LncRNA mediated regulation of aging pathways in *Drosophila melanogaster* during dietary restriction

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ABSTRACT

Dietary restriction (DR) extends lifespan in many species which is a well-known phenomenon. Long non-coding RNAs (IncRNAs) play an important role in regulation of cell senescence and important age-related signaling pathways. Here, we profiled the IncRNA and mRNA transcriptome of fruit flies at 7 day and 42 day during DR and fully-fed conditions, respectively. In general, 102 differentially expressed IncRNAs and 1406 differentially expressed coding genes were identified. Most informatively we found a large number of differentially expressed IncRNAs and their targets enriched in GO and KEGG analysis. We discovered some new aging related signaling pathways during DR, such as hippo signaling pathway-fly, phototransduction-fly and protein processing in endoplasmic reticulum etc. Novel IncRNAs *XLOC_092363* and *XLOC_166557* are found to be located in 10 kb upstream sequences of *hairy* and *ems* promoters, respectively. Furthermore, tissue specificity of some novel IncRNAs had been analyzed at 7 day of DR in fly head, gut and fat body. Also the silencing of IncRNA *XLOC_076307* resulted in altered expression level of its targets including *Gadd45* (involved in FoxO signaling pathway). Together, the results implicated many IncRNAs closely associated with dietary restriction, which could provide a resource for IncRNA in aging and age-related disease field.

INTRODUCTION

Dietary restriction (DR) is the best and nongenetic antiaging strategy without malnutrition, aiming to intervene on environmental factors and reduce the risk of many age-related diseases [1]. DR has been shown to extend lifespan and improve health with the most consistent non-pharmacological intervention during aging in diverse organisms, such as flies [2], yeast [3], nematodes [4] and rodents [5]. These universal effects suggest that there should be some conserved common potential genetic pathways and biochemical processes by virtue of which different organisms delay aging in response to DR [2]. Extensive studies have been devoted to discover such underlying mechanisms of longevity assurance in DR of model organisms including primates (even human) [6]. Previous studies involving whole-genome gene expression analysis have

shown that a number of genes and biological pathways differ between organisms fed on DR and normal-diet [2, 7]. A large number of differentially expressed genes (DEGs) are implicated in regulatory mechanism of DR and molecular pathways, such as lipid metabolism, fatty acid metabolism, immune response, and oxidative phosphorylation are identified as being highly responsive to changes in diet composition [8]. Therefore, coding mRNA genes and signaling pathways involved in DR condition have been extensively studied [9]. The long non-coding RNA (lncRNA) is the key regulatory factor which also participates in the modulation of cell senescence and aging-related disease [10]. Pathologies implicating lncRNAs function include [11], neurodegenerative disorders cancer [12], cardiovascular pathologies [13] and metabolic diseases [14]. Some evidences supporting the role of lncRNAs in age-associated molecular processes are emerging

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recently, for instance, lncRNAs *TERC* and *TERRA* are found to be involved in chromosomal instability and short telomeres, which may contribute to premature senescence and aging [15]. While lncRNAs have significant functions and effect on the course of aging, the number of lncRNAs and their functional implications in anti-aging process are not yet well validated during nutritional interventions especially during DR.

RNA-seq techniques have driven the lncRNAs research in the recent years yielding significant insights in various model species [16]. As the classic model organism, RNA-seq data of coding and non-coding RNA, at different developmental stages, tissue samples, and whole-fly samples treated with environmental perturbations of *D. melanogaster* have been reported [17, 18]. Interestingly fruit-fly being the ideal model organism for aging related studies can be used to understand the role of lncRNAs, which have not yet been explored for their role in aging. We analyzed RNA-seq data including mRNA and lncRNAs, from a set of DR and fully fed samples at 7 day and 42 day, respectively. Present data provides a deep understanding of the dynamic expression of lncRNAs in D. melanogaster transcriptome under DR and fully fed conditions. Our analysis revealed a large number of differentially expressed lncRNAs transcript isoforms and their target genes during DR that spanned most of the genome and can provide valuable insights into aging and age-related disease research field.

RESULTS

Dietary restriction extends lifespan

Similar to our previous report [19], the fruit fly females,

on DR food had median lifespans extended by 21.88% in comparison to fully fed flies in the present study (Fig. 1a). Fecundity of fruit flies in DR group became lower than in fully fed group (P<0.01, Fig. 1b). Flies at day 7 have been considered as young flies in many previous reports [20, 21] and the flies in the present study began to die at day 42. Thus, 7 day and 42 day are the most appropriate time points for carrying out aging specific analysis involving expression patterns of transcriptional dynamics through lncRNA analysis.

Transcriptome profiles of DR and fully fed flies

A total of 86.78 GB of raw sequence data was produced yielding 7.26 billion strand-specific raw reads (Table S1). Value of Q20, Q30 and GC content were not significantly different among samples. After quality check, 95.79% of clean reads were obtained and were aligned to the D. melanogaster genome from FlyBase (Dmel Release 6, http://FlyBase.org/), assigning 87.7% reads to the mRNA sequences (Fig. 2a). The read density (log2) was distributed mainly in 2L, 2R, 3L, 3R and X chromosomes (Fig. 2b). FPKM (fragments per kilobase of transcript sequence per millions base pairs sequenced) distribution was not significantly different in expression levels between lncRNAs and mRNA in DR and fully fed flies ($P \le 0.05$, Fig. 2c).

In total, 3826 redundant lncRNA transcripts and 30413 redundant mRNA transcripts were identified in this study. After BLASTing with FlyBase lncRNA (Dmel_Release_6), these 3826 transcripts corresponded to a total of 134 non-redundant known lncRNAs (Dataset S1) and 1726 non-redundant novel lncRNA (Dataset S2, Fig. 2d and 2e). In those novel lncRNAs,





the number of large intergenic noncoding RNA, intronic transcript lncRNAs and antisense lncRNAs were 821, 695 and 210, respectively. A total of 248 non-redundant novel mRNA transcripts (Dataset S3, Fig. 2f) were recognized when 30413 mRNA transcripts were BLASTed with *D. melanogaster* genome from FlyBase, and the remaining 30165 transcripts aligned to 13917 genes.

Differentially expressed genes analysis

Differentially expressed genes (DEGs) had been analyzed between four comparative groups (Dataset S4), including 7 day DR vs 7 day fully fed, 42 day DR vs 42 day fully fed, 7 day DR vs 42 day DR, 7 day fully fed vs 42 day fully fed. In total, 102 differentially expressed lncRNAs (25 known and 77 novels) and 1406 coding genes were identified between these four comparative groups. A total of 719 differentially expressed transcripts were the most abundant as measured at 7 day between DR and fully fed group, including 30 lncRNAs and 689 coding mRNA genes. Also 39 differentially expressed lncRNAs and 571 differentially expressed coding genes were present at 42 day of DR when compared to fully fed group (Fig. 3a). Out of those differentially expressed transcripts, five common differentially expressed lncRNAs and 204 common coding genes appeared at both 7 day and 42 day between DR and fully fed groups (Fig. 3b, 3c).

Among five differentially expressed lncRNAs, *CR31781* and *XLOC_014901* were up-regulated while *XLOC_189941* was down-regulated in DR when compared to fully fed group at both time frames. Another two lncRNAs (*XLOC_189909* and *XLOC_228709*) were down-regulated at 7 day and up-regulated at 42 day in DR when compared to fully fed group.

In order to validate the RNA-seq analysis finding, we randomly selected 28 differentially expressed lncRNAs and 61 mRNA coding genes, and analyzed their expression using quantitative real-time PCR (qPCR) analysis. All the genes were having expression levels in concordance with the RNA-seq results in different comparison groups with varying levels of significance ($P \le 0.05$) (Dataset S5).

Known IncRNA

When compared to the known lncRNAs existing in FlyBase (Dmel_Release_6), 134 known lncRNAs in our study were detected (Dataset S1). Of 134 annotated lncRNAs, 25 differentially expressed lncRNAs in four different comparisons (7 day DR vs 7 day fully fed, 42 day DR vs 42 day fully fed, 7 day DR vs 42 day DR, 7 day fully fed vs 42 day fully fed). Furthermore, 4 and 14 known lncRNAs displayed differential expression at the 7 day and 42 day when compared between DR and



Figure 2. Overall expression profile in RNA-seq. (a) mapping to fruit fly genome; (b) reads density in chromosomes; (c) FPKM distribution of mRNA and lncRNA; (d) 1726 novel lncRNAs were obtained after four programs filtering; (e) when compared to 2460 known lncRNAs sequences in FlyBase (Dmel_Release_6), 134 non-redundant known lncRNAs and 1726 non-redundant novel lncRNAs were found; (f) When compared to known mRNA sequences in FlyBase, 30165 known and 248 novel transcripts were found.

fully fed groups, respectively. Moreover, out of a total of 134 annotated lncRNAs only 11 lncRNAs obtained 22 annotations from GO enrichment. *CR31781* was the only one differentially expressed lncRNA which got GO annotation and was further validated by qPCR result. A total of 15 out of 22 annotations belonged to lncRNA *CR31781*, such as lateral inhibition, cell-cell signaling involved in cell fate commitment, extracellular space, extracellular region part and cellular component, etc.

Novel IncRNA

We predicted the targets of novel lncRNAs, and then analyzed the GO (Dataset S6) and KEGG enrichment (Dataset S7) of targets (Dataset S8 and Dataset S9). In most GO enrichment annotations, 17 non-redundant differentially expressed mRNA genes were the targets of 13 differentially expressed lncRNAs (Table 1). Six differentially expressed coding genes were the target of six differentially expressed lncRNAs and expressed

Table 1. GO annotations of differentially expressed lncRNA and their targets in DR group when compared to fully fed group

IncRNA(action mode, corrected p-	Targets(corrected p-	GO annotations
value)	value)	
7 day DR vs 7 day fully fed		
$XLOC_052958$ (cis, 0.00715)	CG12374(0.00005)↑	Carboxypeptidase activity
$XLOC_{166557}(\text{trans}, 0.00425)\downarrow$	globin 1(0.0214)↑	Heme binding/Iron ion binding
XLOC_009418(trans, 0.0322) [↑]	CG6048(0.0496)↑	Serine-type endopeptidase activity
42 day DR vs 42 day fully fed	•	
XLOC_001163(trans, $0.0171)$	Hsc70-1(0.0045)↑	Cellular component morphogenesis
XLOC_196039(trans, 0.0028)↑ XLOC_009798(trans	Cyp28d2(0.00835)↑ IscU	Heme binding
$0.01205)^{\uparrow}$	homolog(0.00395) \uparrow	Iron ion binding
7 day DR ys 42 day DR	noniolog(0.00595)+	
XLOC_002137(trans,	Hsc70-3(0.0097)↓	Cell morphogenesis/Cellular component morphogenesis
0.02335)↓		
	CG9733(0.00005)↓	Serine-type endopeptidase activity
$\begin{array}{l} \text{XLOC_076307(trans,} \\ 0.03315) \downarrow \end{array}$	Hsp70Bc(0.00005)↓	Cell morphogenesis/Cellular component morphogenesis/Glycosaminoglycan catabolic process/Glycosaminoglycan metabolic process/Peptidoglycan catabolic process/Peptidoglycan metabolic process/Serine-type endopeptidase activity
	Socs36E(0.00005) \downarrow	Cell morphogenesis/Cellular component morphogenesis
	CG10041(0.0489)↓	Serine-type endopeptidase activity
XLOC_000246(trans, 0.01425) \downarrow	CG15046(0.0405)↓	Serine-type endopeptidase activity
XLOC 071173(trans, 0.0129)↓	SPH93(0.00005)↓	Serine-type endopeptidase activity
XLOC_066439(cis, 0.0113)↓	Cyp6w1(0.0103)↓	Heme binding/Iron ion binding
XLOC 009798(trans, 0.0034)↓	Cyp4p3(0.01165)↓	Heme binding/Iron ion binding
_ 、 、 、 、 、	CG10041(0.0489)↓	Serine-type endopeptidase activity
	IscU homolog $(0.0115)\downarrow$	Iron ion binding
7 day fully fed vs 42 day fully fed	- · · · /	
XLOC_052958(cis, 0.0087)↑	CG12374(0.0001)↑	Carboxypeptidase activity
XLOC_067962(cis, 0.0097)	PGRP-SC1a(0.00005)↑	Carboxypeptidase activity/ Glycosaminoglycan catabolic process/ Glycosaminoglycan metabolic process/Pentidoglycan catabolic process
XLOC_151622(cis, 0.00635)↑	CG33970(0.0346)↓	Iron ion binding

Note: \uparrow , up-regulation; \downarrow , down-regulation.

during both 7 day and 42 day in DR when compared to fully fed fruit flies, and were found to be enriched in carboxypeptidase activity, cellular component morphogenesis, heme binding, iron ion binding and serine-type endopeptidase activity. In all the comparison groups, nine differentially expressed target genes related to fruit fly aging, which has resulted in lethal (including *CG9733*, *SPH93*, *Hsc70-1*, *Cyp4p3*, *IscU* homolog genes) and long lived (including *Socs36E* genes) phenotypes under RNAi system.

In most significant KEGG pathway enrichment (Dataset S7), 27 differentially expressed lncRNAs and 44 differentially expressed targets were found to be involved in 38 pathways out of which 21 targets were related to fly aging. Most of these were important pathways affecting senescence, such as mTOR, FoxO and Wnt signaling pathway. At 7 day and 42 day, 11 of the 26 genes in the mTOR pathway were present in the RNA-seq data, but, just inac gene was upregulated as the target of lncRNA XLOC 056059 at the 42 day in DR in comparison to 42 day in fully fed. Five lncRNAs and three targets existed in FoxO signaling pathway, and were found upregulated at 42 day in DR when compared to fully fed flies at same day (Table 2). Especially, target genes involved in signaling pathways of biosynthesis of unsaturated fatty acids and fatty acid

metabolism were up-regulated in DR group in comparison to fully fed, including *CG9743* (as the target of *XLOC_201255*), *CG15531*, *CG9743*, *CG15531* and *FASN2* at the 7 day, *Acsl* and *CG3961* at the 42 day.

In the present study, we have characterized three novel signaling pathways that may be related to aging, which are, hippo signaling pathway-fly, phototransduction-fly and protein processing in endoplasmic reticulum (Table 2). In hippo signaling pathway-fly 11 differentially expressed coding genes were involved and, three and five genes displayed differential expression at the 7 day and 42 day in DR when compared to fully fed flies, respectively, and five coding genes were the targets of seven novel lncRNAs. In phototransduction-fly signaling pathway eight related coding genes were detected and showed differential expression between various comparison groups in DR and fully fed condition. Novel lncRNA XLOC 092363 and respective target Arr2 were involved on phototransduction-fly signaling pathway. Furthermore, in endoplasmic reticulum pathway 15 differentially expressed coding genes were found in protein processing and 11 of these were related to aging and five genes were the targets of 7 novel lncRNAs. Interestingly enough, 9 of 15 differentially expressed coding genes belonged to heat shock protein gene families.



Figure 3. 102 differentially expressed lncRNA and 1406 differentially expressed coding genes were identified in this study. (a) The number of DEGs in different comparative groups (parentheses presented the number of known lncRNA); (b) Common differentially expressed lncRNA in both 7 day and 42 day between DR and fully fed flies; (c) Common differentially expressed mRNA in both 7 day and 42 day between DR and fully fed flies; \uparrow , upregulation; \downarrow , downregulation

