used as the training set for the algorithm and scanned for conserved motifs as described in [Rouault et al, 2010 ]. The score threshold for motif generation, which sets the searched PWM information content, was varied from 7 to 13 bits in different runs of the algorithm, with a motif width set to 10 bp. In each run, the 5 highest scoring motifs were kept. This resulted in a large number of different motifs. In order to find the most discriminative ones, the 27 negative CRM (Fig. S2) were used as a negative set.

The positive and negative CRM sets were used to evaluate the False Negative Rate (FNR) and False Positive Rate (FPR) of the motifs generated by the algorithm. For each created motif, the two sets were scanned for conserved instances with a scanning threshold varied between 7 and 13 bits. For each threshold, FPR and FNR were computed as the proportion of Positive (resp. Negative) CRMs with at least one conserved instance for the motif with a score higher than the threshold. The best motifs, shown as red and blue dots, were selected based on the minimization of both FPR and FNR in a Pareto plot, as shown in Fig. 4B. These motifs were generated with a threshold of 10.1 bits and were scanned with optimal thresholds of 10.1 and 8.7 bits respectively.

### **Genome wide ranking of enhancers and genes.**

In order to rank enhancers genome wide, we followed the method presented in [Rouault et al, 2010 ]. Coding sequences as well as the training set used for motif generation were masked . Conserved instances of *de novo* svbf7 and blue motifs at optimal threshold were then determined genome wide. Genomic fragment of 1Kbp were scored according to the additive Poisson score introduced in [Rouault et al., 2011] using the negative enhancers as a background set of intergenic fragment. Around each of the determined motif instances, the optimal scoring 1Kbp genomic fragment was defined as a putative enhancer. Each putative enhancer was associated to the nearest gene transcription start site. Each gene was attributed the highest score among its associated enhancers, or 0 if it had no associated enhancers. In order to assess the predictive power of different motif combinations as shown in Fig. 5B, the first 100 genes from the svb affymetrix data were used as True Positives, and a set of 96 negative genes were chosen for False Positive evaluation. A ROC plot was built using results from svbf7 alone (red curve) and the svbf7 and blue motif combination (blue curve). The same procedure was applied to ovoQ6 alone and is shown as the green curve.

### **Microarrays procedure.**

Biotinylated cRNA targets were prepared, starting from 200 ng of total RNA, using the MessageAmp™ Premier RNA Amplification Kit (Ambion CAT# AM1792), according to the manufacturer recommendations. Following fragmentation, 6.5 µg of cRNAs were hybridized for 16 hours at 45°C on GeneChip® Drosophila Genome 2.0 Array interrogating over 18,500 transcripts (Affymetrix, Santa Clara, CA). The chips

were washed and stained using the GeneChip® Fluidics Station 450 and scanned using the GeneChip® Scanner 3000 7G according to Affymetrix recommendations. Raw data (.CEL Intensity files) were extracted from the scanned images using the Affymetrix GeneChip® Command Console (AGCC) version 3.2. CEL files were further processed with Affymetrix Expression Console software version 1.1 to calculate probeset signal intensities using the statistics-based Affymetrix algorithms MAS-5.0 with default settings and global scaling as normalization method. The trimmed mean target intensity of each chip was arbitrarily set to 100.

