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# Lint-O cooperates with L(3)mbt in target gene suppression to maintain homeostasis in fly ovary and brain

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Hitomi Yamamoto-Matsuda<sup>1,†</sup>, Keita Miyoshi<sup>2,3,†</sup>, Mai Moritoh<sup>1</sup>, Hikari Yoshitane<sup>1</sup>, Yoshitaka Fukada<sup>1</sup>, Kuniaki Saito<sup>2,3,\*</sup>, Soichiro Yamanaka<sup>1,\*\*</sup>, Mikiko C Siomi<sup>1,\*\*\*</sup>

## Abstract

Loss-of-function mutations in Drosophila lethal(3)malignant brain tumor [l(3)mbt] cause ectopic expression of germline genes and brain tumors. Loss of L(3)mbt function in ovarian somatic cells (OSCs) aberrantly activates germ-specific piRNA amplification and leads to infertility. However, the underlying mechanism remains unclear. Here, ChIP-seq for L(3)mbt in cultured OSCs and RNA-seq before and after L(3)mbt depletion shows that L(3)mbt genomic binding is not necessarily linked to gene regulation and that L(3) mbt controls piRNA pathway genes in multiple ways. Lack of known L(3)mbt co-repressors, such as Lint-1, has little effect on the levels of piRNA amplifiers. Identification of L(3)mbt interactors in OSCs and subsequent analysis reveals CG2662 as a novel coregulator of L(3)mbt, termed "L(3)mbt interactor in OSCs" (Lint-O). Most of the L(3)mbt-bound piRNA amplifier genes are also bound by Lint-O in a similar fashion. Loss of Lint-O impacts the levels of piRNA amplifiers, similar to the lack of L(3)mbt. The lint-O-deficient flies exhibit female sterility and tumorous brains. Thus, L(3)mbt and its novel co-suppressor Lint-O cooperate in suppressing target genes to maintain homeostasis in the ovary and brain.

Keywords fertility; gene regulation; L(3)mbt; Lint-O; piRNA
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## Introduction

Temperature-sensitive mutations introduced into the *Drosophila* tumor suppressor *lethal(3)malignant brain tumor* [l(3)mbt] cause malignant growth of adult optic neuroblasts and ganglion mother cells in the larval brain (Gateff *et al*, 1993; Janic *et al*, 2010). At

restrictive temperatures, the mutant flies die at the larval stage, while at permissive temperatures, they are viable but infertile (Coux *et al*, 2018). The expression of L(3)mbt in follicle cells in the ovary is particularly crucial for normal oogenesis to occur.

Genome-wide RNA sequencing (RNA-seq) in the l(3)mbt tumorous brain has identified genes under the control of this tumor suppressor, collectively known as the malignant brain tumor signature (MBTS) (Janic *et al*, 2010). MBTS includes germline genes required for the production and amplification of PIWI-interacting RNAs (piRNAs), such as one of the PIWI members *aubergine* (*aub*) and the DEAD-box RNA helicase *vasa*. Forced attenuation of the aberrant expression of these genes in brain tumors makes the tumorous tissue return to normal (Janic *et al*, 2010). This indicates that the function of L(3)mbt in repressing piRNA factors in nongonadal somatic tissues is directly linked to tumor suppression, particularly in the brain.

The piRNAs are a subset of small RNAs enriched in the germline where they silence transposons (Iwasaki *et al*, 2015; Czech *et al*, 2018; Yamashiro & Siomi, 2018; Ozata *et al*, 2019). Upon abrogation of piRNA function, transposons under the control of piRNAs can move within the germline genome. This causes DNA damage, which leads to failure in germline development, resulting in infertility (Schüpbach & Wieschaus, 1991; Klattenhoff *et al*, 2007). Thus, piRNA-mediated transposon silencing is indispensable for a wide range of animals to produce offspring through sexual reproduction.

In cultured ovarian somatic cells (OSCs), which correspond to follicle cells in the ovary, all piRNAs are loaded onto Piwi, one of three PIWI members, giving rise to the piRNA-induced silencing complex (piRISC) (Saito *et al*, 2009). Piwi-piRISC is then localized to the nucleus where it represses transposons transcriptionally by reducing the level of RNA polymerase II at the target loci and/or inducing heterochromatinization around these loci (Yin & Lin, 2007; Klenov *et al*, 2011; Shpiz *et al*, 2011; Wang & Elgin, 2011; Sienski *et al*, 2012; Yashiro *et al*, 2018; Onishi *et al*, 2020, 2021). By contrast, in ovarian germ cells (OGCs), piRNAs are loaded onto all three

3 Department of Genetics, School of Life Science, SOKENDAI, Shizuoka, Japan

\*Corresponding author. Tel: +81 55 981 6823; E-mail: saitok@nig.ac.jp

<sup>1</sup> Department of Biological Sciences, Graduate School of Science, The University of Tokyo, Tokyo, Japan

<sup>2</sup> Department of Chromosome Science, National Institute of Genetics, Research Organization of Information and Systems, Shizuoka, Japan

<sup>\*\*</sup>Corresponding author. Tel: +81 3 5841 4387; E-mail: soichiro.yamanaka@bs.s.u-tokyo.ac.jp

<sup>\*\*\*</sup>Corresponding author. Tel: +81 3 5841 4386; E-mail: siomim@bs.s.u-tokyo.ac.jp

<sup>&</sup>lt;sup>†</sup>These authors contributed equally to this work

PIWI members: Piwi, Aub, and Argonaute3 (AGO3). Piwi-bound piRNAs in both OSCs and OGCs are biased toward the antisense orientation of transposon mRNAs and, as in OSCs, Piwi-piRISC in OGCs represses transposons transcriptionally by targeting nascent transcripts while they are being synthesized on the genome (Saito et al, 2006; Vagin et al, 2006; Czech et al, 2018). Aub-bound piRNAs are also biased toward the antisense orientation, but AubpiRISC silences transposons post-transcriptionally in the cytoplasm by cleaving transposon mRNAs, depending on the endonuclease activity that Aub exhibits (Iwasaki et al, 2015; Czech et al, 2018). AGO3 also has endonuclease activity, but AGO3-bound piRNAs are mostly sense to transposon mRNAs; thus, AGO3 cleaves transposon transcripts in the antisense orientation. RNAs fragmented by AGO3 are subsequently consumed as precursors for Aub-bound piRNAs. In this way, Aub-piRISCs are amplified. Similarly, Aub-dependent RNA cleavage amplifies AGO3-piRISCs. Aub and AGO3 continue this chain reaction, known as the ping-pong cycle, thereby accumulating a great number of piRISCs in the OGCs (Brennecke et al, 2007; Gunawardane et al, 2007; Czech et al, 2018).

OSCs do not operate the ping-pong cycle because of the lack of Aub and AGO3 expression. Other factors essential for piRNA amplification, such as Vasa, are also not expressed in OSCs (Malone et al, 2009; Saito et al, 2009). However, l(3)mbt is expressed in OSCs (Sumiyoshi et al, 2016). As noted above, piRNA factors were aberrantly expressed in the l(3)mbt brains; thus, we reasoned that l(3)mbt depletion in OSCs would allow the cells to express Aub, AGO3, and Vasa, along with other germ-specific ping-pong factors, amplifying piRNAs that act in post-transcriptional silencing. Indeed, CRISPR-Cas9-mediated genome editing to knock out l(3)mbt in OSCs facilitated the expression of Aub and AGO3 (Sumiyoshi et al, 2016). Vasa and other piRNA amplifiers have also been detected in L(3)mbtlacking OSCs (i.e., Ambt-OSCs), where Aub and AGO3 initiate the ping-pong cycle in a manner dependent on Vasa. We hypothesized that L(3)mbt controls genes involved in the piRNA amplification in OSCs, similar to the manner in which it suppresses germline genes in the brain to inhibit tumorigenesis. However, the mechanism by which L(3)mbt controls the target genes in both tissues remains unknown.

In this study, we conducted chromatin immunoprecipitation sequencing (ChIP-seq) for L(3)mbt in cultured OSCs (Saito et al, 2009) concurrently with RNA-seq in the presence and absence of L (3)mbt and found that L(3)mbt controls the expression of piRNA pathway genes in multiple fashions. This function of L(3)mbt does not largely depend on known L(3)mbt co-repressors, such as Lint-1 and Myb (Lewis et al, 2004; Georlette et al, 2007; Meier et al, 2012). We then sought and analyzed L(3)mbt interactors in OSCs and identified CG2662 as a novel L(3)mbt co-repressor, which was termed "L(3)mbt-interacting protein in OSCs" (Lint-O). Comparison of L(3)mbt and Lint-O ChIP-seq reads revealed that the L(3)mbtbound piRNA amplifier genes were mostly bound with Lint-O. The piRNA amplifiers derepressed by L(3)mbt depletion were similarly derepressed by Lint-O depletion. We also found that Lint-O was unstable in the absence of L(3)mbt, but not vice versa, suggesting distinct functionalities of L(3)mbt and Lint-O despite their tight relationship in gene regulatory function. The lint-O knockout flies, Lint- $O^{KO}$ , produced in this study exhibited female sterility at permissive temperatures and developed tumorous brain at restrictive temperatures, similar to the l(3)mbt-deficient flies. We argue that Lint-O is a novel co-suppressor of L(3)mbt that cooperates tightly with L(3)mbt

### Results

#### OSCs express two L(3)mbt variants, L(3)mbt-L and L(3)mbt-S

To conduct genome-wide ChIP-seq for L(3)mbt in OSCs, we first produced an anti-L(3)mbt monoclonal antibody. Western blotting using this antibody detected L(3)mbt as a doublet in OSC lysates (Fig EV1A). Both bands disappeared upon RNA interference (RNAi) treatment for L(3)mbt (Fig EV1A), suggesting that both are L(3) mbt. Hereafter, we refer to the ~ 190 and ~ 150 kDa bands as L(3) mbt-L and L(3)mbt-S, respectively.

A previous study showed that the l(3)mbt gene bears multiple isoforms of which the expression levels change during development (Wismar et al, 1995). We thus inferred that L(3)mbt-L and L(3)mbt-S may correspond to two isoforms. To examine whether this inference is correct, we performed rapid amplification of cDNA ends (RACE) experiments using total RNAs isolated from OSCs. Three different 5' ends of l (3)mbt mRNA were detected (#1-3, Fig EV1B). Two distal 5' ends (#1 and #2) were located within the 5'-untranslated region (UTR) of the l(3)mbt RNA transcript annotated in FlyBase (FBtr0085175). By contrast, the most proximal 5' end (#3) was not within the annotated l(3)mbtsequence. Rather, it was found to be within the 5' long terminal repeat (LTR) of *springer* retrotransposon inserted into the third intron of l(3)mbt in the OSC genome (Sienski et al, 2012). This l(3)mbt isoform consists of a portion of springer (294 bases: nucleotides #152-445) and exons 4 and 5 of the *l*(3)*mbt* gene (Fig EV1B). Western blotting showed that L(3)mbt expressed from the authentic cDNA and its truncated version in OSCs comigrated with endogenous L(3)mbt-L and L(3)mbt-S, respectively (Fig EV1C). Thus, L(3)mbt-L corresponds to the full-length (FL) L(3)mbt, and L(3)mbt-S is its truncated form, which highly likely starts with Met325 of L(3)mbt-L. The level of piRNAs against springer is negligible in OSCs (Sienski et al, 2012). Therefore, the allele encoding L (3)mbt-S is spared from piRNA-mediated regulation, enabling the expression in OSCs. Immunofluorescence of OSCs using anti-L(3)mbt antibody detected the L(3)mbt signals nearly exclusively in the nucleus (Fig EV1D), suggesting that both L(3)mbt isoforms are localized to the nucleus, similarly to L(3)mbt in other cell types such as neuroblasts (Richter et al, 2011) and cultured Kc cells (Meier et al, 2012).

#### L(3)mbt controls piRNA amplifiers in multiple ways in OSCs

We performed L(3)mbt ChIP-seq in OSCs using the anti-L(3)mbt monoclonal antibody. The experiment was conducted twice, and statistical analysis confirmed the high correlation between the two libraries (Appendix Fig S1A). An overview of the ChIP-seq reads mapped on the *Drosophila* genome is presented in Fig EV2A. We then extracted ChIP-seq reads corresponding to 13,951 protein-coding genes in Flybase by allowing the reads to map the promoter region of each gene and analyze. Note that the promoter region in this study refers to the genomic region spanning from 0.35 kilobase (kb) upstream of the transcriptional start site (TSS) to 0.1 kb downstream of the TSS, based on the previously reported DNA-binding status of L (3)mbt in *Drosophila* larval tissues (Richter *et al*, 2011). This analysis showed that L(3)mbt can bind to 8,525 of 13,951 protein-coding genes (61.1%) (Fig 1A). We further classified these genes according to where in each gene L(3)mbt is bound. This revealed that 7,460 genes had promoter region binding of L(3)mbt (53.5% in 13,951 genes). We designated this group as "promoter region binding." The remaining 1,065 genes were designated as "nonpromoter genic binding" (7.6%). The 5,426 genes that did not belong to either group were designated as "unbound with L(3)mbt" (38.9%).

Comparison of the ChIP-seq reads with the OSC RNA-seq reads before and after L(3)mbt depletion revealed that the expression levels of 1,202 genes among the 7,460 "promoter region binding" genes were upregulated by L(3)mbt loss (16.1%), while 1,044 genes were downregulated (14.0%) (Fig 1A). Note that RNA-seq was conducted three times, and principal component analysis (PCA) confirmed the high correlation in the libraries (Fig EV2B). We previously showed that seven germ-specific piRNA biogenesis genes - *vasa, aub, ago3, qin, tejas (tej), bootlegger (boot),* and *CG9925* - were among the genes prominently upregulated by L(3)mbt depletion (Sumiyoshi *et al,* 2016). In this study, we found that five of these genes - *vasa, qin, tej, boot,* and *CG9925* - were within the "upregulated" category of the "promoter region binding" group



#### Figure 1. L(3)mbt controls target gene expression in complex fashions.

- A The 13,951 protein-coding genes of *Drosophila* were classified into "promoter region binding," "nonpromoter genic binding," and "unbound with L(3)mbt" in accordance with the L(3)mbt ChIP-seq reads, and were subsequently divided into "upregulated," "downregulated," and "unchanged" in accordance with the RNA-seq reads from OSCs before and after L(3)mbt depletion [+/- L(3)mbt]. Representatives of piRNA factors are indicated within the groups. ChIP-seq was performed twice technically and RNA-seq three times.
- B–D The genomic regions harboring vasa (B), aub (C), and ago3 (D). The gene structure is shown at the top. The arrow depicts the TSS and the orientation of transcription. The L(3)mbt ChIP-seq reads in normal OSCs (wild-type) and RNA-seq reads from L(3)mbt-depleted [L(3)mbt KD] and control OSCs are shown under the gene structure. The shading in gray corresponds to exons. The y-axis shows the number of reads per million mapped reads (RPM).

(Fig 1A). The patterns of binding of L(3)mbt to these genes and the RNA-seq signals at the loci are shown in Fig 1B (*vasa*) and Fig EV2C (*qin, tej, boot,* and *CG9925*).

The key somatic piRNA factors, *piwi*, *female sterile(1)Yb* (*yb*), *armitage* (*armi*), and *zucchini* (*zuc*), all of which are intrinsically expressed in normal OSCs, belonged to the "promoter region binding" group (Fig 1A). Their expression levels were unchanged by the loss of L(3)mbt (Fig EV2D), agreeing with our previous observation (Sumiyoshi *et al*, 2016). We previously showed that Piwi expression in OSCs depends on the transcriptional factor Traffic jam (Tj) (Saito *et al*, 2009), indicating that as long as Tj is functional, Piwi will be expressed regardless of the presence or absence of L(3)mbt. It seems that the regulation of *piwi* via Tj takes precedence over the regulation via L(3)mbt.

Likewise, the promoter of *flamenco* (*flam*), the piRNA cluster responsible for bearing most piRNAs within OSCs (Brennecke *et al*, 2007), was bound with L(3)mbt via the promoter, but the expression level was not impacted by the lack of L(3)mbt (Fig EV2E). An earlier study showed that the expression of *flam* depends on the transcriptional factor Cubitus interruptus (Goriaux *et al*, 2014). L(3) mbt binds to a relatively wide range of genes, but for genes functioning in OSCs, there appear to be activators that override the repression by L(3)mbt.

The *aub* and *ago3* genes were classified into the "unbound with L(3)mbt" and "nonpromoter genic binding" categories, respectively (Fig 1A). Both genes were upregulated by L(3)mbt depletion (Fig 1C and D), as expected based on our earlier observation (Sumiyoshi *et al*, 2016). At the *aub* locus, the L(3)mbt binding was concentrated in the upstream part of *aub*, but all sites were distant from the TSS (Fig 1C). From the perspective of neighboring genes, the L(3)mbt signals were rich in the promoter regions of *nup154* and *RPL9*. However, the expression levels were not changed by the lack of L(3)mbt (Fig 1C). In this regard, *nup154* and *RPL9* can be considered as equivalents of *piwi* and *yb*. The L(3)mbt ChIP signals at the *ago3* gene were biased to introns but not to the promoter (Fig 1D). It seems that L(3)mbt genomic binding is not always linked to gene regulation and that L(3)mbt regulates piRNA pathway genes in multiple fashions.

L(3)mbt ChIP-seq reads and OSC RNA-seq reads before and after L(3)mbt depletion were also classified based on the distance from most proximal TSS (Appendix Fig S1B and C). Note that the "L(3) mbt in the TSS region" group corresponds to the "promoter region binding" group in Fig 1A.

#### Known L(3)mbt co-suppressors are likely irrelevant for L(3)mbtdriven gene regulation in OSCs

L(3)mbt resides in two repressive chromatin complexes, the LINT complex (Meier *et al*, 2012) and the dREAM complex [*a.k.a.* the Myb–MuvB (MMB) complex] (Lewis *et al*, 2004; Georlette *et al*, 2007; Blanchard *et al*, 2014). An earlier genetic study showed that the L(3)mbt function in the ovaries requires Lint-1, a component of the LINT complex but is independent of the dREAM complex (Coux *et al*, 2018). To understand in which of these two complexes L(3) mbt exerts its function in OSCs, we depleted components of the two complexes by RNAi (Appendix Fig S2A and B) and examined how these treatments affected the levels of *aub*, *ago3*, *piwi*, *and vasa*. The expression of *aub* was upregulated by the loss of Lint-1 and

CoRest, both of which are LINT complex components, but this upregulation was milder than that following L(3) mbt loss (Fig 2A). Upon depletion of E2F2, Mip120, and Mip130, all of which are contained within the dREAM complex, the level of aub was barely changed. Knockdown of Myb in the dREAM complex slightly upregulated aub, but the effect was not as great as that of Lint-1 or CoRest knockdown (Fig 2A). These findings suggest that L(3)mbt function in regulating the aub gene in OSCs is independent of the dREAM complex but dependent on the LINT complex, similar to the circumstances in the ovaries, but with lower extent. The changes in the level of ago3 under these conditions were similar to those of aub (Appendix Fig S2C). The levels of *piwi* remained stable under each condition, as expected (Appendix Fig S2D). In sharp contrast, the increases in the expression of vasa following the loss of all of these known L(3)mbt co-factors were much lower than that following L (3)mbt depletion (Fig 2B). One plausible scenario is that, when L(3) mbt controls target genes via the promoter (e.g., vasa), it is almost independent of both LINT and dREAM complexes, but when L(3) controls target genes via regions other than the promoter (e.g., aub and *ago3*), it may subtly depend on the LINT complex.

#### Lint-O is a novel co-repressor of L(3)mbt in OSCs

Our findings above prompted us to identify novel L(3)mbt cosuppressor(s). To this end, we isolated the L(3)mbt complex from OSCs before and after L(3)mbt RNAi (Fig 2C) and forwarded the materials for mass spectrometric analysis. Peptides corresponding to 100 proteins were obtained from normal OSCs (Fig 2D and Appendix Table S1). The number of peptides corresponding to 21 proteins among these 100 proteins was reduced four-fold or more by L(3)mbt depletion (Appendix Table S1). Exclusion of the ribosomal proteins and L(3)mbt reduced the number of candidate proteins to 17. Gene Ontology (GO) analysis categorized 7 of the 17 proteins as DNA-binding and chromatin regulation factors (Fig 2D and E).

The effects of Lint-1 deficiency on aub, vasa, and ago3 were already examined (Fig 2A and B and Appendix Fig S2C). Histone H3.3A and RNA polymerase II subunit 3 (Rpb3) seemed to be rather general factors and were therefore not considered to be strong candidates. We then examined the contribution of four other factors, CG2662, CG2199, proliferation disrupter (Prod), and Ada2acontaining complex component 3 (Atac3), in the regulation of vasa and aub. Quantitative reverse-transcription PCR (RT-qPCR) showed that the level of vasa was increased upon the depletion of CG2662, similar to that of L(3)mbt, but was unchanged by the depletion of CG2199, Prod, or Atac3 (Fig 2F and Appendix Fig S2E). The level of aub was also influenced by CG2662 loss as efficiently as L(3)mbt loss (Fig 2G). These findings suggested that CG2662 is a co-suppressor of L(3)mbt more closely related to it than any known L(3)mbt cosuppressors, including Lint-1. Thus, we termed CG2662 "L(3)mbtinteracting protein in OSCs" (Lint-O) and continued our investigation to reveal the functional relationship between L(3)mbt and Lint-O.

# The L(3)mbt-Lint-O interaction is necessary for piRNA pathway gene regulation

L(3)mbt contains three malignant brain tumor (MBT) repeats responsible for binding methylated histone marks (Wismar *et al*, 1995; Bonasio *et al*, 2010), a C2H2-type zinc finger, and a sterile



Ε

Protein	SPS	PSM	Function	
Lint-1	37.046	54	L(3)mbt co-suppressor	
CG2662	14.463	14	Unknown	
CG2199	3.391	2	Unknown	
Prod	1.992	2	DNA binding	
Rpb3	2.102	3	RNA polymerase II subunit	
H3.3A	1.259	2	Nucleosome component	
Atac3	0.94	2	Chromatin remodeling	

#### Figure 2. CG2662/Lint-O binds to and functions with L(3)mbt in gene regulation.

- A, B The mRNA levels of *aub* (A) and *vasa* (B) were quantified upon the depletion (RNAi) of L(3)mbt, Lint-1, CoRest, E2F2, Myb, Mip120, and Mip130, and were compared to those in normal OSCs (control). Data represent the mean  $\pm$  SE (n = 3 biological replicates). The P values were calculated with the *t*-test. \*P < 0.05, \*\*P < 0.01. All *t*-tests were performed against samples with  $\lceil$  symbol.
- C Proteins immunoprecipitated with the anti-L(3)mbt antibody from the OSC lysates before (control) and after L(3)mbt knockdown (KD) were silver-stained. The bands corresponding to L(3)mbt-L and L(3)mbt-S are indicated.
- D Flow chart of the identification of L(3)mbt interactors in OSCs. All peptides obtained from LC–MS/MS are listed in Appendix Table S1.
- E Summary of the sum of the –log posterior error probability (Sum Pep Score: SPS), peptide spectra match values (PSM), and known functions of the proteins in (D). Mass spectrometry analysis was performed on biological duplicates.
- F, G The mRNA levels of *vasa* (F) and *aub* (G) were quantified upon the depletion (RNAi) of L(3)mbt, Atac3, Prod, CG2662/Lint-O, and CG2199, and were compared to those in normal OSCs (control). Data represent the mean  $\pm$  SE (n = 3 biological replicates). The *P* values were calculated with the *t*-test. \*\*P < 0.01. All *t*-tests were performed against samples with  $\lceil$  symbol.

Source data are available online for this figure.

alpha motif (SAM) domain that acts in protein–protein interactions (Kim & Bowie, 2003) (Fig 3A). Lint-O consists of two plant homeodomain (PHD) finger domains and a SAM domain (Fig 3A). The PHD finger is often found in chromatin-associated proteins that read histone H3 marks such as H3K4me2/3 to regulate target gene expression (Sanchez & Zhou, 2011).

To confirm the association between L(3)mbt and Lint-O, we ectopically expressed wild-type (WT) Lint-O, tagged with 3x FLAG at the C-terminus, in OSCs. The L(3)mbt complex immunopurified from the OSC lysates was then probed with anti-FLAG and anti-L(3) mbt antibodies. WT Lint-O signal was detected along with that of L (3)mbt (Fig 3B). However, when the Lint-O mutant lacking the SAM domain,  $\Delta$ SAM (Fig EV3A), was expressed instead of WT Lint-O, the mutant failed to co-immunoprecipitate with L(3)mbt (Fig 3B). The  $\Delta$ SAM mutant was localized to the nucleus as was the WT control (Fig 3C). In subsequent experiments, both L(3)mbt-L and L(3) mbt-S, but not their  $\Delta$ SAM mutants, bound to Lint-O (Figs 3D and EV3B and C), although all those proteins were localized to the nucleus (Figs 3E and EV3D). These findings confirm the L(3)mbt-Lint-O association in OSCs and indicate that their interaction depends on the SAM domain of each of the two proteins.