FexD signaling pathway KLOC_000246(A2 ² +B2 0.044, A1 ¹ -A2 0.01425, max) Gadd45 (A2 ² +B2 0.01075, A1 ¹ -A2 0.014) Yang Yang Yang Yang Yang Yang Yang XLOC_00043(A2 ² +B2 0.0136, A1 ¹ -A2 0.01345, trans) Pepck(A2 ² +B2 0.0005, A1 ¹ -A2 0.00005) Yang Hippo signaling pathway-fly XLOC_002137(A1 ¹ -A2 0.02335, trans) Upd2(A1 ² -A2 0.00043) Yang Yang XLOC_002137(A1 ¹ -A2 0.02335, trans) Upd2(A1 ¹ -A2 0.0145) Yang Yang XLOC_002137(A1 ¹ -A2 0.02335, trans) Upd2(A1 ¹ -A2 0.0145) Yang Yang XLOC_002137(A1 ¹ -A2 0.02335, trans) Upd2(A1 ¹ -A2 0.0155) Yang Yang XLOC_002137(A1 ¹ -A2 0.02335, trans) Upd3(A1 ¹ -A2 0.0155) Yang Yang XLOC_000246(A1 ¹ -A2 0.00235, trans) Yang Yang Yang Yang Yang Yang Yang	KEGG pathway	(comparable group and correct pvalue, action mode)	mRNA genes (comparable group and correct pvalue)
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KLOC_221562(A27-B2 0.00275, trans) Egft(A27-B2 0.0204) Hippo signaling pathway-fly KLOC_001163(A27-B2 0.0171, trans) Upd2(A17-A2 0.0043) Microscience XLOC_002137(A14-A2 0.02335, trans) Upd3(A14-A2 0.01585) XLOC_002137(A14-A2 0.02335, trans) Upd3(A14-A2 0.01585) XLOC_000246(A14-A2 0.00455, cis) Zyx(A14-B1 0.046) XLOC_000246(A14-A2 0.00455, trans) baz (A14-A2 0.03595) XLOC_000978(A14-A2 0.00345, trans) wg(B14-B2 0.00905) NLOC_000978(A14-A2 0.00345, trans) wg(B14-B2 0.00905) NLOC_000043(A14-A2 0.00345, trans) wg(B14-B2 0.00905) Proteir processing in endoplasmic reticulum XLOC_07226(A14-B1 0.00885, trans) Hsp70Be(A14-A2 0.0005) XLOC_001163(A27-B2 0.0171, trans) Hsc70-1(A27-B2 0.0045) XLOC_001163(A27-B2 0.0174, trans) XLOC_001163(A27-B2 0.0135, trans) Hsp70Be(A14-A2 0.02335) XLOC_002137(A14-A2 0.02335, trans) XLOC_000043(A27-B2 0.0125, A14-A2 0.01345, trans) I(2)eft(A14-A2 0.0108, A24-B2 0.01715) Trans) XLOC_000236(A14-A2 0.02335, trans) GstD10 (A27-B2 0.0138, A14-A2 0.00175) Trans) XLOC_000246(A27-B2 0.0255, A27-B2 0.00955, trans) GstD10 (A27-B2 0.0138, A14-A2 0.00175) Trans) XLO		trans)	
Hippo signaling pathway-fly XLOC_002137(A14-A2.02335, trans) Upd2(A1 ⁺ -A2.0.043) XLOC_002137(A14-A2.0.02335, trans) Upd3(A14-A2.0.01385) XLOC_002137(A14-A2.0.02335, trans) Upd3(A14-A2.0.01385) XLOC_000236(A14-A2.0.00245, trans) Zyx(A14-B1.0.046) XLOC_000236(A14-A2.0.0034, trans) baz (A14-A2.0.03595) XLOC_000236(A14-A2.0.0034, trans) XLOC_000043(A14-A2.0.0034, trans) baz (A14-A2.0.03595) NLOC_000043(A14-A2.0.0034, trans) wg(B14-B2.0.00905) Arr2(A11^-B1.0.00315, B11^-B2.0.0481) Protein processing in endoplasmic reticulum XLOC_076307(A14-A2.0.03315, trans) Hsp70Bc(A14-A2.0.0005) XLOC_00013(A14-A2.0.03315, trans) Hsc70-1(A21^-B2.0.0045) XLOC_00043(A2^+B2.0.0171, trans) Hsc70-1(A21^+B2.0.0045) XLOC_00043(A21^+B2.0.0136, A14-A2.0.01345, trans) I(2)ef1(A14-A2.0.018, A24-B2.0.01715) XLOC_00043(A21^+B2.0.0136, A14-A2.0.0034, trans) I(2)ef1(A14-A2.0.008, A24-B2.0.0175) Metabolism of xenobiotics by cytochrome P450 XLOC_002137(A14-A2.0.02335, trans) GstD5(A14-A2.0.0005) XLOC_001237(A14-A2.0.02335, trans) GstE12 (A11^+B1.0.0095) XLOC_00175) XLOC_001237(A14-A2.0.02335, trans) GstE12 (A11^+B1.0.0095) XLOC_000175) XLOC_001237(A14-A2.0.02335, tr		XLOC_221562(A2 \uparrow B2 0.00275, trans)	Egfr(A2↑-B2 0.0204)
Hippo signaling pathway-fly XLOC_002137(A14-A2 0.02335, trans) Upd2(A1^-A2 0.0043) XLOC_002137(A14-A2 0.02335, trans) Upd3(A14-A2 0.01585) XLOC_000246(A14-A2 0.00785, cis) Zyx(A14-B1 0.046) XLOC_000246(A14-A2 0.00785, cis) Zyx(A14-A2 0.03595) XLOC_000236(A14-A2 0.0034, trans) baz (A14-A2 0.03595) XLOC_0009798(A14-A2 0.0034, trans) XLOC_0009798(A14-A2 0.0034, trans) XLOC_160411(B14-B2 0.0048, trans) Wg(B14-B2 0.00905) Phototransduction fly XLOC_00236(A14-B1 0.00885, B1^-B2 0.0075, cis) Arr2(A17-B1 0.00315, B1^-B2 0.0481) YLOC_00163(A2^+B2 0.0171, trans) Hsp70Bc(A14-A2 0.0005) XLOC_00481) XLOC_001163(A2^+B2 0.0171, trans) Hsc70-1(A27-B2 0.0045) XLOC_00236(A14-B1 0.00885, trans) XLOC_00236(A14-B1 0.00885, trans) CG8974(A17-B1 0.01945) XLOC_009798(A27-B2 0.0136, A14-A2 0.01345, trans) XLOC_000236(A14-A2 0.02335, trans) Hsc70-3(A14-A2 0.0108, A24-B2 0.01715) Trans) XLOC_000236(A14-A2 0.00235, trans) GstD5(A14-A2 0.0108, A14-A2 0.00175) Trans) XLOC_000236(A14-A2 0.00235, trans) GstD5(A14-A2 0.0108, A14-A2 0.00175) Trans) XLOC_000236(A14-A2 0.00235, trans) GstD10(A14-A2 0.0108, A14-A2 0.00175) Trans)<		XLOC_001163(A2+B2 0.01/1, trans)	
Path/Wdy-Hy XLOC_002137(A14-A2.0.02335, trans) Upd3(A14-A2.0.01585) XLOC_186922(A14-B1.0.00785, cis) Zyx(A14-B1.0.046) XLOC_000246(A14-A2.0.01425, trans) baz (A14-A2.0.03595) XLOC_0009798(A14-A2.0.0055, trans) baz (A14-A2.0.03595) XLOC_0009798(A14-A2.0.0055, trans) baz (A14-A2.0.03595) XLOC_00043(A14-A2.0.0055, trans) xLOC_009798(A14-A2.0.0055, trans) XLOC_00043(A14-A2.0.00315, trans) wg(B14-B2.0.00905) Protein processing in endoplasmic reticulum XLOC_076307(A14-A2.0.03315, trans) Hsp70Bc(A14-A2.0.0005) XLOC_001163(A2^h-B2.0.0171, trans) Hsc70-1(A2^h-B2.0.0045) XLOC_000163(A14-A2.0.02335, trans) XLOC_001163(A2^h-B2.0.0171, trans) Hsc70-3(A14-A2.0.02335) XLOC_000175) XLOC_0002137(A14-A2.0.02335, trans) CG8974(A1^h-B1.0.01995) XLOC_000043(A2^h-B2.0.0136, A14-A2.0.01345, trans) I(2)ef1(A14-A2.0.0108, A24-B2.0.01715) Metabolism of xenobibries by cytochrome P450 XLOC_002137(A14-A2.0.02335, trans) GstD10 (A2^h-B2.0.0138, A14-A2.0.00175) XLOC_002137(A14-A2.0.02335, trans) GstE12 (A11^-B1.0.0495) XLOC_002137(A14-A2.0.00235, trans) XLOC_002137(A14-A2.0.02335, trans) GstE12 (A11^-B1.0.0495) XLOC_000137(A14-A2.0.00235, trans)	Hippo signaling	XLOC_002137(A1↓-A2 0.02335, trans)	Upd2(A1 ⁺ -A2 0.0043)
Metabolism of venobilities of venobilies of venobilies of venobilities of venobilities of venobilities	pathway-ny	XLOC_002137(A1↓-A2 0.02335, trans)	Upd3(A1↓-A2 0.01585)
Metabolism of xenobiotics by cytochrome P450 XLOC_000246(A1↓-A2 0.01425, trans) XLOC_00033(A1↓-A2 0.00355, trans) wg(B1↓-B2 0.003595) Metabolism of xenobiotics by cytochrome P450 XLOC_00236(A1↓-A2 0.0034, trans) wg(B1↓-B2 0.00905) Metabolism of xLOC_00236(A1↓-A2 0.00315, trans) XLOC_00236(A1↓-A2 0.00315, trans) Msp70Bc(A1↓-A2 0.00315, B1^+B2 0.0481) Metabolism of xenobiotics by cytochrome P450 XLOC_076307(A1↓-A2 0.03315, trans) Hsp70Bc(A1↓-A2 0.00005) Metabolism of xenobiotics by cytochrome P450 XLOC_000136(A1↓-A2 0.02335, trans) CG8974(A1↑-B1 0.0188, A1↓-A2 0.01345, trans) XLOC_000236(A1↓-A2 0.02335, trans) CG8974(A1↑-B1 0.0188, A2↓-B2 0.01715) Trans) XLOC_0002137(A1↓-A2 0.02335, trans) I(2)efl(A1↓-A2 0.0108, A2↓-B2 0.01715) Trans) XLOC_000236(A1↓-A2 0.0235, trans) GstD5(A1↓-A2 0.00005) Metabolism of xenobiotics by cytochrome P450 XLOC_002137(A1↓-A2 0.02335, trans) GstD10 (A2↑-B2 0.0138, A1↓-A2 0.00175) XLOC_002137(A1↓-A2 0.02335, trans) GstD10 (A2↑-B2 0.0138, A1↓-A2 0.00175) XLOC_002137(A1↓-A2 0.0235, trans) XLOC_002137(A1↓-A2 0.02335, trans) GstE12 (A1↑-B1 0.0495) XLOC_002137(A1↓-A2 0.00235, trans) XLOC_002137(A1↓-A2 0.02335, trans) GstE12 (A1↑-B1 0.0495) XLOC_002137(A1↓-A2 0.00235, trans)		XLOC_186922(A1↓-B1 0.00785, cis)	Zyx(A1↓-B1 0.046)
XLOC_000236(A14-A2 0.00355, trans) XLOC_0009798(A14-A2 0.0034, trans) XLOC_000043(A14-A2 0.01345, trans) XLOC_000043(A14-A2 0.01345, trans) XLOC_000043(A14-A2 0.01345, trans) Wg(B14-B2 0.00905) Phototransduction- fly Protein processing in endoplasmic reticulum XLOC_001163(A2 ⁺ -B2 0.0171, trans) Hsc70-1 (A2 ⁺ -B2 0.0005) XLOC_00043(A2 ⁺ -B2 0.0171, trans) Hsc70-1 (A2 ⁺ -B2 0.0045) XLOC_00043(A2 ⁺ -B2 0.0171, trans) Hsc70-3(A14-A2 0.02335, trans) KLOC_00043(A2 ⁺ -B2 0.0136, A14-A2 0.01345, trans) XLOC_000043(A2 ⁺ -B2 0.0136, A14-A2 0.01345, trans) XLOC_0002137(A14-A2 0.02335, trans) Hsc70-3(A14-A2 0.00034, trans) XLOC_0002137(A14-A2 0.02335, trans) KLOC_0002137(A14-A2 0.02335, trans) KLOC_0002137(A14-A2 0.02335, trans) StLOC_000246(A2 ⁺ -B2 0.044, A14-A2 0.01425, trans) XLOC_002137(A14-A2 0.00235, trans) XLOC_002137(A14-A2 0.0023		XLOC_000246(A1↓-A2 0.01425, trans)	baz (A1↓-A2 0.03595)
XLOC_009/98(A14-A2.0.0034, trans) XLOC_100041(B14-B2.0.0048, trans) wg(B14-B2.0.00905) Phototransduction- fly XLOC_02363(A14-B1.0.00885, B1^+B2.0.0075,cis) Arr2(A1^+B1.0.00315, B1^+B2.0.0481) Protein processing in endoplasmic reticulum XLOC_076307(A14-A2.0.03315, trans) Hsp70Bc(A14-A2.0.00005) XLOC_001163(A2^+B2.0.0171, trans) Hsc70-1(A2^+B2.0.0045) XLOC_001163(A2^+B2.0.0171, trans) Hsc70-1(A2^+B2.0.0045) XLOC_002137(A14-A2.0.02335, trans) CG8974(A1^+B1.0.01995) XLOC_00043(A2^+B2.0.0120, A14-A2.0.01345, trans) I(2)efl(A14-A2.0.0108, A24-B2.0.01715) XLOC_0009798(A2^+B2.0.01205, A14-A2.0.0034, trans) XLOC_000236(A14-A2.0.0035, XLOC_000236(A14-A2.0.0035, A21-B2.0.00955, trans) Metabolism of xenobiotics by cytochrome P450 XLOC_002137(A14-A2.0.02335, trans) GstD5(A14-A2.0.0005) XLOC_002137(A14-A2.0.02335, trans) GstE12 (A1^+B1.0.0495) XLOC_000175) XLOC_002137(A14-A2.0.0023, trans) GstE12 (A1^+A2.0.0108) XLOC_00135) XLOC_002137(A14-A2.0.0023, trans) GstE12 (A1^+A2.0.0108) XLOC_00135) XLOC_002137(A14-A2.0.0023, trans) GstE12 (A1^+A2.0.0108) XLOC_00135) XLOC_002137(A14-A2.0.0023, trans) GstE12 (A1^+A2.0.0005), G5999(A14-A2.0.00135)		XLOC_000236(A1↓-A2 0.00555, trans)	
Above_00004/(N14+A2.00194z, trans) wg(B14-B2.0.0095) VLOC_100411(B14-B2.0.0048, trans) wg(B14-B2.0.0095) Phototransduction- fly XLOC_092363(A14-B1.0.00885, B1^-B2.0.0075,cis) Arr2(A1^-B1.0.00315, B1^-B2.0.0481) Protein processing in endoplasmic reticulum XLOC_076307(A14-A2.0.03315, trans) Hsp70Bc(A14-A2.0.00005) XLOC_001163(A2^+B2.0.0171, trans) Hsc70-1(A2^+B2.0.0045) XLOC_000137(A14-A2.0.02335, trans) CG8974(A1^+B1.0.01995) XLOC_000137(A14-A2.0.02335, trans) Hsc70-3(A14-A2.0.02335) XLOC_000043(A2^+B2.0.01205, A14-A2.0.0034, trans) XLOC_000236(A14-A2.0.0035, A2^+B2.0.0034, trans) XLOC_000236(A14-A2.0.0055, A2^+B2.0.00955, trans) StLOC_000236(A14-A2.0.0034, trans) XLOC_0002137(A14-A2.0.02335, trans) GstD5(A14-A2.0.0005) XLOC_002137(A14-A2.0.02335, trans) GstD10 (A2^+B2.0.0175) trans) XLOC_002137(A14-A2.0.02335, trans) GstE12 (A1^+B1.0.0495) XLOC_002137(A14-A2.0.02335, trans) GstE12 (A1^+B1.0.0495) XLOC_00135(A14-A2.0.0023, trans) XLOC_00137(A14-A2.0.0023, trans) GstE12 (A1^+A2.0.0005), G5999(A14-A2.0.00135) XLOC_00135(A14-A2.0.00035), G5999(A14-A2.0.00135) XLOC_00137(A14-A2.0.02335, trans) GstE12 (A14^+A2.0.00005), G5999(A14-A2.0.00035), G5999(A14-A2.0.00035), G		$XLOC_{009/98}(A1 \rightarrow A2 0.0034, trans)$	
$ \begin{array}{c} Phototransduction-\\ fly \\ Protein processing in endoplasmic reticulum \\ \hline Multiple Model and Model$		$XLOC_{160411(B1 \downarrow -B2 0.0048, trans)}$	wg(B1↓-B2 0.00905)
$ \begin{array}{c} fly \\ \hline fly \\ fly \\ fly \\ \hline fly \\ fl$	Phototransduction-	$XLOC_{092363}(A1\downarrow -B10.00885_B1^+-B2.0.0075 cis)$	$Arr^{2}(A1^{+}B1 0 00315 B1^{+}B2 0 0481)$
Protein processing in endoplasmic reticulum XLOC_076307(A1↓-A2 0.03315, trans) Hsp70Bc(A1↓-A2 0.00005) XLOC_001163(A2↑-B2 0.0171, trans) Hsc70-1 (A2↑-B2 0.0045) XLOC_002137(A1↓-A2 0.02335, trans) CG8974(A1↑-B1 0.01995) XLOC_00043(A2↑-B2 0.0136, A1↓-A2 0.01345, trans) Hsc70-3(A1↓-A2 0.02335) XLOC_000978(A2↑-B2 0.01205, A1↓-A2 0.0034, trans) I(2)efl(A1↓-A2 0.0108, A2↓-B2 0.01715) Metabolism of xenobiotics by cytochrome P450 XLOC_002137(A1↓-A2 0.02335, trans) GstD5(A1↓-A2 0.00005) XLOC_002137(A1↓-A2 0.02335, trans) GstD10 (A2↑-B2 0.0108, A1↓-A2 0.00175) Trans) XLOC_002137(A1↓-A2 0.02335, trans) GstD10 (A2↑-B2 0.0138, A1↓-A2 0.00175) Trans) XLOC_002137(A1↓-A2 0.02335, trans) GstD10 (A2↑-B2 0.0138, A1↓-A2 0.00175) Trans) XLOC_002137(A1↓-A2 0.02335, trans) GstE12 (A1↑-B1 0.0495) XLOC_002137(A1↓-A2 0.02335, trans) XLOC_002137(A1↓-A2 0.02335, trans) GstE12 (A1↑-B1 0.0495) XLOC_002137(A1↓-A2 0.02335, trans) XLOC_010702(A1↑-A2 0.0023, trans) CG17323(A1↑-A2 0.00005), CG5999(A1↓-A2 0.00135) XLOC_002137(A1↓-A2 0.02335, trans) GstE17(A1↓-A2 0.02137(A1↓-A2 0.02335, trans) GstE17(A1↓-A2 0.00005), CG5999(A1↓-A2 0.00005), CG17323(A1↑-A2 0.00005), CG5999(A1↓-A2 0.00005), CG17323(A1↑-A2 0.00005), CG5999(A1↓-A2 0.00005), CG17323(A1↑-A	fly		
$ \begin{array}{llllllllllllllllllllllllllllllllllll$	Protein processing	XLOC_076307(A1↓-A2 0.03315, trans)	Hsp70Bc(A1↓-A2 0.00005)
$ \begin{array}{c} \text{XLOC}_{072226}(A1\downarrow\text{-B1} 0.00885, trans) & \text{CG8974}(A1\uparrow\text{-B1} 0.01995) \\ \hline \text{XLOC}_{002137}(A1\downarrow\text{-A2} 0.02335, trans) & \text{Hsc70-3}(A1\downarrow\text{-A2} 0.02335) \\ \hline \text{XLOC}_{000043}(A2\uparrow\text{-B2} 0.0136, A1\downarrow\text{-A2} 0.01345, \\ \text{trans}) & \text{XLOC}_{000978}(A2\uparrow\text{-B2} 0.01205, A1\downarrow\text{-A2} 0.0034, \\ \text{trans}) & \text{XLOC}_{000236}(A1\downarrow\text{-A2} 0.00555, A2\uparrow\text{-B2} 0.00955, \\ \text{trans}) & \text{XLOC}_{000236}(A1\downarrow\text{-A2} 0.002335, trans) & \text{GstD5}(A1\downarrow\text{-A2} 0.0005) \\ \hline \text{XLOC}_{000246}(A2\uparrow\text{-B2} 0.044, A1\downarrow\text{-A2} 0.01425, \\ \text{trans}) & \text{XLOC}_{000246}(A2\uparrow\text{-B2} 0.044, A1\downarrow\text{-A2} 0.01425, \\ \text{trans}) & \text{XLOC}_{000246}(A2\uparrow\text{-B2} 0.044, A1\downarrow\text{-A2} 0.01425, \\ \text{trans}) & \text{XLOC}_{002137}(A1\downarrow\text{-A2} 0.02335, trans) & \text{GstD10}(A2\uparrow\text{-B2} 0.0138, A1\downarrow\text{-A2} 0.00175) \\ \hline \text{XLOC}_{002137}(A1\downarrow\text{-A2} 0.02335, trans) & \text{GstE12}(A1\uparrow\text{-B1} 0.0495) \\ \hline \text{XLOC}_{010702}(A1\uparrow\text{-A2} 0.00235, trans) & \text{GstE12}(A1\uparrow\text{-B1} 0.0495) \\ \hline \text{XLOC}_{002137}(A1\downarrow\text{-A2} 0.02335, trans) & \text{GstE7}(A1\downarrow\text{-A2} 0.0108) \\ \hline \text{XLOC}_{002137}(A1\downarrow\text{-A2} 0.02335, trans) & \text{GstE7}(A1\downarrow\text{-A2} 0.0005), \text{CG5999}(A1\downarrow\text{-A2} 0.00135) \\ \hline \text{XLOC}_{002137}(A1\downarrow\text{-A2} 0.02335, trans) & \text{Ugt35}(A1\uparrow\text{-B1} 0.0005), \text{GstD5}(A1\downarrow\text{-A2} 0.00005), \\ \hline \text{Glutathione} & \frac{\text{XLOC}_{002137}(A1\downarrow\text{-A2} 0.02335, trans) & \text{GstD10}(A1\uparrow\text{-A2} 0.00175), \text{GstD5}(A1\downarrow\text{-A2} 0.00005), \\ \hline \text{C}_{002137}(A1\downarrow\text{-A2} 0.02335, trans) & \text{C}_{001722}(A1\uparrow\text{-A2} 0.00035), \\ \hline \text{C}_{002137}(A1\downarrow\text{-A2} 0.02335, trans) & \text{GstE7}(A1\to\text{-A2} 0.00005), \\ \hline \text{C}_{002137}(A1\downarrow\text{-A2} 0.02335, trans) & \text{C}_{001722}(A1\uparrow\text{-A2} 0.00005), \\ \hline \text{C}_{002137}(A1\downarrow\text{-A2} 0.02335, trans) & \text{C}_{001722}(A1\uparrow\text{-A2} 0.00035), \\ \hline \text{C}_{002137}(A1\downarrow\text{-A2} 0.02335, trans) & \text{C}_{00172}(A1\to\text{-A2} 0.00005), \\ \hline \text{C}_{002137}(A1\to\text{-A2} 0.02335, trans) & \text{C}_{00172}(A1\to\text{-A2} 0.00005), \\ \hline \text{C}_{0017}(A1\to\text{-A2} 0$	reticulum	XLOC_001163(A2 ⁺ -B2 0.0171, trans)	Hsc70-1 (A2 ⁺ -B2 0.0045)
$ \begin{array}{l} \mbox{KLOC}_{002137}(A1 \downarrow -A2\ 0.02335, trans) & Hsc70-3(A1 \downarrow -A2\ 0.02335) \\ \hline XLOC_000043(A2^{+}-B2\ 0.0136,\ A1 \downarrow -A2\ 0.01345, \\ trans) \\ XLOC_000798(A2^{+}-B2\ 0.01205,\ A1 \downarrow -A2\ 0.0034, \\ trans) \\ XLOC_000236(A1 \downarrow -A2\ 0.00555,\ A2^{+}-B2\ 0.00955, \\ trans) \\ \hline XLOC_000236(A1 \downarrow -A2\ 0.00555,\ A2^{+}-B2\ 0.00955, \\ trans) \\ \hline XLOC_000246(A2^{+}-B2\ 0.044,\ A1 \downarrow -A2\ 0.00955, \\ trans) \\ \hline XLOC_000246(A2^{+}-B2\ 0.044,\ A1 \downarrow -A2\ 0.01425, \\ trans) \\ \hline XLOC_000246(A2^{+}-B2\ 0.044,\ A1 \downarrow -A2\ 0.01425, \\ trans) \\ \hline XLOC_002137(A1 \downarrow -A2\ 0.02335,\ trans) \\ \hline XLOC_002137(A1 \downarrow -A2\ 0.02335,\ trans) \\ \hline XLOC_002137(A1 \downarrow -A2\ 0.02335,\ trans) \\ \hline XLOC_002137(A1 \downarrow -A2\ 0.002335,\ trans) \\ \hline XLOC_0002137(A1 \downarrow -A2\ 0.002335,\ trans) \\ \hline XLOC_000005),\ CG5999(A1 \downarrow -A2\ 0.00005),\ CG$		XLOC_072226(A1↓-B1 0.00885, trans)	CG8974(A1 ⁺ -B1 0.01995)
$ \frac{XLOC_000043(A2^{+}B2 0.0136, A1^{+}-A2 0.01345, trans)}{XLOC_009798(A2^{+}-B2 0.01205, A1^{+}-A2 0.0034, trans)} \\ XLOC_009798(A2^{+}-B2 0.01205, A1^{+}-A2 0.0034, trans)}{XLOC_000216(A1^{+}-A2 0.00555, A2^{+}-B2 0.00955, trans)} \\ Metabolism of xenobiotics by cytochrome P4500 \\ \frac{XLOC_002137(A1^{+}-A2 0.02335, trans)}{XLOC_002137(A1^{+}-A2 0.02335, trans)} \\ \frac{XLOC_002137(A1^{+}-A2 0.02335, trans)}{XLOC_002137(A1^{+}-A2 0.02335, trans)} \\ \frac{XLOC_002137(A1^{+}-A2 0.02335, trans)}{XLOC_002137(A1^{+}-A2 0.0023, trans)} \\ \frac{XLOC_002137(A1^{+}-A2 0.02335, trans)}{XLOC_002137(A1^{+}-A2 0.0023, trans)} \\ \frac{XLOC_002137(A1^{+}-A2 0.0023, trans)}{XLOC_002137(A1^{+}-A2 0.0023, trans)} \\ \frac{XLOC_002137(A1^{+}-A2 0.02335, trans)}{XLOC_002137(A1^{+}-A2 0.02335, trans)} \\ \frac{XLOC_002137(A1^{+}-A2 0.02335, trans)}{XLOC_00005} \\ \frac{XLOC_002137(A1^{+}-A2 0.02335, trans)}{XLOC_002137(A1^{+}-A2 0.02335, trans)} \\ \frac{XLOC_002137(A1^{+}-A2 0.02335, trans)}{XLOC_00005} \\ \frac{XLOC_002137(A1^{+}-A2 0.02335, trans)}{$		XLOC_002137(A1↓-A2 0.02335, trans)	Hsc70-3(A1↓-A2 0.02335)
$ \begin{array}{c} \mbox{trans} \\ XLOC_009798(A2^{+}B2\ 0.01205, A1^{+}A2\ 0.0034, \\ \mbox{trans} \\ XLOC_000236(A1^{+}A2\ 0.00555, A2^{+}B2\ 0.00955, \\ \mbox{trans} \\ \end{array} \\ \hline \mbox{Metabolism of} \\ \mbox{xenobiotics by} \\ \mbox{cytochrome P450} \\ \hline \mbox{XLOC}_000246(A2^{+}B2\ 0.044, A1^{+}A2\ 0.01425, \\ \mbox{trans} \\ \hline \mbox{XLOC}_000246(A2^{+}B2\ 0.044, A1^{+}A2\ 0.01425, \\ \mbox{trans} \\ \hline \mbox{XLOC}_0002137(A1^{+}A2\ 0.02335, \mbox{trans}) \\ \hline \mbox{XLOC}_002137(A1^{+}A2\ 0.02335, \mbox{trans}) \\ \hline \mbox{XLOC}_002137(A1^{+}A2\ 0.00235, \mbox{trans}) \\ \hline \mbox{XLOC}_010702(A1^{+}A2\ 0.00235, \mbox{trans}) \\ \hline \mbox{XLOC}_010702(A1^{+}A2\ 0.00233, \mbox{trans}) \\ \hline \mbox{XLOC}_010702(A1^{+}A2\ 0.002335, \mbox{trans}) \\ \hline \mbox{XLOC}_010702(A1^{+}A2\ 0.002335, \mbox{trans}) \\ \hline \mbox{XLOC}_010712(A1^{+}A2\ 0.002335, \mbox{trans}) \\ \hline \mbox{XLOC}_106174(A1^{+}-B1\ 0.02315, \mbox{trans}) \\ \hline \mbox{XLOC}_106174(A1^{+}-B1\ 0.02315, \mbox{trans}) \\ \hline \mbox{XLOC}_01072(A1^{+}A2\ 0.00235, \mbox{trans}) \\ \hline \mbox{XLOC}_106174(A1^{+}-B1\ 0.02315, \mbox{trans}) \\ \hline \mbox{XLOC}_106174(A1^{+}-B1\ 0.02315, \mbox{trans}) \\ \hline \mbox{YLOC}_01075), \mbox{GstD5}(A1^{+}-A2\ 0.00005), \\ \hline \mbox{GstD10}(A1^{+}-A2\ 0.00005) \\ \hline \mbox{YLOC}_201255(A1^{+}-B1\ \mbox{trans}) \\ \hline \mbox{YLOC}_201255(A1^{+}-B1\ \mbox{trans}) \\ \hline \mbox{GstD10}(A1^{+}-A2\ 0.00005), \mbox{GstD5}(A1^{+}-A2\ 0.00005), \\ \hline \mbox{GstD5}(A1^{+}-A2\ 0.00005), \\ \hline \mbox{GstD10}(A1^{+}-A2\ 0.00005) \\ \hline \mbox{Hom} \\ \hline \$		XLOC_000043(A2↑-B2 0.0136, A1↓-A2 0.01345,	$l(2)efl(A1\downarrow - A2 \ 0.0108, \ A2\downarrow - B2 \ 0.01715)$
$\frac{\text{XLOC}_009798(A24+B20.01203, A14+A20.0034, trans)}{\text{XLOC}_000236(A14+A20.00555, A2^{+}B20.00955, trans)} \\ \text{Metabolism of xenobiotics by cytochrome P450} \\ \frac{\text{XLOC}_002137(A14+A20.02335, trans)}{\text{XLOC}_000246(A2^{+}B20.044, A14+A20.01425, trans)} \\ \frac{\text{XLOC}_000246(A2^{+}B20.044, A14+A20.01425, trans)}{\text{XLOC}_002137(A14+A20.02335, trans)} \\ \frac{\text{XLOC}_002137(A14+A20.02335, trans)}{\text{XLOC}_002137(A14+A20.0023, trans)} \\ \frac{\text{XLOC}_002137(A14+A20.0023, trans)}{\text{XLOC}_002137(A14+A20.0023, trans)} \\ \frac{\text{XLOC}_010702(A1^{+}A20.00235, trans)}{\text{XLOC}_002137(A14+A20.02335, trans)} \\ \frac{\text{XLOC}_002137(A14+A20.02335, trans)}{\text{XLOC}_002137(A14+A20.02335, trans)} \\ \frac{\text{XLOC}_002137(A14+A20.002335, trans)}{\text{XLOC}_00005), \text{CG5999}(A14+A20.00005), \text{CG5999}(A14+A20.00005), \text{CG5999}(A14+A20.00005), \text{CG599}(A14+A20.00005), \text{CG599}(A14+A20.00005), \text{CG599}(A14+A20.00005), \text{CG599}(A14+A20.00005), \text{CG599}(A14+A20.00005), \text{CG599}(A14+A20.00005), \text{CG599}(A14+A20.00005), \text{CG59}(A14+A20.00005), \text{CG59}(A14+A20.00005), \text{CG59}(A14+A20.00005), \text{CG59}(A14+A20.00005), \text{CG59}(A14+A20.00005), \text{CG59}(A14+A20.00005), \text{CG59}(A14+A20.00005), \text{CG59}(A14+A20.00005), \text{CG59}(A14+A20.00005), \text{CG51}(A14+A20.00005), \text{CG51}($		trans) $XLOC 000708(A2^{+} P2 0.01205 A1^{+} A2 0.0024)$	
$\frac{XLOC_{000236}(A1\downarrow-A2\ 0.00555,\ A2^{+}B2\ 0.00955,\ trans)}{XLOC_{002137}(A1\downarrow-A2\ 0.02335,\ trans)} = GstD5(A1\downarrow-A2\ 0.00005)}$ $\frac{XLOC_{002137}(A1\downarrow-A2\ 0.02335,\ trans)}{XLOC_{002137}(A1\downarrow-A2\ 0.02335,\ trans)} = GstD10\ (A2^{+}B2\ 0.0138,\ A1\downarrow-A2\ 0.00175),\ trans)}{XLOC_{002137}(A1\downarrow-A2\ 0.02335,\ trans)} = GstD10\ (A2^{+}B1\ 0.0495)}$ $\frac{XLOC_{002137}(A1\downarrow-A2\ 0.0023,\ trans)}{XLOC_{002137}(A1\downarrow-A2\ 0.0023,\ trans)} = GstE12\ (A1^{+}B1\ 0.0495),\ CG5999(A1\downarrow-A2\ 0.00135),\ CG5999(A1\downarrow-A2\ 0.00135),\ CG5999(A1\downarrow-A2\ 0.00135),\ CG5999(A1\downarrow-A2\ 0.00135),\ CG5999(A1\downarrow-A2\ 0.00005),\ CG599(A1\downarrow-A2\ 0.00005),\ CG5999(A1\downarrow-A2\ 0.00005),\ CG5999(A1\downarrow-A2\ 0.00005),\ CG5999(A1\downarrow-A2\ 0.00005),\ CG5999(A1\downarrow-A2\ 0.00005),\ CG5999(A1\downarrow-A2\ 0.00005),\ CG5999(A1\downarrow-A2\ 0.00005),\ CG599(A1\downarrow-A2\ 0.00005),\ CG59(A1\downarrow-A2\ 0.00005),\ CG59(A1\downarrow-A2\ 0.00005),\ CG59(A1\downarrow-A2\ 0.00005),\ CG59(A1\downarrow-A2\ 0.00005),\ CG59(A1\downarrow-A2\ 0.00005),\ CG59(A1\downarrow-A2\ 0.00005),\ $		A200 - 00778(A2 + B2 0.01203, A14 - A2 0.0034, trans)	
trans) Metabolism of xenobiotics by cytochrome P450 XLOC_002137(A1↓-A2 0.02335, trans) GstD5(A1↓-A2 0.00005) XLOC_000246(A2↑-B2 0.044, A1↓-A2 0.01425, trans) GstD10 (A2↑-B2 0.0138, A1↓-A2 0.00175) XLOC_002137(A1↓-A2 0.02335, trans) XLOC_002137(A1↓-A2 0.02335, trans) XLOC_010702(A1↑-A2 0.0023, trans) GstE12 (A1↑-B1 0.0495) XLOC_010702(A1↑-A2 0.0023, trans) CG17323(A1↑-A2 0.0108) XLOC_002137(A1↓-A2 0.02335, trans) GstE7 (A1↓-A2 0.00005), CG5999(A1↓-A2 0.00135) XLOC_106174(A1↑B1 0.02315, trans) Ugt35b (A1↑-B1 0.00015) StLOC_002137(A1↓-A2 0.02335, trans) GstD10(A1↓-A2 0.00175), GstD5(A1↓-A2 0.00005), GstE7(A1↓-A2 0.00005) Glutathione metabolism XLOC_002137(A1↓-A2 0.02335, trans) GstD10(A1↓-A2 0.00175), GstD5(A1↓-A2 0.00005), GstE7(A1↓-A2 0.00005) XLOC_002137(A1↓-A2 0.02335, trans) GstD10(A1↓-A2 0.00175), GstD5(A1↓-A2 0.00005), GstE7(A1↓-A2 0.00005)		XLOC_000236(A1↓-A2 0.00555, A2↑-B2 0.00955,	
$ \begin{array}{c} \mbox{Metabolism of} \\ \mbox{xenobiotics by} \\ \mbox{cytochrome P450} \end{array} & \begin{array}{c} \mbox{XLOC}_002137(A1 \downarrow - A2\ 0.02335, trans) & GstD5(A1 \downarrow - A2\ 0.00005) \\ \hline \mbox{XLOC}_000246(A2 \uparrow - B2\ 0.044, A1 \downarrow - A2\ 0.01425, \\ \mbox{trans} & \\ \hline \mbox{XLOC}_002137(A1 \downarrow - A2\ 0.02335, trans) & \\ \hline \mbox{XLOC}_002137(A1 \downarrow - A2\ 0.02335, trans) & \\ \hline \mbox{XLOC}_002137(A1 \downarrow - A2\ 0.0023, trans) & \\ \hline \mbox{XLOC}_010702(A1 \uparrow - A2\ 0.0023, trans) & \\ \hline \mbox{XLOC}_002137(A1 \downarrow - A2\ 0.00235, trans) & \\ \hline \mbox{XLOC}_002137(A1 \downarrow - A2\ 0.00235, trans) & \\ \hline \mbox{XLOC}_002137(A1 \downarrow - A2\ 0.00235, trans) & \\ \hline \mbox{XLOC}_002137(A1 \downarrow - A2\ 0.02335, trans) & \\ \hline \mbox{XLOC}_002137(A1 \downarrow - A2\ 0.02335, trans) & \\ \hline \mbox{XLOC}_002137(A1 \downarrow - A2\ 0.02335, trans) & \\ \hline \mbox{XLOC}_106174(A1 \uparrow - B1\ 0.02315, trans) & \\ \hline \mbox{Ugt35b} (A1 \uparrow - B1\ 0.00015) & \\ \hline \mbox{XLOC}_002137(A1 \downarrow - A2\ 0.02335, trans) & \\ \hline \mbox{GstE7}(A1 \downarrow - A2\ 0.00175), \\ \hline \mbox{GstD10}(A1 \downarrow - A2\ 0.00005), \\ \hline \mbox{GstE7}(A1 \downarrow - A2\ 0.00005) & \\ \hline \mbox{XLOC}_002137(A1 \downarrow - A2\ 0.02335, trans) & \\ \hline \mbox{GstE7}(A1 \downarrow - A2\ 0.000175), \\ \hline \mbox{GstD5}(A1 \downarrow - A2\ 0.00005) & \\ \hline \mbox{KLOC}_002137(A1 \downarrow - B1\ trans) & \\ \hline \mbox{GstE7}(A1 \downarrow - A2\ 0.00005) & \\ \hline \mbox{KLOC}_002137(A1 \downarrow - B1\ trans) & \\ \hline \mbox{GstE7}(A1 \downarrow - A2\ 0.00005) & \\ \hline \mbox{GstE7}(A1 \downarrow - A2\ 0.00005) & \\ \hline \mbox{KLOC}_002137(A1 \downarrow - B1\ trans) & \\ \hline \mbox{GstE7}(A1 \downarrow - A2\ 0.00005) & \\ \hline \mbox{KLOC}_002137(A1 \downarrow - B1\ trans) & \\ \hline \mbox{GstE7}(A1 \downarrow - A2\ 0.00005) & \\ \hline \mbox{GstE7}(A1 \downarrow - A2\ 0.00005) & \\ \hline \mbox{KLOC}_002137(A1 \downarrow - B1\ trans) & \\ \hline \mbox{GstE7}(A1 \downarrow - A2\ 0.00005) & \\ \hline \mbox{GstE7}(A1 \downarrow - A2\ 0.00005) & \\ \hline \mbox{KLOC}_002137(A1 \downarrow - B1\ trans) & \\ \hline \mbox{GstE7}(A1 \downarrow - A2\ 0.00005) & \\ \hline \mbox{GstE7}(A1 \downarrow - A2\ 0.00005) & \\ \hline \mbox{KLOC}_002137(A1 \downarrow - B1\ trans) & \\ \hline \mbox{GstE7}(A1 \downarrow - A2\ 0.00005) & \\ \hline \mbox{KLOC}_002137(A1 \downarrow - B1\ trans) & \\ \hline \mbox{GstE7}(A1 \downarrow - A2\ 0.00005) & \\ \hline \mbox{KLOC}_002137(A1 \downarrow - B1\ trans) & \\ \hline \mbox{KLOC}_002137(A1 \downarrow - B1\ trans) & $		trans)	
$ \begin{array}{c} \text{XEnotiones by} \\ \text{cytochrome P450} \\ & \begin{array}{c} \text{XLOC_000246(A2^+B2\ 0.044,\ A1\downarrow-A2\ 0.01425,} \\ \text{trans} \\ & \begin{array}{c} \text{XLOC_002137(A1\downarrow-A2\ 0.02335,\ trans)} \\ \hline \text{XLOC_201255(A1^+B1\ 0.00515,\ trans)} \\ \hline \text{XLOC_010702(A1^+A2\ 0.0023,\ trans)} \\ \hline \text{XLOC_010702(A1^+A2\ 0.0023,\ trans)} \\ \hline \text{XLOC_002137(A1\downarrow-A2\ 0.02335,\ trans)} \\ \hline \text{XLOC_002137(A1\downarrow-A2\ 0.02335,\ trans)} \\ \hline \text{XLOC_106174(A1^+-B1\ 0.02315,\ trans)} \\ \hline \text{XLOC_106174(A1^+-B1\ 0.02315,\ trans)} \\ \hline \text{Glutathione} \\ \hline \text{metabolism} \\ \hline \begin{array}{c} \text{XLOC_002137(A1\downarrow-A2\ 0.02335,\ trans)} \\ \hline \text{XLOC_002137(A1\downarrow-A2\ 0.02335,\ trans)} \\ \hline \text{XLOC_002137(A1\downarrow-A2\ 0.02335,\ trans)} \\ \hline \begin{array}{c} \text{GstE12(A1^+-B1\ 0.00015)} \\ \hline \text{StD2(A1^+-B1\ 0.00015)} \\ \hline \ StD2(A1^+-A2\ 0.00005),\ StD5(A1^+-A2\ 0.00005),\ S$	Metabolism of	XLOC_002137(A1↓-A2 0.02335, trans)	GstD5(A1↓-A2 0.00005)
$\frac{\text{XLOC}_{002137}(\text{A1}\downarrow-\text{A2}\ 0.02335, \text{trans})}{\text{XLOC}_{201255}(\text{A1}\uparrow-\text{B1}\ 0.00515, \text{trans})} \qquad $	cytochrome P450	XLOC_000246(A2↑-B2 0.044, A1↓-A2 0.01425, trans)	GstD10 (A2↑-B2 0.0138, A1↓-A2 0.00175)
$\frac{XLOC_201255(A1^{+}-B1\ 0.00515, trans)}{XLOC_010702(A1^{+}-A2\ 0.0023, trans)} \qquad GstE12\ (A1^{+}-B1\ 0.0495)}{CG17323(A1^{+}-A2\ 0.0108)} \\ \frac{XLOC_002137(A1^{+}-A2\ 0.02335, trans)}{XLOC_106174(A1^{+}-B1\ 0.02315, trans)} \qquad GstE7\ (A1^{+}-A2\ 0.00005), CG5999(A1^{+}-A2\ 0.00135)}{Ugt35b\ (A1^{+}-B1\ 0.00015)} \\ \frac{Glutathione}{Glutathione} \qquad XLOC_002137(A1^{+}-A2\ 0.02335, trans)}{SLOC_002137(A1^{+}-A2\ 0.02335, trans)} \qquad GstD10(A1^{+}-A2\ 0.00175), GstD5(A1^{+}-A2\ 0.00005), GstE7(A1^{+}-A2\ 0.0000$		XLOC 002137(A1 \downarrow -A2 0.02335, trans)	
$\frac{\text{XLOC}_010702(\text{A1}^-\text{A2}\ 0.0023, \text{trans})}{\text{XLOC}_002137(\text{A1}^-\text{A2}\ 0.02335, \text{trans})} \qquad CG17323(\text{A1}^-\text{A2}\ 0.0108)}{\text{GstE7}\ (\text{A1}^-\text{A2}\ 0.00005), CG5999(\text{A1}^-\text{A2}\ 0.00135)}}{\text{XLOC}_106174(\text{A1}^-\text{-B1}\ 0.02315, \text{trans})} \qquad Ugt35b\ (\text{A1}^-\text{B1}\ 0.00015)}$ $\frac{\text{Glutathione}}{\text{metabolism}} \qquad \frac{\text{XLOC}_002137(\text{A1}^-\text{A2}\ 0.02335, \text{trans})}{\text{SLOC}_102137(\text{A1}^-\text{A2}\ 0.02335, \text{trans})} \qquad \frac{\text{GstD10}(\text{A1}^+\text{-A2}\ 0.00175), \text{GstD5}(\text{A1}^+\text{-A2}\ 0.00005)}, \\ \frac{\text{GstD10}(\text{A1}^+\text{-A2}\ 0.00005)}{\text{GstE7}(\text{A1}^+\text{-A2}\ 0.00005)}, \\ \frac{\text{SLOC}_201255(\text{A1}^+\text{-B1}\ \text{trans})}{\text{SLOC}_102137(\text{A1}^+\text{-B1}\ \text{trans})} \qquad \frac{\text{GstE12}(\text{A1}^+\text{-B1}\ 0.0495)}{\text{GstE12}(\text{A1}^+\text{-B1}\ 0.0495)}$		XLOC 201255(A1 ⁺ -B1 0.00515, trans)	GstE12 (A1 ⁺ -B1 0.0495)
$\frac{\text{XLOC}_{002137}(\text{A1}\downarrow-\text{A2}\ 0.02335, \text{trans})}{\text{XLOC}_{106174}(\text{A1}\uparrow-\text{B1}\ 0.02315, \text{trans})} \qquad $		XLOC_010702(A1 ⁺ -A2 0.0023, trans)	CG17323(A1 ⁺ -A2 0.0108)
XLOC_106174(A1^B1 0.02315, trans) Ugt35b (A1^-B1 0.00015) Glutathione metabolism XLOC_002137(A1↓-A2 0.02335, trans) GstD10(A1↓-A2 0.00175), GstD5(A1↓-A2 0.00005), GstE7(A1↓-A2 0.00005) XLOC_201255(A1↑-B1 trans) GstE12(A1↑-B1 0.0495)		XLOC_002137(A1↓-A2 0.02335, trans)	GstE7 (A1↓-A2 0.00005), CG5999(A1↓-A2 0.00135)
Glutathione metabolismXLOC_002137(A1 \downarrow -A2 0.02335, trans)GstD10(A1 \downarrow -A2 0.00175), GstD5(A1 \downarrow -A2 0.00005), GstE7(A1 \downarrow -A2 0.00005)XLOC_201255(A1 \uparrow -B1 trans)GstE12(A1 \uparrow -B1 0.0495)		XLOC_106174(A1 ⁺ B1 0.02315, trans)	Ugt35b (A1 ⁺ -B1 0.00015)
$\frac{\text{GSEE}/(A1 - A2 0.00005)}{\text{XLOC 201255(A1^-B1 trans)}}$	Glutathione	XLOC_002137(A1↓-A2 0.02335, trans)	GstD10(A1 \downarrow -A2 0.00175), GstD5(A1 \downarrow -A2 0.00005),
	metauonsin	XLOC 201255(A1 \uparrow -B1 trans)	$GstE12(A1^{+}-A2 0.00005)$