### Supplementary information to Fig1

#### List of all genes analyzed by in situ hybridization and their expression pattern:

<u>CG number</u>	<u>symbol</u>	<u>expression in epidermis</u>	<u>other expression</u>	<u>svb dependent</u>	<u>ectopic</u>
CG10175	CG10175	Ventral & Lateral & Dorsal	salivary glands	yes	yes
CG11175	CG11175	Ventral	ubiquitous epidermis	yes	yes
CG12063	mey	Ventral & Lateral & Dorsal	no	yes	yes
CG12814	CG12814	Ventral & Lateral & Dorsal	ubiquitous epidermis	yes	yes
CG13209	sha	Ventral & Lateral & Dorsal	no	yes	yes
CG13913	mwh	Ventral & Lateral & Dorsal	no	yes	yes
CG14395	CG14395	Ventral & Lateral & Dorsal	no	yes	yes
CG1499	nyo	Ventral & Lateral & Dorsal	no	yes	yes
CG15005	CG15005	Lateral	ubiquitous epidermis	yes	yes
CG15013	dyl	Ventral & Lateral & Dorsal	no	yes	yes
CG15022	CG15022	Lateral & Dorsal	no	yes	yes
CG1520	wsp	Ventral & Dorsal	no	yes	yes
CG15335	cyr	Lateral & Dorsal	no	yes	yes
CG15589	CG15589	Ventral & Lateral & Dorsal	trachea	yes	yes
CG16798	CG16798	Ventral & Lateral & Dorsal	no	yes	yes
CG17058	Peritrophin-A	Ventral	ubiquitous epidermis	yes	yes
CG17131	try	Ventral & Lateral & Dorsal	no	yes	yes
CG17905	CG17905	Ventral	no	yes	yes
CG18525	Spn5	Ventral	no	yes	yes
CG2560	crp11A	Ventral & Lateral & Dorsal	no	yes	yes
CG2666	kkv	Ventral & Lateral	ubiquitous epidermis	yes	yes
CG31022	PH4aEFP	Ventral & Lateral & Dorsal	fat body	yes	yes
CG31559	CG31559	Ventral & Lateral & Dorsal	no	yes	yes
CG31973	CG31973	Ventral & Lateral & Dorsal	ubiquitous epidermis	yes	yes
CG32139	Sox21b	Ventral	nervous system	yes	yes
CG32159	dsc73	Ventral & Lateral & Dorsal	no	yes	yes
CG32356	ImpE1	Ventral	trachea	yes	yes
CG32694	CG32694	Ventral & Lateral & Dorsal	no	yes	yes
CG32858	sn	Ventral & Lateral & Dorsal	nervous system	yes	yes
CG3757	y	Ventral	no	yes	yes
CG4376	Actn	Ventral	trachea	yes	yes
CG4702	CG4702	Ventral & Lateral & Dorsal	ubiquitous epidermis	yes	yes
CG5424	f	Ventral & Dorsal	no	yes	yes
CG5847	zye	Ventral	no	yes	yes
CG7356	Tg	Ventral	no	yes	yes
CG7802	neo	Ventral & Lateral & Dorsal	no	yes	yes
CG8303	CG8303	Ventral & Lateral & Dorsal	no	yes	yes
CG9369	m	Ventral & Lateral & Dorsal	no	yes	yes
CG9517	CG9517	Ventral	no	yes	yes
CG10076	spir	Ventral	nervous system	no	ND
CG10244	Cad96Ca	Ventral & Lateral	no	no	ND
CG10917	fj	Ventral & Lateral & Dorsal	no	no*	no
CG12008	kst	Ventral & Lateral & Dorsal	trachea	no*	no
CG13699	CG13699	Ventral & Lateral & Dorsal	ubiquitous epidermis	no	ND
CG14626	CG14626	Ventral	ubiquitous epidermis	no	ND
CG14643	CG14643	Ventral	ubiquitous epidermis	no	ND
CG14830	CG14830	Ventral & Lateral & Dorsal	no	no	no
CG15080	CG15080	Ventral & Lateral & Dorsal	ubiquitous epidermis	no	ND
CG15282	CG15282	Ventral & Lateral & Dorsal	no	no	ND