We next investigated whether the L(3)mbt-Lint-O interaction is important for regulating target gene expression. RT–qPCR showed that *vasa* and *aub* were upregulated in Lint-O-lacking OSCs (Fig 3F and G). We then ectopically expressed RNAi-resistant WT Lint-O in these cells. This treatment rescued the defects caused by the loss of endogenous Lint-O (Fig 3F and G). When the  $\Delta$ SAM mutant, which was also RNAi-resistant, was expressed, the *vasa* and *aub* genes were not re-silenced (Fig 3F and G). These findings indicated that the L(3)mbt-Lint-O interaction via the SAM domain is essential for the cooperative function of L(3)mbt and Lint-O in regulating the gene targets.

These rescue assays were also performed using another Lint-O mutant, 8CA, where eight cysteines within the two PHD finger domains were altered to alanine (Fig EV3A). This mutant was not expected to re-repress *vasa* and *aub* because other PHD finger-

containing proteins have been shown to anchor zinc ions via the cysteines and this ion anchoring is essential for these proteins to exert their functions (Kalkhoven et al, 2002). However, contrary to our expectations, the 8CA mutant re-repressed vasa and aub to an extent similar to that of the WT (Fig 3F and G). Thus, Lint-O may not require zinc ions to regulate its target genes. The 8CA mutant was able to interact with L(3)mbt (Fig 3H) and localize to the nucleus (Fig 31). However, when the PHD finger domains were removed from Lint-O (Fig EV3A), the  $\Delta$ PHD mutant was unable to interact with L(3)mbt (Fig 3H) although its nuclear localization was unaffected by the lack of PHD domains (Fig 3I). These results support the idea that the ability of Lint-O to associate with chromatin via the PHD domains influences the L(3)mbt-Lint-O interaction. This idea was further supported by the observation that the binding activity of L(3)mbt to the vasa promoter was significantly weakened by the absence of Lint-O (Fig 3J). The binding activity of Lint-O to L (3)mbt appeared to be slightly increased by the 8CA mutation (Fig 3H). This may be because the mutation stabilized the binding of Lint-O to chromatin.

In the course of our study, we noticed that, in the absence of L(3) mbt, endogenous Lint-O was barely detected by western blotting using anti-Lint-O antibodies raised in this study (Figs 3K and EV3E). The level of *lint-O* mRNA was not impacted by the lack of L(3)mbt (Fig 3L). By contrast, Lint-O depletion little influenced the level of L (3)mbt (Fig 3K). Thus, the L(3)mbt-Lint-O interaction is required for the stabilization of Lint-O but not of L(3)mbt. These results support the idea that L(3)mbt and Lint-O have distinct functions even though they bind to each other and cooperate in gene regulation in OSCs.

# L(3)mbt and Lint-O cooperate in regulating the expression of piRNA amplifiers in OSCs

We next conducted Lint-O ChIP-seq in OSCs using the anti-Lint-O antibodies. The experiment was conducted twice, and statistical analysis confirmed the high correlation between the two libraries (Appendix Fig S3A). An overview of ChIP-seq reads mapped on the

#### Figure 3. The L(3)mbt-Lint-O interaction is crucial for the repression of target genes.

- A Domain structures of L(3)mbt and Lint-O. L(3)mbt has three MBT repeats (orange), a C2H2-type zinc finger (Zf) (gray), and a SAM domain (blue). Lint-O has two PHD finger domains (green) and a SAM domain (blue).
- B Immunoprecipitation (IP)/western blotting shows that WT Lint-O, but not its ΔSAM mutant (Fig EV3A), co-immunoprecipitated with L(3)mbt from the OSC lysates. n.i., nonimmune IgG.
- C Subcellular localization of WT Lint-O and its  $\Delta$ SAM mutant (green). Both proteins were localized to the nuclei (DAPI: blue). Scale bar: 5  $\mu$ m.
- D IP/western blotting shows that WT L(3)mbt-L, but not its ΔSAM mutant (Fig EV3B), co-immunoprecipitated with Lint-O from the OSC lysates. n.i., nonimmune IgG.
   E Subcellular localization of WT L(3)mbt-L and its ΔSAM mutant (green). Both proteins were localized to the nuclei (DAPI: blue). Scale bar: 5 µm.
- F, G The mRNA levels of *vasa* (F) and *aub* (G) were quantified upon ectopic expression of EGFP, and WT Lint-O and its  $\Delta$ SAM and 8CA mutants (Fig EV3A), in Lint-O-lacking OSCs (Lint-O RNAi) and were compared to those in normal OSCs (control). Data represent the mean  $\pm$  SE (n = 3 biological replicates). The *P* values were calculated with the *t*-test. \*P < 0.05. All *t*-tests were performed against samples with  $\lceil$  symbol.
- H IP/western blotting shows that L(3)mbt co-immunoprecipitated with WT Lint-O and its 8CA mutant, but not with ΔPHD mutant (Fig EV3A). An asterisk shows the background.
- I Subcellular localization of WT Lint-O and its 8CA and ΔPHD mutants (green). All proteins were localized to the nuclei (DAPI: blue). Scale bar: 5 μm.
- J ChIP-qPCR shows that L(3)mbt binding to the *vasa* promoter was weakened after the loss of Lint-O. Data represent the mean  $\pm$  SE (n = 3 biological replicates). The *P* values were calculated with the *t*-test. \*\*P < 0.01. All *t*-tests were performed against samples with  $\lceil$  symbol.
- K Western blotting showing the amounts of L(3)mbt, Lint-O, and histone H3 (H3) in normal (control), L(3)mbt-depleted (RNAi), and Lint-O-depleted (RNAi) OSCs. Asterisks show background signals as in Fig EV3E.
- L The *lint-O* mRNA levels in normal (control), L(3)mbt-depleted (RNAi), and Lint-O-depleted (RNAi) OSCs are shown by fragments per kilobase million (FPKM). Data represent the mean  $\pm$  SE (n = 3 biological replicates). The *P* values were calculated with the *t*-test. \*P < 0.05, \*\*P < 0.01. All *t*-tests were performed against samples with  $\lceil$  symbol.

Source data are available online for this figure.



Figure 3.

*Drosophila* genome is presented in Fig EV4A. The degree of overlap between Lint-O peaks and L(3)mbt peaks is indicated in Fig EV4B. Further analysis showed that Lint-O bound to 7,447 protein-coding genes via their promoter regions (53.4% of a total of 13,951 genes) ("promoter region binding" in Fig 4A). Comparison of the ChIP-seq reads with the OSC RNA-seq reads before and after Lint-O depletion

(Fig EV2B) revealed that 827 genes of the 7,447 "promoter region binding" group were upregulated by the loss of Lint-O (11.1%), whereas 663 genes were downregulated (8.9%) (Fig 4A). The *vasa*, *qin*, *tej*, *boot*, and *CG9925* genes belonged to the "upregulated" category as they belonged to the equivalent in L(3)mbt ChIP-seq (Fig 1A). The expression levels of the other 5,957 genes were little

impacted by Lint-O depletion (80.0%) (Fig 4A). The *piwi*, *yb*, *armi*, and *zuc* genes belonged to this category as they belonged to the counterpart in Fig 1A.

A total of 924 of 13,951 protein-coding genes were classified into the "nonpromoter genic binding" group (6.6%) (Fig 4A). Of these, 154 genes were upregulated by the loss of Lint-O (16.7%) and the *ago3* gene was in this category. In addition, 5,580 genes were "unbound with Lint-O" (40.0%) (Fig 4A). Of these, 231 genes were upregulated by the loss of Lint-O (4.1%), and *aub* belonged to this category. The browser views of Lint-O ChIP-seq and RNA-seq in the presence and absence of Lint-O at the *vasa*, *aub*, and *ago3* loci are shown in Fig 4B–D. Basically, the Lint-O



#### Figure 4. L(3)mbt and Lint-O share genomic binding to orchestrate gene control in OSCs.

- A The 13,951 protein-coding genes of *Drosophila* were classified into "promoter region binding," "nonpromoter genic binding," and "unbound with Lint-O" in accordance with the Lint-O ChIP-seq reads, and were subsequently divided into "upregulated," "downregulated," and "unchanged" in accordance with the RNA-seq reads from the OSCs before and after Lint-O depletion (+/- Lint-O). Representatives of piRNA factors are indicated. ChIP-seq was performed twice technically and RNAseq three times.
- B–D The genomic regions harboring vasa (B), aub (C), and ago3 (D) are indicated. The L(3)mbt and Lint-O ChIP-seq reads and the RNA-seq reads from normal (control), L (3)mbt-depleted, and Lint-1-depleted OSCs are shown. The L(3)mbt ChIP-seq reads and the RNA-seq reads from normal (control) and L(3)mbt-depleted were also shown in Fig 1B–D.
- E Heatmaps show the L(3)mbt ChIP and Lint-O ChIP scores calculated by deeptools (Ramírez *et al*, 2016) within each gene body and the extended regions (*i.e.*, 3 kb upstream of the TSS and 3 kb downstream of the TES). The length of all the genes is normalized to be a constant value, 5 kb. The summary plots show the average score.
- F Venn diagram showing the overlap between L(3)mbt- and Lint-O-regulated genes.

genomic binding patterns are nearly identical to those of L(3)mbt, further indicating the collaborative functions of the two proteins in piRNA amplifier gene regulation.

The five "promoter region binding" genes (*i.e.*, *vasa*, *CG9925*, *tej*, *boot*, and *qin*) and two "nonpromoter genic binding" genes (*i.e.*, *aub* and *ago3*) were similarly upregulated in L(3)mbt- and Lint-O-depleted OSCs (Fig EV4C). In each case, the lack of Lint-O appeared less influential than that of L(3)mbt. Such a trend was also observed in the number of genes affected by the lack of L(3)mbt/Lint-O (based on RNA-seq) (Fig EV4D); namely, the number of genes influenced by the lack of L(3)mbt was slightly higher than that influenced by the lack of Lint-O. This may be related to the observation that Lint-O becomes unstable upon the lack of L(3)mbt (Fig 3K).

Lint-O ChIP-seq reads and OSC RNA-seq reads before and after Lint-O depletion was also classified based on the distance from most proximal TSS (Appendix Fig S3B). We also analyzed the binding frequencies of L(3)mbt and Lint-O to the TSS and transcriptional end sites (TES) of the protein-coding genes. The histogram indicated that both proteins tend to bind strongly to the TSS and weakly to the TES and downstream regions (Fig 4E). L(3)mbt and Lint-O may rarely repress target genes by binding to introns (*e.g., ago3*) or upstream regions far from the TSS (*e.g., aub*). The regulation of *aub* and/or *ago3* by L(3)mbt and Lint-O may also be indirectly mediated by transcription factors or other regulators that are directly activated by the loss of L(3)mbt/Lint-O.

A previous study showed that brain tumors in l(3)mbt mutant flies originated from deregulation of target genes in the Salvador-Warts-Hippo (SWH) pathway (Richter et al, 2011). Another study asserted that inappropriate expression of Nanos (Nos), a translational repressor and key regulator of germline fate, in ovarian follicular (somatic) cells was the main cause of defects in germline development observed in the l(3)mbt mutants (Coux *et al*, 2018). ChIP-seq and RNA-seq at two genes under the control of the SWH pathway, drosophila inhibitor of apoptosis 1 and expanded, showed that both L(3)mbt and Lint-O bound to the promoters of the two genes, albeit weakly, but the mRNA levels were barely changed by the loss of L(3)mbt or Lint-O (Appendix Fig S3C). This suggested that dependence on the L(3)mbt/Lint-O functions varies among cells. The nos promoter was bound with L(3)mbt and Lint-O relatively strongly and the mRNA level was upregulated following L(3)mbt or Lint-O depletion, but the expression was still far lower than that of nos in the ovary in the FlyAtlas 2 (Leader et al, 2018) (Appendix Fig S3D and E). The expression of nos may be activated when OSCs reside in the vicinity of germ cells in the ovary.

# L(3)mbt and Lint-O may function independently of each other in gene regulation

MBTS is not restricted to germ-specific piRNA factors (Janic et al, 2010). For the next part of our study, we collected 1,443 proteincoding genes under the control of L(3)mbt [i.e., genes that were bound with L(3)mbt, irrespective of whether this was promoter binding or nonpromoter binding, and upregulated by the L(3)mbt depletion] (Fig 1A) and 981 genes under the control of Lint-O (i.e., genes that were bound with Lint-O, irrespective of whether this was promoter binding and nonpromoter binding, and upregulated by the loss of Lint-O) (Fig 4A), and compared the gene pools. The Venn diagram showed that 816 genes were shared between the two groups (Fig 4F). We attempted to sort these genes according to GO terms, but the statistical analysis did not enrich for significant terms. We next focused on 627 genes that were suppressed via the L(3)mbt binding but in a Lint-O-independent matter. These genes could be controlled by the combination of L(3)mbt and co-factors other than Lint-O [i.e., "L(3)mbt-dependent and Lint-O-independent"]. However, no significant GO terms were found. A similar result was obtained for "L(3)mbt-independent and Lint-O-dependent" genes (165 genes). We also focused on downregulated genes. We found that 439 genes were downregulated by depletion of both L(3)mbt and Lint-O (Appendix Fig S3F). Again, no significant terms were found. L(3)mbt/Lint-O appears to regulate a wide variety of intracellular pathway genes in OSCs.

# Lint-O is essential for ovarian morphogenesis and oocyte development

To investigate the importance of Lint-O function in flies, we generated *lint-O*-deficient mutants by applying the CRISPR-Cas9 system. A guide RNA was designed to introduce an indel mutation in the *lint-O* coding sequence (Fig 5A). A mutant fly harboring a singlenucleotide deletion was obtained. In this mutant, the *lint-O* expression was severely attenuated (Fig 5B); thus, the *lint-O* mutant was designated *Lint-O*<sup>KO</sup>. The mutant flies were viable at permissive temperatures but exhibited female infertility at 29°C (Fig 5C) as the temperature-sensitive l(3)mbt mutant,  $L(3)mbt^{ts1}$ , showed female sterility at permissive temperatures (Coux *et al*, 2018).

The *Lint-O<sup>KO</sup>* ovaries appeared to be morphologically abnormal at 29°C. To investigate this in more detail, we immunostained the mutant ovaries with antibodies specific for Vasa, oo18 RNA-binding protein (Orb), Fasciclin 3 (Fas3), and Spectrin (Spec), and with phalloidin, a chemical that specifically binds to filamentous actin (F-



Figure 5. The lack of Lint-O in flies leads to abnormal ovarian morphology and female sterility.

- A CRISPR-mediated generation of *lint-O* knockout (KO). Genomic structure of *lint-O* is shown with gRNA targeting *lint-O* exon 1 (triangle). Sequences of *lint-O* DNA in WT (*y w*) (complementary to the gRNA sequence) and the KO mutant, *Lint-O<sup>KO</sup>*, are shown. PAM: protospacer adjacent motif (underlined). E1-3: Exons 1–3. CDS: protein-coding sequence. UTR: untranslated region.
- B RT–qPCR analysis shows the mRNA levels of *lint-O* in y w and *Lint-O<sup>KO</sup>* ovaries. Data are expressed as mean and error bars represent SD. n = 2 biological replicates.
- C The numbers of progeny in y w and Lint-O<sup>KO</sup> are shown. Ten independent crosses were performed. Boxplot central bands, upper edges of boxes, lower edges of boxes, upper whiskers, and lower whiskers show median, third quartile, first quartile, maxima, and minima, respectively.
- D Confocal images of y w and Lint- $O^{KO}$  ovaries immunostained for Vasa. Scale bar: 50  $\mu$ m.
- E Confocal images of y w and Lint-OKO ovarioles immunostained for Vasa. Vasa was ectopically expressed in follicle cells (white arrowheads). Scale bar: 50 µm.

actin). Vasa has been shown to be ectopically expressed in cultured OSCs upon L(3)mbt depletion and somatic cells in  $L(3)mbt^{ts1}$  ovaries (Sumiyoshi *et al*, 2016; Coux *et al*, 2018). Similarly, Vasa was detected in somatic (follicle) cells in the *Lint-O<sup>KO</sup>* ovaries at 29°C (Figs 5D and E and EV5A).

The expression of Orb in the *yellow white* (y w) ovaries that we employed as a WT control was restricted to the developing oocyte at the posterior of egg chambers (Fig EV5B), as reported previously (Lantz et al, 1994). However, in the ovaries of Lint-OKO, Orb was mislocalized to the anterior region of the egg chamber, where a few cells had gathered abnormally (Fig EV5B). Fas3 is a cell adhesion molecule abundant in polar cells during the late stages of oogenesis (Ruohola et al, 1991). The polar cells in y w localize to the edge of the anterior-posterior axis of the follicular cells (Fig EV5C). By contrast, the egg chamber of Lint-OKO had excessive and ectopic polar cells. It seemed that ovarioles were fused during ovary morphogenesis in the absence of *lint-O* expression. Spec localizes to somatic cell membranes and the spectrosome/fusome while the basic F-actin polymer generates a dynamic cytoskeletal network (Theurkauf et al, 1993; Lin et al, 1994). Spec and F-actin immunostaining signals indicated that the egg chambers were indeed fused in Lint-OKO at restrictive temperatures (Fig EV5D and E). These findings indicate that Lint-O plays an essential role in ovarian morphogenesis and oocyte development, similar to L(3)mbt (Coux et al, 2018).

When fly ovaries were immunostained with anti-Lint-O antibody, no signal was detected. Therefore, the gene encoding Venus was knocked in at the *lint-O* genomic loci. Fluorescent signals were detected in both germ and somatic cells (Fig EV5F). It is not yet known whether the ovarian phenotype described above is due to loss of Lint-O expression in germ cells, somatic cells, or both. We infer that somatic cell expression of Lint-O may be important for the maintenance of ovarian morphology, similar to L(3)mbt (Coux *et al*, 2018).

# L(3)mbt and Lint-O cooperatively control target genes in the brain to suppress tumorigenesis

When L(3)mbt was depleted in the third-stage (L3) larvae, germline genes such as vasa, piwi, and aub were ectopically expressed in the brain, resulting in tumorigenesis (Janic et al, 2010; Richter et al, 2011). Remarkably, western blotting showed that Vasa, Piwi, and Aub proteins were ectopically expressed in the brain of *Lint-O<sup>KO</sup>* L3 larvae (Fig 6A). Immunofluorescence detected Vasa relatively strongly in Miranda (MIRA)-positive neuroblast cells (Betschinger et al, 2006) but not in ELAV-positive neuronal cells (Robinow & White, 1991) (Figs 6B and EV5G-J). Lint-O may repress Vasa expression in undifferentiated cells but not in terminally differentiated cells. The *l(3)mbt* mutants ectopically expressed Vasa particularly in the outer proliferative center (OPC) and in the central brain (CB) neuroblasts (Janic et al, 2010; Richter et al, 2011). Similar cell specificity was observed for the *Lint-O<sup>KO</sup>* L3 larval brain (Fig EV5G-J). In addition, the *Lint-O<sup>KO</sup>* brain was enlarged, as was the L(3)*mbt<sup>ts1</sup>* brain, although it was slightly smaller (Fig 6C). These results support the intriguing concept that Lint-O plays an important role in L(3)mbt-mediated inhibition of tumorigenesis in the brain.



#### Figure 6. L(3)mbt and Lint-O cooperatively control target genes in the brain.

- A Western blotting shows that Vasa, Piwi, and Aub were ectopically expressed in *Lint-O<sup>KO</sup>* and *L(3)mbt<sup>ts1</sup>* larval brains at 29°C. Anti-Lint-O, anti-L(3)mbt, anti-Vasa, andi-Piwi, anti-Aub, and anti-Tubulin antibodies were used.
- B Confocal images of y w, Lint-O<sup>KO</sup>, and L(3)mbt<sup>ts1</sup> immunostained for Vasa (magenta), MIRA (green), and ELAV (green). Scale bar: 100 μm.
- C Quantification of brain lobe volume for the following genotypes: Lint-O<sup>KO</sup> -/+ (n = 42 biological replicates), Lint-O<sup>KO</sup> -/- (n = 36 biological replicates), and L(3) mbt<sup>ts1</sup> -/- (n = 34 biological replicates). Boxplot central bands, upper edges of boxes, lower edges of boxes, upper whiskers and lower whiskers show median, third quartile, first quartile, maxima, and minima, respectively. P values were calculated by the Student's t-test. (\*\*\*P-value < 0.001).
- D, E The genomic regions harboring the *uasa* (D) and *aub* (E) genes. The RNA-seq reads in *y w*, *L*(3)*mbt<sup>ts1</sup>*, and *Lint-O<sup>KO</sup>* brains are shown. The shading in gray corresponds to exons. The *y*-axis shows the number of RPM. RNA-seq samples were biological triplicates.
- F Venn diagram shows that 620 protein-coding genes are shared with the I(3)mbt and lint-O libraries.
- G High-ranking GO terms for the 620 protein-coding genes in (F).

Source data are available online for this figure.

We next performed genome-wide RNA-seq in the L3 brains from y w,  $L(3)mbt^{ts1}$ , and  $Lint-O^{KO}$ . The mapping of the RNA-seq reads onto vasa and *aub* confirmed their derepression in  $L(3)mbt^{ts1}$  and  $Lint-O^{KO}$ .

(Fig 6D and E). Computational analysis revealed that 620 genes were upregulated commonly in  $L(3)mbt^{ts1}$  and  $Lint-O^{KO}$  (Fig 6F). GO analysis of these genes showed that the terms with high statistical values

[q-value  $(-\log 10) > 10]$  included "chromosome organization," "meiotic cell cycle," and "nuclear division." The term of "piRNA metabolic process" also appeared [q-value  $(-\log 10) = 2.86]$  (Fig 6G). These results indicate that L(3)mbt/Lint-O tends to regulate genes that function in specific intracellular pathways in the brain, such as the piRNA pathway. In agreement with this, not only the *vasa* and *aub* genes but also other germline-specific piRNA factors (*e.g., piwi, spindle-E, krimper, tej, sister of Yb, vreteno,* and *nxf2*) appeared in the gene set (GSE181802). On the other hand, no significant GO terms were found for the L(3)mbt-independent and Lint-O-independent genes (836 genes) and the L(3)mbt-independent and Lint-O-dependent genes (256 genes). These findings suggest that L(3)mbt and Lint-O may regulate some specific genes independently from each other, but they do not seem to be aimed at regulating any special pathways.

## Discussion

The loss-of-function mutations in the *Drosophila l*(*3*)*mbt* gene cause malignant tumor growth in the brain. This finding was first reported in 1982 (Gateff, 1982). Since then, a number of studies have been conducted to elucidate the function of L(3)mbt and to determine its causal relationship with tumorigenesis. Through this, multiple co-factors, such as Lint-1, CoRest, and Myb, were identified (Lewis et al, 2004; Georlette *et al*, 2007; Meier *et al*, 2012). However, until the present study, Lint-O had never been reported to be an L(3)mbt co-suppressor, showing the complexity of the L(3)mbt-mediated gene regulatory pathway. What was the key leading to the discovery of Lint-O in this study? One plausible answer is the use of OSCs, a cultured cell line composed solely of somatic (follicular) cells derived from *Drosophila* ovary, not from the brain.

Upon the lack of L(3)mbt, OSCs aberrantly induced the expression of germ-specific genes including piRNA amplifiers and activated the ping-pong pathway, in which piRNAs innately generated in naïve OSCs were actually amplified (Sumiyoshi et al, 2016). The Drosophila brain autonomously initiated piRNA biogenesis upon the loss of *l*(3)*mbt* function (Janic *et al*, 2010). Strikingly, when piRNA biogenesis was forcibly attenuated, the tumorigenesis ceased. We previously attempted L(3)mbt knockdown in nongonadal somatic Schneider 2 (S2) cells to examine whether it activated piRNA biogenesis. However, piRNA biogenesis was not carried out because necessary factors were not sufficiently activated. This implies that OSCs and the brain, particularly CB neuroblasts that became Vasapositive upon *l(3)mbt* deficiency (Janic *et al*, 2010; Richter *et al*, 2011; this study), have some commonality, but S2 cells do not. At present, it is unclear what this commonality consists of materially, besides the two main players L(3)mbt and Lint-O. However, the susceptibility of both cells to the loss of function of L(3)mbt and Lint-O is likely to be almost identical. In other words, the degree and mechanism of cooperative gene regulation between L(3)mbt and Lint-O, and the balance with other gene regulatory means, are considered to be equivalent in the two cases. If there was a CB-derived cultured cell line, we could carry out similar experiments in both cells in parallel and compare the outcomes to obtain an understanding of the commonality. However, no such cell line appears to be available in the field of *Drosophila* research.

In this study, by performing genome-wide ChIP-seq and RNA-seq in parallel in OSCs, we were able to understand the implications of the genomic binding of L(3)mbt, such as which binding is actually responsible for the expression of the gene targets. Similar assays can be conducted using the ovary, for example, but its tissue is composed of germarium and egg chambers at different stages of development. Egg chambers are a mixture of nurse cells and oocytes, with follicular cells surrounding them. The follicular cells normally lack Vasa and Aub, and only in abnormal situations such as the depletion of L(3)mbt and/or Lint-O, these proteins are aberrantly upregulated. The nurse cells express Vasa irrespective of the presence or absence of L(3)mbt or Lint-O. With this complexity, it would not be easy to interpret the experimental results accurately and obtain a correct understanding. This reminds us of the usefulness of *in vivo* and *ex vivo* systems and the importance of combining the two.