Table 2. Novle IncRNAs and mRNA genes involved in five KEGG pathways during DR

Note: A1, 7 day in DR; A2, 42 day in DR; B1, 7 day in fully fed; B2, 42 day in fully fed; \uparrow , up-regulation; \downarrow , down-regulation.

Besides, 17 DEGs and 14 DEGs presented in metabolism of xenobiotics by cytochrome P450 and glutathione metabolism pathway, respectively, which were up-regulated in various comparison groups in DR when compared to fully fed condition (Table 2). Out of these, 10 of 17 DEGs and 11 of 14 DEGs belonged to glutathione S transferase, and there are some common glutathione S transferase genes between both pathways such as GstD5, GstD10, GstD6, GstE1, GstE2, GstE3, GstE4, GstE7 and GstE12. Meanwhile seven targets of five novel lncRNAs and four targets of two novel lncRNAs were found in cytochrome P450 and glutathione metabolism pathway, respectively.

Regulatory elements of lncRNA

The promoter positions in genome of fruit fly were first confirmed according to *Drosophila* Core Promoter Database, followed by analysis of lncRNA located in 10kb range (90% identification accuracy and 90% coverage, Dataset S10). Forty four novels and one known lncRNA in our study were found in 10 kb range of 38 promoters. Among 45 lncRNAs, 10 lncRNAs and 12 promoters were present at X chromosome, while one lncRNA and one promoter were present at 2L chromosome. Furthermore, 4 lncRNAs and 4 promoters had the overlapping zones, including *XLOC_067699* (promoter *lcp4*, overlap 92bp), *XLOC_112986* (promoter *s15*, overlap 92bp) and *XLOC_220979* (promoter *G6pd*, overlap 94bp).

Interestingly novel lncRNAs enough. two (XLOC 092363 and XLOC 166557) differentially expressed at the 7 day in DR group when compared to fully fed group. lncRNA XLOC 092363 was located in promoter hairy in the up-stream of sense strand of 3L chromosome. Five differentially expressed targets of XLOC 092363 were also located in 3L chromosome through *cis*-acting mode (Fig. 4a). It's noteworthy that hairy gene as associated promoter and as target of *XLOC* 092363, differentially expressed at 7 day and 42 day of DR in comparison to fully fed flies. Target arr2 has the same tendency of being differentially expressed with promoter hairy gene. Other three targets Cp16, Cp18 and Cp19 differentially expressed at the 7 day in DR when compared to fully fed group, and their molecular function was being the structural constituent of chorion. In addition, promoter ems sited in the downstream of XLOC 166557 in sense strand of 3R chromosome is involved in heme binding and iron ion binding of GO annotations (Fig. 4a). The target of XLOC 166557 was globin 1 by cis-acting mode, and



Figure 4. Two promoters associated IncRNA *XLOC_092363* and *XLOC_166557* in 10 kb range. (a) the positional relationship of two differentially expressed IncRNA and targets in chromosome of fruit fly (\uparrow , up-regulated in DR when compared to fully fed group in RNA-seq data; \downarrow , down-regulated in DR when compared to fully fed group in RNA-seq profile); (b) expression level of two promoters, IncRNA and their targets between DR and fully fed flies by qPCR. **, *P*≤0.01; *, *P*≤0.05.

XLOC_166557 was found to be down-regulated while globin 1 was up-regulated in DR when compared to fully fed flies. The qPCR results were consistent with RNA-seq data up to certain extent (Dataset S3), and revealed differential expression between DR and fully fed flies (Fig. 4b).

Tissue specificity of lncRNA

Differentially expressed lncRNA and mRNA in this study were BLASTed with the transcripts from D. melanogaster from cultured cell lines, dissected organ systems and under environmental perturbations and 5 known lncRNAs from the present study showed the tissue specificity (Dataset S11). In five lncRNAs, CR31781 and target CG31810 (cis-acting mode) were upregulated in DR group when compared to fully-fed group, which were mainly expressed in head, carcass, digestive system, central nervous system and under environmental perturbations (including caffeine, paraquat, Cd, Zn, Cu) in fruit fly. Another target CG13284 was seen upregulated at the 42 day when compared between DR and fully-fed groups. The molecular function of CG31810 and CG13284 is described with steroid dehydrogenase activity. Besides, lncRNA CR43641 (up-regulated at the 7 day when compared to fully fed group) along with the differentially expressed targets *Dip-B*, *tal-AA* and *CG34383* (*cis*-acting mode), were highly expressed in fat or fat body. The remaining lncRNA (*CR43148*, *CR40469* and *CR44095*) and their differentially expressed targets did not have the obviously same tissue specificity.

A total of 20 novel differentially expressed lncRNAs at 7 day under DR condition were randomly selected for analysis in fly head, gut, and fat body using qPCR to determine the tissue specificity (Fig. 5a, primers in Table S2). The results showed that lncRNA XLOC 066439 were at significantly higher expression level in gut compared to head and fat body ($P \le 0.05$). Also the expression levels of XLOC 076307 and XLOC 009418 in head were significantly higher than that of gut and fat body (P≤0.05). XLOC 166557 was mainly expressed in fatbody of fruit flies. Tissue specificity of several IncRNA was consistent with their targets (Table S3), such as XLOC 076307 (Socs36E, head), XLOC 166557 (globin 1, fatbody), XLOC 067962 (PGRP-SC1a, PGRP-SC2 and CG8740, gut and fatbody). On the other hand, 21 differentially expressed lncRNAs were identified in cytoplasm or nucleus of Schneider's line 2 cells by qPCR (Fig. 5b). Among these lncRNA, XLOC 073604 was specially expressed in S2 cell's nucleus. LncRNA XLOC 009798, XLOC 010702, XLOC 071213, XLOC 118356, XLOC 009418 and XLOC 076307 were particularly located in S2 cell's cytoplasm. We also found that lncRNA XLOC 000071, XLOC 056059 and XLOC 196039 were expressed in S2 cell's nucleus and cytoplasm.



Figure 5. Tissue specificity of differentially expressed lncRNA. (a) the tissue specificity of 20 differentially expressed lncRNA at 7 day under DR condition had been analyzed in gut, head, and fat body of flies; (b) 21 differentially expressed lncRNA whether located in cytoplasm or nucleus of Schneider's line 2 cell were detected.



Figure 6. **Expression levels of three targets after 72h of transfection XLOC_076307 siRNA and function enrichment.** (a) expression level of IncRNA XLOC_076307 was significantly down regulated with target Hsp70Bc down-regulation and Gadd45 and Socs36E up-regulation; (b) function enrichment (including GO and KEGG) of XLOC_076307 and its targets.

Inhibition of a novel lncRNA expression in fly S2 cell

A novel lncRNA, targets among other few, the *Gadd45* gene which is involved in FoxO signaling pathway (Fig. 6). In order to understand the role of this novel lncRNA *XLOC_076307*, we silenced it in fruit fly S2 cells by small interfering RNA (siRNA). The results showed that the expression level of *XLOC_076307* and its target *Hsp70Bc* decreased significantly ($P \le 0.01$), while targets *Gadd45* and *Socs36E* showed significant increases after 72h of transfection, confirming the association between lncRNA and its predicted targets through *trans* action model.

DISCUSSION

Long non-coding RNAs make up the majority of the mammalian transcriptome, many of which are emerging as regulators of genome expression/stability and modulators of cell senescence [22, 23]. Previous studies have shown that lncRNAs are involved in aging process and age-related diseases [24, 25]. Although DR is the best-studied intervention known to delay aging and extend lifespan in evolutionarily distant organisms ranging from fruit flies to mammals in the laboratory, the molecular mechanisms of DR are still elusive. In our study, we analyzed lncRNA and mRNA gene expression patterns of transcriptional dynamics in fruit flies at the 7 day and 42 day during DR and fully-fed conditions, respectively, and identified the differentially expressed lncRNAs and their target genes and revealed their possible regulatory roles in DR process.

A large number of candidate lncRNAs have been identified in *Drosophila* during different developmental

stages, dissected tissue samples, cultured cell lines and under environmental perturbations [17, 25, 26]. In this study, we found only 134 known lncRNAs when compared to 2460 annotated lncRNAs from FlyBase (Dmel_Release_6). The reason may be the technical differences between ours and previous studies. Also the lncRNAs at the time of DR have not been identified before and thus, the number of novel lncRNAs (1726) was far more than known lncRNA (134) related to DR, demonstrating that DR impact on lncRNAs remains largely unexplored.

LncRNA in known aging pathways

Upon comparison of aging-related signaling pathways with previously published data on fruit flies [26], we found differentially expressed coding genes as the targets of lncRNA which were enriched in signaling pathways, such as mTOR, FoxO and Wnt signaling pathway, biosynthesis of unsaturated fatty acids, and fatty acid metabolism. Especially in FoxO signaling pathway, three (Gadd45, Pepck, Egfr) of seven differentially expressed coding genes were found to be up-regulated at the 42 day of DR when compared to fully fed flies as the targets of novel lncRNA XLOC 076307, (XLOC 000246, XLOC 000043. XLOC 221562 and XLOC 001163). Gadd45 and Egfr had been reported to be involved in Drosophila senescence [27, 28]. Adipose tissue is a major source of energy, which declines in old age [23, 29]. In our study, DR activates the level of biosynthesis of unsaturated fatty acids and fatty acid metabolism and may rescue the declining stored fat with advancing age to extend healthspan of Drosophila flies. CG9743 (up-regulated at the 7 day of DR versus fully fed flies) as the target of novel differentially expressed lncRNA XLOC_201255 participates in lipid metabolic process [30], such as unsaturated fatty acids and fatty acid metabolism, suggesting a possible involvement in regulation of lipid metabolic process. In this study, 1 gene (inac gene) out of 11 mTOR pathway genes were found to be differentially expressed, and the remaining genes were not significantly different between any of the comparative groups. This result is consistent with what has been previously reported [2]. We presume that the effects of DR on the mTOR pathway genes may occur post-transcriptionally and could not be detected in RNA-seq data. From those results, DR alters the expressing profile of mRNA and lncRNA to activate of the conserved nutrient-signaling pathways.

IncRNA in potential novel aging pathways

Besides known aging-related signaling pathways, we also identified novel pathways which might be related to senescence in DR process. In present study, 11 DEGs were detected which were involved in Hippo pathway and nine of these had been demonstrated to be related to *Drosophila* aging, such as *Upd2*, *Upd3*, *Zyx*, *Pp2A-29B*, *baz*, *wg*, etc. The Hippo pathway is an evolutionarily conserved and pleiotropic mediator of growth control, cell fate decisions and stem cell identity, cell type specification and differentiation during development [31], and, Hippo pathway components also mediated crosstalk with other pathways, for example Wnt, TGF and BMP pathways[32], and also five targets of seven lncRNAs were present in Hippo pathway in the present study.

Phototransduction-fly was another interesting pathway, and had eight DEGs (27.57% of the total 28 coding genes) upregulated during DR when compared to fully fed group in present study. Transient receptor potential (*trp*) was the essential element of the transduction cascade [33], which was upregulated at the 7 day and 42 day during DR in comparison to fully fed flies in our study. Furthermore, the differentially expressed *Arr2* and *inaC* genes were the targets of differentially expressed lncRNA *XLOC_092363* and *XLOC_056059*, respectively. These results indicated DR to be the pleiotropic mediator of *Drosophila* aging for affecting various physiological processes. LncRNA may also take part in regulation of these similar pathways.

IncRNA and its relation with gene promoters

Previous studies have documented the important connection of lncRNA to promoter. Promoter region could be transcribed into lncRNA in quiescent cells to block DHFR gene expression through both direct interactions of the RNA and promoter-specific interference [34]. In our study, we found that 4 lncRNA and 4 promoters had the overlapping zones, which illustrates that these lncRNAs may be transcribed from corresponding promoters.

Another study showed lncRNA HSR1 (heat shock was required for HSF1 (heat-shock RNA-1) transcription factor 1) activation, and the activated HSF1 affect the promoter of related genes to open the transcription in mammalian cells[35]. In this study, we found two differentially expressed lncRNA had the position correlation with promoters. As promoter and target of lncRNA XLOC 092363, hairy gene upregulation in DR had been proven to be a lethal factor after mutagen treatment [36]. Furthermore, Drosophila sirtl is required for heterochromatic silencing and euchromatic hairy/E(Spl) bHLH repression in segmentation and sex determination[36], which is a key member of the sirtuin family of proteins and mammalian homolog of the yeast silent information regulator protein that influence lifespan in several model organisms[37]. XLOC 092363 and targets Cp16, Cp18 and Cp19 were down-regulated at 7 day of DR while promoter hairy was up-regulated. Cp16, Cp18 and Cp19 are involved in biological process of multicellular organismal development and eggshell chorion assembly[38]. We also observed a decrease in egg production in DR flies suggesting that promoter hairy mav have special correlation with IncRNA XLOC 092363 and downstream targets to affect fecundity in DR flies.

Another lncRNA *XLOC_166557* was located in upstream of promoter ems and the expression level of ems was up-regulated at the 7 day during DR when compared to fully fed flies. Its target globin1 located in downstream participated in biological process of oxygen transport [39]. In summary, these results demonstrate that differentially expressed lncRNA and promoters may play a role in DR for extending lifespan *in Drosophila*.

Tissue specificity of lncRNA

In this study, two differentially expressed annotated lncRNA (CR31781 and CR43641) and its targets have the consistent tissue specificity. CR31781 presented specific expression at the 42 day of DR when compared to fully fed flies, and its molecular function is lateral inhibition in cell fate determination [40]. CR31781 and two targets had the similar tissue specificity in carcass from mated female after 4 days [17]. The previous studies reported the variable expression level of CR31781 (presenting up-regulation) in myopathic lamin mutations and lifespan extension of flies over-expressing a small mitochondrial chaperone Hsp22

[41]. Furthermore, its potential targets *CG31810* and *CG13284* are involved in steroid metabolic process, had steroid dehydrogenase activity and upregulated in DR. *CG13284* also participated in negative regulation of cell proliferation and phagocytosis with relevant senescence [42]. These observations suggest that annotated lncRNA *CR31781* and its predicted targets may play an important role in DR, and the specific mechanism of action should be studied in the future research.

Another lncRNA CR43641 and targets Dip-B, tal-AA and CG34383 were highly expressed in Drosophila fat body, a major immune organ, that undergoes immunosenescence and mounts strong systemic inflammation leading to dysregulation of immune deficiency signaling in the midgut of old flies [43]. RNAi system of target CG34383 (Scer\GAL4pnr-MD237) had been a lethal factor before end of pupal stage [40] related to Drosophila aging. Target Dip-B participated in proteolysis process while *tal-AA* took part in biological process of actin filament organization and morphogenesis of an epithelium [44]. Based on these findings, we would speculate that lncRNA CR43641 and its predicted targets may have the positive function in enhancing the immune system and anti-aging in DR conditions.

IncRNA *XLOC_076307* relationship with its targets

We have identified in the Schneider's line 2 cells, the novel lncRNA XLOC 076307, which was hypothesized to possibly take part in cell morphogenesis, cellular morphogenesis, component glycosaminoglycan metabolic process, peptidoglycan metabolic process, spliceosome and FoxO signaling pathway according to its potential targets (Hsp70Bc, Socs36E and Gadd45), and was found mainly located in flies head and S2 cell cytoplasm. Loss of Hsp70 in Drosophila is pleiotropic, with effects on thermotolerance, recovery from heat shock, neurodegeneration and aging defects [45]. Also the target Hsp70Bc was related to heat shock-mediated polytene chromosome puffing [45]. Another target Socs36E played a critical role in a genetic circuit that establishes a boundary between the motile border cell cluster and its non-invasive epithelial neighbors through STAT attenuation [46]. Furthermore, phenotypes Socs36E^{Scer/UAS.P/T.cCa} could reduce death in some flies dying during pharate adult stage [46]. The overexpression of target Gadd45 in the nervous system of D. melanogaster increased the lifespan [47]. Expression level of three targets changed after 72h of transfection of XLOC 076307 siRNA in our study. Thus, we hypothesize that XLOC 076307 may play a role in Drosophila aging.

MATERIALS AND METHODS

Sample collection and preparation

The wild-type stock (Dahomey) were reared at 25°C on a 12-hour on/off light cycle at 50% humidity. Female flies were sorted in two groups which were given DR and fully fed treatment [48]. Median lifespan was calculated as the mean life span of the longest surviving 50% of the population. Egg count was measured according to Emran et al [19]. Ten vials (100 females) of flies were randomly collected for RNA-seq at the 7 day and 42 day in experimental groups (including DR and fully fed group), respectively. A total of eight samples (two biological replicates at day 7 and 42 for each treatment group) were chosen for paired-end (PE read length of 100bp) sequencing using Hiseq2000.

RNA isolation, library preparation, sequencing and lncRNA prediction

Total RNA was extracted using TRIzol Reagent (Invitrogen, CA), and treated with DNase and purified on an RNAeasy column (Qiagen). The quality, quantity and integrity were measured using standard laboratory procedures. Subsequently, sequencing libraries were generated using the rRNA-depleted RNA by NEBNext[®] Ultra[™] Directional RNA Library Prep Kit for Illumina® (New England Biolabs, USA) following manufacturer's recommendations and library quality was assessed on the Agilent Bioanalyzer 2100 system. After cluster generation, the libraries were sequenced on an Illumina Hiseq 2000 platform (provided by Novogene Co. China) and 100 bp paired-end reads were generated. After removing low quality reads (QV\20) and trimming the adapters, paired-end clean reads were aligned to the fly reference genome using TopHat v2.0.9 [49].