<b>CG15598</b>	<i>osi17</i>	<b>Ventral &amp; Lateral &amp; Dorsal</b>	<b>ubiquitous epidermis</b>	<b>no</b>	<b>ND</b>
<b>CG16885</b>	<i>CG16885</i>	<b>Ventral</b>	<b>trachea</b>	<b>no</b>	<b>no</b>
<b>CG17786</b>	<i>CG17786</i>	<b>Ventral &amp; Lateral &amp; Dorsal</b>	<b>no</b>	<b>no</b>	<b>ND</b>
<b>CG1869</b>	<i>Cht7</i>	<b>Ventral &amp; Lateral &amp; Dorsal</b>	<b>trachea</b>	<b>no</b>	<b>ND</b>
<b>CG2467</b>	<i>CG2467</i>	<b>Ventral &amp; Lateral &amp; Dorsal</b>	<b>ubiquitous endoderm</b>	<b>no</b>	<b>ND</b>
<b>CG2767</b>	<i>CG2767</i>	<b>Ventral &amp; Lateral &amp; Dorsal</b>	<b>ubiquitous endoderm</b>	<b>no*</b>	<b>no</b>
<b>CG30092</b>	<i>jbug</i>	<b>Ventral &amp; Lateral &amp; Dorsal</b>	<b>trachea</b>	<b>no*</b>	<b>no</b>
<b>CG32137</b>	<i>CG32137</i>	<b>Ventral</b>	<b>no</b>	<b>no</b>	<b>ND</b>
<b>CG32239</b>	<i>Gef64C</i>	<b>Ventral &amp; Lateral &amp; Dorsal</b>	<b>no</b>	<b>no*</b>	<b>ND</b>
<b>CG3244</b>	<i>CG3244</i>	<b>Ventral &amp; Lateral &amp; Dorsal</b>	<b>no</b>	<b>no</b>	<b>ND</b>
<b>CG33196</b>	<i>dp</i>	<b>Ventral &amp; Lateral &amp; Dorsal</b>	<b>no</b>	<b>no*</b>	<b>no</b>
<b>CG3541</b>	<i>pio</i>	<b>Ventral &amp; Lateral &amp; Dorsal</b>	<b>no</b>	<b>no*</b>	<b>no</b>
<b>CG4761</b>	<i>knrl</i>	<b>Ventral &amp; Lateral</b>	<b>trachea</b>	<b>no</b>	<b>ND</b>
<b>CG5058</b>	<i>grh</i>	<b>Ventral &amp; Lateral &amp; Dorsal</b>	<b>hémocytes</b>	<b>no</b>	<b>ND</b>
<b>CG5065</b>	<i>CG5065</i>	<b>Ventral &amp; Lateral &amp; Dorsal</b>	<b>ubiquitous epidermis</b>	<b>no</b>	<b>ND</b>
<b>CG5756</b>	<i>CG5756</i>	<b>Ventral &amp; Lateral &amp; Dorsal</b>	<b>ubiquitous epidermis</b>	<b>no</b>	<b>ND</b>
<b>CG6433</b>	<i>qua</i>	<b>Ventral &amp; Lateral &amp; Dorsal</b>	<b>no</b>	<b>no*</b>	<b>no</b>
<b>CG7100</b>	<i>CadN</i>	<b>Ventral &amp; Lateral &amp; Dorsal</b>	<b>nervous system</b>	<b>no*</b>	<b>no</b>
<b>CG7337</b>	<i>CG7337</i>	<b>Ventral &amp; Lateral &amp; Dorsal</b>	<b>ubiquitous epidermis</b>	<b>no</b>	<b>ND</b>
<b>CG9196</b>	<i>CG9196</i>	<b>Ventral &amp; Lateral &amp; Dorsal</b>	<b>no</b>	<b>no*</b>	<b>no</b>
<b>CG9889</b>	<i>yellow-d</i>	<b>Lateral &amp; Dorsal</b>	<b>no</b>	<b>no*</b>	<b>no</b>
<b>CG9990</b>	<i>CG9990</i>	<b>Ventral &amp; Lateral &amp; Dorsal</b>	<b>trachea</b>	<b>no*</b>	<b>no</b>
<b>CG8170</b>	<i>CG8170</i>	<b>Ventral &amp; Lateral &amp; Dorsal</b>	<b>ubiquitous epidermis</b>	<b>no*</b>	<b>no</b>
<b>CG17045</b>	<i>ye -e3</i>	<b>Lateral &amp; Dorsal</b>	<b>no</b>	<b>no</b>	<b>ND</b>
<b>CG17914</b>	<i>CG17914</i>	<b>Ventral</b>	<b>gut</b>	<b>no*</b>	<b>no</b>
<b>CG31558</b>	<i>CG31558</i>	<b>Ventral &amp; Lateral &amp; Dorsal</b>	<b>ubiquitous epidermis</b>	<b>no*</b>	<b>no</b>

\* : it was sometimes difficult to conclude whether there was or not a significant decrease in svb mutants; in this case, a lack of responsiveness to svb ectopic expression was analyzed  
ectopic svb expression was performed as described in Chanut et al., 2006 by  
ectopically expressing svb in naked cells (wgGAL4 > uasSvb<sup>ACT</sup>)