Lint-1 was present in the L(3)mbt interactors in OSCs. This led us to speculate that L(3)mbt interacts with not only Lint-O but also Lint-1 to assemble a highly ordered complex to regulate the target genes in a cooperative manner. However, the *lint-O* brain was tumorigenic, similar to the l(3)mbt brain (but it showed slightly less brain enlargement). This implies that L(3)mbt and Lint-1, likely as the LINT complex with CoRest, contribute less to the regulation of germline genes in the brain. The situation could be similar in OSCs. Another plausible idea is that, in the absence of Lint-O, Lint-1 may become unstable as Lint-O became unstable in the absence of L(3) mbt. Given our present understanding, this is not an unreasonable proposition, but further research is required to properly understand the relationship among these three proteins.

The l(3)mbt gene is conserved from nematodes to humans, although the domain structures may not be strictly identical among them (Bonasio *et al*, 2010). Humans express four L(3)mbt orthologs, L3MBTL1 to L3MBTL4. Of these, L3MBTL1, L3MBTL3, and L3MBTL4 contain three MBT repeats, a zinc finger, and a SAM domain, similar to *Drosophila* L(3)mbt, but L3MBTL2 contains four MBT repeats and a zinc finger but lacks the SAM domain (Boccuni *et al*, 2003; Bateman, 2019). According to their peptide sequences, the protein sizes of human L3MBTLs are approximately half that of the fly L(3)mbt (Boccuni *et al*, 2003; Bateman, 2019). These interspecies differences suggest that L(3)mbt orthologs may exert their function(s) in different ways in individual organisms.

Are there any human orthologs of Lint-O? Previous proteomics analysis identified the sterile alpha motif domain containing 13 (SAMD13) as an interactor of human L(3)MBTL3 (Hauri et al, 2016; Huttlin et al, 2017). SAMD13 has a SAM domain but lacks the PHD domain that Lint-O has, but it is recognized as a human ortholog of Lint-O based on a BLAST search. Although this study did not go so far as to remark the function of the PHD domain of Lint-O, we found that the PHD domain is required for the functional expression of Lint-O. In this regard, SAMD13 may not be the human version of Lint-O. One possibility is that factors that bind to SAMD13 may have a PHD domain or something similar. However, this is also a matter of conjecture, and further research is needed before any conclusions are drawn. It is still unclear whether loss of L3MBTLs causes brain tumors or infertility in humans. It is also unclear whether loss of SAMD13 causes serious damage to the human brain and germline. Future research results on these interesting issues are awaited.

Previous studies showed that L(3)mbt binds to insulator elements of several insulator factors such as CP190, CTCF, and BEAF-32 (Richter *et al*, 2011; Bortle *et al*, 2012). Although these factors did not appear as interacting factors for L(3)mbt in OSCs in this

## **Materials and Methods**

#### Cell culture

OSCs (Saito *et al*, 2009; RRID:CVCL\_IY73) were cultured at 26°C in Shields and Sang M3 Insect Medium (US Biological) supplemented with 10% fly extract (Saito *et al*, 2009), 10% fetal bovine serum (Funakoshi), 10 mU/ml insulin, and 0.6 mg/ml glutathione.

#### **Plasmid construction**

To construct L(3)mbt-L-3xFLAG, L(3)mbt-S-3xFLAG, myc-Lint-Oand Lint-O-3xFLAG-expressing plasmids, a full-length L(3)mbt-L/-S/ Lint-O cDNA was amplified from cDNA library produced from total RNAs of OSCs using First Strand cDNA Synthesis Kit (Roche). The 5'-end of L(3)mbt-L/S was determined by 5' RACE using the SMARTer RACE 5'/3' Kit (Clontech). Then, amplified cDNA was cloned into vectors that have the promoter of actin and myc/ 3xFLAG tags using NEBuilder HiFi DNA Assembly Cloning Kit (NEB). For the rescue assays, Lint-O-3xFLAG expressing plasmids were modified to be siRNA-resistant using inverse PCR and infusion. The ΔSAM and ΔPHD mutants were produced by inverse PCR on L (3)mbt-L/S-3xFLAG and Lint-O-3xFLAG (siRNA-resistant) and ligation. The Lint-O-8CA mutant was produced by mutagenesis using inverse PCR on Lint-O-3xFLAG (siRNA-resistant) and ligation. Primers used are summarized in Appendix Table S2.

#### **RNAi and plasmid transfection**

For performing RNAi, up to  $6 \times 10^6$  trypsinized OSCs were prepared and suspended in 20 µl of Solution SF from the Cell Line Nucleofector Kit SF (Lonza Bioscience) to which 400 pmol siRNA duplex was added. Transfection was performed with the Nucleofector 96-well Shuttle Device (Lonza Bioscience). For performing transfection of the plasmids along with siRNAs, up to  $1 \times 10^7$  trypsinized OSCs were prepared and suspended in buffer [180 mM sodium phosphate buffer for Church and Gilbert hybridization (pH 7.2) containing 15 mM MgCl<sub>2</sub>, 5 mM KCl, and 50 mM D-mannitol], modified from the original protocol (Nye et al, 2014). A total of 6 µg of the plasmids and 600 pmol of the siRNA duplex were added to the suspended cells, and transfection was performed with the Nucleofector 2b Device (Lonza Bioscience) using the N-020 program. Transfected cells were cultured at 26°C in a fresh OSC medium for 48 h for further experiments. For the rescue assays, RNAi-treated cells were incubated for 48 h before co-transfection of the plasmids and siRNA duplex. After co-transfection, the cells were cultured for another 48 h. The sequences of siRNA duplexes are listed in Appendix Table S2.

#### **Production of antibodies**

The recombinant L(3)mbt peptide (Lys401-Thr600) tagged with glutathione S-transferase [GST-L(3)mbt] was purified from *E. coli* and used for mouse immunization. The production and selection of hybridomas were performed as described in a previous report (Nishida *et al*, 2015). To produce the anti-Lint-O antibody, a part of the protein (Gln340-Ser353) was used to immunize rabbits. The antibody was purified from the serum and then dialyzed against PBS. The Lint-O peptide and antibody were prepared by Eurofins Scientific. A Lint-O peptide (Met1-Arg130) fused to 6 x His was expressed in and purified from *E. coli*, and then injected into 8week-old female Ts1:BALB/cCr[GF] mice (Sankyo Lab) for immunization. The blood serum was used for experiments using flies. Mouse procedures were approved by the Animal Research Committee of the University of Tokyo (Animal plan16-3).

#### Nuclear extraction and immunoprecipitation

Nuclear lysates were prepared and immunoprecipitation was performed as described previously (Onishi et al, 2020). Briefly, cells were suspended in hypotonic buffer [10 mM HEPES-KOH (pH 7.3), 10 mM KCl, 1.5 mM MgCl<sub>2</sub>, 0.5 mM dithiothreitol (DTT), 2 µg/ml pepstatin A, 2 µg/ml leupeptin, and 0.5% aprotinin], and the cells were fractured by passing them three times through a 25-gauge needle. The nuclear fraction was first centrifuged at 400 g for 10 min, washed with hypotonic buffer by centrifugation at 13,600 g for 20 min, and resuspended in chromatin co-immunoprecipitation (co-IP) buffer [50 mM HEPES-KOH (pH 7.3), 200 mM KCl, 1 mM EDTA, 1% Triton X-100, 0.1% sodium deoxycholate, 2 µg/ml pepstatin A, 2 µg/ml leupeptin, and 0.5% aprotinin]. The nuclear fraction was sonicated on ice using a Branson Digital Sonifier and then centrifuged at 20,000 g for 20 min at 4°C. The supernatant was collected as the nuclear extract. For immunoprecipitation, the nuclear lysate was incubated with antibodies bound to Dynabeads Protein G (Thermo Fisher Scientific) at 4°C for 2 h. The beads were washed five times with co-IP buffer. Proteins were eluted from the beads by heating at 95°C for 3 min in buffer containing SDS. After electrophoresis, the samples for LC-MS/MS were visualized by silver staining using SilverQuest (Invitrogen) or processed for western blotting.

#### Western blotting

Western blotting was performed as described previously (Miyoshi *et al*, 2005). For primary antibodies, anti-L(3)mbt (culture supernatant from the hybridoma) (this study), anti-Lint-O (rabbit blood serum, 1:10 dilution) (this study), anti-FLAG (SIGMA M2, 1:5,000 dilution), anti-Vasa (8E12, purified, 1:1,000 dilution) (Nishida *et al*, 2015), anti-Piwi (4D2 cultured supernatant) (Saito *et al*, 2006), anti-Aub (4D10, purified, 1:1,000 dilution) (Nishida *et al*, 2015), anti-Tubulin [E7 culture supernatant, Developmental Studies Hybridoma Bank (DSHB)], anti-histone H3 (Abcam ca#ab1791, 1:2,000 dilution), and anti-Myc monoclonal (Fujifilm Wako Pure Chemical 9E10, 1:1,000 dilution) antibodies were used.

#### Immunofluorescence

Immunofluorescence was performed as described previously (Saito *et al*, 2010). The primary antibodies used in this study were anti-L (3)mbt (1:500 dilution) and anti-FLAG monoclonal (MBL FLA-1, 1:1,000 dilution, and SIGMA M2, 1:1,000 dilution) antibodies. The secondary antibodies used were Alexa 488-conjugated anti-mouse

antibody (Thermo Fisher Scientific, 1:500 dilution). The cells were mounted with the VECTASHIELD Mounting Medium and stained with DAPI (Vector Laboratories), followed by observation using an LSM 710 or LSM 980 laser scanning confocal microscope (Carl Zeiss). Immunostaining of ovaries was performed following standard procedures. Fixation of ovaries was carried out with 4% paraformaldehyde phosphate buffer. Mouse anti-Vasa (1:500 dilution) (Nishida et al, 2015), mouse anti-Spectrin (1 µg/ml, 3A9, DSHB), mouse anti-Fas3 (1 µg/ml, 7G10, DSHB), and mouse anti-Orb (1 µg/ml, 4H8, DSHB) antibodies were used as primary antibodies. The specificity of the staining for F-actin was verified by Phalloidin-iFluor488 (1:1,000 dilution, #23115, AAT Bioquest). Larval brains were dissected in cold PBS and fixed in 4% paraformaldehyde for 40 min. Samples were incubated with primary antibodies diluted in PBS containing 0.3% Triton X-100 and 5% BSA (PBSTB) overnight at 4°C. Primary antibodies used were as follows: mouse anti-Vasa (8E12, 1:50 dilution) (Nishida et al, 2015), rat anti-MIRA (1:500 dilution, ab197788, Abcam), and rat anti-ELAV (1:100 dilution, 7E8A10, DSHB). Brains were washed three times for 10 min in PBST and then incubated in secondary antibodies overnight at 4°C. Secondary antibodies were used as follows: Alexa 546-conjugated anti-mouse IgG (1:1,000 dilution, Molecular Probes) or Alexa 488conjugated anti-rat IgG (1:1,000 dilution, Molecular Probes). Samples were incubated with secondary antibodies overnight at 4°C. After washing three times for 10 min in PBST, samples were mounted in the VECTASHIELD Mounting Medium and stained with DAPI (Vector Laboratories). Images of ovaries and larval brains were collected using a confocal microscope (Zeiss LSM900).

#### RNA extraction and RT-qPCR

Total RNAs were extracted from OSCs with the ISOGEN II reagent (Nippon Gene). After digestion of the contaminated DNAs by DNase (Life Technologies) and subsequent purification, a cDNA library was prepared using the reverse-transcription kit ReverTra Ace (Toyobo). For RT–qPCR, cDNAs or DNA products from ChIP were amplified using the StepOnePlus Real-Time PCR System (Applied Biosystems) with PCR enzymes and the PowerUp SYBR Green Master Mix (Thermo Fisher Scientific). The efficiency of qPCR amplification was calculated based on the slope of the standard curve. After determining the amplification efficiency values (between 95% and 105%), the relative steady-state RNA levels were calculated from the threshold cycle for amplification. The sequences of primers are listed in Appendix Table S2.

#### Preparation of protein samples for LC–MS/MS

For the preparation of immunoprecipitated samples for LC–MS/MS, the anti-L(3)mbt antibody used for immunoprecipitation was crosslinked to beads by dimethyl pimelimidate (Thermo Fisher Scientific). Immunoprecipitation was performed using control OSCs and L(3)mbt knockdown (KD) OSCs. The cells were washed after incubation six times with 800 mM NaCl in HEMG buffer [25 mM HEPES-KOH (pH 7.3), 12.5 mM MgCl<sub>2</sub>, 0.1% Nonidet P-40, 0.1 mM EDTA, 20% glycerol, 2  $\mu$ g/ml pepstatin A, 2  $\mu$ g/ml leupeptin, and 0.5% aprotinin] and then twice with 200 mM NaCl in HEMG buffer. The immunoprecipitants were eluted in elution buffer containing 125 mM Tris–HCl (pH 6.8), 4% SDS, and 0.01% bromophenol blue by heating at 70°C for 10 min. The products were precipitated in acetone containing 20% trichloroacetic acid. The same experiment was performed again to generate a replicate. The pellets containing immunoprecipitated samples were lysed in 100 µl of PTS buffer [100 mM NH<sub>4</sub>HCO<sub>3</sub>, 12 mM sodium deoxycholate, 12 mM sodium N-lauroylsarcosinate, and phosphatase inhibitor cocktails 2 and 3 (Sigma-Aldrich)]. Each sample in the PTS buffer was reduced with 10 mM DTT at 60°C for 30 min and then alkylated by incubation with 22 mM iodoacetamide at 37°C for 30 min in the dark. Next, the samples were diluted with 100 mM NH<sub>4</sub>HCO<sub>3</sub> solution up to a volume of 500 µl and digested with 0.4 µg of trypsin (Roche) by incubation at 37°C for 18 h in the dark. After the digestion, an equal volume of ethyl acetate was added to the samples, and the mixture was acidified with 0.5% TFA and mixed to transfer the detergents into the organic phase. After the samples were centrifuged at 15,700 g for 1 min at room temperature, the aqueous phases containing the peptides were collected. The samples were concentrated by a centrifugal evaporator (Eyela) and desalted using a MonoSpin C18 column (GL Sciences). The eluted products were dried prior to LC-MS/MS analysis.

#### LC–MS/MS analysis

The dried and desalted peptides were dissolved in distilled water containing 2% acetonitrile and 0.1% TFA. The LC-MS/MS analyses were performed using a mass spectrometer (Q Exactive Plus, Thermo Fisher Scientific) equipped with a nano ultra-highperformance liquid chromatography system (Dionex Ultimate 3000, Thermo Fisher Scientific). The peptides were loaded onto the LC-MS/MS system with a trap column (0.3  $\times$  5 mm, L-column, octadecylsilyl groups; Chemicals Evaluation and Research Institute) and a capillary column (0.1 × 150 mm, L-column, octadecylsilyl groups, Chemicals Evaluation and Research Institute) at a flow rate of 10 µl/min. The loaded peptides were separated by a gradient using the mobile phases A (1% formic acid in distilled water) and B (1% formic acid in acetonitrile) at a flow rate of 300 nl/min (2% to 35% B in 133 min, 35% to 50% B in 20 min, 50% to 95% B in 2 min, 95% B for 10 min, 95% to 2% B in 0.1 min and 2% B for 10 min). The eluted peptides were electrosprayed (2.0 kV) and introduced into the MS equipment (positive ion mode, data-dependent MS/ MS). Each of the most intense precursor ions (the top 10) was isolated and fragmented by higher collision energy dissociation with normalized collision energy (27%). For full MS scans, the scan range was set to 350-1,500 m/z at a resolution of 70,000, and the AGC target was set to 3e6 with a maximum injection time of 60 ms. For the MS/MS scans, the precursor isolation window was set to 1.6 m/z at a resolution of 17,500 and the AGC target was set to 5e5 with a maximum injection time of 60 ms. The Orbitrap mass analyzer was operated with the "lock mass" option to perform shotgun detection with high accuracy. The raw spectra were extracted using Proteome Discoverer 2.2 (Thermo Fisher Scientific) and searched against the Drosophila UniProt database (TaxID = 7,227 and subtaxonomies) with the following settings: the parameter for the cleavage was set to trypsin, and a maximum missed number of cleavages of two were allowed. The mass tolerances were set to 10 ppm for the precursor ion and 0.02 Da for the fragment ion. As for protein modifications, we set carbamidomethylation (+ 57.021 Da) at Cys as a fixed modification of the peptide, oxidation (+ 15.995 Da) at Met as a dynamic (nonfixed) modification of the peptide, and acetylation (+ 42.011 Da) at the N-terminus as a dynamic modification of the protein terminus. The amount of each peptide was semi-quantified using the peak area with Precursor Ions Quantifier in Proteome Discoverer 2.2.

#### ChIP and ChIP-seq library preparation

For chromatin immunoprecipitation, cultured OSCs ( $1 \times 10^7$  cells/reaction) were fixed by incubation with an OSC medium including 0.75% formaldehyde for 5 min at room temperature, following which glycine was added to the medium (final concentration, 125 mM) to stop the fixation. Cells were scraped and suspended with hypotonic buffer [25 mM HEPES-KOH (pH 7.3), 1.5 mM MgCl<sub>2</sub>, 10 mM KCl, 1 mM DTT, 0.1% NP-40, 2 µg/ml pepstatin A, 2 µg/ml leupeptin, and 0.5% aprotinin] and the nuclei were centrifuged into pellets at 1,000 g for 10 min. The nuclei were diluted in sonication buffer [50 mM HEPES-KOH (pH 7.3), 140 mM NaCl, 1% Triton X-100, 0.1% sodium deoxycholate, 0.1% SDS, 1 mM EDTA, 2 µg/ml pepstatin A, 2 µg/ml leupeptin, and 0.5% aprotinin] and sonicated with a Covaris S220 Focused ultrasonicator for 10 min at 4°C. The settings used for the sonication were as follows: peak power 140, duty factor 5.0, and 200 cycle/burst. Next, the lysates were centrifuged at 20,000 g for 20 min, and the supernatants were collected for immunoprecipitation. Anti-L(3)mbt and anti-Lint-O antibodies were added to the supernatants and incubated for 16 h at 4°C. Dynabeads Protein G (Thermo Fisher Scientific) was added to each sample and incubated for 1 h at 4°C. After incubation, beads were washed once with low-salt buffer [20 mM Tris-HCl (pH 8.0), 150 mM NaCl, 2 mM EDTA, 0.1% Triton X-100, 0.1% SDS, and 1 mM phenylmethylsulfonyl fluoride (PMSF)], high-salt buffer [20 mM Tris-HCl (pH 8.0), 500 mM NaCl, 2 mM EDTA, 0.1% Triton X-100, 0.1% SDS, and 1 mM PMSF], and LiCl buffer [20 mM Tris-HCl (pH 8.0), 200 mM LiCl, 2 mM EDTA, 1% NP-40, 1% sodium deoxycholate, and 1 mM PMSF], and twice with TE buffer [20 mM Tris-HCl (pH 8.0), 1 mM EDTA, and 1 mM PMSF]. The beads were dissolved in elution buffer [50 mM Tris-HCl (pH 8.0), 10 mM EDTA, and 1% SDS] and incubated at 65°C for 30 min. The supernatant containing the immunoprecipitated materials was collected, to which NaCl was added to a final concentration of 200 mM, and the supernatant was incubated at 65°C for 8 h for decrosslinking. Next, 2 µl of RNase A (10 mg/ml) was added to the samples and incubated at 37°C for 30 min to digest the RNAs, and 5 µl of proteinase K (20 mg/ml) was added and incubated at 55°C for 1 h to digest the proteins. The DNA was purified with the FastGene Gel/PCR Extraction Kit (Nippon Genetics), in accordance with the manufacturer's protocol and eluted in nucleasefree water. DNA products from ChIP were amplified using the StepOnePlus Real-Time PCR System (Applied Biosystems) with PCR enzymes and the PowerUp SYBR Green Master Mix (Thermo Fisher Scientific) and qualified for ChIP-seq libraries. ChIP-seq libraries were prepared in accordance with the instructions accompanying the NEBNext Ultra II FS DNA Library Prep Kit for Illumina (New England BioLabs). In the adaptor ligation step, the original adaptor reagent was diluted 10-fold. After adapter ligation, the DNA was purified with AMPure XP beads (Beckman Coulter) for size selection. Then, the DNA was PCR-amplified with Illumina primers for 13-16 cycles and the library fragments of  $\sim 325$  bp (insert plus adaptor and the PCR primer sequences) were purified with AMPure XP beads (Beckman Coulter). Duplicate samples were prepared for each condition. The purified DNA was captured on an Illumina flow cell for cluster generation. The libraries were sequenced on the Illumina HiSeq in accordance with the manufacturer's protocols. The ratio of the abundances of the peptides [control/L(3)mbt KD > 4] and the peptide spectrum matches (> 1) were used for candidate selection.

#### **RNA-seq library preparation**

The ribosomal RNAs were excluded from the total RNAs using a Ribo-Zero rRNA Removal Kit (Human/Mouse/Rat), in accordance with Illumina's protocol, and the RNA-seq libraries were prepared following the instructions accompanying the TruSeq Stranded mRNA Library Prep Kit (Illumina). Poly-A selected mRNAs were submitted for library preparation. Triplicate samples were prepared for each RNAi-treated condition. Libraries were sequenced on the Illumina HiSeq following the manufacturer's protocol.

#### Computational analysis of RNA-seq and ChIP-seq

For ChIP-seq analysis, the sequence reads were mapped to the genome of Drosophila melanogaster (dm6) using Bowtie 2 (Langmead & Salzberg, 2012). Only unique mapped reads were used in the analysis and PCR amplicons were excluded using Picard tools (https://broadinstitute.github.io/picard/). Peak calling was completed with MACS2 (Zhang et al, 2008) with default settings. From the output file of peak coordinate, the peaks with log10-converted *q*value over -100 were removed. Pearson's correlation coefficient between L(3)mbt ChIP duplicate reads mapped on merged peaks was 0.983 and that between Lint-O ChIP duplicate reads mapped on merged peaks was 0.981. Common peaks, not merged peaks, between the duplicate samples were selected and used for further analysis. Peaks were annotated with in-house scripts according to dmel-all-r6.43.gtf (ftp://ftp.flybase.org/genomes/dmel/current/gtf/ ). For heatmaps and summary plots, ChIP scores were calculated by deeptools (Ramírez et al, 2016). Bigwig files of ChIP were produced by the bamCoverage program of deeptools and matrix data were calculated by the computeMatrix program of deeptools using bigwig files and plotted. Motif detection was performed using the peak bed files produced by MACS2 and findMotifsGenome.pl program of Homer (Heinz et al, 2010). For RNA-seq analysis, sequence reads mapped to rRNAs were excluded and the remaining reads were mapped to the genome of Drosophila melanogaster (dm6) using HISAT2 (Kim et al, 2015). Differential expression analysis was performed using the triplicate samples and DESeq2 package in R (Love et al, 2014) The resulting lists of differentially expressed genes [FDR (false discovery rate) < 0.01] were categorized into upregulated and downregulated genes by the fold change of the expression and applied for further analysis (Appendix Table S3). PCA analysis of RNA-seq samples of OSC was performed in R by using the dataset of reads for each gene normalized by million mapped reads. GO analysis of the biological process shown in Fig 6G was performed using clusterProfiler package in R (Yu et al, 2012; Wu et al, 2021).

#### Fly stock

The *yellow white*  $(y^1 w^{1118})$  strain was used as a WT strain. The mutants used in this study were:  $y^1 w^{1118}$ ,  $y^1 w^{1118}$  Lint-O<sup>KO</sup>/FM7, Kr

> *GFP* (this study), *w*\*; *L*(3)*mbt<sup>ts1</sup>/TM6b* (gift from C. Gonzalez). A mutant allele of *Lint-O<sup>KO</sup>* was generated using the transgenic CRISPR-Cas9 technique as previously described (Kondo & Ueda, 2013) The following strains were used for the mutagenesis: *y*<sup>1</sup> *v*<sup>1</sup> *nos-phiC31*; *attP40* host (NIG-FLY stock TBX-0002), *y*<sup>2</sup> *cho*<sup>2</sup> *v*<sup>1</sup>; *Sp hs-hid/CyO* (NIG-FLY stock TBX-0009), *y*<sup>1</sup> *w*<sup>1118</sup>; +; *attP2*{*nos-cas9*} (Kondo *et al*, 2020), and *Df*(1)*JA27/FM7c*, *P*{*w*[+*mC*]=*GAL4-Kr.C*} *DC1*, *P*{*w*[+*mC*]=*UAS-GFP S65T*}*DC5*, *sn*[+] (Bloomington Drosophila Stock Center #5193). Mutant files were validated by PCR and sequencing of the target region. Oligo DNA sequences are shown in Appendix Table S4.

#### RNA extraction from flies and RT-qPCR

Total RNAs were extracted from ovaries using ISOGEN (Nippon Gene). RT–qPCR was performed as reported previously (Saito *et al*, 2009). In accordance with the manufacturer's instructions, 1  $\mu$ g of total RNA from each sample was used to reverse-transcribe target sequences using a Transcriptor First Strand cDNA Synthesis Kit (Roche). The resulting cDNAs were amplified with a TB Green Premix Ex Taq II (Takara). The primers used are shown in Appendix Table S2.

