BLIMP-1/BLMP-1 and Metastasis-Associated Protein Regulate Stress Resistant Development in *Caenorhabditis elegans*

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ABSTRACT Environmental stress triggers multilevel adaptations in animal development that depend in part on epigenetic mechanisms. In response to harsh environmental conditions and pheromone signals, *Caenorhabditis elegans* larvae become the highly stress-resistant and long-lived dauer. Despite extensive studies of dauer formation pathways that integrate specific environmental cues and appear to depend on transcriptional reprogramming, the role of epigenetic regulation in dauer development has remained unclear. Here we report that BLMP-1, the BLIMP-1 ortholog, regulates dauer formation via epigenetic pathways; in the absence of TGF-β signaling (in *daf-7* mutants), lack of *blmp-1* caused lethality. Using this phenotype, we screened 283 epigenetic factors, and identified *lin-40*, a homolog of metastasis-associate protein 1 (MTA1) as an interactor of BLMP-1. The interaction between LIN-40 and BLMP-1 is conserved because mammalian homologs for both MTA1 and BLIMP-1 could also interact. From microarray studies, we identified several downstream target genes of *blmp-1*: *npr-3*, *nhr-23*, *ptr-4*, and *sams-1*. Among them S-adenosyl methionine synthase (SAMS-1), is the key enzyme for production of SAM used in histone methylation. Indeed, *blmp-1* is necessary for controlling histone methylation level in *daf-7* mutants, suggesting BLMP-1 regulates the expression of SAMS-1, which in turn may regulate histone methylation and dauer formation. Our results reveal a new interaction between BLMP-1/BLIMP-1 and LIN-40/MTA1, as well as potential epigenetic downstream pathways, whereby these proteins cooperate to regulate stress-specific developmental adaptations.

KEYWORDS stress resistant development; BLMP-1; epigenetics; TGF-β; dauer

DURING development, epigenetic changes in gene expression are passed on to the daughter cells to dictate cell fate without changing the DNA sequence itself (Hemberger *et al.* 2009). Epigenetic regulation is critical not only for normal development but also for tumor proliferation (Jones and Baylin 2007). The PRDM (PR domain-containing genes) family regulates many epigenetic events through interactions with histone modification and nucleosome remodeling factors (Hohenauer and Moore 2012; Pinheiro *et al.* 2012). Within this family, PRDM-1/BLIMP-1 regulates differentiation of various tissues and cell types including germ cells and B cells (Turner *et al.* 1994; Bikoff *et al.* 2009; John and Garrett-Sinha 2009). PRDM-1/BLIMP-1 is a transcriptional repressor, interacting with chromatin factors, such as the SET domain protein G9a (Yu *et al.* 2000), histone deacetylase HDAC1/2 (Gyory *et al.* 2004), and demethylase LSD1 (Su *et al.* 2009). Defects in the gene function are associated with certain type of lymphoma (Mandelbaum *et al.* 2010), demonstrating its critical role in B cell development. Termination of B cell differentiation is controlled by PRDM-1/BLIMP-1 (Kallies *et al.* 2004) and an abnormal downregulation of PRDM-1/BLIMP-1 may prevent the terminal differentiation process in diffuse large B-cell lymphoma (Nie *et al.* 2010).

Recently, Horn *et al.* (2014) and Huang *et al.* (2014) reported that BLMP-1, which encodes a homolog of PRDM-1/BLIMP-1, regulates the *Caenorhabditis elegans* developmental

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process. Both groups showed that *blmp-1* is required for cell migration and the molting process via its interaction with DRE-1 (a *C. elegans* homolog of FBXO11). Their results show that BLMP-1 in *C. elegans* plays a significant role in development with several conserved features. Both BLIMP-1 of mammals and BLMP-1 of *C. elegans* interact with the conserved molecule FBXO11 or DRE-1, respectively. In addition, both BLIMP-1 and BLMP-1 regulate similar development processes in mammals and in *C. elegans*, such as germ cell migration. These results demonstrate that *C. elegans blmp-1* has a conserved function and operates through similar molecular pathways as those of mammals.