ND: not determined

expression pattern are listed from BDGP and this  
study

### Supplementary Information to Figure 2 and 3

<b>CRM name</b>	<b>related gene</b>	<b>genomic position (2006)</b>				<b>activity</b>
EminB	miniature	chrX	11654097	11655097		positive
Emin	miniature	chrX	11650982	11651144		positive
155589	CG15589	chr3R	2027050	2028050		positive
17058	Peritrophin-A	chrX	20113835	20115016		positive
32159	dsx-c73A	chr3L	16435341	16436341		positive
Cyra	cypher	chrX	8019397	8020397		positive
dyl2	dusky like	chr3L	4298268	4299468		positive
sha1	shavenoid	chr2R	7209659	7210257		positive
sha3	shavenoid	chr2R	7215630	7216294		positive
tyn2	tryunity	chrX	77484	78384		positive
4702B	CG4702	chr3R	7951250	7952250		positive
31559	CG31559	chr3R	1977200	1978200		positive
nyo1	nyobe	chr3R	27384231	27384921		positive
snE1	singed	chrX	7869678	7870390		positive
32356	ImpE1	chr3L	8370153	8371153		negative
nyo2	nyobe	chr3R	27381479	27382574		negative
sox21b	sox21b	chr3L	14121641	14122852		negative
f4	forked	chrX	17162096	17163096		negative
f5	forked	chrX	17158996	17160096		negative
4702	CG4702	chr3R	7950428	7950586		negative
1499-1	nyobe	chr3R	27370295	27370415		negative
12063	morpheyus	chr3R	27320842	27321073		negative
15013-1	dusky like	chr3L	4299768	4299927		negative
15013-2	dusky like	chr3L	4300420	4300715		negative
CyRB	cypher	chrX	8017597	8018797		negative
dyl1	dusky like	chr3L	4303968	4304768		negative
dyl3	dusky like	chr3L	4305468	4306468		negative
f1	forked	chrX	17153478	17154756		negative
f2	forked	chrX	17159378	17160246		negative
neyo	neyo	chr3R	25647300	25648300		negative
tyn1	tryunity	chrX	86343	87613		negative
snE5	singed	chrX	7871996	7872659		negative
sn-enh1	singed	chrX	7864407	7869657		negative
snH5	singed	chrX	7868528	7868978		negative
snB2	singed	chrX	7869989	7870390		negative
nyo3	nyobe	chr3R	27377275	27378274		negative
sha-int	shavenoid	chr2R	7216771	7220065		negative
snP	singed	chrX	7862910	7864103		negative
snE4	singed	chrX	7871432	7872096		negative

### Supplementary information to Fig6

**A: Genes used as control from microarray experiments: these genes show no variation of their expression in svb and pri mutants.**

Using microarrays analysis, genes with significant level of expression in wild type condition were used. Among these 5000 genes, 100 of them with a  $0.8 \leq \text{pvalue} \leq 1$  associated to *svb* and *pri* mutant are selected. Gray line indicates a gene that is validated as a true *Svb* non target gene by *in situ* hybridization. For each gene, expression pattern, predictions for *svbF7* and blue motifs, and ChIP peak in a 5kb window are mentioned.

name	CG Number	expression pattern	svb*	pri*	chip in 5kb
robo	CG13521	ND	91,22	73,45	no
CG8090	CG8090	ND	85,52	115,10	yes
blow	CG1363	not epidermal	101,79	104,82	no
ush	CG2762	ep stripes	100,46	98,55	yes
RpS30	CG15697	ND	115,96	77,01	no
Bap55	CG6546	not epidermal	108,19	109,38	yes
lack	CG4943	ND	109,29	111,22	no
ttk	CG1856	ep stripes	97,50	80,48	yes
CG12164	CG12164	ND	83,20	93,45	no
CG3305	CG3305	ND	88,29	79,96	yes
CG11877	CG11877	not epidermal	113,94	118,58	no
CG14229	CG14229	not epidermal	105,43	109,87	no
Rga	CG2161	not epidermal	93,53	108,09	yes
Rpb5	CG11979	not epidermal	81,38	91,59	no
bsf	CG10302	ND	98,81	94,84	no
hkl	CG10473	not epidermal	97,76	103,84	yes
CG15099	CG15099	ND	88,57	94,68	yes
gry	CG17569	ND	97,01	89,65	no
slik	CG4527	ND	90,39	88,72	yes
trr	CG3848	ND	80,15	106,49	yes
CG14442	CG14442	ND	111,93	120,36	no
CG12375	CG12375	not epidermal	103,42	122,64	no
RpS27	CG10423	not epidermal	106,16	76,13	no
cenG1A	CG31811	not epidermal	108,36	102,03	no
Rgl	CG8865	not epidermal	137,42	100,20	yes
MBD-R2	CG10042	not epidermal	99,57	106,58	no
CG6230	CG6230	ND	95,47	123,11	no
kis	CG3696	ND	112,50	96,17	yes
CG4210	CG4210	ND	91,21	118,02	yes
betaTub56D	CG9277	ep stripes	105,75	105,22	no
RhoGAP1A	CG40494	ND	73,46	113,54	yes
CG9293	CG9293	ND	99,22	92,58	yes
CG10731	CG10731	ND	97,43	96,07	yes
CG2249	CG2249	ND	97,42	83,94	no
CG18549	CG18549	not epidermal	98,92	90,20	yes
CG9776	CG9776	ND	107,81	92,47	no
Bre1	CG10542	ND	108,66	134,50	no
vsg	CG16707	not epidermal	113,76	107,51	yes
CBP	CG1435	not epidermal	102,78	91,76	yes