Cuffcompare software [49] was used to combine the transcripts, which at least existed in two samples. The \geq 200bp transcripts were selected and the number of extrons was ≥ 1 . Those transcripts were BLASTed (evalue=1e-10) to FlyBase dataset. The mapped transcripts were directly described as known lncRNAs or mRNA genes. The remaining transcripts were BLASTed (evalue=1e-10) to non-mRNA transcripts. such as rRNA, tRNA, snRNA, snoRNA, pre-miRNA, pseudogenes. And, the similar or same transcripts were filtered out. Then, CNCI (Coding-Non-Coding-Index) (v2) profiles [50], CPC (Coding Potential Calculator) (0.9-r2) [51], Pfam Scan (v1.3) [52], and PhyloCSF substitution (phylogenetic codon frequency) (v20121028) [53] were performed to analyse the coding potential of transcripts. Transcripts predicted with coding potential by either/all of the four tools mentioned above, were filtered out, and those without coding potential were our candidate set of novel lncRNAs. The non-coding transcripts were BLASTed to mRNA in FlyBase dataset to screen the lincRNA, intronic lncRNA, anti-sense lncRNA transcripts by Cuffcompare according to class_code (http://cufflinks.cbcb.umd.edu/manual.html#class_codes) [54] and the transcripts with coding potential were the novel mRNA transcripts.

Quantification of gene expression level

Cuffdiff (v2.1.1) [49] was used to calculate FPKMs (expected number of fragments per kilobase of transcript sequence per millions base pairs sequenced) of both lncRNAs and coding genes in each sample. Gene FPKMs were computed by summing up the FPKMs of transcripts in each gene group.

Target gene prediction

LncRNAs have regulatory roles in gene expression at both the transcriptional and post-transcriptional levels in diverse cellular contexts and biological processes. lncRNAs are responsible for nuclear structure integrity, and can regulate the expression of either nearby genes (acting in cis in the nucleus) or genes elsewhere in cells (acting in trans in the nucleus or cytoplasm) by interacting with proteins, RNAs, and DNAs [55, 56]. Cis acting lncRNAs are those acting on neighboring target genes [55]. We searched coding genes 10k/100k upstream and downstream of lncRNAs and then analyzed their function next. Trans acting targets were identified by expression levels of both lncRNAs and mRNA transcripts [56]. While there were eight samples, we calculated the expressed correlation between lncRNAs and coding genes with custom scripts; otherwise, we clustered the genes from different samples with WGCNA [57] to search common expression modules and then analyzed their function through functional enrichment analysis.

Differential gene expression analysis

Cuffdiff (v2.1.1) [49] was used to calculate FPKMs and p value of both lncRNAs and coding genes in each sample. A differential expression correct p value (using BH orthosis) \leq 0.05 and fold change>1.5 assigned as differentially expressed in four different comparisons (7 day DR vs fully fed, 42 day DR vs fully fed, 7 day DR vs 42 day DR, 7 day fully fed vs 42 day fully fed). qRT-PCR was used to validate 28 differentially expressed lncRNAs and corresponding 61 targets using eight samples from two biological duplicates including DR and fully fed groups at the 7 day and 42 day, and the relative gene expression level was calculated according

to Livak and Schmittgen methods [58]. All custom primers were purchased from Sangon Biotech, and the primers of internal reference and identified transcripts in the qPCR were presented in Table S3. The SYBR green method was used for qRT-PCR using LightMix® Swiss) kit (Roche. following manufacturer's instructions. Gene expression levels were identified according to the cycle threshold values and values are expressed as $2-\Delta\Delta CT$ [59]. The relative levels of lncRNAs and targets were normalized to glyceraldehyde 3-phosphate dehydrogenase (GAPDH). Differential expression levels were compared by independent-samples multiple comparison methods between four different comparisons.

GO and KEGG enrichment analysis

Gene Ontology (GO) enrichment analysis of differentially expressed genes or lncRNAs target genes was implemented by the GOseq R package, in which gene length bias was corrected. GO terms with corrected P-value less than 0.05 were considered significantly enriched by differentially expressing genes. KOBAS software [60] was performed to test the statistical enrichment of differentially expressed genes or lncRNAs target genes in KEGG pathways (http://www.genome.jp/kegg/).

Evaluation of tissue specificity

In order to analyze tissue specificity, we downloaded RNA-seq data from paired-end sequencing of $poly(A)^+$ RNA in biological duplicates from 29 dissected tissue samples (including the nervous, digestive, reproductive, endocrine, epidermal and muscle organ systems of larvae, pupae and adults), cultured cell lines and under environmental perturbations [17]. The known identified mRNA and lncRNAs in the present study were BLASTed with the above mentioned transcripts dataset generated in the previous study [17]. Then, 18 novel lncRNAs were randomly selected to analyze the tissue specificity of head, gut and fat body of fruit flies at the 7 day during DR process. Furthermore, 21 novel IncRNAs were picked at random from RNA-seq data to analyze the expression level in Drosophila S2 cell nucleus and cytoplasm using qRT-PCR method. Differential expression levels were compared by independent-samples t-test between groups. The heat map was drawn by MEV4 software [61] and heat map visualizations were conducted with TreeView program.

Regulatory elements

In order to find whether these lncRNAs have analogy to regulatory elements, a list of 205 *Drosophila*

melanogaster core promoters were obtained from database (http://labs.biology.ucsd.edu/Kadonaga/DCPD. htm) and were used to blast with upstream 10kb sequences of identified lncRNAs.

Knockdown of IncRNA in Drosophila S2 cells

Drosophila S2 cells were cultured at 25°C in Hyclone SFX-Insect serum free medium (Thermo Scientific, USA) containing 100 U/mL penicillin and 100 µg/mL streptomycin. The lncRNA XLOC 076307 silencer was synthesized by RiboBio (GuangZhou, China). LncRNA silencer with non-specific nucleotide sequences was used as negative control (lncRNA silencer NC). LncRNA XLOC 076307 silencer and NC were transfected into Drosophila S2 cells in 6-well cell culture plates. For each lncRNA silencer, Drosophila S2 cells were transfected in triplicates with a final concentration of 150 nM in each well. The transfection was performed using transfection reagent (Biotool, China). The cells were harvested after 72 hours of transfection, to extract total RNA and expression levels of lncRNA XLOC 076307 and predicted interacting genes (hsp70BC, Gadd45, Socs36E) were measured by qPCR program as the above described method. LncRNA XLOC 076307 silencers oligonucleotide sequences and primers used in qPCR are listed in Table S2.

Data availability

The RNA-seq data used for this analysis are accessible through (SRP073695).

CONCLUSION

In conclusion, a substantial number of DR-specific lncRNAs and corresponding targets involved in multiple signaling pathways were identified in this study. We have predicted potential functions for novel lncRNA based on target function enrichment and also found important known lncRNA and their targets having the tissue specificity. Moreover, we obtained the result of the tissue specificity of some novel lncRNA in flies and the location of lncRNAs in fly S2 cell. Furthermore we have detected the expression levels of two lncRNA, their targets, and some genes related to aging signaling pathways. As the role of lncRNAs in DR specific lifespan extension have not yet been fully identified and understood, this analysis could serve as the beginning point for exploring the valuable insights into aging and aging-related disease research field for the future studies.

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CONFLICTS OF INTEREST

The authors declare no competing financial interests.

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SUPPLEMENTARY MATERIAL

Sample name	Raw reads	Clean reads	Clean bases	Error rate (%)	Q20 (%)	Q30 (%)	GC content (%)
DR_42d_1_1	46563239	44306160	5.54G	0.03	96.36	92.55	51.09
DR _42d_1_2	46563239	44306160	5.54G	0.04	94.57	89.71	50.32
DR _42d_2_1	45239902	43388011	5.42G	0.03	96.24	92.32	50.81
DR _42d_2_2	45239902	43388011	5.42G	0.04	94.4	89.37	50
DR _7d_1_1	44319390	42475291	5.31G	0.03	96.93	93.69	51.9
DR _7d_1_2	44319390	42475291	5.31G	0.04	93.01	87.43	50.92
DR _7d_2_1	43316530	41506696	5.19G	0.03	96.87	93.59	51.57
DR _7d_2_2	43316530	41506696	5.19G	0.04	93.13	87.61	50.64
Fully fed_42d_1_1	45976024	43999316	5.5G	0.03	96.21	92.21	52.06
Fully fed _42d_1_2	45976024	43999316	5.5G	0.04	94.18	88.98	51.19
Fully fed _42d_2_1	45648001	43880922	5.49G	0.03	96.4	92.59	50.84
Fully fed _42d_2_2	45648001	43880922	5.49G	0.04	94.11	88.92	50.01
Fully fed _7d_1_1	46944441	45018051	5.63G	0.03	96.89	93.59	51.94
Fully fed _7d_1_2	46944441	45018051	5.63G	0.04	92.81	87.1	51
Fully fed _7d_2_1	44797568	42951957	5.37G	0.03	96.83	93.46	51.92
Fully fed _7d_2_2	44797568	42951957	5.37G	0.04	92.8	87.04	51.01

Supplementary Table S1. Transcriptome profiles of DR and fully fed flies

Supplementary Table S2. RT-qPCR primers of 89 genes

			Product		
Gene name	Gene name	Primers(5'-3')	size	Tm (°C)	
Arr2	FBgn0000121-F	GGCACCTGGAACCATTGAGA	85		63.3
	FBgn0000121-R	ATAGCCCTTCACATTGCGGT			
cp16	FBgn0000356-R	CGTTATGGATGGGAGCAGGG	157		63.3
	FBgn0000356-F	ACGCATTCTCGCCGTAAGAT			
cp18	FBgn0000357-F	AGCTCCTCTGGTCTGGAAGG	88		63.3
	FBgn0000357-R	GTCCGTACTCCTGGTTCACG			
cp19	FBgn0000358-F	GAGCTACGGACAGCGATCTT	182		63.3
	FBgn0000358-R	CATATCCACCGCTGACCTGG			
ems	FBgn0000576-F	AGCATCGAGTCCATTGTGGG	146		63.3
	FBgn0000576-R	ATCAAGGTGAGTGTGGCTGG			
hairy	FBgn0001168-F	GGACATCAAGCCATCGGTCA	89		63.3
	FBgn0001168-R	GCTCCTCCTCCTTGATCTGC			
Cyp6w1	FBgn0033065-F	ATCGTCCGGCACTTGTCATT	93		63.3
	FBgn0033065-R	CAGTTTGAAGGACGCGGTTG			
Gadd45	FBgn0033153-F	CATCGGACGCACCATCAAGT		126	63.3
	FBgn0033153-R	GCCATCAGGCAGAAGAGGG			
CG12374	FBgn0033774-F	TCGTTGGTCCCTTGTTCCAC		121	63.3
	FBgn0033774-R	GAATCGTCGCCAACAGAGGA			