The nematode *C. elegans* undergoes specialized development to become a stress-resistant larva called a dauer to survive harsh conditions such as starvation or high temperatures (Cassada and Russell 1975). Dauers are characterized by a distinct morphology and behavior: dauers are stress resistant, can survive for many months under adverse conditions, and do not eat (Cassada and Russell 1975). These differences indicate that dauer larvae employ a specific development program that nondauers do not execute in order to maximize their fitness under stress. Dauer formation is controlled by the nuclear hormone receptor DAF-12, a vitamin D and liver-X receptor homolog that functions as a ligand-regulated switch between dauer and nondauer programs (Fielenbach and Antebi 2008; Wang *et al.* 2015). Notably, worms that have been dauers have been shown to retain persistent histone modifications that change gene expression to affect life span and brood size of the postdauer adult animals, demonstrating that going through a different form of development leaves epigenetic marks (Hall *et al.* 2010). However, the mechanisms by which BLMP-1 regulates dauer formation in an epigenetic manner have not been investigated.

Here we report a new molecular pathway where BLMP-1 interacts with a MTA1 homolog of LIN-40 to specifically regulate dauer development in the absence of TGF-β signaling. Although both BLIMP-1 and MTA1 are known to interact with the TGF-β pathway, it is unknown whether MTA1 interacts with BLIMP-1. Through the study of the dauer development process, we have discovered a new and potentially conserved pathway whereby two tumorigenic and epigenetic factors (BLIMP-1 and MTA1/LIN-40) interact to enable an animal to be resistant to stress. Furthermore, our study reveals that the stress-resistant developmental process employs a distinct molecular pathway from that of a reproductive (nonstress resistant) development process. These results are consistent with prior reports for a role of BLIMP-1 in *C. elegans* development, but further extend those findings by showing a role for BLIMP-1 in dauer formation that is DRE-1 independent through a novel epigenetic mechanism (Horn *et al.* 2014). Our study suggests that in the absence of TGF-β signal, BLMP-1 interacts specifically with LIN-40 to differentially regulate the transcription profile to execute a dauer-specific development program.

Materials and Methods

Strains and culture conditions

Worms were maintained as described previously (Sulston and Hodgkin 1988) with the following modifications: worms were routinely grown on NGM containing streptomycin plates (Avery 1993) . Worms were maintained at 20° on *Escherichia coli* strain HB101 unless indicated differently. The wild-type strain was *C. elegans* variant Bristol, N2. Mutant strains used were DR40 *daf-1(m40ts)* IV, CB1393 *daf-8(e1393ts)* I, DR77 *daf-14(m77ts)* IV, CB1372 *daf-7(e1372ts)* III, YJ99 *daf-7(m62ts)* III, CB1376 *daf-3(e1376)* X, YJ55 *blmp-1(tm548)* I, YJ56 *blmp-1 (tm548)* I; *daf-7(e1372ts)* III, YJ57 *daf-7(e1372ts)* III; *daf-3(e1376)* X, MH1951 *unc-119(ed3)* III; *Ex[lin-40*::*gfp unc-119(+)]*, YJ78 *blmp-1(tm548)* I; *uyEx74[blmp-1p*::*blmp-1 rol-6p*::*GFP]*.

Cell culture, transfection, and Western blot

HEK 293T cells were maintained in DMEM (Invitrogen) supplemented with 10% FBS. Flag/MTA1 expression plasmids were obtained from Dr. Paul Wade. His-BLIMP-1 expression plasmids were obtained from Dr. Adam Antebi. Cells were seeded at 50–70% confluence/six-well plate in DMEM media for 24 hr. Total plasmid DNA (5 μg) of Flag-MTA1 and BLIMP-1/His were cotransfected into 293T cells using FuGENE HD transfection reagent (Promega, Madison, WI; E2311). After 72 hr, cells were washed by 1× PBS (pH 7.4) and then harvested. The pellet was resuspended in lysis buffer (50 mM Tris·HCl, pH 7.4, 150 mM NaCl, 1 mM EDTA, 10% glycerol and protease inhibitor cocktail) and then the lysates were spinned down by centrifugation (10,000 × *g* for 10 min), precleared by protein G agarose beads (Millipore, 16-266) then incubated with either anti-BLIMP-1 (Abcam, Ab96479; 1:100 dilution) antibody or anti-Flag antibody (Sigma, F1804, 1:100) and mouse IgG (Cell Signaling, 5415) for 16 hr at 4°. A total of 20 μl of protein G agarose was added to each sample and incubated for 2 hr at 4°. The precipitate samples were washed and then analyzed by Western blot.