#### Generation of the Lint-O-Venus strain

The *Lint-O-Venus* strain was generated by CRISPR/Cas9-mediated targeted transgene integration (Kondo *et al*, 2020). The gene encoding Venus fluorescent protein was inserted immediately in front of the stop codon of the *Lint-O* gene so that Lint-O-Venus was translated as a C-terminal fusion protein. The donor vector (pBS-Lint-Oarm-Venus-3xP3-dsRed-Express2) carried approximately 800 bp and 500 bp homology arms on the left and left sides of a knock-in cassette comprising genes encoding Venus and 3xP3-dsRed-Express2 flanked by loxP sites from pPV-RF3 (Kondo *et al*, 2020). The donor and gRNA vector (pBFv-U6.2-Lint-O-gRNA5) containing a guide RNA were co-injected into fertilized eggs laid by *nos*-Cas9 flies. Transformants were selected by eye-specific red fluorescence of the 3xP3-dsRed-Express2 transgene. Homozygous Lint-O-Venus strain was used for the microscopy analysis. DNA oligo sequences for plasmid vectors are shown in Appendix Table S2.

#### Female fertility assay

Adults after eclosion were immediately transferred to  $29^{\circ}$ C and incubated for 2 days. Single females were then incubated with three  $y^{1} w^{1118}$  control males at  $29^{\circ}$ C for 5 days for mating. Ten independent crosses were performed. The number of adult offspring per cross was counted.

#### L3 larval brain

L3 larval brains were isolated from  $y^{1} w^{1118}$ ,  $y^{1} w^{1118}$  Lint-O<sup>KO</sup>/FM7 Kr > GFP,  $y^{1} w^{1118}$  Lint-O<sup>KO</sup>, and L(3)mbt<sup>ts1</sup> grown at 29°C for 5– 6 days after spawning at 25°C, and used for western blotting, volume calculation, immunostaining, and RNA-seq analysis. The orthogonal major and minor axes across the brain lobes were measured using an SZX16 stereo microscope and cellSens standard (Olympus). The volume (*V*) of brain lobes was calculated as  $V = 4/3\pi ab^2$ , where *a* is the major semiaxis and *b* is the minor semiaxis. Significance was calculated by the Student's *t*-test.

## Data availability

OSC RNA-seq and ChIP-seq data are deposited at Gene Expression Omnibus (GSE) (GSE181802: https://www.ncbi.nlm.nih.gov/geo/ query/acc.cgi?acc = GSE181802). Fly RNA-seq data are also available at GSE (GSE205541: https://www.ncbi.nlm.nih.gov/geo/query/acc. cgi?acc = GSE205541). LC–MS/MS data are deposited at PRIDE (PXD026945: http://proteomecentral.proteomexchange.org/cgi/Get Dataset?ID = PXD026945).

Expanded View for this article is available online.

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#### Author contributions

Hitomi Yamamoto-Matsuda: Data curation; investigation; writing – original draft; writing – review and editing. Keita Miyoshi: Funding acquisition; investigation; writing – review and editing. Mai Moritoh: Investigation; writing – review and editing. Hikari Yoshitane: Funding acquisition; investigation; methodology. Yoshitaka Fukada: Funding acquisition; methodology. Kuniaki Saito: Conceptualization; supervision; funding acquisition; writing – review and editing. Soichiro Yamanaka: Data curation; supervision; investigation; writing – original draft; writing – review and editing. Mikiko, C Siomi: Conceptualization; supervision; funding acquisition; writing – original draft; writing – curation; supervision; funding acquisition; writing – original draft; writing – curation; writing – curation; writing – original draft; writing – curation; w

In addition to the CRediT author contributions listed above, the contributions in detail are:

HY-M and MM performed biochemical experiments. HY-M and SY performed bioinformatic analysis. HY and YF performed mass spectrometric analysis. KM and KS produced *lint-O* mutant flies and analyzed them. HY-M, KM, KS, SY, and MCS conceived the project and designed the experiments. All authors contributed to the writing of the manuscript.

#### Disclosure and competing interest statement

The authors declare that they have no conflict of interest.

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# **Expanded View Figures**

#### Figure EV1. Two isoforms of L(3)mbt, L(3)mbt-L, and L(3)mbt-S, in OSCs.

- A Western blotting using an anti-L(3)mbt antibody that we raised in this study detected L(3)mbt as a doublet in the OSC nuclear lysates. The doublet disappeared upon L(3)mbt RNAi. Histone H3 (H3) served as a loading control.
- B The exon-intron structures of the *l(3)mbt* gene in dm6 (provided by UCSC) and in OSCs (Sienski *et al*, 2012). Note that the *l(3)mbt* gene in OSCs has an LTR-type transposon, *springer*. RACE detected three different 5' ends of *l(3)mbt* mRNA (#1, #2, and #3).
- C Top: Western blotting using the anti-L(3)mbt antibody shows that L(3)mbt-L-3xFLAG and L(3)mbt-S-3xFLAG exogenously expressed in OSCs co-migrate with endogenous L(3)mbt-L and L(3)mbt-S (control), respectively. Middle: Western blotting was performed using anti-FLAG antibody. Bottom: Histone H3 (H3) was detected as a loading control.
- D Immunofluorescence analysis using the anti-L(3)mbt antibody detected L(3)mbt (green) mostly in the OSC nuclei. The L(3)mbt signals disappeared upon L(3)mbt RNAi (KD). DAPI (blue) indicates the nuclei. Scale bar: 10  $\mu$ m.

Source data are available online for this figure.

#### Figure EV2. Genomic distribution of L(3)mbt and the effects of L(3)mbt loss on the expression levels of piRNA factors in OSCs.

- A Genomic browser views of L(3)mbt ChIP-seq signals. All fly chromosomes are shown. The *vasa*, *ago3*, and *aub* loci are indicated. The total number of L(3)mbt ChIP peaks is shown in upper right.
- B PCA shows the correlation in the RNA-seq libraries. Control: GFP siRNA was used.
- C-E The genomic regions harboring qin, tej, boot, and CG9925 (C), piwi, yb, armi, and zuc (D), and flam (E).



Figure EV2.



#### Figure EV3. Doman structures of L(3)mbt, Lint-O and their mutants and behavior of L(3)mbt-S in OSCs.

- A Domain structures of WT Lint-O and its  $\Delta$ SAM and 8CA mutants. The  $\Delta$ SAM mutant is composed of Met1-Val371 and Ser437-Asp446. The Cys-to-Ala mutations in the 8CA mutant are indicated at the bottom (asterisks in the structure).
- B Domain structures of WT L(3)mbt-L, WT L(3)mbt-S, and their ΔSAM mutants. The ΔSAM mutant of L(3)mbt-L is composed of Met1-Leu1278 and Val1367-Ser1477 of WT L(3)mbt-L. The ΔSAM mutant of L(3)mbt-S is composed of Met325-Leu1278 and Val1367-Ser1477 of WT L(3)mbt-L.
- C IP/western blotting shows that WT L(3)mbt-S, but not its  $\Delta$ SAM mutant, co-immunoprecipitated with Lint-O from the OSC lysates. n.i., nonimmune IgG.
- D Subcellular localization of WT L(3)mbt-S and its  $\Delta$ SAM mutant (green). Scale bar: 5  $\mu$ m.
- E Western blotting using the anti-Lint-O antibodies raised in this study. The Lint-O band (~60 kDa) was observed in normal OSCs (Lint-O RNAi-) but not in Lint-O-depleted OSCs (Lint-O RNAi+). Histone H3 (H3) was detected as a loading control. An asterisk shows the background.

Source data are available online for this figure.



#### Figure EV4. Lint-O OSC ChIP-seq and RNA-seq before and after Lint-O depletion in OSCs.

- A Genomic browser views of the Lint-O ChIP-seq reads. All fly chromosomes are shown. The *y*-axis shows the number of RPM. The *vasa*, *ago3*, and *aub* loci are indicated. The total number of Lint-O ChIP peaks is shown in upper right.
- B Overlap between Lint-O ChIP peaks in (A) and L(3)mbt ChIP peaks (Fig EV2A).
- C uasa, CG9925, tej, boot, qin, aub, and ago3 were identified as upregulated genes (\* q-value <0.05) in RNA-seq analysis. The log fold change of the differential expression for each piRNA pathway gene was calculated based on the RNA-seq data from normal (control), L(3)mbt-depleted (KD), and Lint-O-depleted (KD) OSCs. The y-axis shows the ratio of the read counts between L(3)mbt- and Lint-O-depleted OSCs and the normal OSCs.
- D Overview and comparison of the gene classification in Figs 1A and 4A.

## Figure EV5. Lint-O <sup>KO</sup> ovaries and larval brains.

- A Schema depicting the experiment. Eggs were transferred to 29°C after spawning at 25°C and incubated for 13 days. Ovaries were dissected from adult flies.
- B–E Confocal images of brains of *y w*, *Lint-O<sup>KO</sup>*, and *L(3)mbt<sup>ts1</sup>* larvae (grown at 29°C) for Orb (B), Fas3 (C), Spectrin (Spec) (D), and F-actin (E). *Lint-O<sup>KO</sup>* ovariole showed defects in follicle cell layer integrity. DAPI (blue): nuclei. Scale bars: 50 μm.
- F The *Lint-O-Venus* fly line (*y w Lint-O-Venus*) was generated using the CRISPR /Cas9 system. The Venus sequence was inserted before the stop codon of Lint-O. The Lint-O-Venus signal (green) was detected in the nucleus of both germ and follicle cells in the ovaries. Nuclei were stained with DAPI (blue). Wild-type (*y w*) was used as a negative control. Scale bars: 50 μm.
- G Confocal images of *y w*, *Lint-O<sup>KO</sup>*, and *L(3)mbt<sup>ts1</sup>* immunostained for Vasa (magenta) and MIRA (green). Merged images were also presented in Fig 6B. Scale bars: 100 μm.
- H Enlarged views of insets in (G). Scale bars: 50 μm.
- I Confocal images of y w, Lint-O<sup>KO</sup>, and L(3)mbt<sup>ts1</sup> immunostained for Vasa (magenta) and ELAV (green). Merged images were also presented in Fig 6B. Scale bars: 100 μm.
- J Enlarged views of insets in (I). Scale bars: 100 μm.



Figure EV5.

## Appendix PDF

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## Appendix Figure S1. Relationship between L(3)mbt ChIP peaks and TSS.

(A) Scatter plot of sequenced reads, mapped onto each L(3)mbt ChIP peak defined by MACS2 for each replicate. Each dot denotes a detected ChIP peak. (B) Distribution of L(3)mbt ChIP peaks is shown according to the distance to most proximal TSS. (C) The 13,951 protein-coding genes of *Drosophila* were classified into "L (3)mbt in TSS region," "L(3)mbt in TSS +/- 1kb," "L(3)mbt in TSS +/- 5kb," and "L(3)mbt in TSS > 5kb," in accordance with the L(3)mbt ChIP-seq signals, and were subsequently divided into "upregulated," "downregulated," and "unchanged" in accordance with the RNA-seq reads from OSCs before and after L(3)mbt depletion [+/- L(3)mbt]. Representatives of piRNA factors are indicated within the groups. Note that the "L(3)mbt in TSS region" corresponds to the "promoter region binding" in Fig 1A.

А

L(3)mbt-containing complex	components
LINT	L(3)mbt, Lint-1, CoRest
dREAM/MMB	L(3)mbt, Myb, E2F2, RBF, p53, Mip120, Mip130, Mip140





Appendix Figure S2. The mRNA levels of *ago3* and *piwi* upon the depletion of L(3)mbt interactors in OSCs.

(A) Known L(3)mbt cofactors within the LINT and dREAM complexes (Lewis et al. 2004; Meier et al. 2012; Blanchard et al, 2014). (B) Knockdown (KD) efficiencies of members of the LINT and dREAM complexes were verified by RT-qPCR. Control: EGFP siRNA was used. Data represent the mean  $\pm$  SE (n = 3). The *p* values were calculated with the t-test. \**p*: < 0.05, \*\**p*: < 0.01. (C, D) The mRNA levels of *ago3* (C) and *piwi* (D) were quantified in L(3)mbt-, Lint-1-, CoRest-, E2F2-, Myb-, Mip120-, and Mip130-depleted (RNAi) OSCs, and were compared with those in normal (control) OSCs. (E) KD efficiencies were verified by RT-qPCR for the indicated genes.

## Yamamoto-Matsuda, Miyoshi\_Appendix Figure S3



## Appendix Figure S3. Genes bound and controlled by Lint-O.

(A) Scatter plot of sequenced reads, mapped onto each Lint-O ChIP peak defined by MACS2 for each replicate. Each dot denotes a detected ChIP peak. (B) The 13,951 protein-coding genes of Drosophila were classified into "Lint-O in TSS region," "Lint-O in TSS +/- 1kb," "Lint-O in TSS +/- 5kb," and "Lint-O in TSS > 5kb," in accordance with the Lint-O ChIP-seq reads, and were subsequently divided into "upregulated," "downregulated," and "unchanged" in accordance with the RNA-seq reads from OSCs before and after Lint-O depletion [+/- Lint-O]. Representatives of piRNA factors are indicated within the groups. Note that the "Lint-O in TSS region" corresponds to the "promoter region binding" in Fig 4A. (C, D) The genomic regions harboring the *diap1* (C), *ex* (C), and *nos* (D) genes. The L (3)mbt and Lint-O ChIP-seq reads in normal OSCs (wild-type) and RNA-seq reads from L(3)mbt- and Lint-O-depleted [L(3)mbt KD and Lint-O KD] and control OSCs are shown. The shades in gray correspond to exons. The *y*-axis shows the number of RPM. (E) The levels of *nos* mRNA in the ovary and cultured OSCs following L(3)mbt depletion are shown. (F) Venn diagram shows that 439 protein-coding genes are commonly present in the I(3)mbt and lint-O libraries as downregulated genes. **4** 

#### Appendix Table S1. List of proteins in LC/MS/MS analysis. excluded in first selection, excluded in second selection, excluded in third selection, and final selected proteins

				Abundance	es (control)	Abundances	(L(3)mbt KD)	
Accession	Description	Sum PEP Scor	PSMs	1	2	1	2	FC of (abunda
E8NH29	LD46071p (Fra	92.506	778	128.5	50.4	91.6	129.5	0.809136137
Q9VZ22	L(3)mbt intera	37.046	54	326	70.2	1.9	1.9	104.2631579
Q9VB52	LD05287p OS=	23,163	17	381.4	18.6	0	0	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
E4NKN3	GM13963n OS	17002	61	2473	8.89	325	515	3 763005238
		16.042	01	247.3	00.0	32.5	J1.J	3.703093238
	ATP synthase	10.043	20	39.Z	201.2	30.0	41.1	4.023123028
076866	EG:100G10.6 p	14.463	14	383.8	14.2	0	1.9	209.4736842
Q9VLK1	U3 small nucle	14.345	9	274.4	0	27.3	98.3	2.184713376
P56538	Eukaryotic tra	12.677	17	38.8	163.9	188.8	8.6	1.026849037
P29844	Endoplasmic r	12.448	13	168.8	90.3	85.5	55.4	1.838892832
Q9VJD1	Glucosidase 2	11.363	13	131.1	176.4	35.6	56.9	3.324324324
A0A0B4KHY6	Ets at 97D, iso	10.881	7	164.5	94.6	107.7	33.2	1.838892832
007HI2	123A ribosom	9 2 9 3	5	242.3	54.7	80.4	22.7	2 880698351
001/1170	Tranalagan-ag	0.200	15	242.0	262.7	67.1	21.4	2.060012706
037020	And it is the second se	0.109	11	30.0	202.7	07.1	51.4	3.000913700
P17704	405 ribosomal	7.807	14	253	52.9	41.8	52.3	3.250797024
D2NUK9	Hoi-polloi, iso	7.659	18	174.1	161.8	21.2	42.9	5.24024961
A0A0B4LH50	Actin 87E, iso	7.612	18	3.1	193.1	121.8	82	0.962708538
P55830	40S ribosomal	7.37	8	93.7	223.6	28.3	54.4	3.836759371
M9NE89	Lamin, isoform	7.079	7	3.9	214.1	68	114	1.197802198
P50887	60S ribosomal	6.947	51	146.9	95.5	127.6	30	1.538071066
C0HKA1	40S ribosomal	6.738	7	130	136.5	103.4	30.1	1.996254682
Q06559	40S ribosomal	6 5 9 8	7	182.4	100.9	56.7	60	2 427592117
	Dre L hemeler	5.000	14	00.7	172	04.2	42	1.024702061
	Dhaj nomolog	0.00	14	90.7	1/3	94.3	42	1.934702601
X2JF59	Thioredoxin pe	4.989	8	0	261.5	62	/6.5	1.888086643
Q7JZ53	CG4866 OS=D	4.883	1	218.1	0	181.9	0	1.199010445
Q9VGN9	Probable ribos	4.666	2	205.6	0	194.4	0	1.057613169
P08736	Elongation fac	4.588	12	39.6	193.4	102.3	64.8	1.394374626
A0A023GQA5	Lethal (2) 37C	4.276	2	0	357.9	0	42.1	8.501187648
Q9VTP4	60S ribosomal	3.676	2	30.2	270.2	85.3	14.3	3.016064257
A0A0B4KeN1	40S ribosomel	2 5 2 0	1	400	270.2	00.0	14.0	~~~~~
D11147	Heat alter 1 70	3.528		400	0100	0	1100	0.026110400
0114/	THEAL SHOCK /U	3.513	6	61.3	218.8	0	119.9	2.330113428
P46222	oUS ribosomal	3.448	2	400	0	0	0	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
HURNL4	FI17108p1 (Fra	3.391	2	327.7	0	72.3	0	4.532503458
B5RIJ9	FI02875p (Frag	2.925	1	0	338.7	0	61.3	5.525285481
Q8STI6	RE53401p OS	2.831	1	400	0	0	0	∞
P13469	DNA-binding	2.563	1	0	0	0	0	-
Q8T479	AT12489n OS	2 5 5 3	1	0	331.4	0	68.6	4,83090379
A0A0F7.13F0	MIP06027-1 0	2.533	2	225.0	53.4	Q0 1	30.5	2 315020309
001/507	60S rikeser-1	2.324	1	105 5	33.4	204 5	30.5	0.05500000
041074	503 ribosomal	2.51	· ·	195.5	0	204.5	0	0.95599022
P413/4	Eukaryotic tra	2.424	1	63.9	259.1	0	11	4.194805195
A0A0B4KH25	Histone H2A (	2.41	6	193.5	85.5	79.8	41.2	2.305785124
Q7KLW6	LD06837p (Fra	2.318	1	0	400	0	0	∞
Q4V5X9	IP07888p OS=	2.316	3	287.3	0	112.7	0	2.549245785
A0A023T5E7	GEO01108p1 0	2.224	2	123.8	114.4	86.7	75.1	1.472187886
P02283	Histone H2B (	2.166	10	238	41.1	75	45.9	2.308519438
097183	GH07456p_OS	2 102	3	33.6	305.3	19.7	41.3	5 555737705
A0A0R4LC52	CE009220m1 (	2.05	2	109.0	120.2	10.7	152	1.620226042
AUAUB4LG52	GEOU6239p1 C	2.05	2	106.9	139.2	0	152	1.032230642
	Non-histone c	1.992	2	0	346.7	0	53.3	0.504690432
Q08473	RNA-binding p	1.98	3	68.2	197.7	46./	87.4	1.98284862
Q9VWD9	LD38919p OS=	1.957	2	213	187	0	0	00
C6SV50	40S ribosomal	1.919	2	134.6	216.8	0	48.6	7.230452675
A8DY43	Uncharacterize	1.858	2	0	0	0	0	-
Q9VHG5	Insulator bindi	1.854	11	87.5	86.9	212.1	13.6	0.772707133
A9UN96	LD25519p OS=	1.853	1	400	0	0	0	∞
P54397	39 kDa EK506	1 795	1	400	0	0	0	00
D06602	Tubulin alaba-	1.700	1	561	0	242.0	0	0.162120017
07//0003		1.701	1	30.1	1775	343.9	541	1.000005001
Q/K5MZ	GH05836p US	1./48	2	88.3	177.5	80.1	54.1	1.980625931
P09180	60S ribosomal	1.604	1	186.5	0	213.5	0	0.8735363
B7ZWP7	RH14172p (Fra	1.601	1	91	159.3	81.7	68	1.672010688
M9PFN1	RuvB-like heli	1.576	2	12.3	211.3	94.6	81.9	1.266855524
Q7KRI2	Longitudinals	1.34	1	16.7	313.9	69.4	0	4.763688761
Q9VHX4	LD24679p OS=	1.314	3	27.4	127.3	134.1	111.2	0.630656339
Q8IR16	No on or off tr	1.28	2	305.8	0	94.2	0	3246284501
	Histops H22A	1 250	2	400	0	01.2	0	0.210201001
	OCTORE instal	1.255	1	400	056.0	0	1427	1 702576006
	UD01600 000	1.259		0	256.3	0	143./	1.783576896
Q972W1	LD21662p OS=	1.228	2	0	355.3	0	44.7	7.948545861
Q9I7W5	Something abo	1.154	1	400	0	0	0	00
Q9VQ29	Cytochrome b	1.145	1	0	371.1	0	28.9	12.84083045
Q9V7A4	Integrin alpha-	1.136	4	400	0	0	0	∞
A8DYH1	Muscle wasted	1.073	14	22.8	332.2	11.6	33.4	7.888888889
Q9V3P3	LD45860p OS=	1.067	2	0	341.5	0	58.5	5.837606838
Q9VA91	40S ribosomal	1.049	1	400	0	0	0	∞
	GE004460p1 (	1 044	i i	364.3	0	357	0	10,20448179
	Uncharacteria	1.044		100	100.0	110.0	00.7	1005012521
	CU1E760 CC	1.037	2	12.3	188.2	118.8	80.7	1.000012031
03VIVI14	GEL9/08p US	0.998	5	0	0	400	0	0
M9PDW8	Uncharacterize	0.99	11	400	0	0	0	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
11V500	Supercoiling fa	0.961	1	33.9	294.2	71.9	0	4.563282337
Q9VVH5	AT13736p OS	0.947	1	266.9	0	133.1	0	2.005259204
A0A0B4KF15	Mangetout, iso	0.942	5	400	0	0	0	∞
M9NFF9	Ada2a-contair	0.94	2	207.2	114.8	22.2	55.8	4.128205128
Q24156	Transcription	0.937	2	84.5	56.9	232.6	25.9	0.547001934
094901	RNA-binding	0.007	1	400	00.0			~ ~
B77072	SOSS again	0.919		400	400	0	0	
12013	SUSS complex	0.898	1	0	400	0	0	0.000010
J/K9E8	Sin3A (Fragme	0.852	1	0	35.2	0	364.8	0.096491228
Q5BI31	LD15043p OS=	0.839	2	0	115.5	180	104.5	0.405975395
Q9VLP4	Protein mitosh	0.838	1	400	0	0	0	∞
F0JAS9	TD01073p (Fra	0.828	8	0	0	400	0	0
Q9VNA3	GH21273n OS	0.824	1	376.6	0	23.4	0	16,09401709
226686	Serine-arginin	0.024	1	400	0	0	0	~ ~
0051154	CHO6271- CO	0.010	4	400	0	400	0	
	Dimension Contraction Contraction	0.813	4	0	0	400	0	0
	Drongo, Isofori	0.764	1	0	0	400	0	0
Q967T6	Gag protein O	0.757	1	155.3	136.4	0	108.3	2.693444137
A1ZBL0	Tubulin beta c	0.757	2	0	196.1	0	203.9	0.961745954
M9Z4Q3	MIP26177p1 O	0.754	1	0	0	0	0	-
Q8MT08	Dynein regulat	0.738	1	0	400	0	0	00
Q59E37	Uncharacterize	0.735	2	0	.30	400	0	0
Q9W1R1	GH10600- 05	0.725	1	1/11	0	258.0	0	0.544998060
00\/\/N4	ATP_interest	0.725	1	141.1	205.1	200.9	040	2.014060110
006001	DE OSOGA	0.719		0	303.1	0	94.9	3.214903119
Q86PC1	RE03224p OS=	0.68	1	0	0	400	0	0
P20007	Phosphoenolpy	0.675	9	0	0	400	0	0

experiment	name	sense	antisense	
RNAi in OSCs	siEGFP	GGCAAGCUGACCCUGAAGU TT	ACUUCAGGGUCAGCUUGCC TT	
	siL(3)mbt	CCUCUGGAGAUGUCCGUAA TT	UUACGGACAUCUCCAGAGG TT	
	siLint-1	GCAGAAUCUCCACCAGUAA TT	UUACUGGUGGAGAUUCUGC TT	
	siCoRest	AACGAGGAGUCUGAUAACGAU TT	AUCGUUAUCAGACUCCUCGUU TT	
	siE2F2	CCAAAUCUUGGACGUACA TT	UGUACGUCCAAGAUUUUGG TT	
	siMyb	GGAGAACGACCAUUCCAU TT	AUGGAAUGGUCGAUUCUCC TT	
	siMip120	GUCAUCUUUGUCCAGAAGU TT	UAUGUGGACCACGUUCUUC TT	
	siMip130	GGACUCCGUUUCCAUGCUA TT	UAGCAUGGAAACGGAGUCC TT	
	siAtac3	CGAAUGGAUGUCCUAGAAA UU	UUUCUAGGACAUCCAUUCG UU	
	siProd	CGAUUGGAAGAACACCACU UU	AGUGGUGUUCUUCCAAUCG UU	
	siCG2662(siLint-O)	GAUUGAGAAGCUAGCCAAA UU	UUUGGCUAGCUUCUCAAUC UU	
	siCG2199	CAGACGUACUGGAGACCAU UU	AUGGUCUCCAGUACGUCUG UU	
experiment	name	forward primer (5' > 3')	reverse primer (5' > 3')	
RT-qPCR	L(3)mbt	AGGAGACGTCTTTCGCTTGG	AGGAGACGTCTTTCGCTTGG	
	Lint-1	CGCCTCAACGATAGCCTACA	TATCACGAGCCATCACCGAC	
	CoRest	CCAGTTCCACGGGAAGAGC	CTGGCTATGGATTTGTCTGGC	
	E2F2	CCAAGGACCAAGAGAACTAC	ATACGACCTATTCGAGGGAT	
	Муb	TTGAAGATATGGATCTGCGG	GACTCTTGTGTGGAGTTTCT	
	Mip120	GAAACCAATACCCAGCAGTA	TCTGGACAAAGATGACTTGG	
	Mip130	CTGCCAGATTAAGATCTCCC	AAGTTCTCCGACACAATCTC	
	Atac3	CGATGGCACAAAGCTAGTCA	CTTGTCCCCTAAGCGAACTG	
	Prod	ATGTCGAGGAGGATCCCCAA	ACGCGGCGCATTTTTAACTT	
	CG2662 (siLint-O)	AAGTGTGGCAAAAGCGAACC	ACGTTGCATAACCGGCAGTA	
	CG2199	TGCAAAAAGAGGTGCGATGC	ATGGGATGCTTCTGTGGGTG	
	Vasa	AGCCGTCCAACGATGCA	AACATCGCTGCCGGTCA	
	Aub	ACGGCATTTGTGACGAGTAG	ACGTCCACGAGCAATTACAG	
	AGO3	CTGCATTTGTGGCCTCCATA	GGGGAGTTTGCCATTCCTTT	
	Piwi	CAAGGCCGGATAATTGGACA	CCATCGCTCGGAGTGGTAAG	
	control(heterochromatin)	CAGTTGATGGGATGAATTTGG	TGCCTGTGGTTCTATCCAAAC	
	vasa promoter	TGAATGAATCACTTAGGTTGCTTG	TGGTGGAATTTCCCATTGTGC	
	rp49	CCGCTTCAAGGGACAGTATCTG	ATCTCGCCGCAGTAAACGC	
RT-qPCR	rp49	CCGCTTCAAGGGACAGTATCTG	ATCTCGCCGCAGTAAACGC	
using mes	CG2662 (Lint-O)	CCAAGGACGAAGACAAGGAG	CGAGGGATCGTACACCTGTT	