CG11192 FBgn0034507-R CTGGCAACTATCCCGACCTGAT 119 63.3 FBgn0037637-R CTGGCAACTATCCCGACCTGATC 137 63.3 FBgn0037637-R GTTTCATCACATCGCGCACG 123 63.3 FBgn0038083-R CACTTGGAGGAATACGG 123 63.3 GG9743 FBgn0039756-F CTTCACCTGGACCCTAACG 115 63.3 G79733 FBgn0039759-R CACGAGGAGACAATGGGAC 27 53.3 G79733 FBgn0039759-R CACCGAGGAGACAATGGGAC 86 63.3 FBgn0041184-F TTCGGCGATGTTTCGAGGC 86 61.4 FBgn0041184-F TTCGGCGAACTACAATGGACAATGGAGGT 71 63.3 FBgn0043575-F TTCGGCGACTACTCTCGC 145 63.3 FBgn0043575-R TACGTTGACCTCTCCCC 71 63.3 FBgn0043570-F GCCAACGACATAGACGCACTG 26 63.3 FBgn0053970-F GGCATGTGGACTTCCACCT 71 63.3 FBgn0053970-F GGCACGAAGACACACGCGGAG 85 63.3 FBgn0053970-F GGCACGTGGAACTACACCCGT 71 63.3 </th <th></th> <th></th> <th></th> <th></th> <th></th>					
FBgn0034507-R CTGGCAACTATCCCGACCTG IscU FBgn0037637-F TGTCCCGGGGCATTGTATC 137 6.3.3 FBgn0037637-R GTTCATCACATCGCCCCAG 123 6.3.3 CG5999 FBgn0038083-F CACTTGGAGGAGAAAGCCGT 123 6.3.3 FBgn0039756-F CTTCACCTGCGGCTCAACG 115 6.3.3 FBgn0039759-F CCAGCAGGAGACAATGGGAG 6.3.3 FBgn0039759-F CCAGTGAGTGAGAGTGTCG 86 6.3.3 FBgn0039759-F CCAGTGAGTGAGAGTGTCG 5.3.3 FBgn00439759-R GCACGGAGTGAGAGTGTCG 5.3.3 FBgn0043575-F TTCGGCCGACTACTCTCTCG 145 6.3.3 FBgn0043575-F TCCCAAAGTGGCTACCTCTCGC 71 6.3.3 FBgn0043575-R TAGTTTCAGCGGTGTGTT 95 6.3.3 FBgn0043576-F TCCAAAGTGGCTCCCCCCT 71 6.3.3 FBgn0053970-F GGCATGTTGAGACGTCTCCTCCT 71 6.3.3 FBgn0053970-F GGCACGAGAGTGTGGCT 5.3.3 FBgn0053970-F GCTGGCTTAGCACACGGGGGTGTTT 95 6.3.3	CG11192	FBgn0034507-F	TTCGTTTCGTGGACGTGGAT	119	63.3
IseUFBgn0037637-FTGTCCCGGTGGCATTGTATC1376.3.3CG5999FBgn003088-FCACTTGGAGGAGAAGCGT1236.3.3CG743FBgn0039756-FCTTCACCTGAGCGGTCATCGG1156.3.3CG9733FBgn0039756-RCACGCGGAGACAATGGGGG866.3.3FBgn0039759-RCCACGCGAGACAATGGGGGG1396.1.4GS038759-RGCACGGAGTAGAGTGTCTGG156.3.3FBgn0039759-RGCACGGAGTAGAGTGCTGGG1396.1.4FBgn0041184-RACCGTGTATTCACGGGGTG1456.3.3FBgn0041184-RACCGTGTTATTCACGGGTGGGGG156.3.3FBgn0041575-RTAGTTTCCAGCGGTGGGGGG156.3.3FBgn0043575-RTAGTTTCCAGCGGTGGGGGGG156.3.3FBgn0043576-FGCCAAAGGCCTCTCCTCCT716.3.3FBgn0043570-FGGCATGTGAGACATAGAGCGCCTG1266.3.3FBgn0053970-RGTCTGGCTTAGCATCACCGGT1266.3.3FBgn0053970-RGCACAGAAAGACCAGGGAGG1266.3.3FBgn0053228-RGACACGAAAGACCAGGGAGG156.3.3FBgn0052813-FCGGACAGCACACTAGCGGGA156.3.3FBgn00529697-RGGCAAGCTTCACCATAGC1206.3.3FBgn0032614-FGTAGGACACCTAGGGGAGA1206.3.3FBgn0032614-FGAAAGACGAGCGCGAAGACATAGG1206.3.3FBgn0032614-FGAAAGACGAGCGCGAGACCAAGG1206.3.3FBgn0032614-FGAAAGGCGCTGCCCCTTTTGG1326.3.3FBgn000278-RGCACGGATCCCCACTGGGAGACACA1206.3.3 <td></td> <td>FBgn0034507-R</td> <td>CTGGCAACTATCCCGACCTG</td> <td></td> <td></td>		FBgn0034507-R	CTGGCAACTATCCCGACCTG		
HBgn0037637-RGTTTCATCACATCGCCGCAGCGS999FBgn003808-RCACTTTGGAGGAGAACCCTI.3I.5CG9743FBgn0039756-FCTTCACCTGGACCCTCAACGI.15I.5.3CG9733FBgn0039759-RCCACGGGAGACAATGGAGCI.5I.5.3CG9733FBgn0039759-RCCACGGGAGACAATGGAGCI.5.9I.5.3CG9733FBgn0039759-RGCACGGAGTAGAGTGTCTGGI.5.9I.5.9Socs36EFBgn0041184-FTTCGCTGAATGCAAATGGGCI.5.9I.5.9PGRP-SC2FBgn0043575-FTTCTGGCCGTACCTTCTCTCI.5.3I.5.9FBgn0043575-FTCCAAAGTGGCTCTCCTCCT71I.6.3FBgn0043576-FTCCAAAGTGGCTTGCTACCATCCCT71I.6.3FBgn0043576-FTCCAAAGTGGCCTTCCTCAAI.2.6I.3.3FBgn003570-FGCGACGAAGGGCTTTCTAAI.2.6I.3.3FBgn003570-FGCGACAAGGGCTTTCTCAAI.2.6I.3.3FBgn00328-FTGGCACAAGGGCTTTCTCAAI.2.6I.3.3FBgn00328-RGCACCGAAAGACCAGGGAGI.3.2I.3.3FBgn003513-RCTTGAACCACACCCGTI.2.6I.3.3FBgn003513-RCTGGGAAGCAACTTGTGTGTI.2.6I.3.3FBgn003513-RCTGGACAAGGGCGAGACACCI.2.6I.3.3FBgn003513-RCTGGACCAAGGGCGAGACACCI.3.2I.3.3FBgn003514-RCCTCGCATCTCACCATCCI.3.2I.3.3FBgn003514-RGTAGGACTGCCCCCCCCCCI.3.3I.3.3FBgn003514-RGTAGGACTGCCCCCCCCCI.3.3I.3.3FBgn003514-RGCACGGAGCACACCGGGAGACACC	IscU	FBgn0037637-F	TGTCCCGGTGGCATTGTATC	137	63.3
CG5999FBgn0038083-FCACTTTGGAGGAGAAGCCGT1236.3.3FBgn003875-FCATTCCCTAGCGGTCATCGGCG9743FBgn003975-FCCAGCAGGAGACAATGGAGAGCG973FBgn0039759-FCCAGCGAGTAGAGTGTCGGCG973FBgn0039759-RGCACGGATAGAGTGTCGGGFBgn0039759-RGCACGGATAGAGAAATGGAGC </td <td></td> <td>FBgn0037637-R</td> <td>GTTTCATCACATCGCCGCAG</td> <td></td> <td></td>		FBgn0037637-R	GTTTCATCACATCGCCGCAG		
FBgn003808-RGATTCCCTAGCGGTCATCGGCG9733FBgn0039756-FCTTCACCTGGACCCTCAACG1156.3.3FBgn0039759-RCCAGTCAGATTGAGGTGCC&63.3FBgn0039759-RGCACGGAGTAGAATGGGC	CG5999	FBgn0038083-F	CACTTTGGAGGAGAAGCCGT	123	63.3
CG9743FBgn0039750-FCTTCACCTGGACCCTCAACG1156.3.3FBgn0039759-RCCACGGGAGACAATGGAGCSG9733FBgn0039759-RGCACGGAGTAGAGTGTCGGSocs36EFBgn0041184-FTTCGCTGAATGCAAATGGGC13961.4FBgn0041184-RACCGTTGTTATTCACGGGC14563.3FBgn0043575-FTTCTGGCCGACTCTCTCGC14563.3FBgn0043575-RTAGTTICCACGGGTGTGGTGGPGRP-TCCAAAGTGGCTCTCCTCCT7163.3FBgn0043576-RGAGACGACATAGACGCCCTGFBgn0043576-RGGCATGTTGGAGGCTGTCTCAA12663.3FBgn0035970-FGGCATGTGGACATCACCCTGFBgn00328-RGACACGAAAGACAAGGCGTTCTCAA12663.3FBgn0032828-FTGGACACAAAGGCATTGACGGGAGFBgn0085213-RCTTGAAGCTTGACGGGAG3.3FBgn0085213-RCTGGAGAAGCAACTGTGGTGT1326.3.3FBgn0085413-RCTGGAGCAACTGTGGTGT1326.3.3FBgn0032614-RGTAGGACTGCTCACCAATACCCG31810FBgn0032614-RGTAGGACGACGAGCACATCFBgn0032614-RGTAGGACTGCTCACCATCGGFBgn0051810-RGTACGAACTGGGAGAGACAACT1963.3FBgn0051810-RGTACGAGCAGCAGCAGGAGCACAAC826.3.3FBgn0051810-RGCACGGGTGGAGTAGGAGCACAT1963.3FBgn00051810-RGCACGGGTGGAGAGACACAT716.3.3FBgn00051810-RGCACGGTGGGGGGGAGCACACAT6.3.3		FBgn0038083-R	GATTCCCTAGCGGTCATCGG		
FBgn0039756-RCAGCAGGGAGACAATGGGAGCG9733FBgn0039759-FCCAGTCAGATTCGAGGTGCC86FBgn0039759-RGCACGAGTAGAGTGTCTGG50.33FBgn0041184-FTTCGCTGAATGCAAATGGGC13961.4FBgn0041184-RACCGTTGTTATTCACGGGGT50.33FBgn0041575-RTTCTGCCGCAACTCTTCTGC14563.3FBgn0043576-FTCCAAGGGCTCTCCTCT7163.3FBgn0043576-FGCACGACATAGACGCCCGG50.33FBgn0043576-RGGCATGTTGGAGCCTTCTCAA12663.3FBgn0043576-RGGCACGACATAGACGCCCGG50.33FBgn003970-FGGCATGTTGGAGCGTTGTT9563.3FBgn003270-RGTCGCGCAAGGGCGGGAG8563.3FBgn003228-FTGGCACAAGGGCCCGGGAG563.3FBgn0085282-RGACACGAAGACCAGGGAGG563.3FBgn0085282-RGCAACGAAGACCAGGGAGG563.3FBgn0085282-RGCAACGAAGACCAAGGGAGG563.3FBgn0085413-FCGAACGAAGACCAGGGAGG563.3FBgn0085413-FCGAACGACTCACCGGGAG8263.3FBgn00529697-RGCAACGCTCCACATAGG263.3FBgn0032614-FGTAGGACTGCCACATGGGAGGA8463.3FBgn0032614-FGTAGGACTGCCACTGGAACAAC8263.3FBgn0032614-FGAAAGCGAGCGAAGCAAC8263.3FBgn0032614-FGAAAGCGAGCGAGCAAC8463.3FBgn00051810-RGTAGGACTCCACTGGACCAT7163.3FBgn00051810-RGCACGCAGCACAGGAACTAGGAA11963.3FBgn000	CG9743	FBgn0039756-F	CTTCACCTGGACCCTCAACG	115	63.3
CG9733FBgn0039759-FCCAGTCAGATTCGAGGTGCC\$66.3.3FBgn003759-RGCACGGAGTAGAGTGTCTGGSocs36EFBgn0041184-FTTCGCTGAATGCAATGGGC1.9FBgn0041184-RACCGTTGTTATTCACGGGCTPGRP-SC2FBgn0043575-FTTCTGGCCGTACTCTTCTGC1.456.3.3FBgn0043575-RTAGTTTCCAGCGGTGTGGTGPGRP-FBgn0043576-FTCCAAAGTGGCTCCTCCTC716.3.3FBgn0043576-RGAGACGACATAGACGCCCTGCG33970FBgn0053970-RGTCTGGCTTAGCATCACCCGFFgn0053970-RGTCTGGCTTAGCATCACCCGFFg2FBgn0053970-RGTCTGGCAAAGGGGCTTTCTCAA1.266.3.3FBgn0053970-RGTCTGGCAAAGAGCAGGGAGG53.3FBgn0053970-RGCCACAAAGACCAGGGAGG53.3FBgn0085413-FCGACCGAAAGATGCGGGAGG53.3FBgn0085413-FCGACAGAACATGTGTGTGT1.326.3.3FBgn00259697-FTGGGGAAGCAACTTGTGGTGT1.326.3.3FBgn0025164-RCAAGTGGGCTGGAAGTAACC526.3.3FBgn0025164-RCAAGTGGGCTGGAAGACACAC846.3FBgn005810-FGAAAGACGAGCGAGACCAAC826.3.3FBgn005810-FGAAAGACGAGCGGAGAGACACAC716.3.3FBgn005810-FGAAAGTGGCTGCGGGAGGA1.196.3.3FBgn005810-FGAAAGTGCGCCGCCC716.3.3FBgn005810-FGAAGCGGAGCAGCGAGACCACAC846.3FBgn000541-RCGTGATCCCACTGGGAGGA1.196.3.3FBgn0005810-FGCAGGGAGCGCGCGCGGAGGACCAC716		FBgn0039756-R	CAGCAGGGAGACAATGGGAG		
FBgn0039759-R GCACGGAGTAGAGTGTCTGG Socs36E FFbgn0041184-R TTCGCTGAATGGCAATGGGC 13 61.4 FBgn0041184-R ACCGTTGTTATTCACGGGCT - - - PGRP-SC FFbgn0043575-R TAGTTGCCGACTCTTCTGC 145 - <td< td=""><td>CG9733</td><td>FBgn0039759-F</td><td>CCAGTCAGATTCGAGGTGCC</td><td>86</td><td>63.3</td></td<>	CG9733	FBgn0039759-F	CCAGTCAGATTCGAGGTGCC	86	63.3
Soes36EFBgn0041184-FTTCGCTGAATGCAAATGGCC13961.4FBgn0041184-RACCGTTGTTATTCACGGGCTPGRP-SC2FBgn0043575-RTAGTTTCCAGCGGTGTGGGGPGRP-SC1aFBgn0043576-RTCCAAAGTGGCTCCTCCTC71SC1aFBgn003576-RGGCATGTTGCAGCGCGTGTGTT95CG33970FBgn003576-RGGCATGTTGGACGCTTGTCACCCGTFrg2FBgn0053970-RGTCTGGCTTAGCATCACCGTFrg2FBgn0083228-FTGGCACAAGGCGCTTCTCAA126CG34384FBgn0085413-RCTGCACAAGGCGGGG85FBgn0085413-RCTGGACCAAAGACCAGGGGAG132FBgn0055970-RGCACCGTCCCCACTGG963.3FBgn0055413-RCTGGAGCACATTGTGTGT13263.3FBgn0055413-RCTGGAGCCAACAGGGGGGG8563.3FBgn0055413-RCTGGAGCCACATTGTGTGT13263.3FBgn0055414-RGCAACGCTCCCACATACC33CG31810FBgn0051810-FGAAAGACGAGCGGAGCCAAC8263.3FBgn0051810-FGAAAGACGAGATGGGACCAAC8463.3FBgn0051810-RGTACGAATATCCATGGGAGCAA8463.3FBgn0051810-RGTACGAATATCCATGGCAGGACCAAC336FBgn0005412-RCGTGATCCCCCTGGAACAAC11963.3FBgn0005412-RGCACCGGTGGAGCACAGTGGAACA11963.4FBgn000078-FGCACCGGTGGAGGACCAGTGGAACA11963.4FBgn000078-FGCACCGGTGGGGGGGAGACCAGTGGAACA13763.4FBgn0001089-RCCGTCACCGGTGGGGGGGAGACCAGTGGAGA13763.4FBgn00012		FBgn0039759-R	GCACGGAGTAGAGTGTCTGG		
FBgn0041184-R ACCGTTGTTATTCACGGGCT PGRP-SC2 FBgn0043575-F TTCTGGCCGTACTCTTCTGC 145 $6.3.3$ FBgn0043575-R TAGTTTCCAGCGGTGTGGGTG V $6.3.3$ FBgn0043576-R GAGACGACATAGACGCCCTG T $6.3.3$ FBgn0035970-R GGCATGTTGGAGCGTTGTT 95 $6.3.3$ FBgn0035970-R GGCACGACAAGGCGCTGTCTCCAA 126 $6.3.3$ FBgn0035970-R GGCACGAAAGAGCCAGGGGAGG V V $6.3.3$ FBgn0035970-R GGCACGAAAGAGCAGGGGAGG V $6.3.3$ FBgn0083228-R GACACGAAAGAGCAGGGGAG 85 $6.3.3$ FBgn0083228-R GACACGAAAGAGCGGGGA 85 $6.3.3$ FBgn0085413-R CTTGAAGCTTGCACCATGGGGAG 85 $6.3.3$ FBgn0025697-R GGCAACGCACACATAGCCCC $CG13284$ FBgn0025697-R GCAACGCAACACACACACAC 82 $6.3.3$ FBgn002514-R CAAGTGGGCAGAAGAAGCAGCACACACA 82 $6.3.3$ 6.33 6.33 6.33 6.33 6.33 6.33 6.33 6.33 <	Socs36E	FBgn0041184-F	TTCGCTGAATGCAAATGGGC	139	61.4
PGRP-SC2 FBgn0043575-F TTCTGGCCGTACTCTTCTGC 145 63.3 PGRP- SC1a FBgn0043575-R TAGTTTCCAGCGGTGTGGTG PGRP- SC1a FBgn0043576-R GAGACGACATAGACGCCCTG 71 63.3 FBgn003370-F GCCATGTTGGACGTGTGTT 95 6.3.3 FBgn0053970-F GCCATGTTGGACCTCACCGT Frag0053970-R GTCTGGCTTAGCATCACCGGT 6.3.3 FBgn003228-F TGGCACAAGGGCTTCTCAA 126 6.3.3 FBgn0083228-R GACACGAAAGAGTGCGGGAG 85 6.3.3 FBgn0085413-F CGACCAGAAGATGCGGGGG 6.3.3 FBgn0025697-R TGGGGAAGCAACTTGTGTGT 132 6.3.3 FBgn0025697-R GCAACGGCTCACCACTCGG 99 6.3.3 FBgn0032614-F GTAGGACTGCTCACCATCGG 99 6.3.3 FBgn0051810-F GAAAGCAGCGGAGCAGACTTGGGAACCAC 82 6.3.3 FBgn0051810-R GTACGAAATATCCATGGGAGCCACA 2 6.3.3 FBgn0051810-R GTACGAAATATCGTGGGAACACAT 71 6.3<		FBgn0041184-R	ACCGTTGTTATTCACGGGCT		
FBgn0043575-R TAGTTTCCAGCGGTGTGGTG PGRP- SC1a FBgn0043576-F TCCAAAGTGGCTCTCCTCCT 71 63.3 FBgn0043576-R GAGACGACATAGACGCCCTG CG33970 FBgn0053970-R GTCTGGCTTAGCATCACCGT	PGRP-SC2	FBgn0043575-F	TTCTGGCCGTACTCTTCTGC	145	63.3
PGRP- SC1a FBgn0043576-F TCCAAAGTGGCTCTCCTCTCT 71 63.3 FBgn0043576-R GAGACGACATAGACGCCTG 5 63.3 GG33970 FBgn0053970-F GGCATGTTGGAGCGTTGTT 95 63.3 FBgn0053970-R GTCTGGCTTAGCATCACCGT 126 63.3 FBgn0053970-R GTCTGGCTAGCATCACCGG 5 63.3 GG34384 FBgn0085413-F CGACAGAAAGACCAGGGGAG 85 63.3 FBgn0259697-F TGGGGAAGCAACTGTGTGTGT 132 63.3 FBgn0259697-R GCAACGGAAGCACACTGTGTGTGT 132 63.3 FBgn0259697-R GCAACGGACACACTGGGGA 82 63.3 FBgn0032614-F GTAGGACTGCTCACCATCGG 99 63.3 FBgn0032614-R CAAGTGGGGCTGGAAGTAGG 82 63.3 FBgn0032614-R GAAAGACGAGCAGACAACA 82 63.3 FBgn0035810-F GAAAGACGGCACCACACACAC 82 63.3 FBgn0051810-R GTACGAATATCCATGGGACACAT 71 63.3 FBgn000539733-F GCTGGATCCCACTGGAACAT 71 63.3		FBgn0043575-R	TAGTTTCCAGCGGTGTGGTG	•	
SC1aFBgn0043576-FTCCAAAGTGGCTCTCCTCT7163.3FBgn0043576-RGAGACGACATAGACGCCTGCG33970FBgn0053970-FGGCATGTTGGACTGTGTT956.3FBgn0083228-RGACACGAAAGGGCTTTCTCAA1266.3.3FBgn0083228-RGACACGAAAGACCAGGGAGGCG34384FBgn0085413-FCGACCAGAAGATGCGGGAG856.3.3FBgn0055907-RGCGACAGAAGATCCGGGAG856.3.3FBgn0259697-FTGGGGAAGCAACTTGTGTGT1326.3.3FBgn0259697-FGCGACGCTCCACCATAGC2CG13284FBgn0032614-FGTAGGACTGCTCACCATCGG996.3.3FBgn0032614-RCAAGTGGGGCTGGAAGTAGG826.3.3FBgn0035810-FGAAAGACGAGCGACCAAC826.3.3FBgn0058110-FGAAAGACGAGCGAGCAACACA826.3.3FBgn005812-FAAAATACGGGCACCAGTGGA846.3.3FBgn005812-RGATCGAATATCCATGGGAGCCAA63.3FBgn005812-RGCTGGATCCACTGGAACACA846.3.3FBgn0059733-RGCTCGTGTCCCGCTCTTTGG3.3FBgn0000454-RCCGTGTTGTCCAGGCAGAA1176.3.3FBgn0000078-FGCACCGGTCGTAGGGAGAA1176.3.3FBgn0000078-RCACAGGGGAGACCTGAACAC906.3.3FBgn0001216-FCAAGCAGCAGGAACTGGAGAA1176.3.3FBgn0001216-FCAAGCAGCAGGGAACTGGAGAACTGGAGAA1176.3.3FBgn0001216-FCAAGCAGCAGCAGGGAACTGGAGAACTGGAGAA1176.3.3FBgn0001216-FCAAGCAGCAGCAGGAACTGGAGAACTGG	PGRP-				
FBgn0043576-R GAGACGACATAGACGCCCTG CG33970 FBgn0053970-F GGCATGTTGGAGCGTTGTTT 95 63.3 FBgn0053970-R GTCTGGCTTAGCATCACCGT 126 63.3 FFq2 FBgn0083228-F TGGCACAAGGGCTTTCTCAA 126 63.3 FBgn0083228-R GACCGAAAGACCAGGGAG 85 63.3 CG34384 FBgn0085413-F CGACCGAAAGACCAGGGGGG 85 63.3 FBgn005813-R CTTGAAGCTTGCACGCGCT 132 63.3 FBgn0055413-R CGACACGACAACATGGTGTGTGT 132 63.3 FBgn00529697-F TGGGGAAGCAACTTGGTGTGT 132 63.3 FBgn0032614-F GTAGGACTGCTCACATACG 90 63.3 FBgn0032614-F GTAGGACGAGCAAGCAACA 82 63.3 FBgn0051810-F GAAAGACGACGACGACAAC 82 63.3 FBgn0051810-F GAAAGACGCACGCGGGAGGAGACAACA 84 63.3 FBgn0051810-F GATGAATATCCATGGGAACAAC 84 63.3 FBgn00051810-F GAAAGCTGCACACGCGCTGAACAT 71 61.3 GATCCCGTCAGTGGAAGCAGCACACA	SC1a	FBgn0043576-F	TCCAAAGTGGCTCTCCTCCT	71	63.3
CG33970FBgn0053970-FGGCATGTTGGAGCGTTGTT9563.3FBgn0053970-RGTCTGGCTTAGCATCACCGTFrq2FBgn0083228-RGGCACAAGAGGCTTTCTCAA12663.3FBgn0085413-FCGACCAGAAGACCAGGGAGG63.3CG34384FBgn0085413-RCTTGAAGCTTGACGCGCT13263.3FBgn0085413-RCTTGAAGCTTGACGCGCT13263.3FBgn0259697-FTGGGGAAGCAACTGTGTGT13263.3FBgn0259697-RGCAACGGTCCACACATACCCG1284FBgn0032614-FGTAGGACTGCTCACCATACCFBgn0032614-FGTAGGACTGCTGAGAGTAGGCG31810FBgn0051810-FGAAAGACGAGCAGCAAC8263.3FBgn0051810-FGAAAGACGGCAGCAGCGAGCAAC8263.3FBgn0051810-RGTACGAATATCCATGGGAGCACAAC8463.3FBgn0051810-RGTACGAATATCCATGGAACAT7163.3FBgn00051810-RGCTGGATCCACTGGAACAT7163.3FBgn0005412-RCGTGAATGCGTCTCGGCTTGJip-BFBgn0000454-FGGAAAGGTGATTGCCAGCAGAGAACAT11963.3FBgn0000058-FCCACCGGTGTAGTGGAACAT7163.3FBgn0001216-FCAACGGGGAGACCTGAACACFBgn0001216-FCAACGGGGAGACCTGAACAC11963.3FBgn0001216-FCAACGGCGGGAGCCTGAACACFBgn001216-FCAACGGGGAGGCGTTTGTGTGFBgn001216-FCAACGGCGAGGGGAGCTGAACACFBgn001216-F		FBgn0043576-R	GAGACGACATAGACGCCCTG		
FBgn0053970-R GTCTGGCTTAGCATCACCGT Frq2 FBgn0083228-F TGGCACAAGGGCTTCTCAA 126 $<$ 3.3 FBgn0083228-R GACACGAAGAGCAGGGGAG $<$ $<$ CG34384 FBgn0085413-F CGACCAGAAGATGCGGGAG $<$ $<$ CG34384 FBgn0085413-R CTTGAAGCTTGACGCGCT $<$ $<$ $<$ nvd FBgn0259697-F TGGGGAAGCAACTGTGTGTGT $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$	CG33970	FBgn0053970-F	GGCATGTTGGAGCGTTGTTT	95	63.3
Frq2FBgn0083228-FTGGCACAAGGGCTTTCTCAA12663.3FBgn0083228-RGACACGAAAGACCAGGGAGGCG34384FBgn0085413-FCGACCAGAAGATGCGGGAG8563.3FBgn0085413-RCTTGAAGCTTTGACGCGGTnvdFBgn0032614-RGCAACGCTGCCACATACC9963.3CG31810FBgn0032614-RCAAGTGGGGCGGAAGCAAC8263.3FBgn0032614-RCAAGTGGGGCGGAGACCAAC8263.3CG31810FBgn0032614-RGAAAGACGAGCGAGCAAC8263.3FBgn0032614-RGAAAGACGAGCGAGAGCAAC8263.3CG31810FBgn0051810-RGTACGAATATCCATGGGAGCCAA8463.3FBgn0051810-RGTACGAATATCCATGGGAGCCAAC8463.3FBgn0051810-RGCTGGATCCCACTGGAACAT7163.3FBgn0051810-RGCTGGATCCCACTGGAACAT7163.3FBgn0051810-RGCTGGATCCCACTGGAACAT7163.3FBgn0005131-RAGTCCTGTCGCTCTTTTGG11963.3GC34383FBgn000054-RGCTGGATCCACTGAGCAGACAT11963.3FBgn0000454-RGCAACGGTGATGGCAACAT11763.3GaFBgn000078-RCACAGGGGAGACTGAACAC11763.3GaFBgn000078-RCCCGCTCTAATGGTTGGCAGACAC11763.3GaFBgn0001216-RCTCACCGTTGGCGAGAACTGGAGAACT13763.3FBgn0001216-RCCTCCTCAATGGTTGGCAGGAACTGGAGAC13763.3FBgn0001218-RTGTCACCACAGGCAGGAACTGTGGGAGAC13563.3FBg		FBgn0053970-R	GTCTGGCTTAGCATCACCGT		