Ufd1-like	CG6233	not epidermal	112,22	110,15	no
CG8928	CG8928	ND	91,78	113,34	no
Ald	CG7643	not epidermal	84,52	91,17	no
Atg18	CG7986	not epidermal	100,61	98,82	no
Chd1	CG3733	ND	97,28	94,33	no
mRpS11	CG5184	not epidermal	114,70	108,13	no
CG6852	CG6852	ND	111,03	109,18	yes
Krn	CG32179	not epidermal	102,68	108,51	yes
CG7852	CG7852	ND	106,54	113,74	no
CG8931	CG8931	not epidermal	110,33	111,09	yes
mRpL33	CG3712	ND	105,01	112,98	yes
RanBPM	CG42236	ND	124,37	103,44	no
CG8289	CG8289	not epidermal	101,82	109,37	no
CG5931	CG5931	not epidermal	123,35	92,97	no
CG32267	CG32267	ND	95,97	115,07	no
CG32164	CG32164	not epidermal	98,31	125,93	no
CG10365	CG10366	not epidermal	100,39	101,34	yes
kst	CG12008	ep stripes	127,31	103,42	yes
mRpS11	CG5184	not epidermal	114,70	108,13	no
CG2249	CG2249	ND	97,42	83,94	no
Ssdp	CG7187	not epidermal	111,89	87,21	no
CG17082	CG17082	ND	91,18	94,01	yes
CG4841	CG4841	ND	110,54	95,91	no
Stlk	CG40293	not epidermal	105,66	87,23	no
CG9715	CG9715	ND	119,34	97,89	yes
Rap2l	CG3204	ND	108,16	107,35	yes
drl	CG17348	ep stripes	115,07	78,43	yes
CG8878	CG8878	not epidermal	103,04	96,89	yes
Trim9	CG31721	not epidermal	96,29	91,91	yes
CG9917	CG9917	not epidermal	126,61	102,54	no
CG12006	CG12006	not epidermal	114,23	113,87	yes
crp	CG7664	not epidermal	82,88	111,58	yes
Cad87A	CG6977	ND	109,50	112,09	no
CG7028	CG7028	not epidermal	101,44	109,71	yes
zormin	CG33484	ND	130,13	114,51	yes
bbx /// waw	CG1414	ND	101,98	109,42	yes
CG1965	CG1965	ND	90,48	108,38	yes
CG1371	CG1371	not epidermal	115,46	100,11	yes
RpS30	CG15697	not epidermal	115,96	77,01	no
CG32676	CG32676	ND	90,95	93,01	yes
msn	CG16973	ND	114,08	115,00	yes
CG31108	CG31108	not epidermal	103,94	105,91	no
CG2918	CG2918	epidermal ubiquitous	103,01	88,58	no
mmy	CG9535	not epidermal	95,52	97,92	no
Nat1	CG3845	not epidermal	108,49	82,47	no
Taf1	CG17603	not epidermal	107,83	109,83	no
CG5869	CG5869	ND	89,39	108,39	yes
CG13284	CG13284	not epidermal	100,89	92,66	yes
CG12404	CG12404	ND	104,22	90,36	yes
tra2	CG10128	not epidermal	95,99	79,72	yes
CG6406	cg6406	not epidermal	90,56	87,00	yes
Fip1	CG1078	ND	104,96	87,54	no
Ubp64E	CG5486	not epidermal	130,11	101,59	no
CG14636	CG14636	ep stripes	112,31	88,23	no
gp210	CG7897	ND	110,61	106,95	no
dbr	CG11371	ND	139,91	126,84	no
bru-2	CG43065	ND	118,64	112,13	no

CG3493	CG3493	ND	126,41	109,19	yes
betaggt-I	CG3469	ND	110,78	130,95	yes
gek	CG4012	ND	110,94	96,43	no
bip2	CG2009	not epidermal	146,43	130,23	yes

\* : expression in mutant / WT (%)

Svb non-regulated genes  
analysed par Hybridization in situ