# Appendix Table S2. List of siRNAs and primers. RNA is shown in italics.

Sequence CG2662gRNA1\_seq Validation of Lint-O fly mutant

AACTGATCTCCTTATCCAACCGATGGAAGG

experiment	name	sequence	vector
Expression	L3mbt-ATGR	CCCGATCCGGGGTCTCTGG	pAcF-L(3)mbt-S-3xFLAG
vector for OSC	L3mbt-ATG4	ATGAGCCTAATTAAATCCAAGCCCG	pAcF-L(3)mbt-S-3xFLAG
	pAcM-Lint-O_F	AACAAGCTTGGTACCAAACAATCCAAGGACGAAGA	pAcM-Lint-O
	pAcM-Lint-O_R	GACTCGAGCGGCCGCCTAATCTAGCCAGGCGAGGC	pAcM-Lint-O
	pAcM_F	GCGGCCGCTCGAGTCTAGAG	pAcM
	pAcM_R	GGTACCAAGCTTGTTCAGGT	pAcM
	pAc-C3F_F	CTCGAGGACTACAAAGACCA	pAc-C3F_vector
	pAc-C3F_R	CATGGTGGCTAGCCCGATCC	pAc-C3F_vector
	pAc-L3mbt-3xFLAG_F	GGGCTAGCCACCATGCTGCCATTGTCGATGGCCAG	pAc-L3mbt-3xFLAG
	pAc-L3mbt-3xFLAG_R	TTTGTAGTCCTCGAGAGAGGACGTGCGCAAGGGCG	pAc-L3mbt-3xFLAG
	pAc-Lint-O-3xFLAG_F	GGGCTAGCCACCATGAAACAATCCAAGGACGAAGA	pAc-Lint-O-3xFLAG
	pAc-Lint-O-3xFLAG_R	TTTGTAGTCCTCGAGATCTAGCCAGGCGAGGCCAA	pAc-Lint-O-3xFLAG
	siRNA resistant_F	AAAATCGAAAAACTGGCTAAGCGTAGACAGCCCTT	pAc-Lint-O_siRNA_resistant
	siRNA resistant_R	CTTAGCCAGTTTTTCGATTTTCGCTGGCTTTTCTT	pAc-Lint-O_siRNA_resistant
	8CA1_vector_F	GCCCGGTTAGCCAACGTGAGGGGGGCCA	pAc-Lint-O_8CA-3xFLAG
	8CA1_vector_R	GGCCTTCTGGGCCGTGTCGAAGTTGCG	pAc-Lint-O_8CA-3xFLAG
	8CA1_insert_F	CGGCCCAGAAGGCCGGCAAAAGCGAACCCA	pAc-Lint-O_8CA-3xFLAG
	8CA1_insert_R	GTTGGCTAACCGGGCGTAGCGACACTTGTC	pAc-Lint-O_8CA-3xFLAG
	8CA2_vector_F	GCCAGTTTAGCCGTGGATGCCTATCAC	pAc-Lint-O_8CA-3xFLAG
	8CA2_vector_R	GGCGCCCTTGGCAGTGAGGAAGTTGCT	pAc-Lint-O_8CA-3xFLAG
	8CA2_insert_F	ACTGCCAAGGGCGCCATGCAGAAATGGCAC	pAc-Lint-O_8CA-3xFLAG
	8CA2_insert_R	CACGGCTAAACTGGCAATGGAAAGACCTGG	pAc-Lint-O_8CA-3xFLAG
	Lint-O-∆SAM-3xFLAG_F	AAGCCATCCATCCAATGACGTTGGCCTCGC	pAc-Lint-O-∆SAM-3xFLAG
	Lint-O-∆SAM-3xFLAG_R	CGTCATTGGATGGATGGCTTCTTCTCTCTA	pAc-Lint-O-∆SAM-3xFLAG
	Lint-O-∆PHD-3xFLAG_F	CTTCGCAACTTCGACGCGTGTAACATCGGC	pAc-Lint-O-∆PHD-3xFLAG
	Lint-O-∆PHD-3xFLAG_R	GCCGATGTTACACGCGTCGAAGTTGCGAAG	pAc-Lint-O-∆PHD-3xFLAG
	L(3)mbt-L/S_∆SAM_F	GGACCACAGTTCCTGGTCGTCTGCAAGTTTGATTC	pAcF-L(3)mbt-L/S_∆SAM
	L(3)mbt-L/S_∆SAM_R	AAACTTGCAGACGACCAGGAACTGTGGTCCATAGT	pAcF-L(3)mbt-L/S_∆SAM

experiment	name	sequence	vector
Lint-O fly	gRNA_CG2662_1F	CTTCGACGACCCACAATTCCAGCGC	pBFv-U6.2-Lint-O-gRNA1
mutagenesis	gRNA_CG2662_1R	AAACGCGCTGGAATTGTGGGTCGTC	pBFv-U6.2-Lint-O-gRNA1
Lint-O-Venus	Lint-O gRNA5_F	CTTCGACATTAGGTGCTAAGGAGGT	pBFv-U6.2-Lint-O-gRNA5
construction	Lint-O gRNA5_R	AAACACCTCCTTAGCACCTAATGTC	pBFv-U6.2-Lint-O-gRNA5
	Lint-O 5'arm_F	GCTTGATATCGAATTCCTTGCCGATCACGTTCCACAAC	pBS-Lint-Oarm-Venus-3xP3-dsRed-Express2
	Lint-O 5'arm_R	AGTTGGGGGGCGTAGGATCTAGCCAGGCGAGGCCAACGTC	pBS-Lint-Oarm-Venus-3xP3-dsRed-Express2
	Lint-O 3'arm_F	TAGTATAGGAACTTCCGTCCCCACCCACCTCCTTAGCAC	pBS-Lint-Oarm-Venus-3xP3-dsRed-Express2
	Lint-O 3'arm_R	CGGGCTGCAGGAATTC TAAAAGGCGTATTTTACTCCATC	pBS-Lint-Oarm-Venus-3xP3-dsRed-Express2

# Appendix Table S3. Genes upregulated in L(3)mbt KD

FBgn0000053	FBgn0004919	FBgn0020391	FBgn0028916	FBgn0030742	FBgn0032105	FBgn0033431	FBgn0034988	FBgn0036503	FBgn0037853
FBgn0000071	FBgn0005390	FBgn0021800	FBgn0028983	FBgn0030778	FBgn0032123	FBgn0033438	FBgn0035019	FBgn0036536	FBgn0037885
FBgn0000084	FBgn0005558	FBgn0022160	FBgn0028984	FBgn0030793	FBgn0032135	FBgn0033446	FBgn0035032	FBgn0036565	FBgn0037896
FBan0000108	FBan0005631	FBan0022359	FBan0028996	FBan0030816	FBan0032161	FBan0033448	FBan0035034	FBan0036574	FBan0037902
EBap0000158	EBan0005660	EBan0022702	EBan0028997	EBap0030841	EBan0032178	EBap0033451	EBan0035035	EBgn0036612	EBon0037921
EBgn0000190	EBan0005606	EBgn0022700	EBgp0020002	EBgp0020847	EBgn0022102	EBgn0022452	EBan0035056	EBgn0026622	EBgp0027020
FB910000180	FBg10003090	FBg110022709	FBy110029002	FBy110030647	FB910032192	FB910033455	FBy110035050	FB910030022	FBy110037930
Fbgn0000246	FBgn0010014	FBgri0022768	Fbgn0029094	Fbgn0030864	FBgri0032210	FBgn0033459	FBgn0035073	FBg10036640	FB910037950
FBgn0000289	FBgn0010097	FBgn0022770	FBgn0029105	FBgn0030869	FBgn0032211	FBgn0033468	FBgn0035086	FBgn0036641	FBgn0037999
FBgn0000299	FBgn0010226	FBgn0022960	FBgn0029131	FBgn0030876	FBgn0032213	FBgn0033486	FBgn0035094	FBgn0036652	FBgn0038016
FBgn0000317	FBgn0010246	FBgn0023023	FBgn0029137	FBgn0030884	FBgn0032221	FBgn0033538	FBgn0035146	FBgn0036687	FBgn0038037
FBgn0000320	FBgn0010263	FBgn0023094	FBgn0029147	FBgn0030937	FBgn0032228	FBgn0033554	FBgn0035151	FBgn0036689	FBgn0038038
FBgn0000346	FBgn0010314	FBgn0023097	FBgn0029508	FBgn0030941	FBgn0032233	FBgn0033555	FBgn0035157	FBgn0036698	FBgn0038042
EBgn0000422	EBgn0010317	EBgn0023171	EBgn0029514	EBan0030955	EBan0032249	EBgn0033627	EBan0035167	EBan0036732	EBan0038045
EBgp0000463	EBgp0010342	EBgn0023179	EBgn0020573	EBgp0030068	EBgn0032204	EBgn0033654	EBgp0035169	EBgn0036738	EBgp0038047
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FBgn0000633	FBgn0010470	FBgn0023540	FBgn0029722	FBgn0031053	FBgn0032428	FBgn0033767	FBgn0035390	FBgn0036815	FBgn0038250
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# Appendix Table S3. Genes downregulated in L(3)mbt KD

FBgn0000036	FBgn0010265	FBgn0023081	FBgn0027836	FBgn0031169	FBgn0033086	FBgn0034543	FBgn0036035	FBgn0037648	FBgn0039274
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FBgn0261602	FBgn0288310	FBgn0036665	
FBgn0261800	FBgn0000326	FBgn0036970	
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# Appendix Table S3. Genes upregulated in Lint-O KD