FBgn0083228-RGACACGAAAGACCAGGGAGGCG34384FBgn0085413-FCGACCAGAAGATGCGGGAG8563.3FBgn0085413-RCTTGAAGCTTTGACGCGCT13263.3nvdFBgn00259697-FGGAACGACTCCACCAATACG13263.3FBgn0032614-FGCAACGCTTCCACCAATAGG963.3FBgn0032614-RCAAGTGGGGCTGGAAGTAGG5263.3FBgn0051810-FGAAAGACGAGCGAGACCAAC8263.3FBgn0051810-FGAAAGACGAGCGAGCAGACCAAC8263.3FBgn0051810-RGTACGAATATCCATGGGAGCCAC8463.3FBgn0051810-RGTACGAATATCCATGGGAGCCAC5263.3FBgn0051810-RGTACGAATATCCATGGGAACCAC8263.3FBgn0051810-RGTACGAATATCCATGGGAACCAC8463.3FBgn0051810-RGCTGGATCCCACTGGAACAT11763.3FBgn0051810-RGCTGGATCCCACTGGAACAT11763.3FBgn000531-FGCTGGATCCCACTGGAACAT11763.3FBgn0005412-RGCTGGATCCCACTGGAACAT11763.3FBgn000078-FGCACCGGTGTAGTGGAAT11763.3FBgn000078-FGCACCGGTGTAGGAACT11763.3FBgn000078-FCTCACCGTTGGGCTTTCGT7063.3FBgn000189-FCTCACCGTGGAGAGCAGACC13763.3FBgn0001216-FCAAGCAGCAGGAGTGTTCTCA9063.3FBgn0001216-FCAAGCAGCAGGAGTGTTGCC13763.3FBgn0001218-FGAAGTCCGAGGGAATCGGAACC13763.3FBgn0001218-FGAAGTCCGAGGGAATCGGAACCC13763.3 </td <td>Frq2</td> <td>FBgn0083228-F</td> <td>TGGCACAAGGGCTTTCTCAA</td> <td>126</td> <td>63.3</td>	Frq2	FBgn0083228-F	TGGCACAAGGGCTTTCTCAA	126	63.3
CG34384FBgn0085413-FCGACCAGAAGATGCGGGAG8563.3FBgn0085413-RCTTGAAGCTTTGACGCGCT13263.3nvdFBgn0259697-RGCAACGCTTCCACCATACC13263.3FBgn0259697-RGCAACGCTTCCACCATCGG9963.3CG13284FBgn0032614-FGTAGGACTGCTCACCATCGG9963.3FBgn0032614-RCAAGTGGGGGCTGGAAGTAGC8263.3CG31810FBgn0051810-FGAAAGACGAGCGAGACCAAC8263.3FBgn0051810-RGTACGAATATCCATGGGAGCCAAC8463.3FBgn0051810-RGTACGAATATCCATGGGAGCCAAC8463.3FBgn0051810-RGTACGAATATCCATGGGAGCAGAGGAG8463.3FBgn0051810-RGTACGAATATCCATGGGAGCAGAGAGA8463.3FBgn0051810-RGCTGAATAGCGTCTCGGCTTG11963.3GBgn0085412-RCGTTAATGCGTCTGGCTTTGGG11963.3FBgn00559733-RAGTCCTGTCGCCTCTTTGG11963.3FBgn0000454-RCCGTGTTTGTCCAGTCAGAACA11763.3FBgn000078-RGCACCGGGCGAGACCTGAACAC11763.3GalFBgn000078-RCACAGGGGAGACCTGAACAC13763.3FBgn000128-RTCGTAAACCTTGGCTGTCC13563.3FBgn0001216-FCAAGCAGCAGGAACTGGAGAC13763.3GC1-1FBgn0001216-FCAAGCAGCAGGAACTGGAGAC13763.3FBgn0001218-RTTGTCCTGGCTATGGGAGC13563.3FBgn0001218-RGCACCAAAGCCAAGGAACTGGGAACC13563.3FBgn0003067-RGAAGCCAGAAGCGAATCGGAACCC <td< td=""><td></td><td>FBgn0083228-R</td><td>GACACGAAAGACCAGGGAGG</td><td></td><td></td></td<>		FBgn0083228-R	GACACGAAAGACCAGGGAGG		
FBgn0085413-RCTTGAAGCTTTGACGCGCTnvdFBgn0259697-FTGGGGAAGCAACTTGTGTGT13263.3FBgn0259697-RGCAACGCTTCCACCAATACCCG13284FBgn0032614-FGTAGGACTGCTCACCATCGG9963.3FBgn0032614-RCAAGTGGGGCTGGAAGTAGGCG31810FBgn0051810-FGAAAGACGAGCGAGACCAAC8263.3FBgn0051810-RGTACGAATATCCATGGGAGCCAAC8263.3CG34383FBgn0051810-RGTACGAATATCCATGGGAGGCA8463.3CG34383FBgn0085412-RAAAATACGGCAGCAGCAGGAGGAGC8263.3Bgn0085412-RGCTGGATCCCACTGGAACGA7163.3GETAATGCGTCTGGCACTGGAACAFBgn0059733-FGCTGGATCCCACTGGAACA11963.3PBgn00454-RCCGTGTTTGTCCAGTCCAGA11963.3FBgn000078-FGCAACGGGGAGACCTGAACAC11763.3GalFBgn000078-RCACAGGGGAGACCTGAACAC11763.3FBgn0001089-FCTCACCGTTGGCTGTTGTGT7063.3GalFBgn0001216-FCAAGCAGCAGGAACTGGAGA13763.3FBgn001216-RCCTCCTCAATGGTTGGACCC13763.3FBgn001216-RCCTCCTCAATGGTGGAGCG13763.3FBgn001218-RTTGTCTTGGTCATGGGACCC13563.3FBgn001218-RTTGTCTTGGTCATGGGAACT13563.3FBgn0001218-RCAGGGTCAATGGCAAACTCTTGGCAGC13563.3FBgn000367-RCAGGGTCAATGGCAAACTCTTGGGCAGC13563.3FBgn003131-RATGTCTTGTGTGGCAGGGAACTCT	CG34384	FBgn0085413-F	CGACCAGAAGATGCGGGAG	85	63.3
nvdFBgn0259697-FTGGGGAAGCAACTTGTGTGT13263.3FBgn0259697-RGCAACGCTTCCACCAATACCCG13284FBgn0032614-FGTAGGACTGCTCACCATCGG9963.3FBgn0032614-RCAAGTGGGGCTGGAAGTAGGCG31810FBgn0051810-FGAAAGACGAGCGAGACCAAC8263.3FBgn0051810-RGTACGAATATCCATGGGAGCCAAC8263.3FBgn0051810-RGTACGAATATCCATGGGAGCCAAC8463.3FBgn0051810-RGTACGAATATCCATGGGAGCCAAC8463.3FBgn0055412-RCGTTAATGCGTCTCGGCTTG8463.3FBgn0055412-RCGTGGATCCCACTGGAACAAT7163.3FBgn0055412-RGCTGGATCCCACTGGAACAAT7163.3FBgn0055412-RGCTGGATCCCACTGGAACAAT7163.3FBgn0055412-RGCTGGATCCGCTCTTTTGG11963.3FBgn0005454-RGCGTGTTGTCCAGTCAGAACAT11963.3FBgn000078-FGCACGGGGAGACTGAAGACAC11963.3GalFBgn000078-RCACAGGGGAGACCTGGAACAC11763.3GalFBgn0001216-FCTCACCGTTGGGCTTTGTGT11763.3GalFBgn001216-RCCTCCTCAATGGTGAACC113763.3FBgn001216-RCCTCCTCAATGGTGTCCC13063.3FBgn001218-RTTGTCCTTGGTCATGGGACG13763.3FBgn001218-RTTGCCTTGGCCAGGGAACTGGAACG13563.3FBgn0003067-FCAGGGTAATGCGAAACTCGGAACG13563.3FBgn003067-RGACCAGAACTCCTTGGGCAGC13563.		FBgn0085413-R	CTTGAAGCTTTGACGCGCT		
FBgn0259697-RGCAACGCTTCCACCAATACCCG13284FBgn0032614-FGTAGGACTGCTCACCATCGG9963.3FBgn0032614-RCAAGTGGGGGCTGGAAGTAGGFBgn0032614-RCAAGTGGGGCGGAGACCAAC8263.3CG31810FBgn0051810-FGAAAGACGAGCGAGCCAAC8263.3FBgn0051810-RGTACGAATATCCATGGGAGCCAAC8263.3CG34383FBgn0055412-FAAAATACGGGCAGCAGCAGTGGA8463.3FBgn0055412-RCGTTAATGCGTCTCGGCTTG8463.3FBgn00559733-FGCTGGATCCCACTGGAACAT7163.3FBgn00259733-RAGTCCTGTCGCCTCTTTTGG11963.3FBgn000454-FGGAAAGGTGATTGGCGAGGA11963.3FBgn000078-FGCATCCGGTCGTAGTGGAAT11763.3GalFBgn000078-RCACAGGGGAGACCTGAACAC11763.3GalFBgn0001216-FCTAACCGTTGGGCTGTTCC7063.3FBgn0001216-FCAAGCAGCAGGAACTGGAGAA13763.3GalFBgn0001216-FCAAGCAGCAGGAACTGGAGAAC13763.3FBgn001216-RCCTCCTCAATGGTTGGCAGC9063.3FBgn001218-RTTGTCCTTGGTCATGGGAACC9063.3FBgn0001218-RGAGCCAGAATGGCGAATCCT13563.3FBgn000367-RCAGGGTCAATGGCAATCCT13563.3FBgn003731-RATGTTCCTTGTTGTGTGAGGGCA10963.3FBgn003731-RATGTTCCTTGTTGTGTGAGGGCA10963.3	nvd	FBgn0259697-F	TGGGGAAGCAACTTGTGTGT	132	63.3
CG13284FBgn0032614-FGTAGGACTGCTCACCATCGG9963.3FBgn0032614-RCAAGTGGGGCTGGAAGTAGG </td <td></td> <td>FBgn0259697-R</td> <td>GCAACGCTTCCACCAATACC</td> <td></td> <td></td>		FBgn0259697-R	GCAACGCTTCCACCAATACC		
FBgn0032614-RCAAGTGGGGCTGGAAGTAGGCG31810FBgn0051810-FGAAAGACGAGCGAGACCAAC8263.3FBgn0051810-RGTACGAATATCCATGGGAGCCAC8263.3CG34383FBgn0085412-FAAAATACGGGCAGCAGTGGA8463.3al-AAFBgn0085412-RCGTTAATGCGTCTCGGCTTG8463.3g1-AAFBgn0259733-FGCTGGATCCCACTGGAACAT7163.3p1-BFBgn000454-FGGAAAGGTGATTGGCGAGGA11963.3p1-BFBgn000078-FGCATCCGGTCGTAGTGGAACAT11963.3my-dFBgn000078-FGCATCCGGTCGTAGTGGAAT11763.3GalFBgn001089-FCTCACCGTTGGGCTGTAGTGAACAC11763.3GalFBgn001089-FCTCACCGTTGGGCTGTAGTGAACAC11763.3GalFBgn001216-FCAAGCAGCAGCAGAACTGGAGAA13763.3f5gn001216-RCCTCCTCAATGGTTGGACCC13763.3FBgn001218-RTTGTCCTTGGTCATGGGACGAG9063.3f5gn003067-FCAGGGTCAATGGCGAATCCT9063.3f5gn003067-FCAGGGTCAATGGCGAATCCT13563.3f5gn003067-FCAGGGTCAATGGCGAATCCT13563.3f5gn003067-FCAGGGTCAATGGCGAATCCT13563.3f5gn00331-FCATCACCACAAAGCTCATCGGCAA10963.3f5gn003731-RATGTTCCTTGTTGTGGAGGCA10963.3	CG13284	FBgn0032614-F	GTAGGACTGCTCACCATCGG	99	63.3
CG31810FBgn0051810-FGAAAGACGAGCGAGACCAAC8263.3FBgn0051810-RGTACGAATATCCATGGGAGCCA63.3CG34383FBgn0085412-FAAAATACGGGCAGCAGTGGA8463.3FBgn0085412-RCGTTAATGCGTCTGGGCTTG1163.3al-AAFBgn0259733-FGCTGGATCCCACTGGAACAT7163.3fBgn0259733-RAGTCCTGTCGCCTCTTTTGG11963.3jp-BFBgn0000454-FGGAAAGGTGATTGGCGAGGA11963.3fBgn000078-FGCATCCGGTCGTAGTGGAAT11763.3fBgn000078-FGCATCCGGTCGTAGTGGAAT11763.3GalFBgn000078-RCACAGGGGAGACCTGAACAC11763.3GalFBgn0001089-FCTCACCGTTGGGCTGTTGTGT7063.3FBgn001089-RCCTCCTCAATGGTGGAGAA13763.3FBgn0001216-FCAAGCAGCAGGAACTGGAGAA13763.3FBgn0001218-RTTGTCCTTGGTCATGGGACCC13563.3FBgn0001218-RTTGTCCTTGGTCATGGGAACC9063.3FBgn000367-FCAGGGTCAATGGCGAATCCT13563.3FBgn0003067-FCAGGGTCAATGGCGAATCCT13563.3FBgn003067-RGACCAGAACTCCTTGGGCAG13563.3FBgn00331-FCATCACCACAAAGCTCATGGGAAC13563.3FBgn003731-RATGTTCCTTGTTGTTGGTAGTGGCA10963.3		FBgn0032614-R	CAAGTGGGGCTGGAAGTAGG		
FBgn0051810-RGTACGAATATCCATGGGAGCCAACG34383FBgn0085412-FAAAATACGGGCAGCAGTGGA8463.3FBgn0085412-RCGTTAATGCGTCTCGGCTTG163.3al-AAFBgn0259733-FGCTGGATCCCACTGGAACAT7163.3Dip-BFBgn000454-FGGAAAGGTGATTGGCGAGGA11963.3Mmy-dFBgn000078-FGCATCCGGTCGTAGTGGAAT11763.3GalFBgn000078-RCACAGGGGAGACCTGAACAC11763.3GalFBgn001089-FCTCACCGTTGGCGTTGTGT7063.3FBgn001089-RCCTCCTCAATGGTGGAGA13763.3FBgn0001216-FCAAGCAGCAGGAACTGGAGAC13763.3FBgn0001216-RCCTCCTCAATGGTTGGACCC13563.3FBgn0001218-FGAAGTCGCAGGTGTTCTCAA9063.3FBgn0001218-RTTGTCCTTGGTCATGGGAGG13563.3FBgn000367-FCAGGGTCAATGGCGAATCCT13563.3FBgn003067-RGACCAGAACTCCTTGGGCAG13563.3FBgn00331-RATGTTCCTTGTTGGAGGCA10963.3	CG31810	FBgn0051810-F	GAAAGACGAGCGAGACCAAC	82	63.3
CG34383FBgn0085412-FAAAATACGGGCAGCAGTGGA8463.3FBgn0085412-RCGTTAATGCGTCTGGGCTTGal-AAFBgn0259733-FGCTGGATCCCACTGGAACAT7163.3FBgn0259733-RAGTCCTGTCGCCTCTTTGGDip-BFBgn0000454-FGGAAAGGTGATTGGCGAGGA11963.3FBgn0000454-RCCGTGTTTGTCCAGTCCAGA11763.3Amy-dFBgn000078-FGCATCCGGTCGTAGTGGAAT11763.3GalFBgn000078-RCACAGGGGAGACCTGAACACGalFBgn001089-FCTCACCGTTGGCTGTTCC7063.3FBgn001216-FCAAGCAGCAGGAACTGGAGA13763.3FBgn001216-RCCTCCTCAATGGTTGGACCCHsc70-3FBgn0001218-FGAAGTCGCAGGTGTTCCAGGACG9063.3FBgn0001218-RTTGTCCTTGGTCATGGGACG9063.3FBgn0003067-FCAGGGTCAATGGCGAATCCT13563.3FBgn003067-RGACCAGAACTCCTTGGGCAG10963.3FBgn003731-RATGTTCCTTGTTGGAGGGCA10963.3		FBgn0051810-R	GTACGAATATCCATGGGAGCCAA		
FBgn0085412-RCGTTAATGCGTCTCGGCTTGal-AAFBgn0259733-FGCTGGATCCAACTGGAACAT7163.3FBgn0259733-RAGTCCTGTCGCCTCTTTGGDip-BFBgn0000454-FGGAAAGGTGATTGGCGAGGA11963.3FBgn0000454-RCCGTGTTTGTCCAGTCCAGA11763.3Amy-dFBgn000078-FGCATCCGGTCGTAGTGGAACAC11763.3GalFBgn000078-RCACAGGGGAGACCTGAACAC11763.3GalFBgn001089-FCTCACCGTTGGGCTGTTGTGT7063.3FBgn001089-RTCGTAAACCTTGGCTGTTCCHsc70-1FBgn0001216-FCAAGCAGCAGGAACTGGAGA13763.3FBgn001216-RCCTCCTCAATGGTTGGACCCHsc70-3FBgn0001218-FGAAGTCGCAGGTGTTCTCA9063.3FBgn001218-RTTGTCCTTGGTCATGGGACG13563.363.3PepckFBgn00367-FCAGGGTCAATGGCGAATCCT13563.3FBgn003067-RGACCAGAACTCCTTGGGCAG10963.3FBgn003731-FCATCACCACAAGGTCATCGG10963.3FBgn003731-RATGTTCCTTGTTGGAGGCA10963.3	CG34383	FBgn0085412-F	AAAATACGGGCAGCAGTGGA		84 63.3
al-AAFBgn0259733-FGCTGGATCCCACTGGAACAT7163.3Dip-BFBgn0000454-FGGAAAGGTGATTGGCGAGGA11963.3FBgn0000454-RCCGTGTTTGTCCAGTCCAGA11763.3Amy-dFBgn000078-FGCATCCGGTCGTAGTGGAAT11763.3FBgn000078-RCACAGGGGAGACCTGAACAC56GalFBgn0001089-FCTCACCGTTGGGCTTTGTGT7063.3FBgn0001089-RCCCTCCTCAATGGTGGAGA13763.3FBgn0001216-FCAAGCAGCAGGAACTGGAGA13763.3FBgn0001216-RCCTCCTCAATGGTTGGACCC9063.3FBgn0001218-RTTGTCCTTGGTCATGGGACG9063.3PepckFBgn0003067-FCAGGGTCAATGGCGAATCCT13563.3FBgn0003067-RGACCAGAACTCCTTGGGCAG10963.3FBgn0003731-RATGTTCCTTGTTGGAGGGCA10963.3		FBgn0085412-R	CGTTAATGCGTCTCGGCTTG		
FBgn0259733-RAGTCCTGTCGCCTCTTTGGDip-BFBgn000454-FGGAAAGGTGATTGGCGAGGA11963.3FBgn0000454-RCCGTGTTTGTCCAGTCCAGA11763.3Amy-dFBgn000078-FGCATCCGGTCGTAGTGGAAT11763.3GalFBgn000078-RCACAGGGGAGACCTGAACAC63.3GalFBgn0001089-FCTCACCGTTGGGCTTTGTGT7063.3FBgn001089-RTCGTAAACCTTGGCTGTTCC13763.3Hsc70-1FBgn0001216-FCAAGCAGCAGGAACTGGAGA13763.3FBgn0001216-RCCTCCTCAATGGTTGGACCC9063.3Hsc70-3FBgn0001218-FGAAGTCGCAGGTGTTCTCCA9063.3FBgn0001218-RTTGTCCTTGGTCATGGGACG9063.3PepckFBgn0003067-FCAGGGTCAATGGCGAATCCT13563.3FBgn0003067-RGACCAGAACTCCTTGGGCAG10963.3FBgn0003731-RATGTTCCTTGTTGGAGGGCA10963.3	al-AA	FBgn0259733-F	GCTGGATCCCACTGGAACAT		71 63.3
Dip-BFBgn0000454-FGGAAAGGTGATTGGCGAGGA11963.3Amy-dFBgn000078-FGCATCCGGTCGTAGTGGAAT11763.3Amy-dFBgn000078-RCACAGGGGAGACCTGAACAC11763.3GalFBgn0001089-FCTCACCGTTGGGCTTTGTGT7063.3FBgn0011089-RCTCACCGTTGGCTGTTCC13763.3Hsc70-1FBgn0001216-FCAAGCAGCAGGAACTGGAGA13763.3FBgn001216-RCCTCCTCAATGGTTGGACCC9063.3Hsc70-3FBgn001218-FGAAGTCGCAGGTGTTCTCCA9063.3FBgn001218-RTTGTCCTTGGTCATGGGACG9063.3PepckFBgn003067-FCAGGGTCAATGGCGAATCCT13563.3FBgn003067-RGACCAGAACTCCTTGGGCAG10963.3FBgn003731-FCATCACCACAAGCTCATCGG10963.3FBgn003731-RATGTTCCTTGTTGGAGGGCA10963.3		FBgn0259733-R	AGTCCTGTCGCCTCTTTTGG		
FBgn0000454-RCCGTGTTTGTCCAGTCCAGAAmy-dFBgn000078-FGCATCCGGTCGTAGTGGAAT11763.3FBgn000078-RCACAGGGGAGACCTGAACACGalFBgn0001089-FCTCACCGTTGGGCTTTGTGT7063.3GalFBgn0001089-RTCGTAAACCTTGGCTGTTCCT063.3Hsc70-1FBgn0001216-FCAAGCAGCAGGAACTGGAGA13763.3FBgn0001216-RCCTCCTCAATGGTTGGACCCHsc70-3FBgn0001218-FGAAGTCGCAGGTGTTCTCCA9063.3Hsc70-3FBgn0001218-RTTGTCCTTGGTCATGGGACGT53.3PepckFBgn0003067-FCAGGGTCAATGGCGAATCCT13563.3EgfrFBgn0003731-FCATCACCACAAGCTCATCGG10963.3	Dip-B	FBgn0000454-F	GGAAAGGTGATTGGCGAGGA		119 63.3
Amy-d FBgn000078-F GCATCCGGTCGTAGTGGAAT 117 63.3 FBgn000078-R CACAGGGGAGACCTGAACAC 63.3 Gal FBgn0001089-F CTCACCGTTGGGCTTTGTGT 70 63.3 FBgn0001089-R TCGTAAACCTTGGCTGTTCC 70 63.3 Hsc70-1 FBgn0001216-F CAAGCAGCAGGAACTGGAGA 137 63.3 FBgn0001216-R CCTCCTCAATGGTTGGACCC 90 63.3 Hsc70-3 FBgn0001218-F GAAGTCGCAGGTGTTCTCCA 90 63.3 FBgn0001218-R TTGTCCTTGGTCATGGGACG 90 63.3 Pepck FBgn0003067-F CAGGGTCAATGGCGAATCCT 135 63.3 Egfr FBgn0003731-F CATCACCACAAGCTCATCGG 109 63.3		FBgn0000454-R	CCGTGTTTGTCCAGTCCAGA		
FBgn0000078-RCACAGGGGAGACCTGAACACGalFBgn0001089-FCTCACCGTTGGGCTTTGTGT7063.3FBgn0001089-RTCGTAAACCTTGGCTGTTCCHsc70-1FBgn0001216-FCAAGCAGCAGGAACTGGAGA13763.3FBgn0001216-RCCTCCTCAATGGTTGGACCCHsc70-3FBgn0001218-FGAAGTCGCAGGTGTTCTCCA9063.3FBgn0001218-RTTGTCCTTGGTCATGGGACGPepckFBgn0003067-FCAGGGTCAATGGCGAATCCT13563.3EgfrFBgn0003731-FCATCACCACAAGCTCATCGG10963.3FBgn0003731-RATGTTCCTTGTTGGAGGCA10963.3	Amy-d	FBgn0000078-F	GCATCCGGTCGTAGTGGAAT		117 63.3
GalFBgn0001089-FCTCACCGTTGGGCTTTGTGT7063.3FBgn0001089-RTCGTAAACCTTGGCTGTTCCHsc70-1FBgn0001216-FCAAGCAGCAGGAACTGGAGA13763.3FBgn0001216-RCCTCCTCAATGGTTGGACCCHsc70-3FBgn0001218-FGAAGTCGCAGGTGTTCTCCA9063.3FBgn0001218-FGAAGTCGCAGGTGTTCTCCA9063.3PepckFBgn0003067-FCAGGGTCAATGGCGAATCCT13563.3FBgn0003067-RGACCAGAACTCCTTGGGCAG10963.3FgfrFBgn0003731-FCATCACCACAAGCTCATCGG10963.3		FBgn0000078-R	CACAGGGGAGACCTGAACAC		
FBgn0001089-RTCGTAAACCTTGGCTGTTCCHsc70-1FBgn0001216-FCAAGCAGGAAGGAACTGGAGA13763.3FBgn0001216-RCCTCCTCAATGGTTGGACCC58gn0001218-FGAAGTCGCAGGTGTTCTCCA9063.3FBgn0001218-RTTGTCCTTGGTCATGGGACG7063.363.3PepckFBgn0003067-FCAGGGTCAATGGCGAATCCT13563.3FBgn0003067-RGACCAGAACTCCTTGGGCAG563.363.3EgfrFBgn0003731-FCATCACCACAAGCTCATCGG10963.3	Gal	FBgn0001089-F	CTCACCGTTGGGCTTTGTGT		70 63.3
Hsc70-1FBgn0001216-FCAAGCAGCAGGAACTGGAGA13763.3FBgn0001216-RCCTCCTCAATGGTTGGACCCHsc70-3FBgn0001218-FGAAGTCGCAGGTGTTCTCCA9063.3FBgn0001218-RTTGTCCTTGGTCATGGGACGPepckFBgn0003067-FCAGGGTCAATGGCGAATCCT13563.3FBgn0003067-RGACCAGAACTCCTTGGGCAG53.3EgfrFBgn0003731-FCATCACCACAAGCTCATCGG10963.3FBgn0003731-RATGTTCCTTGTTGGAGGGCA53.3		FBgn0001089-R	TCGTAAACCTTGGCTGTTCC		
FBgn0001216-RCCTCCTCAATGGTTGGACCCHsc70-3FBgn0001218-FGAAGTCGCAGGTGTTCTCCA9063.3FBgn0001218-RTTGTCCTTGGTCATGGGACG70063.3PepckFBgn0003067-FCAGGGTCAATGGCGAATCCT13563.3FBgn0003067-RGACCAGAACTCCTTGGGCAG10963.3EgfrFBgn0003731-FCATCACCACAAGCTCATCGG10963.3FBgn0003731-RATGTTCCTTGTTGGAGGGCA500500	Hsc70-1	FBgn0001216-F	CAAGCAGCAGGAACTGGAGA		137 63.3
Hsc70-3FBgn0001218-FGAAGTCGCAGGTGTTCTCCA9063.3FBgn0001218-RTTGTCCTTGGTCATGGGACGPepckFBgn0003067-FCAGGGTCAATGGCGAATCCT13563.3FBgn0003067-RGACCAGAACTCCTTGGGCAGEgfrFBgn0003731-FCATCACCACAAGCTCATCGG10963.3FBgn0003731-RATGTTCCTTGTTGGAGGGCA53.3		FBgn0001216-R	CCTCCTCAATGGTTGGACCC	÷	•
FBgn0001218-RTTGTCCTTGGTCATGGGACGPepckFBgn0003067-FCAGGGTCAATGGCGAATCCT13563.3FBgn0003067-RGACCAGAACTCCTTGGGGCAGEgfrFBgn0003731-FCATCACCACAAGCTCATCGG10963.3FBgn0003731-RATGTTCCTTGTTGGAGGGCAFBgn0003731-RFBgn0003731-RFBgn0003731-RFBgn0003731-R	Hsc70-3	FBgn0001218-F	GAAGTCGCAGGTGTTCTCCA		90 63.3
PepckFBgn0003067-FCAGGGTCAATGGCGAATCCT13563.3FBgn0003067-RGACCAGAACTCCTTGGGCAGEgfrFBgn0003731-FCATCACCACAAGCTCATCGG10963.3FBgn0003731-RATGTTCCTTGTTGGAGGGCA		FBgn0001218-R	TTGTCCTTGGTCATGGGACG		I
FBgn0003067-R GACCAGAACTCCTTGGGCAG Egfr FBgn0003731-F CATCACCACAAGCTCATCGG 109 63.3 FBgn0003731-R ATGTTCCTTGTTGGAGGGCA 63.3	Pepck	FBgn0003067-F	CAGGGTCAATGGCGAATCCT		135 63.3
EgfrFBgn0003731-FCATCACCACAAGCTCATCGG10963.3FBgn0003731-RATGTTCCTTGTTGGAGGGCA	-	FBgn0003067-R	GACCAGAACTCCTTGGGCAG	•	1
FBgn0003731-R ATGTTCCTTGTTGGAGGGCA	Egfr	FBgn0003731-F	CATCACCACAAGCTCATCGG		109 63.3
	Ŭ	FBgn0003731-R	ATGTTCCTTGTTGGAGGGCA		

	1				
Hsp70Bc	FBgn0013279-F	TGCGATGACGAAGGACAACA	106		63.3
	FBgn0013279-R	GGCGTCCAAGTCGAAGGTTA			
Spat	FBgn0014031-F	GCATCCGAAAGCGAAAGACC	106		63.3
	FBgn0014031-R	ATGGTGTGGTGGTAGATGCG			
CG8740	FBgn0027585-F	GAAATCGGGAAGTGGGCAGA	143		63.3
	FBgn0027585-R	GGTTTTCTCCATCCTGGGCA			
glob1	FBgn0027657-F	GATTCTGGAGCGGCGATACT	85		63.3
	FBgn0027657-R	CCAAAGGAACATCGCGGAAG			
CG6048	FBgn0029827-F	AACTTTTGGCGGTAGCCCTT	81		63.3
	FBgn0029827-R	TCGTGTCCAAGTGTGTTCGT			
CG15046	FBgn0030927-F	ACTGTCCGCTGTTCGAGATG	91 63		63.3
	FBgn0030927-R	CTGCCCAGATCCTGAACTCC			
Cyp28d2	FBgn0031688-F	TGATGCTGGGACGTAATCCG	139		63.3
	FBgn0031688-R	TGCGGTGAAAACAAACGCAA			
SPH93	FBgn0032638-F	GAGTTAGGCCGCGATACCTG	79		63.3
	FBgn0032638-R	ACACACCAGAGTTCTCCCCT			
CG17323	FBgn0032713-F	GCAGCACATGAACTTTGGGG	90		63.3
	FBgn0032713-R	GCAGCGGGAACCGATAGTAA			
CR31781	FBgn0051781-F	GGATACTCTGCCTCGCTCAC	88		59.4
	FBgn0051781-R	ACTCACAGACTTTCTGCCCG			
Cg25C	FBgn0000299-F	GGACGGGTTACTCCCTGTTG	147		59.2
8	FBgn0000299-R	TTCTGGAGGCGTAGTTGCAG			
αTrv	FBgn0003863-F	TGCGCTTACTCCAACTACCC	70		60.4
	FBgn0003863-R	CAGTGCTCACCACCCAAGAG			
5-HT1A	FBgn0004168-F	TCTCCAGCCCTCCAACTGAT	94		59.2
	FBgn0004168-R	CGAGGAGGAGCGTGTCATTT			
inaC	FBgn0004784-F	TTTACGCTGTGGAAGTGGCT	112 594		59.4
	FBgn0004784-R	AGCTTTACATGCCCCTCACC			
ash1	FBgn0005386-F	AGTCAGCCACCCAGTTTAGC	108 594		59.4
	FBgn0005386-R	TTGGGGGTTTCTTGGTTGCT			
δTry	FBgn0010358-F	GGATGGGGGCACTCTCTCCTA		84	58.3
	FBgn0010358-R	CTGGCTCTGGCTAACGATGT			
εTrv	FBgn0010425-F	CGCTCGGATGAGTTCGGATA		149	59.4
	FBgn0010425-R	CATCCATAGCCCCAGGACAC	.1		
nTry	FBgn0011554-F	AGAGAACGGCTTGTCATCCG		136	59.2
	FBgn0011554-R	CTTTCCGCCCTCCGATAGTC	.1		
θTrv	FBgn0011555-F	GGTCGGTAACACTCTGGTGG		71	59.2
	FBgn0011555-R	AAACACCGGGCAGTAGGTTC	.1		
ζTrv	FBgn0011556-F	ACCCAAGGTCTTCCCCTTCT	1	118	59.2
55	FBgn0011556-R	TGTAGCGCAGGGAAATCTGG	J		
Zvx	FBgn0011642-F	CGTTAATGAAACTGACAACGAAAAA		104	59.2
	FBgn0011642-R	ATTCCAAAGTGGCGTGACGA	.1	- • •	
ıTrv	FBgn0015001-F	GTTTGATTCCCGCTTCCTGC	TCCTGC 78 5		57
	FBgn0015001-R	CTCGTTGAGAGGCCAAAGGT	<u>.I</u>	10	51
vkg	FBgn0016075-F	AGGCATCTCTCGGGTCTTCT		124	60.4
	FBgn0016075-R	CCATGCGTCCCTTGATTCCT	4	141	00.1
Ugt35h	FBgn0026314-F	CAGAAACCCTTTTGCCACCG	1	79	60.4
09.000	FBgn0026314-R		1	17	т
	1 D 51100 200 1 4 IC				