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FBgn0029514 FBgn0029514 FBgn0029514 FBgn0029514 FBgn0029573 FBgn0029712 FBgn0029754 FBgn0029754 FBgn0029754 FBgn0029754 FBgn0029830 FBgn0029765 FBgn00297	FBgn0030876 FBgn0030984 FBgn0030937 FBgn0030968 FBgn0030968 FBgn0031053 FBgn0031053 FBgn0031091 FBgn0031101 FBgn0031116 FBgn0031117 FBgn0031171 FBgn0031228 FBgn0031228 FBgn0031228 FBgn0031228 FBgn0031245 FBgn0031254 FBgn0031264 FBgn0031630 FBgn0031630 FBgn0031630 FBgn0031630 FBgn0031637 FBgn0031646 FBgn0031740 FBgn0	FBgn0032752 FBgn0032779 FBgn0032708 FBgn0032800 FBgn0032813 FBgn0032815 FBgn0032815 FBgn0032821 FBgn0032821 FBgn0032821 FBgn0032881 FBgn0032884 FBgn0032884 FBgn0032955 FBgn0032955 FBgn0032955 FBgn0033031 FBgn0033031 FBgn0033031 FBgn0033103 FBgn0033159 FBgn0033159 FBgn0033174 FBgn0033174 FBgn0033174 FBgn0033214 FBgn0033214 FBgn0033214 FBgn0033214 FBgn0033214 FBgn0033373 FBgn003373 FBgn003374 FBgn003374 FBgn003374 FBgn003374 FBgn003374 FBgn003374 FBgn003374 FBgn003374 FBgn003374 FBgn003374 FBgn003374 FBgn003374 FBgn003374 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FBgn0037764 FBgn0037764 FBgn0037764 FBgn0037764 FBgn0037764 FBgn0037764 FBgn0037764 FBgn0037764 FBgn0037764 FBgn0037764 FBgn0037765 FBgn0037764 FBgn0037764 FBgn0037841 FBgn0037841 FBgn0037844 FBgn0037845 FBgn0037865 FBgn0037897 FBgn0037897 FBgn0037921 FBgn0037921 FBgn0037920 FBgn0037927 FBgn0	FBgn0039277 FBgn0039567 FBgn0039640 FBgn0039640 FBgn0039640 FBgn0039640 FBgn0039640 FBgn0039752 FBgn0039702 FBgn0039702 FBgn0039774 FBgn0039755 FBgn0039774 FBgn0039863 FBgn0039863 FBgn0039863 FBgn0039986 FBgn0039986 FBgn0039986 FBgn0039986 FBgn0039986 FBgn0040009 FBgn0040009 FBgn0040009 FBgn0040021 FBgn0040021 FBgn0040022 FBgn0040032 FBgn0040323 FBgn0040323 FBgn0040324 FBgn0040351 FBgn0040551 FBgn0040752 FBgn075 FBgn075 FBgn075 FBgn075 FBgn075 FBgn075 FBg	FBgn0051636 FBgn0051658 FBgn0051720 FBgn0051720 FBgn0051789 FBgn0051789 FBgn0051989 FBgn0052088 FBgn0052088 FBgn0052177 FBgn0052195 FBgn0052363 FBgn0052363 FBgn0052363 FBgn0052436 FBgn0052436 FBgn0052476 FBgn0052476 FBgn0052476 FBgn0052476 FBgn0052476 FBgn0052476 FBgn0052477 FBgn0052476 FBgn0052477 FBgn0052477 FBgn0052626 FBgn0052577 FBgn0052626 FBgn0052577 FBgn0052626 FBgn0052679 FBgn0053108 FBgn0053108 FBgn0053494 FBgn0053494 FBgn0053494 FBgn0053792 FBgn0	FBgn0260933 FBgn0260970 FBgn0261041 FBgn0261243 FBgn0261243 FBgn0261260 FBgn0261262 FBgn0261363 FBgn0261363 FBgn0261367 FBgn0261377 FBgn0261574 FBgn0261671 FBgn0261671 FBgn0261797 FBgn0261797 FBgn0261802 FBgn0261802 FBgn0261802 FBgn0261985 FBgn0261985 FBgn0261987 FBgn0262985 FBgn0262503 FBgn0262562 FBgn0262563 FBgn0262563 FBgn0262564 FBgn0262564 FBgn0262578 FBgn0262788 FBgn0262788 FBgn0262782 FBgn0262782 FBgn0262782 FBgn0262955 FBgn0262782 FBgn0262955 FBgn0262782 FBgn0262782 FBgn0263023 FBgn0263023 FBgn0263023 FBgn0263143 FBgn0263143 FBgn0263232 FBgn0263232 FBgn0263232 FBgn0263232 FBgn0263232 FBgn0263232 FBgn0263232 FBgn0263232 FBgn0263232 FBgn0263232 FBgn0263232 FBgn0263232 FBgn0263232 FBgn0263232 FBgn0263232	FBgn0000075 FBgn0000277 FBgn0003028 FBgn0003028 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FBgm032205         FBgm023216         FBgm003210         FBgm003210         FBgm003211           FBgm003214         FBgm023116         FBgm0032178         FBgm003340           FBgm003212         FBgm0221696         FBgm0032178         FBgm003340           FBgm003210         FBgm003225         FBgm003340         FBgm003322           FBgm003221         FBgm002225         FBgm003222         FBgm003225           FBgm003321         FBgm022267         FBgm003222         FBgm003324           FBgm003365         FBgm022267         FBgm003222         FBgm003324           FBgm003363         FBgm022841         FBgm0032831         FBgm003324           FBgm003462         FBgm0022831         FBgm003324         FBgm003383           FBgm003447         FBgm026845         FBgm003287         FBgm003895           FBgm003447         FBgm026845         FBgm003897         FBgm003891           FBgm003447         FBgm026812         FBgm003891         FBgm003891           FBgm003450         FBgm003891         FBgm003891         FBgm003891           FBgm003476         FBgm003891         FBgm003891         FBgm003891           FBgm003891         FBgm003891         FBgm003891         FBgm003891           FBgm003891         <	FBgn0032040	FBgn0259108	FBgn0031887	FBgn0038260
FBgn002216         FBgn021174         FBgn0032175           FBgn0022175         FBgn002116         FBgn0023175           FBgn0022176         FBgn0022175         FBgn00232175           FBgn00232175         FBgn0022217         FBgn0023225           FBgn0023222         FBgn0023257         FBgn0023252           FBgn0023221         FBgn0023275         FBgn0023257           FBgn0023222         FBgn0023271         FBgn0023275           FBgn0023247         FBgn0023271         FBgn0023275           FBgn0023247         FBgn0023271         FBgn0023272           FBgn002427         FBgn0023272         FBgn0023272           FBgn002447         FBgn0023272         FBgn0023272           FBgn002447         FBgn0023272         FBgn0023272           FBgn002447         FBgn002372         FBgn002372           FBgn002447         FBgn002372         FBgn002372           FBgn002477         FBgn002372         FBgn002372           FBgn002347         FBgn002373         FBgn003373           FBgn002347         FBgn002373         FBgn003373           FBgn002347         FBgn002373         FBgn003373           FBgn002347         FBgn002373         FBgn003473           FBgn0002375         FBgn0	FBgn0032055	FBgn0259216	FBgn0031920	FBgn0038261
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FBp         FBp <td>FBqn0032345</td> <td>FBan0261016</td> <td>FBan0032003</td> <td>FBan0038407</td>	FBqn0032345	FBan0261016	FBan0032003	FBan0038407
Fig.0003210         FBgn0032173         FBgn0038163           FBgn0033006         FBgn028057         FBgn0038123         FBgn0038123           FBgn0033203         FBgn028257         FBgn0038222         FBgn003822           FBgn003322         FBgn003822         FBgn003822         FBgn003822           FBgn0033257         FBgn0038267         FBgn0038242         FBgn003824           FBgn003365         FBgn0286211         FBgn003242         FBgn003824           FBgn0034052         FBgn028645         FBgn003273         FBgn003867           FBgn003447         FBgn028652         FBgn003273         FBgn003861           FBgn003476         FBgn028652         FBgn003273         FBgn003861           FBgn003476         FBgn028652         FBgn003273         FBgn003873           FBgn003476         FBgn028612         FBgn003873         FBgn003873           FBgn003474         FBgn003875         FBgn003873         FBgn003875           FBgn003874         FBgn003873         FBgn003873         FBgn003875           FBgn003874         FBgn003875         FBgn004862         FBgn003875         FBgn004863           FBgn003874         FBgn003875         FBgn004863         FBgn004874         FBgn004864         FBgn004874         FBgn0048	EBan0032726	EBan0261859	EBan0032082	FBan0038435
Fig.0032749         FBg100257         FBg1003225         FBg1003225           FBg1003310         FBg102257         FBg1003225         FBg1003325           FBg1003222         FBg1022531         FBg1003252         FBg1003357           FBg10033246         FBg1022537         FBg1003357         FBg1003357           FBg10033904         FBg1022521         FBg10033222         FBg10033275         FBg10033275           FBg10034052         FBg1022511         FBg10032734         FBg10033275         FBg10033275           FBg1003404         FBg1026405         FBg10032773         FBg10033904           FBg1003404         FBg1026527         FBg1003273         FBg1003991           FBg1003404         FBg1026527         FBg1003391         FBg1003991           FBg10034043         FBg10025274         FBg1003391         FBg1003911           FBg1003444         FBg1003151         FBg1003115         FBg1003115           FBg1003524         FBg1003177         FBg10033115         FBg10031315           FBg1003524         FBg1003375         FBg1003524         FBg1003573           FBg1003524         FBg1003375         FBg1003573         FBg1003575           FBg1003524         FBg1003375         FBg1003575         FBg1003575      >	FDgn0002720	FD==0001000	FD:==0000170	FD==0000400
Flagn033096         FBgn0282057         FBgn033225         FBgn033716           FBgn033101         FBgn0282501         FBgn033226         FBgn033242           FBgn033226         FBgn028251         FBgn033242         FBgn033242           FBgn033365         FBgn0282511         FBgn033242         FBgn033963           FBgn033661         FBgn033252         FBgn033242         FBgn033963           FBgn033657         FBgn028655         FBgn033273         FBgn033963           FBgn034447         FBgn028652         FBgn033290         FBgn033963           FBgn034474         FBgn028652         FBgn033973         FBgn039816           FBgn034474         FBgn0286129         FBgn033973         FBgn039816           FBgn033113         FBgn03973         FBgn039816         FBgn03973           FBgn0381474         FBgn039175         FBgn03979         FBgn034974           FBgn038163         FBgn003131         FBgn034974         FBgn034974           FBgn03979         FBgn034974         FBgn034974         FBgn034974           FBgn03979         FBgn034974         FBgn034974         FBgn034974           FBgn03176         FBgn033711         FBgn034974         FBgn034974           FBgn0303264         FBgn033787         F	FBgn0032749	FB910261996	FB910032178	FBgn0038492
FBgn003221         FBgn003222         FBgn003222         FBgn003223           FBgn003322         FBgn003224         FBgn003223         FBgn003325           FBgn003322         FBgn0032271         FBgn0033275         FBgn0033261           FBgn003304         FBgn0232181         FBgn0033261         FBgn0033261           FBgn003402         FBgn024415         FBgn0032714         FBgn0033261           FBgn003404         FBgn0264455         FBgn0032734         FBgn0033661           FBgn003449         FBgn0226424         FBgn003273         FBgn003961           FBgn003449         FBgn022672         FBgn003273         FBgn003961           FBgn0034447         FBgn026874         FBgn003377         FBgn003972           FBgn003443         FBgn003501         FBgn003971         FBgn003972           FBgn0034474         FBgn000153         FBgn003371         FBgn004372           FBgn003524         FBgn000371         FBgn004373         FBgn004373           FBgn003524         FBgn003373         FBgn004373         FBgn004373           FBgn003524         FBgn003773         FBgn003373         FBgn004375           FBgn003524         FBgn003775         FBgn004572         FBgn004572           FBgn003777         FBgn003775	FBgn0033096	FBgn0262057	FBgn0032225	FBgn0038530
FBgn033203         FBgn222509         FBgn003225         FBgn003322           FBgn0033246         FBgn225287         FBgn0033242         FBgn003394           FBgn003367         FBgn2252817         FBgn0032422         FBgn0033943           FBgn0033963         FBgn2252811         FBgn0032741         FBgn0033943           FBgn003404         FBgn226415         FBgn003273         FBgn0033963           FBgn003447         FBgn026625         FBgn0032803         FBgn003974           FBgn003447         FBgn0266129         FBgn0032973         FBgn003973           FBgn003447         FBgn000159         FBgn003311         FBgn003973           FBgn003497         FBgn000159         FBgn003311         FBgn004162           FBgn003151         FBgn003151         FBgn004123         FBgn004123           FBgn003152         FBgn003151         FBgn004123         FBgn004123           FBgn003152         FBgn003157         FBgn004304         FBgn004304           FBgn003504         FBgn003157         FBgn004304         FBgn004305           FBgn003505         FBgn00317         FBgn004304         FBgn004305         FBgn004305           FBgn003505         FBgn001121         FBgn003375         FBgn004305         FBgn003575         FBgn00357	FBgn0033110	FBgn0262477	FBgn0032252	FBgn0038761
FBgn033222         FBgn028251         FBgn033274         FBgn033274           FBgn033546         FBgn0282671         FBgn033275         FBgn033924           FBgn033507         FBgn028121         FBgn033261         FBgn033924           FBgn033604         FBgn028121         FBgn033261         FBgn033273           FBgn034052         FBgn028465         FBgn033273         FBgn033676           FBgn034076         FBgn028774         FBgn033773         FBgn033676           FBgn034707         FBgn028672         FBgn033773         FBgn033876           FBgn034706         FBgn028672         FBgn033773         FBgn033971           FBgn034497         FBgn028678         FBgn033873         FBgn033972           FBgn03474         FBgn028679         FBgn033813         FBgn003972           FBgn03448         FBgn003131         FBgn041710         FBgn04372           FBgn035103         FBgn003173         FBgn043524         FBgn043525           FBgn03524         FBgn003177         FBgn033868         FBgn043562           FBgn035264         FBgn003177         FBgn043563         FBgn043563           FBgn035612         FBgn033763         FBgn043564         FBgn043563           FBgn035616         FBgn0037677         FBgn	FBgn0033203	FBgn0262509	FBgn0032253	FBgn0038957
FBgn033246         FBgn028267         FBgn033275         FBgn03392           FBgn033363         FBgn028271         FBgn033275         FBgn033923           FBgn033963         FBgn028219         FBgn033263         FBgn033923           FBgn03404         FBgn028415         FBgn033273         FBgn033923           FBgn03404         FBgn028615         FBgn033273         FBgn033923           FBgn03404         FBgn028652         FBgn033283         FBgn03393           FBgn034497         FBgn028652         FBgn033973         FBgn033973           FBgn034497         FBgn003153         FBgn033973         FBgn034973           FBgn034974         FBgn000158         FBgn033113         FBgn044974           FBgn0303113         FBgn042862         FBgn003317         FBgn044974           FBgn00317         FBgn03387         FBgn044974         FBgn003175           FBgn03524         FBgn00317         FBgn043866         FBgn044974           FBgn003524         FBgn003177         FBgn043876         FBgn043867           FBgn03524         FBgn003177         FBgn043867         FBgn043867           FBgn03524         FBgn003172         FBgn043875         FBgn043876           FBgn03517         FBgn003177         FBgn003177 <td>FBgn0033222</td> <td>FBgn0262531</td> <td>FBgn0032262</td> <td>FBgn0039006</td>	FBgn0033222	FBgn0262531	FBgn0032262	FBgn0039006
FBgn0033657         FBgn0032875         FBgn0033826           FBgn0033904         FBgn028111         FBgn0033821         FBgn0033821           FBgn003402         FBgn0284115         FBgn0032873         FBgn0033821           FBgn003404         FBgn028465         FBgn003273         FBgn0038261           FBgn0034497         FBgn0285624         FBgn003871         FBgn003891           FBgn0034497         FBgn0285624         FBgn003891         FBgn003992           FBgn0034497         FBgn028574         FBgn003891         FBgn003992           FBgn003497         FBgn003891         FBgn003992         FBgn003992           FBgn003493         FBgn003891         FBgn003981         FBgn003981           FBgn003494         FBgn0001296         FBgn003391         FBgn004170           FBgn003504         FBgn000373         FBgn0033284         FBgn004375           FBgn003505         FBgn003386         FBgn0033763         FBgn00357           FBgn003893         FBgn003875         FBgn003875         FBgn003875           FBgn003893         FBgn003875         FBgn003875         FBgn003875           FBgn003893         FBgn003875         FBgn003875         FBgn003875           FBgn003894         FBgn003875         FBgn003875 <td>FBan0033246</td> <td>FBan0262867</td> <td>FBan0032374</td> <td>FBan0039124</td>	FBan0033246	FBan0262867	FBan0032374	FBan0039124
Fg.n003394         FBg.n028311         FBg.n003242         FBg.n003842           FBg.n0033943         FBg.n0283219         FBg.n003863         FBg.n003863           FBg.n003404         FBg.n028415         FBg.n003863         FBg.n003863           FBg.n003404         FBg.n028615         FBg.n003873         FBg.n003873           FBg.n0034407         FBg.n028612         FBg.n003873         FBg.n003971           FBg.n0034407         FBg.n028612         FBg.n003873         FBg.n003973           FBg.n0034406         FBg.n003871         FBg.n003871         FBg.n003871           FBg.n0034465         FBg.n003521         FBg.n004726         FBg.n003871           FBg.n003503         FBg.n003753         FBg.n004766         FBg.n003874         FBg.n004766           FBg.n003513         FBg.n003875         FBg.n003875         FBg.n003876         FBg.n003875         FBg.n003876         FBg.n003875	EBan0033657	EBan0262871	EBan0032375	FBan0039282
Fig.003306         FBgn023819         FBgn003861         FBgn003862           FBgn03462         FBgn024415         FBgn003763         FBgn003962           FBgn03440         FBgn226612         FBgn003763         FBgn003962           FBgn03440         FBgn226612         FBgn003290         FBgn003961           FBgn034470         FBgn026672         FBgn0032972         FBgn003971           FBgn034440         FBgn026679         FBgn003391         FBgn003927           FBgn034446         FBgn003173         FBgn003927         FBgn003927           FBgn003486         FBgn003175         FBgn003115         FBgn0041701           FBgn003524         FBgn0001796         FBgn0033274         FBgn0043027           FBgn003524         FBgn0001796         FBgn003375         FBgn004367           FBgn003524         FBgn0003767         FBgn0033763         FBgn004586           FBgn003524         FBgn0003775         FBgn003775         FBgn005170           FBgn003803         FBgn0033763         FBgn005172         FBgn005172           FBgn003803         FBgn0033775         FBgn005172         FBgn003477         FBgn005172           FBgn003804         FBgn0033783         FBgn005172         FBgn003472         FBgn005172	EBgp0033904	EBgp0262111	EBgp0032422	EBgn0030204
Fig0033863         FBg0/284219         FBg0/032683         FBg0/032683           FBg0/03404         FBg0/025662         FBg0/032774         FBg0/03969           FBg0/03449         FBg0/025672         FBg0/03273         FBg0/03997           FBg0/03449         FBg0/025674         FBg0/032972         FBg0/03997           FBg0/03449         FBg0/025679         FBg0/032973         FBg0/03997           FBg0/03449         FBg0/025679         FBg0/033973         FBg0/03997           FBg0/03449         FBg0/02597         FBg0/03397         FBg0/04123           FBg0/034495         FBg0/00159         FBg0/033211         FBg0/04123           FBg0/03504         FBg0/00159         FBg0/03321         FBg0/04302           FBg0/03524         FBg0/003268         FBg0/04302           FBg0/03550         FBg0/003680         FBg0/033753         FBg0/04580           FBg0/03561         FBg0/003775         FBg0/05375         FBg0/05468           FBg0/03561         FBg0/003775         FBg0/05468         FBg0/05476           FBg0/03687         FBg0/003775         FBg0/05469         FBg0/05476           FBg0/03677         FBg0/03763         FBg0/05476         FBg0/05476           FBg0/03776         FBg0/03776         FBg0/05477	FD 0000000	T Dg10203111	T Dg110032422	T Dy10039294
FBgn034052         FBgn0254615         FBgn033274         FBgn033825           FBgn034449         FBgn0256052         FBgn033273         FBgn033875           FBgn034706         FBgn0256052         FBgn033273         FBgn033871           FBgn034471         FBgn0256052         FBgn033871         FBgn033971           FBgn034474         FBgn025672         FBgn033971         FBgn033971           FBgn034474         FBgn025673         FBgn033713         FBgn003927           FBgn034485         FBgn0033713         FBgn003927         FBgn003927           FBgn035284         FBgn003113         FBgn0041710         FBgn0041710           FBgn035284         FBgn003273         FBgn004328         FBgn004328           FBgn035284         FBgn003286         FBgn0033753         FBgn004387           FBgn035284         FBgn003486         FBgn0033753         FBgn003503           FBgn035803         FBgn003468         FBgn0033753         FBgn00350137           FBgn035803         FBgn003475         FBgn003575         FBgn003576           FBgn03617         FBgn003776         FBgn003776         FBgn003776           FBgn03686         FBgn003776         FBgn003776         FBgn003776           FBgn03687         FBgn003776	FBgn0033963	FBgn0263219	FBgn0032601	FBgn0039321
FBgn034094         FBgn024495         FBgn032773         FBgn033675           FBgn03449         FBgn025524         FBgn032803         FBgn033975           FBgn03449         FBgn025524         FBgn032872         FBgn003971           FBgn03447         FBgn025524         FBgn033773         FBgn003971           FBgn034443         FBgn0256709         FBgn0032773         FBgn003971           FBgn034447         FBgn0256709         FBgn0033713         FBgn0041233           FBgn0303446         FBgn003521         FBgn004175         FBgn004172           FBgn030313         FBgn0032824         FBgn004303         FBgn004303           FBgn03526         FBgn003387         FBgn003565         FBgn003565           FBgn03526         FBgn003387         FBgn003565         FBgn003565           FBgn03526         FBgn003573         FBgn003564         FBgn003573         FBgn003563           FBgn036876         FBgn003687         FBgn003573         FBgn003517         FBgn003573         FBgn003517           FBgn036876         FBgn0036421         FBgn0033763         FBgn003517	FBgn0034052	FBgn0264815	FBgn0032683	FBgn0039504
FBgn034427         FBgn0255045         FBgn032803         FBgn039978           FBgn034489         FBgn026524         FBgn032972         FBgn039917           FBgn034470         FBgn026574         FBgn032973         FBgn039917           FBgn034447         FBgn026574         FBgn032973         FBgn039915           FBgn034446         FBgn026579         FBgn033113         FBgn0041230           FBgn034474         FBgn0001259         FBgn033211         FBgn0041230           FBgn035504         FBgn0001259         FBgn033224         FBgn0041230           FBgn035504         FBgn0001259         FBgn033224         FBgn0043037           FBgn035504         FBgn0001259         FBgn033224         FBgn0043037           FBgn035524         FBgn0003137         FBgn033237         FBgn0043047           FBgn035561         FBgn0003767         FBgn03375         FBgn003564           FBgn035612         FBgn003477         FBgn03375         FBgn03176           FBgn036479         FBgn0004512         FBgn03375         FBgn03176           FBgn036479         FBgn0001258         FBgn03317         FBgn03176           FBgn036477         FBgn03177         FBgn036462         FBgn0303672           FBgn03687         FBgn03172	FBgn0034094	FBgn0264895	FBgn0032774	FBgn0039629
FBgn0034489         FBgn025052         FBgn0032900         FBgn003490           FBgn0034497         FBgn025274         FBgn0032973         FBgn003915           FBgn0034403         FBgn02872         FBgn003973         FBgn003975           FBgn0034966         FBgn002165         FBgn0033113         FBgn0041235           FBgn003504         FBgn003226         FBgn003221         FBgn004375           FBgn0035214         FBgn0003175         FBgn003224         FBgn004375           FBgn003524         FBgn000308         FBgn003385         FBgn004375           FBgn003550         FBgn000386         FBgn003375         FBgn003375           FBgn003551         FBgn000386         FBgn003375         FBgn003175           FBgn003622         FBgn003375         FBgn003175         FBgn003175           FBgn0036512         FBgn003375         FBgn005176         FBgn003477           FBgn003677         FBgn0004512         FBgn003413         FBgn005176           FBgn003677         FBgn0004512         FBgn003473         FBgn005176           FBgn003753         FBgn001473         FBgn003753         FBgn005176           FBgn003757         FBgn001473         FBgn003753         FBgn005207           FBgn003775         FBgn003753	FBgn0034247	FBgn0265045	FBgn0032783	FBgn0039655
FBgn0034497         FBgn0285274         FBgn0032900         FBgn003911           FBgn0034706         FBgn02873         FBgn003911         FBgn003911           FBgn003496         FBgn000153         FBgn0033115         FBgn004037           FBgn0035034         FBgn000153         FBgn0033221         FBgn004296           FBgn0035034         FBgn0001296         FBgn0033221         FBgn004296           FBgn0035244         FBgn003377         FBgn003324         FBgn004397           FBgn0035244         FBgn003377         FBgn003387         FBgn004397           FBgn0035244         FBgn003375         FBgn004396         FBgn003368         FBgn003369           FBgn0035612         FBgn003380         FBgn003375         FBgn005475         FBgn003477         FBgn003476         FBgn003477         FBgn003476	FBan0034489	FBan0265052	FBan0032803	FBan0039678
Fig.nc.         Fig.nc.         Fig.nc.         Fig.nc.           Fig.nc.         Fig.nc.         Fig.nc.         Fig.nc.         Fig.nc.         Fig.nc.           Fig.nc.	EBan0034497	FBan0265274	EBan0032900	FBan0039818
Feglinosario         Feglinosario         Feglinosario           Fegno34496         Fegno2273         Fegno33113         Fegno3474           Fegno34496         Fegno3113         Fegno33113         Fegno3473           Fegno335034         Fegno32273         Fegno32214         Fegno32214           Fegno35244         Fegno32214         Fegno322321         Fegno322321           Fegno35234         Fegno33234         Fegno32324         Fegno33234           Fegno35254         Fegno33244         Fegno33234         Fegno33585         Fegno33585           Fegno35565         Fegno33585         Fegno351375         Fegno33586         Fegno33585         Fegno33585         Fegno33585         Fegno351375         Fegno351375         Fegno351375         Fegno351375         Fegno35146         Fegno35146         Fegno35147         Fegno35147         Fegno35147         Fegno35147         Fegno35147         Fegno35147         Fegno35147         Fegno35147         Fegno35147         Fegn	FD==0004700	FD==0000100	FD==000002000	ED==0000011
Hgn0034943         FHgn003496         FHgn003496           FHgn0034965         FHgn0020513         FHgn003051           FHgn0034965         FHgn000153         FHgn0033113         FHgn0041233           FHgn0035044         FHgn0001296         FHgn0033224         FHgn0043037           FHgn0035054         FHgn0003175         FHgn0033284         FHgn0043037           FHgn0035055         FHgn000308         FHgn0033284         FHgn0043965           FHgn0035056         FHgn0003868         FHgn0033763         FHgn0045962           FHgn0035056         FHgn0003868         FHgn0033763         FHgn0051017           FHgn0036822         FHgn0003868         FHgn0033763         FHgn0051017           FHgn0036727         FHgn0034512         FHgn0033175         FHgn0051464           FHgn0036727         FHgn0034512         FHgn0034133         FHgn0051644           FHgn003677         FHgn001241         FHgn003453         FHgn005207           FHgn003677         FHgn001258         FHgn003453         FHgn005273           FHgn003776         FHgn001426         FHgn003473         FHgn005273           FHgn003776         FHgn0014384         FHgn0034957         FHgn005273           FHgn003776         FHgn0014396         FHgn0034957	FBgn0034706	FBgn0200129	FBgn0032972	FBgn0039911
FBgn034966         FBgn0244435         FBgn033079         FBgn003927           FBgn034974         FBgn0000153         FBgn033113         FBgn004170           FBgn035044         FBgn0001259         FBgn033221         FBgn00470           FBgn0350304         FBgn0001296         FBgn033221         FBgn004376           FBgn035244         FBgn0003175         FBgn0033284         FBgn004375           FBgn035505         FBgn0003475         FBgn003368         FBgn003368         FBgn003561           FBgn03503         FBgn0003808         FBgn0033753         FBgn005148           FBgn003615         FBgn000380         FBgn003375         FBgn0051436           FBgn0036479         FBgn0004512         FBgn003477         FBgn003477         FBgn003477           FBgn003666         FBgn0034279         FBgn0051436         FBgn003689         FBgn003469         FBgn003697         FBgn003697         FBgn003697         FBgn003697         FBgn003697         FBgn003697         FBgn0037714         FBgn0037714         FBgn0037714         FBgn0037714         FBgn0037714         FBgn0037714         FBgn003771         FBgn003771         FBgn003771         FBgn003771         FBgn003771         FBgn003768         FBgn003768         FBgn003768         FBgn003768         FBgn003768         FBgn003768 <td>FBgn0034943</td> <td>FBgn0266709</td> <td>FBgn0032973</td> <td>FBgn0039915</td>	FBgn0034943	FBgn0266709	FBgn0032973	FBgn0039915
FBgn0034974         FBgn0001146         FBgn0033113         FBgn0040372           FBgn003504         FBgn0001256         FBgn0033115         FBgn004123           FBgn003504         FBgn0001256         FBgn0033221         FBgn004303           FBgn003503         FBgn000317         FBgn0033284         FBgn004303           FBgn003505         FBgn003475         FBgn003358         FBgn004356           FBgn003550         FBgn003466         FBgn0033753         FBgn005448           FBgn003615         FBgn0003466         FBgn0033753         FBgn005142           FBgn003650         FBgn0003466         FBgn003375         FBgn005143           FBgn003656         FBgn0004512         FBgn003477         FBgn005143           FBgn003667         FBgn001241         FBgn0034279         FBgn0051464           FBgn003677         FBgn001226         FBgn0034273         FBgn0051462           FBgn003776         FBgn0011226         FBgn003462         FBgn005206           FBgn003771         FBgn0011226         FBgn003453         FBgn005276           FBgn003776         FBgn0011226         FBgn003452         FBgn003775           FBgn003771         FBgn001348         FBgn003452         FBgn003775           FBgn003771         FBgn00377	FBgn0034966	FBgn0284435	FBgn0033051	FBgn0039927
FBgn0034985         FBgn000153         FBgn0033113         FBgn004123           FBgn003504         FBgn002126         FBgn003221         FBgn004170           FBgn0035103         FBgn0001266         FBgn0032284         FBgn004375           FBgn0035244         FBgn0003175         FBgn0033568         FBgn003565           FBgn003505         FBgn0003475         FBgn0033659         FBgn003561           FBgn003503         FBgn0003808         FBgn0033753         FBgn0051468           FBgn003503         FBgn0003809         FBgn0033753         FBgn0051426           FBgn0036479         FBgn0005427         FBgn003477         FBgn003143           FBgn003666         FBgn003477         FBgn003479         FBgn005143           FBgn003680         FBgn003471         FBgn003479         FBgn005143           FBgn003687         FBgn001473         FBgn003478         FBgn005143           FBgn003771         FBgn0011226         FBgn003452         FBgn005272           FBgn003771         FBgn001122         FBgn003456         FBgn003773           FBgn003771         FBgn0011438         FBgn003496         FBgn003775           FBgn003771         FBgn0014417         FBgn003496         FBgn003775           FBgn003771         FBgn00277	FBgn0034974	FBgn0000146	FBgn0033079	FBgn0040370
FBgn0035034         FBgn001259         FBgn0033211         FBgn004268           FBgn003504         FBgn003137         FBgn003324         FBgn003324         FBgn003324           FBgn003524         FBgn0003137         FBgn003328         FBgn004380           FBgn003524         FBgn000346         FBgn003368         FBgn003686           FBgn003505         FBgn000346         FBgn0033753         FBgn005448           FBgn003512         FBgn000346         FBgn0033753         FBgn005143           FBgn003522         FBgn000118         FBgn003375         FBgn005143           FBgn003656         FBgn003477         FBgn005143         FBgn005143           FBgn003686         FBgn001225         FBgn003473         FBgn005146           FBgn0036875         FBgn001125         FBgn003473         FBgn003277           FBgn003775         FBgn001128         FBgn003482         FBgn003277           FBgn003771         FBgn0011381         FBgn003478         FBgn003775           FBgn003775         FBgn001348         FBgn003476         FBgn003877           FBgn003771         FBgn001439         FBgn003476         FBgn003877           FBgn003876         FBgn003277         FBgn003876         FBgn003846           FBgn003876	FBgn0034985	FBgn0000153	FBgn0033113	FBgn0041233
Figur0035094         Figur001236         Figur0033221         Figur004286           Figur0035103         Figur0001296         Figur0033244         Figur0043043           Figur0035244         Figur000308         Figur0033268         Figur0043043           Figur0035505         Figur003086         Figur003368         Figur003368         Figur003368           Figur0035612         Figur0033686         Figur0033753         Figur003642           Figur0036222         Figur0034612         Figur0033477         Figur003647           Figur0036806         Figur003407         Figur003647         Figur003647           Figur0036807         Figur003642         Figur0034047         Figur003647           Figur0036807         Figur001628         Figur0034413         Figur0036473           Figur0036807         Figur001428         Figur003462         Figur003479           Figur0036807         Figur001472         Figur003462         Figur003773           Figur003771         Figur001348         Figur003462         Figur003774           Figur0037750         Figur001348         Figur003467         Figur003764           Figur003771         Figur001436         Figur003506         Figur003768           Figur003771         Figur001400         Figur0034787	FBgn0035034	FBan0001259	FBgn0033115	FBan0041710
Fight003503         FBgn00313         FBgn003224         FBgn004304           FBgn003503         FBgn0003264         FBgn0003265         FBgn0033268         FBgn004306           FBgn003505         FBgn0003268         FBgn0033268         FBgn0045805           FBgn003505         FBgn0003475         FBgn0033659         FBgn0051375           FBgn003503         FBgn0003486         FBgn003375         FBgn0051426           FBgn0036822         FBgn0004512         FBgn003375         FBgn0051465           FBgn0036877         FBgn0004512         FBgn0034479         FBgn0051466           FBgn0036877         FBgn0001228         FBgn0034530         FBgn0052027           FBgn0036875         FBgn0011226         FBgn003462         FBgn0052027           FBgn003776         FBgn0011226         FBgn003462         FBgn0052027           FBgn003776         FBgn0011828         FBgn0034789         FBgn0052702           FBgn0037714         FBgn0011828         FBgn0034789         FBgn0052702           FBgn0037717         FBgn0014395         FBgn0034789         FBgn0052702           FBgn003771         FBgn0014395         FBgn0034789         FBgn0052702           FBgn003771         FBgn0014395         FBgn0035147         FBgn0055141 <tr< td=""><td>EBan0035094</td><td>EBgp0001296</td><td>EBan0033221</td><td>EBan0042696</td></tr<>	EBan0035094	EBgp0001296	EBan0033221	EBan0042696
Fegn(0033:03         FEgn(00323:04         FEgn(00323:05         FEgn(00323:05         FEgn(0033:05         FEgn(003:05:02         FEgn(003:05:02	FD:::0005004	FD==0001001	FD:==000000221	ED==0040040
FBgn0035234         FBgn0003375         FBgn0003328         FBgn0043505           FBgn0035505         FBgn0003465         FBgn003365         FBgn003365         FBgn003365           FBgn0035612         FBgn0003486         FBgn0033753         FBgn0050435           FBgn0035612         FBgn0003886         FBgn0033753         FBgn0051375           FBgn0036479         FBgn0004512         FBgn0033917         FBgn0051463           FBgn003668         FBgn0005427         FBgn003413         FBgn0051463           FBgn003668         FBgn0010241         FBgn0034530         FBgn0051463           FBgn00366875         FBgn001128         FBgn0034530         FBgn0052037           FBgn003776         FBgn0011826         FBgn0034662         FBgn005273           FBgn0037716         FBgn0011828         FBgn003456         FBgn005273           FBgn0037751         FBgn001431         FBgn003456         FBgn005273           FBgn0037751         FBgn001331         FBgn003456         FBgn005273           FBgn003775         FBgn001331         FBgn0035104         FBgn005273           FBgn003775         FBgn0013518         FBgn003517         FBgn005276           FBgn003775         FBgn0013518         FBgn002576         FBgn002576	FB910035103	FBGNUUU 1991	FB910033234	FBgn0043043
FBgn0035264         FBgn0003308         FBgn003387         FBgn0045900           FBgn0035505         FBgn0003475         FBgn003569         FBgn005369         FBgn005369           FBgn0035195         FBgn0003868         FBgn0033753         FBgn0051437           FBgn0036195         FBgn0004512         FBgn0033775         FBgn0051432           FBgn0036677         FBgn0004512         FBgn003447         FBgn0051463           FBgn003668         FBgn001241         FBgn0034530         FBgn0051463           FBgn003660         FBgn0011286         FBgn0034530         FBgn0052027           FBgn003677         FBgn0011286         FBgn0034531         FBgn0052027           FBgn003776         FBgn0011286         FBgn0034531         FBgn0052702           FBgn003776         FBgn0011286         FBgn003462         FBgn0052703           FBgn0037716         FBgn0013813         FBgn0034928         FBgn0053775           FBgn0037717         FBgn0014305         FBgn0035056         FBgn005877           FBgn0037751         FBgn0014305         FBgn003517         FBgn0082802           FBgn0038070         FBgn002379         FBgn003517         FBgn0082804           FBgn0038071         FBgn0028745         FBgn0028744         FBgn0028744 <t< td=""><td>FBgn0035234</td><td>FBgn0003137</td><td>FBgn0033268</td><td>FBgn0043575</td></t<>	FBgn0035234	FBgn0003137	FBgn0033268	FBgn0043575