GstE12	FBgn0027590-F	TATGCCACCCTAAGTCCCCC 91			59.2
	FBgn0027590-R	TCAGCAGGTTAATTGGCCGT			
CG9220	FBgn0030662-F	ACCCTGCACTTGGAACTACG	77		56.3
	FBgn0030662-R	GTTTGCCCGTGTACGCATTT			
CG8974	FBgn0030693-F	CTGCTGCTAATCGGGGAACA	80		58.3
	FBgn0030693-R	CCACACAACGGCCAAATACG			
CG15531	FBgn0039755-F	TCACCCTCCTTGGCACTTTG	96		58.3
	FBgn0039755-R	TGAGGAAAACCTTCAGGGGC			
λTry	FBgn0043470-F	ACAACACACTCCTGGGCATT	118		58.3
	FBgn0043470-R	TTATCCGCAACGGTCTCCAC			
Pp2A-29B	FBgn0260439-F	GATCCCGTTGCCAATGTTCG	99		58.3
`	FBgn0260439-R	TGTGGGCTTTACTTGGGCAT			
GLS	FBgn0261625-F	AGGACAGCATCAGGCAGAAG	109		59.4
	FBgn0261625-R	TCCACCTTCTCCTCCTCCAC			
Vha68-1	FBgn0265262-F	CCATTGTCGGAGCTGTGTCT	83		594
	FBgn0265262-R	GAACACCTGCACGATACCCA			
	XLOC 000246-F	GTCATAACTGGGCTAAA	115		563
	XLOC 000246-R	CACAATCTGATTTCCCT			
	XLOC 076307-F	TTCCTGGCTTCTTCGCCTAC	103		594
	XLOC 076307-R	GCGCCACCGGCAAAATATAG	105		57.1
	XLOC 000071-F		71		583
	XLOC_000071-R				50.5
	XLOC_009418-F		133		583
	XLOC_009418-R	GAGCGTTTGGCAGTGGTATC	155		50.5
	XLOC_052958-F	TAGGGGTTGCTCCTTTTGGT	81		58.3
	XLOC_052958_R	GCTGAATCCAACGGGTGCTT	01		50.5
	XLOC_052050-R		125		58.2
	XLOC_056059-P				56.5
	XLOC_030039-K	TTGTACTCCCCTCCTTTTGG	00		58.3
	XLOC_072226-P))		56.5
	<u>XLOC_072220-K</u>			74	50.4
	<u>XLOC_101301-1</u> <u>VLOC_161201 P</u>			/4	39.4
	<u>XLOC_101301-K</u>			144	50.2
	XLOC_186022-F		ſ	144	38.5
	XLOC_180922-K			121	50 2
	XLOC_201255-F	TTCCCACACACAACCACCAC		121	30.5
	XLOC_201255-K			72	(2,2)
	XLOC_067962-F			13	03.3
	XLOC_00/902-K			104	(2.2
	XLOC_0/11/3(trans)-F			104	63.5
	XLOC_0/11/3(trans)-R	GACGCGACACAAIGCICICC		100	(2.2
	$\frac{\text{ALUC}_{0/1213}(\text{trans})-\text{F}}{\text{VLOC}_{071212}(\text{trans})-\text{F}}$			122	03.5
	ALOC_0/1213(trans)-R			107	(2.2
	ALUC_0/3004-F			127	63.5
	ALUC_0/3004-K			00	(2.2
	XLUC_09/4/5-F			93	63.3
	XLOC_09/4/5-K		I	01	(2.2
	XLOC_106174(trans)-F			91	63.3
	XLOC_106174(trans)-R	GTAGAGCCAGCCGTATCTGAA			

	XLOC_118356-F	AAGCGAGTGCAAGCTACAGA	73	63.3
	XLOC_118356-R	AATGCCCCACGAAAACCCAA		
	XLOC_151622-F	CAAAAGGGGGGCGTGGTCAAA	104	63.3
	XLOC_151622-R	ACAAAGGACGACAAAGGACGA		
	XLOC_166557(trans)-F	CCTGGAGAGGGGGTTGGATGT	98	63.3
	XLOC_166557(trans)-R	TGAGGCGCAATTTACAGAGC		
	XLOC_196039(trans)-F	TAGGCAAGAATGTACCAAGAACT	83	59
	XLOC_196039(trans)-R	GCCAAAATACGGCGGGAAA		
	XLOC_201602-F	CCAGCTCTTTGGCGATTTGG	104	61.4
	XLOC_201602-R	GAAAATGGCAAACCCGTGGA		
	XLOC 000043(trans)-F	AGTTTGGGCCAATTTTCGCAT	214	63.3
	XLOC_000043(trans)-R	CGTTTTTCCAAGTTTCGGTCA		
	XLOC_002137-F	TCCCAATTCAAAATCGCGTCA	109	63.3
	XLOC 002137-R	ACCGTGTGTTCAATTCCTACC		
	XLOC_007686-F	TCTACGTCATTTGGCATTGGC	85	63.3
	XLOC_007686-R	ACACTTCACACATCGACAAACA		
	XLOC_009798(trans)-F	TTGTTAGCCAGCCAGTCCAG	144	59
	XLOC_009798(trans)-R	GCCCCTGACACGCAAAAGTA		
	XLOC_010702(trans)-F	GGCGGCTGTCACTTTTCATT	126	59
	XLOC 010702(trans)-R	AGGAACCGCAGGACAAAACA		
	XLOC_059066(-inf)-F	CAGCGAAAGAAAACAGGTTAGTCA	122	63.3
	XLOC_059066(-inf)-R	GCGAGAGTATTAAGCCAGCCA		
	XLOC 066439-F	TGCTCCTCCCATATTTCGCAT	144	63.3
	XLOC_066439-R	GCCTCATTGGTTTTGCTATGT		
	XLOC_092363-F	TCTGTCGTCGGGGTATTTGCT	70	63.3
	XLOC_092363-R	GGGTGGGGTTTTATTTGCGG		
GAPDH	FBgn0001128-F	GTTGCGGCTGAGGGCGGATT	94	55-65
	FBgn0001128-R	AGTTGATGTTGGCCGGGTCGC		
GAPDH	XLOC_002137-R XLOC_007686-F XLOC_007686-R XLOC_009798(trans)-F XLOC_009798(trans)-R XLOC_010702(trans)-R XLOC_010702(trans)-R XLOC_059066(-inf)-F XLOC_059066(-inf)-F XLOC_059066(-inf)-R XLOC_066439-F XLOC_066439-R XLOC_092363-F XLOC_092363-R FBgn0001128-F FBgn0001128-R	ACCGTGTGTTCAATTCCTACC TCTACGTCATTTGGCATTGGC ACACTTCACACATCGACAAACA TTGTTAGCCAGCCAGTCCAG GCCCCTGACACGCAGTCCAG GCCGGCTGTCACTTTTCATT AGGAACCGCAGGACAAAACA CAGCGAAAGAAAACAGGTTAGTCA GCGAGAGTATTAAGCCAGCCA TGCTCCTCCCATATTTCGCAT GCCTCATTGGTTTGCTATGT TCTGTCGTCGGGGTATTTGCT GGGTGGGGGTTTTATTTGCGG GTTGCGGCGGAGGGCGGATT AGTTGATGTTGGCCGGGTCGC	85 144 126 122 144 70 94	63. 5 63. 63. 55-65

IncRNA Name	Tissue specificity of lncRNA in	Target Nmae	Tissue specificity from flybase
XLOC 076307	Head	Hsp70Bc	Spermatozoon
		Soce ²⁶ E	Digestive system (midgut, hindgut), brain, head
		SUCSOLE	eve
		CG10041	Male accessory gland
XLOC_009798	Head, gut, fatbody	CG10041	Male accessory gland
		Cyp4p3	Malpighian tubules, Male accessory gland
		IscU homolog	Head, eye, brain, thoracic-abdominal ganglion, gut, heart, carcass, ect
XLOC_166557	Fatbody	globin 1	Head, crop, hindgut, fatbody, carcass, ect
XLOC_000043	Head, gut, fatbody	Pepck	Head, eye, hindgut, fatbody, heart, carcass, ect
XLOC_066439	Gut	Cyp6w1	Head, hindgut, fatbody, heat, carcass, ect
XLOC_106174	Gut, fatbody	Cg25C	Adult heart, fatbody, carcass, ect
		Ugt35b	Head, brain, malpighian tubules, male accessory
NH OC 0(70(2		DODD CC1	gland, digestive system, ect
XLOC_06/962	Gut, fatbody	PGRP-SCIa	Digestive system, fatbody, ect
		PGRP-SC2	Midgut, carcass, salivary gland, ect
		CG8740	Adult hindgut, adult salivary gland, head, ect
XLOC_073604	Head, gut, fatbody	Amy-d	Adult midgut, carcass
XLOC_097475	Gut, fatbody	inaC	Eye, head
XLOC_092363	Gut, fatbody	Hairy	Midgut, hindgut, crop, fatbody, carcass, ect
		Cp16	Adult heart, ovary, carcass, ect
		Cp18	Digestive system, ovary, carcass
		Cp19	Digestive system, ovary, carcass
XLOC_000071	Head, fatbody	CG33970	Adult head, crop, hindgut, ect
XLOC_009418	Head	CG6048	Midgut, hindgut, ect
		Pp2A-29B	Brain, hindgut, heart, ovary, ect
XLOC_056059	Head, fatbody	inaC	Eye, head

Supplementary Table S3. Tissue specificity of IncRNA and its targets