FBgn0035612         FBgn003466         FBgn0033659         FBgn0050365           FBgn0033612         FBgn0003866         FBgn0033753         FBgn0050485           FBgn0033613         FBgn0003866         FBgn0033753         FBgn0051437           FBgn0036282         FBgn0004118         FBgn0033753         FBgn0051432           FBgn0036686         FBgn0005427         FBgn003413         FBgn0051463           FBgn0036675         FBgn0010258         FBgn003413         FBgn0052037           FBgn0036875         FBgn0011228         FBgn003462         FBgn0052037           FBgn003776         FBgn0011728         FBgn003462         FBgn0052702           FBgn003776         FBgn0011828         FBgn003462         FBgn0052702           FBgn0037714         FBgn0013813         FBgn0034457         FBgn0052702           FBgn0037714         FBgn0014395         FBgn0034457         FBgn0053775           FBgn0037714         FBgn0014395         FBgn003566         FBgn0052702           FBgn0037716         FBgn0014395         FBgn003571         FBgn005377           FBgn003771         FBgn0014395         FBgn003526         FBgn003526         FBgn003526           FBgn003807         FBgn0015312         FBgn0025317         FBgn0025261         FBgn	FBgn0035264	FBgn0003308	FBgn0033387	FBgn0043806
FBgn0035612         FBgn003466         FBgn0033659         FBgn005467           FBgn0035903         FBgn003890         FBgn003773         FBgn0051375           FBgn003682         FBgn0004512         FBgn003397         FBgn0051407           FBgn003668         FBgn0005667         FBgn003477         FBgn0051407           FBgn003677         FBgn0005666         FBgn0034530         FBgn0051407           FBgn003677         FBgn0011226         FBgn0034530         FBgn0052020           FBgn003678         FBgn0011728         FBgn003462         FBgn0052037           FBgn003718         FBgn0011728         FBgn003462         FBgn0052703           FBgn0037714         FBgn0011828         FBgn0034789         FBgn0053775           FBgn0037717         FBgn001338         FBgn003497         FBgn0053775           FBgn0037711         FBgn0014306         FBgn003276         FBgn005377           FBgn0037716         FBgn0014396         FBgn0035104         FBgn0052437           FBgn003876         FBgn0014396         FBgn003517         FBgn0052437           FBgn003876         FBgn001532         FBgn0035147         FBgn0052437           FBgn003879         FBgn002379         FBgn003517         FBgn0026248           FBgn0038201	FBgn0035505	FBgn0003475	FBgn0033658	FBgn0045980
FBgn0035803         FBgn0003886         FBgn003753         FBgn0051101           FBgn0036195         FBgn0004118         FBgn0037753         FBgn00511017           FBgn0036282         FBgn0004512         FBgn0033775         FBgn0051403           FBgn0036727         FBgn0005427         FBgn003417         FBgn0051403           FBgn0036806         FBgn0010241         FBgn003413         FBgn0051020           FBgn0036875         FBgn0011258         FBgn0034602         FBgn0052027           FBgn0036893         FBgn0011226         FBgn0034602         FBgn0052703           FBgn0037716         FBgn0011226         FBgn0034602         FBgn0052703           FBgn0037717         FBgn0011338         FBgn003462         FBgn0052737           FBgn0037711         FBgn0011331         FBgn0034956         FBgn0052775           FBgn0037751         FBgn0014316         FBgn0034957         FBgn0058775           FBgn0037751         FBgn0014396         FBgn003506         FBgn003506         FBgn0038079           FBgn0038079         FBgn0014396         FBgn003514         FBgn0082402           FBgn0038079         FBgn002479         FBgn003514         FBgn002506           FBgn0038079         FBgn002279         FBgn0023717         FBgn0028431 <t< td=""><td>FBan0035612</td><td>FBan0003486</td><td>FBan0033659</td><td>FBan0050345</td></t<>	FBan0035612	FBan0003486	FBan0033659	FBan0050345
Fig.n003030         FBgn003703         FBgn003703         FBgn0051137           FBgn0038479         FBgn0004512         FBgn0033875         FBgn0051432           FBgn0036479         FBgn0005427         FBgn0033875         FBgn0051433           FBgn0036678         FBgn0005427         FBgn003413         FBgn0051443           FBgn0036677         FBgn0011256         FBgn0034530         FBgn0052005           FBgn0036678         FBgn0011226         FBgn0034602         FBgn0052702           FBgn003776         FBgn0011226         FBgn0034602         FBgn0052702           FBgn0037714         FBgn0011828         FBgn0034789         FBgn0053775           FBgn0037717         FBgn0013348         FBgn0034956         FBgn0053775           FBgn0037717         FBgn0014300         FBgn0034972         FBgn0058470           FBgn0037711         FBgn0014396         FBgn0035147         FBgn0058470           FBgn0037711         FBgn0014417         FBgn0035147         FBgn0058470           FBgn0038076         FBgn001532         FBgn0035141         FBgn0085428           FBgn0038079         FBgn002719         FBgn003511         FBgn002844           FBgn0038070         FBgn002752         FBgn003580         FBgn025907           FBgn00380	EBan0035903	EBan0003886	EBan0033753	EBan0050485
Fegn003819         Fegn0033763         Fegn0033763           Fegn003867         Fegn0004118         Fegn0033763         Fegn0051370           Fegn003668         Fegn0005427         Fegn0034279         Fegn0051463           Fegn0036675         Fegn0010241         Fegn0034279         Fegn0051463           Fegn0036675         Fegn00110241         Fegn0034538         Fegn0052003           Fegn0036675         Fegn0011722         Fegn0034538         Fegn0052003           Fegn0037716         Fegn0011722         Fegn003462         Fegn0052703           Fegn0037714         Fegn0011328         Fegn003428         Fegn005375           Fegn0037750         Fegn001439         Fegn0034928         Fegn005376           Fegn0037751         Fegn0014395         Fegn0035056         Fegn0065470           Fegn003756         Fegn0014395         Fegn0035056         Fegn0065262           Fegn003750         Fegn001532         Fegn0035056         Fegn0065262           Fegn0038076         Fegn001532         Fegn003517         Fegn008540           Fegn0038079         Fegn002379         Fegn0035317         Fegn008540           Fegn0038079         Fegn002379         Fegn0035317         Fegn025402           Fegn0038079         Fegn002379	T Dg110033303	T Dg10003000	FD 0000733	T Dg110050405
FBgn003622         FBgn0004118         FBgn003875         FBgn0051432           FBgn0036568         FBgn0005427         FBgn003407         FBgn0051436           FBgn0036806         FBgn0010258         FBgn003413         FBgn0052007           FBgn00368075         FBgn0010258         FBgn003453         FBgn0052007           FBgn0036978         FBgn0011296         FBgn003453         FBgn0052007           FBgn003726         FBgn0011226         FBgn003462         FBgn0052703           FBgn0037761         FBgn0011828         FBgn0034928         FBgn0052703           FBgn0037714         FBgn001348         FBgn0034927         FBgn0054737           FBgn0037750         FBgn0014395         FBgn0034957         FBgn0055104           FBgn0037750         FBgn0014395         FBgn0035104         FBgn0085425           FBgn003876         FBgn0015519         FBgn0035114         FBgn0085424           FBgn003807         FBgn0002379         FBgn0035412         FBgn008548           FBgn003802         FBgn0023416         FBgn0035412         FBgn008548           FBgn003903         FBgn0023957         FBgn0026060         FBgn0260643           FBgn003920         FBgn002395         FBgn003594         FBgn02605907           FBgn003950 <td>FBgn0036195</td> <td>FBgn0003890</td> <td>FBgn0033763</td> <td>FBgn0051017</td>	FBgn0036195	FBgn0003890	FBgn0033763	FBgn0051017
FBgn0036479         FBgn0004512         FBgn003917         FBgn0051423           FBgn0036568         FBgn0005427         FBgn0034279         FBgn0051463           FBgn0036806         FBgn0010281         FBgn0034530         FBgn0052037           FBgn0036875         FBgn0011296         FBgn0034632         FBgn0052073           FBgn003776         FBgn0011282         FBgn0034662         FBgn0052725           FBgn0037716         FBgn0011828         FBgn0034662         FBgn0053775           FBgn0037714         FBgn0011828         FBgn0034662         FBgn0053775           FBgn0037750         FBgn0014395         FBgn0034957         FBgn0054747           FBgn0037751         FBgn0014395         FBgn0034957         FBgn0055477           FBgn0037750         FBgn0014395         FBgn003506         FBgn0065428           FBgn0037751         FBgn0015519         FBgn0035286         FBgn0085246           FBgn0038079         FBgn002379         FBgn0035317         FBgn0085432           FBgn0038079         FBgn002379         FBgn0035571         FBgn0026042           FBgn003807         FBgn002379         FBgn00358412         FBgn0026042           FBgn003804         FBgn0026144         FBgn003580         FBgn0260502           FBgn00	FBgn0036282	FBgn0004118	FBgn0033875	FBgn0051370
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FBgn0036806         FBgn0010241         FBgn0034413         FBgn0051997           FBgn0036875         FBgn0010258         FBgn0034530         FBgn0052006           FBgn0036993         FBgn0011296         FBgn0034602         FBgn0052072           FBgn003776         FBgn0011282         FBgn0034662         FBgn0052702           FBgn003776         FBgn0011828         FBgn0034962         FBgn0052703           FBgn0037711         FBgn0011438         FBgn0034957         FBgn0053775           FBgn0037751         FBgn0014395         FBgn0034957         FBgn005877           FBgn0037751         FBgn0014395         FBgn0034972         FBgn0085298           FBgn0038076         FBgn001532         FBgn0035141         FBgn0085298           FBgn0038076         FBgn002379         FBgn0035141         FBgn0085298           FBgn003800         FBgn002379         FBgn003511         FBgn008543           FBgn003801         FBgn002379         FBgn003511         FBgn0250907           FBgn003810         FBgn0022472         FBgn003594         FBgn0250907           FBgn0039201         FBgn0027070         FBgn003614         FBgn0260865           FBgn003950         FBgn0027070         FBgn003644         FBgn0260433           FBgn003979	FBqn0036727	FBqn0005666	FBgn0034279	FBqn0051464
Fighn038875         FBgn0010288         FBgn0034530         FBgn0052006           FBgn0036978         FBgn0011226         FBgn0034530         FBgn0052007           FBgn003776         FBgn0011722         FBgn0034602         FBgn0052702           FBgn003776         FBgn0011286         FBgn003498         FBgn0052703           FBgn0037714         FBgn00113813         FBgn003495         FBgn0052703           FBgn0037750         FBgn0014396         FBgn0034957         FBgn0054775           FBgn0037750         FBgn0014396         FBgn0034957         FBgn005510           FBgn0037750         FBgn0014396         FBgn003506         FBgn0055245           FBgn0038076         FBgn0015519         FBgn0035104         FBgn0085245           FBgn0038079         FBgn002379         FBgn0035412         FBgn0085483           FBgn003800         FBgn002379         FBgn0035412         FBgn00250907           FBgn003840         FBgn002372         FBgn0035434         FBgn0250907           FBgn003841         FBgn0025703         FBgn0035434         FBgn0250907           FBgn0039500         FBgn002707         FBgn0035985         FBgn0250977           FBgn0039501         FBgn002707         FBgn003640         FBgn0266133           FBgn003997<	EBan0036806	EBan0010241	EBan0034413	EBan0051997
Fbgn003673         Fbgn001473         Fbgn0034353         Fbgn0052037           Fbgn0036993         Fbgn0011226         Fbgn0034602         Fbgn0052073           Fbgn0037716         Fbgn0011226         Fbgn0034622         Fbgn0052732           Fbgn0037717         Fbgn0011384         Fbgn0034926         Fbgn005775           Fbgn0037717         Fbgn0013435         Fbgn0034956         Fbgn0053461           Fbgn0037750         Fbgn0014395         Fbgn0034957         Fbgn0058470           Fbgn0037751         Fbgn0014395         Fbgn0034972         Fbgn0058470           Fbgn0038076         Fbgn0014395         Fbgn0035461         Fbgn0085245           Fbgn0038079         Fbgn0015032         Fbgn003511         Fbgn0085245           Fbgn0038079         Fbgn002379         Fbgn0035412         Fbgn0085433           Fbgn0038079         Fbgn002379         Fbgn0035412         Fbgn00250907           Fbgn003802         Fbgn0022709         Fbgn0035880         Fbgn0250907           Fbgn0039201         Fbgn0026593         Fbgn003584         Fbgn026403           Fbgn003950         Fbgn0027070         Fbgn0036131         Fbgn026403           Fbgn003950         Fbgn0027073         Fbgn0036131         Fbgn0264032           Fbgn00398	EBgp0036975	EBgp0010258	EBgp0034530	EBgn0052006
FBgn00369/8         FBgn00114/3         FBgn0034602         FBgn0052073           FBgn0037276         FBgn0011296         FBgn0034602         FBgn0052073           FBgn0037276         FBgn0011828         FBgn0034662         FBgn0052703           FBgn0037714         FBgn0011828         FBgn0034956         FBgn0053775           FBgn0037750         FBgn0014395         FBgn0034957         FBgn0053775           FBgn0037751         FBgn0014395         FBgn0034972         FBgn0055477           FBgn0037751         FBgn0014395         FBgn003506         FBgn0085296           FBgn0038079         FBgn0015519         FBgn0035114         FBgn0085298           FBgn0038070         FBgn002379         FBgn003511         FBgn0085298           FBgn0038200         FBgn002379         FBgn003511         FBgn0085298           FBgn0038201         FBgn002379         FBgn003511         FBgn00260861           FBgn0038201         FBgn002379         FBgn003594         FBgn0023904         FBgn0250907           FBgn0039501         FBgn0024732         FBgn003594         FBgn00260862         FBgn003614         FBgn0260864           FBgn0039504         FBgn0027070         FBgn003614         FBgn0260864         FBgn0260864           FBgn003986 <td< td=""><td>FD 0000075</td><td>T Dg10010230</td><td>T Dg110034550</td><td>T Dg110052000</td></td<>	FD 0000075	T Dg10010230	T Dg110034550	T Dg110052000
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FBgn0037618         FBgn0011828         FBgn0034789         FBgn0057747           FBgn0037714         FBgn0013813         FBgn0034956         FBgn0053775           FBgn0037750         FBgn0014000         FBgn0034957         FBgn0055477           FBgn0037751         FBgn0014395         FBgn0034957         FBgn0055477           FBgn0037751         FBgn0014396         FBgn0034972         FBgn0085296           FBgn0038076         FBgn001532         FBgn003504         FBgn0085296           FBgn0038079         FBgn0015519         FBgn003511         FBgn0085298           FBgn0038290         FBgn002379         FBgn003511         FBgn008548           FBgn0038200         FBgn002379         FBgn003571         FBgn0250907           FBgn0039201         FBgn0024732         FBgn0035904         FBgn0250907           FBgn003950         FBgn0026583         FBgn003640         FBgn0250907           FBgn003950         FBgn0027070         FBgn003641         FBgn0260666           FBgn0039789         FBgn0027521         FBgn003644         FBgn0261933           FBgn003986         FBgn002755         FBgn003667         FBgn0262594           FBgn0040372         FBgn002755         FBgn003667         FBgn02626134           FBgn0039897 <td>FBgn0037276</td> <td>FBgn0011722</td> <td>FBgn0034662</td> <td>FBgn0052702</td>	FBgn0037276	FBgn0011722	FBgn0034662	FBgn0052702
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FBgn0037717         FBgn0013813         FBgn0034956         FBgn0053775           FBgn0037750         FBgn0014000         FBgn0034957         FBgn0058470           FBgn0037751         FBgn0014395         FBgn0034957         FBgn0065407           FBgn0037751         FBgn0014396         FBgn003506         FBgn0065264           FBgn0038076         FBgn0015032         FBgn0035104         FBgn0085286           FBgn0038079         FBgn0015519         FBgn0035117         FBgn0085433           FBgn0038002         FBgn0022709         FBgn0035571         FBgn0026014           FBgn0038740         FBgn0022416         FBgn0035571         FBgn0250907           FBgn0039201         FBgn0024732         FBgn0035880         FBgn0250907           FBgn0039500         FBgn0026562         FBgn0036131         FBgn0260662           FBgn0039501         FBgn0026562         FBgn0036131         FBgn0260662           FBgn0039501         FBgn0027507         FBgn0036131         FBgn02606626           FBgn0039789         FBgn002751         FBgn0036131         FBgn0261333           FBgn0039861         FBgn0027521         FBgn003657         FBgn0262033           FBgn004096         FBgn0027550         FBgn0036575         FBgn0262547           F	FBgn0037714	FBqn0013348	FBgn0034928	FBgn0053481
Figur0037750         FBgn0014000         FBgn0034957         FBgn005475           FBgn0037751         FBgn0014395         FBgn0034957         FBgn0055470           FBgn0037751         FBgn0014395         FBgn003506         FBgn0065247           FBgn0038076         FBgn0015519         FBgn003506         FBgn0085248           FBgn0038079         FBgn0015519         FBgn003511         FBgn008543           FBgn0038330         FBgn002379         FBgn0035412         FBgn0025090           FBgn0038700         FBgn0022416         FBgn003571         FBgn0250904           FBgn0039201         FBgn0024732         FBgn003580         FBgn0250907           FBgn003901         FBgn0024732         FBgn0035904         FBgn0250907           FBgn003901         FBgn0026593         FBgn0036040         FBgn0260643           FBgn003950         FBgn0027070         FBgn0036131         FBgn0261341           FBgn0039789         FBgn0027750         FBgn0036644         FBgn0261343           FBgn003986         FBgn0027550         FBgn0036677         FBgn0262634           FBgn0040372         FBgn002750         FBgn0036677         FBgn0262634           FBgn0040372         FBgn002750         FBgn0036677         FBgn02626134           FBgn004037	EBan0037717	EBan0013813	EBan0034956	EBan0053775
Fighn003753         Fighn003751         Fighn003751         Fighn003751           Fighn003751         Fighn0014395         Fighn0034972         Fighn0065110           Fighn003751         Fighn0014395         Fighn003526         Fighn0085245           Fighn0038076         Fighn0015519         Fighn0035112         Fighn0085483           Fighn003800         Fighn002379         Fighn0035412         Fighn0025081           Fighn003800         Fighn0023495         Fighn0035412         Fighn0250907           Fighn0039201         Fighn0024495         Fighn003594         Fighn0250907           Fighn0039500         Fighn0026562         Fighn003594         Fighn0260907           Fighn0039501         Fighn0027070         Fighn003618         Fighn026083           Fighn0039789         Fighn0027070         Fighn0036208         Fighn0261341           Fighn0039866         Fighn0027521         Fighn0036637         Fighn0261561           Fighn0039897         Fighn0027550         Fighn0036637         Fighn0262033           Fighn004091         Fighn0027550         Fighn0036637         Fighn0262033           Fighn004092         Fighn002752         Fighn0264134         Fighn0264134           Fighn004093         Fighn0026752         Fighn0264134         Fighn	EBap0037750	EBap0014000	EBap0034957	EBan0058470
FBgn0037/51         FBgn0014395         FBgn00347/2         FBgn0065104           FBgn0037/51         FBgn0014396         FBgn0035066         FBgn0065245           FBgn0038076         FBgn0015032         FBgn0035104         FBgn0085246           FBgn0038077         FBgn0023791         FBgn0035112         FBgn0085246           FBgn003800         FBgn002379         FBgn0035412         FBgn008704           FBgn003800         FBgn002379         FBgn0035414         FBgn0025081           FBgn0038740         FBgn002416         FBgn003584         FBgn0250907           FBgn0039201         FBgn0024722         FBgn003594         FBgn0250907           FBgn003950         FBgn0026562         FBgn003594         FBgn0260565           FBgn0039561         FBgn0026553         FBgn003613         FBgn0260565           FBgn0039789         FBgn0027507         FBgn003618         FBgn0261533           FBgn0039789         FBgn0027550         FBgn003657         FBgn0262035           FBgn004091         FBgn0027551         FBgn003657         FBgn0262052           FBgn004092         FBgn0027550         FBgn003657         FBgn0262035           FBgn004123         FBgn0027551         FBgn003657         FBgn0262052           FBgn004172	FB910037750	FBy10014000	FBy110034957	FB910036470
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Fegn0041234         FBgn0029986         FBgn0036722         FBgn00265137           FBgn0041723         FBgn0029986         FBgn0036762         FBgn0265137           FBgn0041723         FBgn0029986         FBgn0036765         FBgn02655417           FBgn005102         FBgn0030244         FBgn0036910         FBgn02655647           FBgn005102         FBgn0030308         FBgn0037028         FBgn0265564           FBgn0051202         FBgn0030590         FBgn0037028         FBgn0265564           FBgn0051201         FBgn0030590         FBgn0037028         FBgn0265564           FBgn0051279         FBgn0030590         FBgn0037222         FBgn0265564           FBgn0051279         FBgn0030591         FBgn0037304         FBgn0037304           FBgn0052036         FBgn0030748         FBgn0037375         FBgn003527           FBgn0053027         FBgn003104         FBgn0037363         FBgn003368           FBgn0053257         FBgn0031144         FBgn0037653         FBgn003144           FBgn0031255         FBgn0037807         FBgn008544         FBgn0031548           FBgn0085421         FBgn0031548         FBgn0037934         FBgn0031548           FBgn0085421         FBgn0031548         FBgn0037973         FBgn0085421         FBgn003154	T Dg110040372	T Dgri0029710	FD	T Dy10204034
FBgn0041723         FBgn0029986         FBgn0036765         FBgn0265137           FBgn0050502         FBgn0030288         FBgn0036890         FBgn0265176           FBgn0050502         FBgn0030028         FBgn0036891         FBgn02655767           FBgn0051161         FBgn0030244         FBgn0037028         FBgn0266534           FBgn0051202         FBgn0030500         FBgn0037028         FBgn0266566           FBgn0051279         FBgn0030503         FBgn0037222         FBgn0265666           FBgn0051706         FBgn0030653         FBgn0037222         FBgn0285896           FBgn0051706         FBgn0030659         FBgn0037304         FBgn0035225         FBgn00285205           FBgn0053059         FBgn003104         FBgn0037563         FBgn0035563         FBgn0035563         FBgn0035563           FBgn0053519         FBgn0031148         FBgn0037659         FBgn003156         FBgn003156           FBgn008546         FBgn0031144         FBgn0037867         FBgn0085421         FBgn003155           FBgn0085421         FBgn0031548         FBgn003793         FBgn0085421         FBgn003154           FBgn0085421         FBgn0031548         FBgn003793         FBgn0085421         FBgn003154           FBgn0085421         FBgn0031715         FBgn0037973 <td>FBgn0041234</td> <td>FBgn0029856</td> <td>FBgn0036752</td> <td>FBgn0265048</td>	FBgn0041234	FBgn0029856	FBgn0036752	FBgn0265048
FBgn0042133         FBgn0029987         FBgn0036890         FBgn0265417           FBgn0050502         FBgn0030028         FBgn0036891         FBgn02656417           FBgn0051161         FBgn0030244         FBgn0036991         FBgn0265653           FBgn0051202         FBgn0030530         FBgn0037028         FBgn02657402           FBgn0051202         FBgn0030530         FBgn0037028         FBgn02657402           FBgn0051207         FBgn0030653         FBgn0037222         FBgn0267408           FBgn0051706         FBgn00300653         FBgn0037225         FBgn0287205           FBgn0052036         FBgn0030748         FBgn0037375         FBgn0037375           FBgn0053099         FBgn0031044         FBgn0037375         FBgn0033745           FBgn0053519         FBgn0031187         FBgn0037659         FBgn003155           FBgn0061356         FBgn0031143         FBgn0037807         FBgn008384           FBgn008384         FBgn0031343         FBgn0037934         FBgn008384           FBgn0083143         FBgn003155         FBgn0037973         FBgn0085431           FBgn0085431         FBgn0031745         FBgn0037974         FBgn0085434           FBgn0085434         FBgn0031745         FBgn0037974         FBgn00250816 <t< td=""><td>FBgn0041723</td><td>FBgn0029986</td><td>FBgn0036765</td><td>FBgn0265137</td></t<>	FBgn0041723	FBgn0029986	FBgn0036765	FBgn0265137
FBgn0050502         FBgn0030028         FBgn0036891         FBgn0265767           FBgn0051101         FBgn0030244         FBgn0036910         FBgn0265563           FBgn0051202         FBgn0030310         FBgn0037028         FBgn02655636           FBgn0051201         FBgn0030500         FBgn0037060         FBgn02655636           FBgn0051279         FBgn0030503         FBgn0037222         FBgn0285896           FBgn0051706         FBgn003748         FBgn0037304         FBgn0037304           FBgn0052036         FBgn003104         FBgn0037375         FBgn0032577         FBgn003104         FBgn0037375           FBgn0053257         FBgn00310104         FBgn0037653         FBgn003563         FBgn0037653         FBgn003563           FBgn0053519         FBgn0031157         FBgn0037807         FBgn0037807         FBgn003800         FBgn0037807           FBgn0063364         FBgn0031155         FBgn0037915         FBgn0037915         FBgn0037914         FBgn0031515         FBgn0037934         FBgn003544         FBgn0031548         FBgn0037973         FBgn0085431         FBgn0031548         FBgn0037973         FBgn0085434         FBgn0031715         FBgn0037974         FBgn0085434         FBgn0031715         FBgn0037975         FBgn0036607         FBgn0260866         FBgn0031775	FBgn0042133	FBgn0029987	FBgn0036890	FBgn0265417
FBgn0051161         FBgn0030244         FBgn0036910         FBgn0266534           FBgn0051202         FBgn0030303         FBgn0037028         FBgn0266534           FBgn0051221         FBgn0030530         FBgn0037028         FBgn02667408           FBgn0051279         FBgn0030631         FBgn0037222         FBgn02667408           FBgn0051279         FBgn0030691         FBgn0037222         FBgn0267408           FBgn0051276         FBgn0030691         FBgn0037225         FBgn0287209           FBgn0052036         FBgn003104         FBgn0037304         FBgn003755           FBgn0053257         FBgn003104         FBgn0037563         FBgn0037563           FBgn0053468         FBgn0031143         FBgn0037659         FBgn0037659           FBgn0053551         FBgn0031144         FBgn0037807         FBgn0085421           FBgn0085421         FBgn0031548         FBgn003793         FBgn0085421           FBgn0085421         FBgn0031548         FBgn0037973         FBgn0085431           FBgn0085431         FBgn0031745         FBgn0037973         FBgn008666           FBgn008544         FBgn0031716         FBgn0037974         FBgn0086906           FBgn00866         FBgn0031775         FBgn0038067         FBgn0280807           FBgn	FBgn0050502	FBgn0030028	FBgn0036891	FBgn0265767
FBgn0051202         FBgn0030310         FBgn0037028         FBgn0266566           FBgn0051231         FBgn0030590         FBgn0037028         FBgn0267408           FBgn0051279         FBgn0030653         FBgn0037222         FBgn0267408           FBgn0051706         FBgn0030631         FBgn0037225         FBgn0285896           FBgn0052036         FBgn0030748         FBgn0037347         FBgn0053099           FBgn0053099         FBgn0030859         FBgn0037347         FBgn0053099           FBgn0053099         FBgn0031004         FBgn0037375         FBgn0053563           FBgn0053557         FBgn0031157         FBgn0037659         FBgn0037659           FBgn0061356         FBgn0031157         FBgn0037867         FBgn0037867           FBgn0063364         FBgn0031143         FBgn0037915         FBgn008384           FBgn008384         FBgn003155         FBgn0037934         FBgn003541           FBgn0085421         FBgn0031548         FBgn0037973         FBgn0037973           FBgn0085434         FBgn0031745         FBgn0037974         FBgn0085434           FBgn0085434         FBgn0031716         FBgn0037975         FBgn0031767           FBgn0086906         FBgn0031737         FBgn0037975         FBgn003176           FBg	FBgn0051161	FBgn0030244	FBgn0036910	FBgn0266534
Fbgn0051231         Fbgn0030500         Fbgn0037060         Fbgn0287400           Fbgn0051231         Fbgn0030590         Fbgn0287400         Fbgn0287400           Fbgn0051279         Fbgn0030653         Fbgn0037222         Fbgn0287400           Fbgn0051706         Fbgn0030691         Fbgn0037225         Fbgn0287209           Fbgn0052036         Fbgn0030748         Fbgn0037375         Fbgn0287209           Fbgn0052039         Fbgn003104         Fbgn0037375         Fbgn0037375           Fbgn0053257         Fbgn0031010         Fbgn0037375         Fbgn003559           Fbgn0053519         Fbgn0031157         Fbgn0037659         Fbgn008366           Fbgn0061356         Fbgn0031144         Fbgn0037907         Fbgn008384           Fbgn008384         Fbgn0031343         Fbgn0037915         Fbgn008384           Fbgn008584         Fbgn0031515         Fbgn0037934         Fbgn0085431           Fbgn0085431         Fbgn0031548         Fbgn0037973         Fbgn0085434           Fbgn0085434         Fbgn0031745         Fbgn0037974         Fbgn0085067           Fbgn0085086         Fbgn0031776         Fbgn0037975         Fbgn0036017           Fbgn0086906         Fbgn0031737         Fbgn00308017         Fbgn0036067	EBan0051202	EBan0030310	EBan0037028	EBan0266566
Fbgn0051237         Fbgn0030530         Fbgn0037202         Fbgn0237202           FBgn005179         FBgn0030653         FBgn0037222         FBgn023653           FBgn0051706         FBgn0030653         FBgn0037222         FBgn0237202           FBgn0052036         FBgn0030748         FBgn0037304           FBgn0053059         FBgn003784         FBgn0037347           FBgn0053257         FBgn0031004         FBgn0037563           FBgn0053468         FBgn0031018         FBgn0037563           FBgn0053468         FBgn0031187         FBgn0037659           FBgn0053456         FBgn0031184         FBgn0037807           FBgn0085484         FBgn003155         FBgn0037807           FBgn0085421         FBgn003155         FBgn0037934           FBgn0085421         FBgn0031548         FBgn0037973           FBgn0085421         FBgn0031745         FBgn0037974           FBgn0086424         FBgn0031746         FBgn0037975           FBgn0086906         FBgn0031745         FBgn0037974           FBgn0086906         FBgn0031746         FBgn0037974           FBgn0086906         FBgn0031776         FBgn0038067	EBgp00E1221	EBan0020500	EBgp0027060	EBgn0267409
Fogmous12/9         Fogmous12/9         Fogmous12/9         Fogmous12/9         Fbgmous12/9         Fbgmous12/22	EBap0054070	EBan0000050	EBap0007000	EPar000505
Fegnous1/06         Fegno030621         FBgn0037225         FBgn0237225           FBgn0052036         FBgn0030748         FBgn003704         FBgn003704           FBgn0053099         FBgn0030859         FBgn0037375           FBgn0053257         FBgn003104         FBgn0037375           FBgn0053468         FBgn0031187         FBgn0037659           FBgn0061356         FBgn0031187         FBgn0037807           FBgn0063569         FBgn0031255         FBgn0037807           FBgn008384         FBgn0031143         FBgn0037915           FBgn008584         FBgn0031515         FBgn0037934           FBgn008584         FBgn0031548         FBgn0037973           FBgn0085431         FBgn0031548         FBgn0037974           FBgn0085434         FBgn0031715         FBgn0037975           FBgn0086906         FBgn0031737         FBgn003797           FBgn0086907         FBgn0031776         FBgn0037974           FBgn0086906         FBgn0031775         FBgn0037975           FBgn0086906         FBgn0031776         FBgn0037975           FBgn00250816         FBgn003176         FBgn0038017           FBgn00250869         FBgn0031786         FBgn0038067	1 Dy100512/9	- Dy10030053	- Dy110037222	-bynu285896
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FBgn0053099         FBgn0030859         FBgn0037347           FBgn0053257         FBgn0031004         FBgn0037375           FBgn0053468         FBgn0031108         FBgn0037563           FBgn0053519         FBgn0031157         FBgn0037659           FBgn0063056         FBgn0031184         FBgn0037607           FBgn008500         FBgn0031255         FBgn0037835           FBgn0085421         FBgn0031515         FBgn0037934           FBgn0085431         FBgn0031548         FBgn0037973           FBgn0085434         FBgn0031548         FBgn0037974           FBgn0086406         FBgn0031715         FBgn0037975           FBgn0085086         FBgn0031737         FBgn0037975           FBgn0208690         FBgn0031737         FBgn0036017           FBgn0250816         FBgn0031789         FBgn0038017           FBgn0250869         FBgn0031869         FBgn0038017	FBgn0052036	FBgn0030748	FBgn0037304	
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FBgn0053468         FBgn0031018         FBgn0037563           FBgn0053519         FBgn0031157         FBgn0037659           FBgn0061356         FBgn0031255         FBgn0037807           FBgn0083960         FBgn0031255         FBgn0037815           FBgn0085384         FBgn0031343         FBgn00379315           FBgn0085421         FBgn0031515         FBgn0037934           FBgn0085431         FBgn0031548         FBgn0037973           FBgn0086906         FBgn0031715         FBgn0037974           FBgn0086906         FBgn0031716         FBgn0037975           FBgn0086906         FBgn0031737         FBgn0037975           FBgn0086906         FBgn0031737         FBgn0037975           FBgn0208690         FBgn0031737         FBgn0030177           FBgn0208690         FBgn0031789         FBgn00308067	FBgn0053257	FBgn0031004	FBgn0037375	
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Egno03139         FBgn003139         FBgn0037639           FBgn0061356         FBgn0031184         FBgn0037805           FBgn008580         FBgn0031255         FBgn0037835           FBgn008584         FBgn0031515         FBgn0037934           FBgn0085421         FBgn0031548         FBgn0037973           FBgn0085431         FBgn0031548         FBgn0037974           FBgn00868906         FBgn0031715         FBgn0037975           FBgn0086906         FBgn0031767         FBgn0037975           FBgn0208164         FBgn0031767         FBgn0036017           FBgn0250816         FBgn0031869         FBgn003167	EBap0052510	EBan0031157	EBap0037650	
Hsgnubilitis         FBgn0037807           FBgn0083960         FBgn0031255         FBgn0037807           FBgn008584         FBgn0031255         FBgn0037815           FBgn0085421         FBgn0031515         FBgn0037934           FBgn0085431         FBgn0031548         FBgn0037934           FBgn0085434         FBgn0031548         FBgn0037973           FBgn0086434         FBgn0031755         FBgn0037974           FBgn00866906         FBgn0031716         FBgn0037975           FBgn0208690         FBgn0031776         FBgn0037975           FBgn0208690         FBgn0031737         FBgn0030177           FBgn0208690         FBgn0031869         FBgn0030177	FB910053519	FB910031157	FB910037659	
FBgn0083960         FBgn0031255         FBgn0037835           FBgn0085384         FBgn0031343         FBgn0037915           FBgn0085421         FBgn0031515         FBgn0037934           FBgn0085431         FBgn0031515         FBgn0037934           FBgn0085431         FBgn0031715         FBgn0037973           FBgn0085434         FBgn0031715         FBgn0037974           FBgn00866906         FBgn0031716         FBgn0037975           FBgn0260816         FBgn0031737         FBgn0038017           FBgn0250869         FBgn0031869         FBgn0038067	⊢Bgn0061356	⊢Bgn0031184	⊢Bgn0037807	
FBgn0085384         FBgn0031343         FBgn0037915           FBgn0085421         FBgn0031515         FBgn0037934           FBgn0085431         FBgn0031548         FBgn0037973           FBgn0085434         FBgn0031715         FBgn0037973           FBgn0085430         FBgn0031716         FBgn0037975           FBgn0086906         FBgn0031767         FBgn00308017           FBgn0250816         FBgn0031869         FBgn0038017           FBgn0250869         FBgn0031869         FBgn0036067	FBgn0083960	FBgn0031255	FBgn0037835	
FBgn0085421         FBgn0031515         FBgn0037934           FBgn0085431         FBgn0031548         FBgn0037973           FBgn0085434         FBgn003175         FBgn0037974           FBgn0086906         FBgn0031716         FBgn0037975           FBgn0250816         FBgn0031737         FBgn00308017           FBgn0260869         FBgn0031869         FBgn003067	FBgn0085384	FBgn0031343	FBgn0037915	
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Egn0005434         FBgn0031715         FBgn0037974           FBgn0086906         FBgn0031716         FBgn0037975           FBgn0250816         FBgn0031737         FBgn0038017           FBgn0250869         FBgn0031869         FBgn0038067	FBan0085431	FBan0031548	FBan0037973	
Egnov304v3         Ebgno031716         Ebgn0037976           FBgn086906         FBgn0031716         FBgn0037975           FBgn0250816         FBgn0031737         FBgn0038017           FBgn0250869         FBgn0031869         FBgn0038067	EBan0005404	EBan0021715	EBap0027074	
Fbgnu032908         Fbgnu031/16         Fbgn0037975           FBgn0250816         FBgn0031737         FBgn0038017           FBgn0250869         FBgn0031869         FBgn0038067	1 Dy10085434	EDer0001715	- by1003/9/4	
FBgn0250816         FBgn0031737         FBgn0038017           FBgn0250869         FBgn0031869         FBgn0038067	-Bgnu086906	⊢вgn∪031/16	-вgnu03/975	
FBgn0250869 FBgn0031869 FBgn0038067	FBgn0250816	FBgn0031737	FBgn0038017	
		EBap0031860	FBan0038067	

# Appendix Table S3. Genes downregulated in Lint-O KD

EBan0000116	EBan0011726	FBan0026666	EBan0031651	EBan0034447	EBan0036686	FBan0039419	EBgn0261380	FBan0030983
EBgn0000181	EBgn0011737	FBgn0027055	EBgn0031660	FBgn0034451	EBgn0036702	FBgn0039488	FBgn0261535	FBgn0031227
FBy10000181	FB910011737	FB910027055	FBg110031000	FB9110034451	FB910030702	FB9110039466	FByII0201555	FB910031227
FBgn0000250	FBgn0011762	FBgn0027057	FBgn0031673	FBgn0034494	FBgn0036734	FBgn0039602	FBgn0261560	FBgn0031805
FBgn0000253	FBgn0013269	FBgn0027079	FBgn0031710	FBgn0034528	FBgn0036754	FBgn0039626	FBgn0261565	FBgn0031857
EBan0000261	EBan0013432	EBan0027081	EBan0031736	EBon0034534	EBan0036805	FBan0039636	EBan0261596	EBan0031888
FD	FD	FD0007000	FD0001000	FD 000 1570	FD	FD 0000054	FD0001500	ED
FB910000326	FBg10014020	FBg110027082	FB910031832	Fbgn0034579	Fbgn0036828	FBg110039654	FB910261599	FB910033592
FBgn0000370	FBgn0014028	FBgn0027086	FBgn0031851	FBgn0034617	FBgn0036838	FBgn0039735	FBgn0261822	FBgn0033725
FBgn0000395	FBgn0014163	FBgn0027088	FBgn0031881	FBgn0034631	FBgn0036886	FBgn0039740	FBgn0261931	FBgn0035158
EBgn0000412	EBan0014366	- FBan0027090	EBgn0031902	EBan0034703	EBan0036892	EBan0039765	EBgn0261933	EBan0035189
FD	FD: 00114000	FD0007001	FB. 0001002	FD:::0004700	FD0000002	FD	FD:::0001001	FD
FBgn0000426	FBgn0014411	FBgn0027091	FBgn0031992	FBgn0034724	FBgn0036916	FBgn0039828	FBgn0261984	FBgn0035281
FBgn0000560	FBgn0014877	FBgn0027094	FBgn0032016	FBgn0034741	FBgn0036973	FBgn0039868	FBgn0262081	FBgn0035727
FBqn0000579	FBqn0015000	FBqn0027330	FBgn0032034	FBgn0034792	FBgn0037011	FBqn0039909	FBqn0262169	FBqn0036597
EBap0001092	EBap0015024	EBap0027554	EBan0032050	EBap0034802	EBap0037012	EBan0030020	EBan0262527	EBan0037672
F Dg11000 1032	T Dg10013024	T Dg110027334	T Dg110032030	T Dg110034002	T Dg110037012	T Dg110033323	T Dg110202327	T Dg110037072
FBgn0001139	FBgn0015218	FBgn0027556	FBgn0032051	FBgn0034858	FBgn0037019	FBgn0039993	FBgn0262601	FBgn0037941
FBgn0001149	FBgn0015221	FBgn0027587	FBgn0032101	FBgn0034877	FBgn0037051	FBgn0040064	FBgn0262732	FBgn0040256
FBan0001168	FBan0015222	FBan0027599	FBan0032138	FBan0034914	FBan0037073	FBan0040066	FBan0262734	FBan0040259
EBgp0001186	EBap0015220	EBap0027610	EBap0032108	EBap0034015	EBap0037081	EBap0040075	EBap0262736	EBap0040600
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FBgn0001202	FBgn0015245	FBgn0027785	FBgn0032217	FBgn0034918	FBgn0037102	FBgn0040271	FBgn0262954	FBgn0041087
FBgn0001215	FBgn0015268	FBgn0027836	FBgn0032222	FBgn0034925	FBgn0037137	FBgn0040309	FBgn0263133	FBgn0042173
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ED==0001000	FD==0015507	ED==00000001	ED==00000000	ED0005000	ED==0007000	ED==0040000	ED==00000000	ED==0054547
FB910001220	FB910015527	FBgr10028331	FB910032236	FB910035020	Fbgn0037293	FBg110040389	FB910263396	FB910051547
FBgn0001247	FBgn0015754	FBgn0028341	FBgn0032248	FBgn0035027	FBgn0037382	FBgn0040394	FBgn0263510	FBgn0063491
FBgn0001258	FBgn0015765	FBgn0028429	FBgn0032258	FBgn0035039	FBgn0037391	FBgn0040529	FBgn0263594	FBgn0259243
EBgn0001301	EBan0015776	EBan0028473	EBan0032261	EBan0035063	EBgn0037487	FBan0040985	EBan0263605	EBan0263118
FD	FD:::0015770	FD	FD. 00002201	FD. 0005005	FD	FD:::0044447	FD. 0000740	T Dg10200110
-вgnuu01316	FBgn0015778	⊢Bgn0028504	⊢Bgn0032296	FBgn0035085	FBgn0037489	FB900041147	FBgnu263740	⊢Bgn0264907
FBgn0001341	FBgn0015790	FBgn0028527	FBgn0032321	FBgn0035121	FBgn0037543	FBgn0041184	FBgn0263773	
FBgn0001961	FBgn0015795	FBgn0028690	FBgn0032346	FBgn0035131	FBgn0037555	FBgn0041210	FBgn0263929	
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1 Dyn0002031	1 Dy10013/9/	1 Dy10020/44	1 Dy110032397	1 Dy110035137	1 Dy11003/301	1 Dy110041004	1 Dy10204000	
FBgn0002413	FBgn0015829	FBgn0028836	FBgn0032408	FBgn0035165	FBgn0037608	FBgn0041629	FBgn0264294	
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FBgn0003206	FBgh0016694	FBgn0029117	FBgn0032512	FBgn0035213	FBgn0037710	FBgn0044323	FBgn0265574	
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T Dg110003274	T Dg110013024	T Dg110023072	T Dg110032307	T Dynoossoo	T Dg110037734	T Dg110050000	T Dg110200301	
FBgn0003275	FBgn0020238	FBgn0029689	FBgn0032620	FBgn0035337	FBgn0037852	FBgn0050035	FBgn0266668	
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EBan0003360	EBgn0020414	EBan0029785	EBan0032731	EBan0035383	EBan0037958	EBan0050349	EBan0266720	
T Dynood3300	T Dg110020414	T Dg110023703	T Dg110032731	T Dynoossoos	T Dg110037330	T Dg110050549	T Dg110200720	
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FBgn0003512	FBgn0020443	FBgn0029887	FBgn0032849	FBgn0035422	FBgn0038057	FBgn0050493	FBgn0267385	
FBqn0003525	FBan0020445	FBan0029894	FBan0032859	FBqn0035425	FBqn0038146	FBan0051111	FBan0267975	
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FBgn0003714	FBgn0021768	FBgn0030052	FBgn0032891	FBgn0035440	FBgn0038196	FBgn0051361	FBgn0283659	
FBgn0003748	FBgn0021874	FBgn0030060	FBgn0032901	FBgn0035462	FBgn0038224	FBgn0051363	FBgn0283680	
EBan0003885	EBan0021895	EBan0030061	EBan0032919	EBgn0035488	EBan0038235	EBan0051852	EBan0283681	
FD	FD0001005	FD0000007	FD0000005	FD	FD00000274	FD0050000	FD0004040	
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FBgn0003984	FBgn0022029	FBgn0030177	FBgn0032974	FBgn0035524	FBgn0038275	FBgn0052103	FBgn0284248	
FBgn0004050	FBqn0022069	FBgn0030208	FBqn0032981	FBgn0035541	FBgn0038294	FBqn0052176	FBgn0284251	
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F Dg11000+177	T DG10022200	FD	T Dg110002000	T Dg10000000	T Dg110000000	T Dg110002207	T Dg10204200	
FBgn0004359	FBgn0022288	FBgn0030321	FBgn0033000	FBgn0035591	FBgn0038307	FBgn0052344	FBgn0285937	
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FBgn0004926	FBgn0023514	FBgn0030608	FBgn0033454	FBgn0035866	FBgn0038585	FBgn0053329	FBgn0026160	
FBqn0005278	FBgn0023519	FBgn0030672	FBgn0033483	FBgn0035877	FBgn0038593	FBgn0053542	FBgn0026319	
EBan0005e1e	EBan0022507	FBan0030697	EBan0033495	FBan0025070	EBan0039eeee	EBap0062440	EBap0028544	
- Dyn0000010	1 Dy10023027	1 Dy10030087	1 Dy110033465	1 Dy100308/8	1 Dy110030000	1 Dy10002449	1 Dy110020041	
rвgn0005648	rBgn0023542	⊢Bgn0030692	⊢Bgn0033507	⊢⊔gn0035901	r⊔gn0038678	⊢Bgn0085339	⊢Bgn0029896	
FBgn0005672	FBgn0024245	FBgn0030720	FBgn0033540	FBgn0036000	FBgn0038742	FBgn0086347	FBgn0030318	
FBgn0010038	FBgn0024321	FBgn0030752	FBgn0033544	FBgn0036018	FBgn0038746	FBgn0086443	FBgn0030870	
FBan0010172	FBan002/262	FBan0030950	FBan0033547	FBan0036035	EBan0039769	FBan0086656	FBan0032640	
- Dyn00101/3	1 Dy110024302	1 Dy10030850	i byil0033547	1 Dy110030035	1 Dy110038768	1 0910000000	1 Dy110032040	
⊢Bgn0010220	⊢Bgn0024364	⊢Bgn0030853	⊢Bgn0033548	FBgn0036038	FBgn0038787	FBgn0086711	FBgn0035023	
FBgn0010235	FBgn0024556	FBgn0030854	FBgn0033571	FBgn0036124	FBgn0038854	FBgn0086855	FBgn0035049	
FBgn0010238	FBgn0024993	FBgn0030863	FBgn0033649	FBgn0036126	FBgn0038869	FBgn0086904	FBgn0035101	
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- Dynoo 10270	1 Dg110020000	1 Dy10030094		1 Dyno030173	1 0910030090	1 Dy10000912	1 Dyn0030470	
⊢Bgn0010333	⊢Bgn0025394	FBgn0030904	⊢Bgn0033741	FBgn0036187	FBgn0038893	FBgn0250785	FBgn0036316	
FBgn0010340	FBgn0025582	FBgn0030969	FBgn0033816	FBgn0036207	FBgn0038964	FBgn0259152	FBgn0039257	
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- Dynou 10389	1 Dy110020074	1 Dy110031043	1 0910033918	1 Dy110030230	1 Dy110039004	1 Dy10239/11	1 0910039858	
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FBgn0010504	FBgn0025809	FBgn0031057	FBgn0034029	FBgn0036334	FBgn0039175	FBgn0259832	FBgn0263256	
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FBqn0010774	FBgn0026084	FBgn0031392	FBgn0034118	FBgn0036522	FBgn0039259	FBgn0260632	FBgn0003285	
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- Dgnuu10786		FB910031456	r bynu034232		F Dgn0039274	FD910260648	F Dg10004034	
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FBgn0010808	FBgn0026252	FBgn0031500	FBgn0034259	FBgn0036614	FBgn0039306	FBgn0260855	FBgn0015037	
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5020	J	5	3	J	3	5	5	
EBan0011004	EBap0000070	EBan0024507	EBaboooddaad	EBannooccod	EBannoocoro	EBabooctoro	EBannonana	
FBgn0011204	FBgn0026372	FBgn0031597	FBgn0034401	FBgn0036661	FBgn0039358	FBgn0261258	FBgn0029804	

Appendix table S Related to Figs 5-	<b>4</b> 6 and Figs EV5. Experimental genotypes used in this study.			
Fig 5B-5E				
уw	$y^{1} w^{1118}$			
Lint-O <sup>KO</sup>	$y^{1} w^{1118} Lint - O^{KO} / y^{1} w^{1118} Lint - O^{KO}$			
Fig 6A, 6B, 6D-6G	ì			
уw	$y^{1} w^{1118}, y^{1} w^{1118} / Y$			
Lint-O <sup>KO</sup>	$y^{1} w^{1118} Lint-O^{KO} / y^{1} w^{1118} Lint-O^{KO},$ $y^{1} w^{1118} Lint-O^{KO} / Y$			
L(3)mbt <sup>ts1</sup>	$w^*$ ; +; L(3)mbt <sup>ts1</sup> /L(3)mbt <sup>ts1</sup> , $w^*$ /Y; +; L(3)mbt <sup>ts1</sup> /L(3)mbt <sup>ts1</sup>			
Fig 6C				
Lint-O <sup>KO</sup> –/+	y <sup>1</sup> w <sup>1118</sup> Lint-O <sup>KO</sup> / FM7 Kruppel>GFP, FM7 Kruppel>GFP / FM7 Kruppel>GFP, FM7 Kruppel>GFP / Y			
Lint-O <sup>KO</sup> —/—	$y^{1} w^{1118} Lint-O^{KO} / y^{1} w^{1118} Lint-O^{KO},$ $y^{1} w^{1118} Lint-O^{KO} / Y$			
L(3)mbt <sup>ts1</sup> –/–	$w^*$ ; +; L(3)mbt <sup>ts1</sup> / L(3)mbt <sup>ts1</sup> , $w^*$ / Y; +; L(3)mbt <sup>ts1</sup> / L(3)mbt <sup>ts1</sup>			
Fig EV5				
уw	$y^{1} w^{1118},$ $y^{1} w^{1118} / Y$			
Lint-O <sup>KO</sup>	$y^{1} w^{1118}$ Lint-O <sup>KO</sup> / $y^{1} w^{1118}$ Lint-O <sup>KO</sup> , $y^{1} w^{1118}$ Lint-O <sup>KO</sup> / Y			
L(3)mbt <sup>ts1</sup>	$w^*$ ; +; L(3)mbt <sup>ts1</sup> /L(3)mbt <sup>ts1</sup> , w <sup>*</sup> /Y; +; L(3)mbt <sup>ts1</sup> /L(3)mbt <sup>ts1</sup>			
yw Lint-O-Venus	y <sup>1</sup> w <sup>1118</sup> Lint-O-Venus / y <sup>1</sup> w <sup>1118</sup> Lint-O-Venus			