For Western blot, the following primary antibodies were used: anti-BLIMP-1 antibody (Abcam, Ab96479; 1:1,000 dilution) and anti-Flag antibody (Sigma, F1804; 1:1,000 dilution). Secondary antibody used was anti-mouse antibody conjugated with HRP (GE Healthcare, NA931V; 1: 5,000 dilution). The bands were detected using ECL Plus Kit (GE Healthcare, RPN2232).

Analysis of dauer formation

Mutants were grown at a permissive temperature (15°) until they became L4 larva (fourth larva stage). They were then transferred to and kept at a nonpermissive temperature (25°) throughout the test period. For dauer formation assays, 5–10 L4s were allowed to grow and lay eggs for ~24 hr at 25°, a nonpermissive temperature, and then removed. The scoring time points were selected for each genotype (96 hr for *daf-2* and 72 hr for *daf-7* and *daf-11*, because *daf-2* grows a lot

slower than *daf-7* or *daf-11* at 25°) so that all animals had passed L2 stages at the time of scoring. Dauers were scored based on intestinal reorganization and radial shrinkage of the body and the pharynx. Dauer morphology was observed under the DIC setting of an optical magnification of ×100. To confirm dauer formation, worms were also tested for resistance to 1% SDS (Cassada and Russell 1975).

Growth assay

Worms were prepared and synchronized by egg preparation (Lewis and Fleming 1995). After each day of L1 starvation, ~100 L1s were plated on each of three *E. coli*-seeded NGM plates to grow at 20°. Every hour from 42 hr after plating, worms were examined under a dissecting microscope at ×50 magnification to count worms that had molted into young adults (Lee *et al.* 2012).

RNA interference screen

The bacteria-mediated feeding RNA interference (RNAi) screen was performed as described (Fraser *et al.* 2000), with the following modifications. The wild-type and CB1372 strain were screened with the clones of nucleosome modification and chromatin remodeling factor genes from the Ahringer feeding library (Fraser *et al.* 2000; Kamath and Ahringer 2003). The plates containing NGM agar with 1 mM IPTG and 50 mg/ml carbenicillin were inoculated with bacterial cultures grown 16–18 hr for each targeted gene. L4 stage worms were transferred in the plates for each gene at 25°. Twenty-four hours later, adults were removed. Five days later, the number of progeny that had become dauers was counted.

Quantitative RT- PCR

Total RNA preparation: *C. elegans* (from mixed and individual stages) were grown on NGM plates at 20° or 25°, washed with M9 buffer, and resuspended in TRIzol (Invitrogen). After vortexing for 60 sec, the mixture was frozen in liquid nitrogen and thawed at room temperature. After chloroform extraction, DNA was removed using DNase I. After ethanol precipitation, the air-dried pellet was dissolved in DEPC water.

Complimentary DNA preparation: Approximately 1–2 μg of total RNA in a 20-μl reaction was used to synthesize the complimentary DNA (cDNA) (Biovision, Bio65043 synthesis kit). Quantitative RT-PCR (qPCR) was carried out in a C-1000 thermal cycler Real-Time PCR system (Bio-Rad, Hercules, CA, CFX96 optics module) and analyzed using the Ct method (Lee *et al.* 2009). The mRNA levels of *ama-1* (RNA polymerase II) and *inf-1* (Initiation factor 4A) were used for normalization as previously described (Potts *et al.* 2009). The average of at least three repeats was used for each data point. qPCR was performed using primers as described in the Supplemental Material, Table S11.

Western blot analysis and antibodies

Worms were washed from NGM plates (approximately one to two plates, 1000 worms) with M9 buffer. Worm pellets were resuspended in lysis buffer (1× PBS, pH 7.4, 10% glycerol, protease inhibitor cocktail tablet (Roche, 11836170001) and lysed by sonication (Misonix Sonicator 3000, 10 bursts at 10-sec intervals). Then Western blot analysis was performed as described (You *et al.* 2006). We used the following antibodies: anti-BLMP-1 antibody (Novus Biologicals, 42010002; 1:5000 dilution), anti-GFP (You *et al.* 2006), anti-di/trimethylhistone H3K9 (Cell Signaling, 5327; 1:1000 dilution), anti-trimethylhistone H3K4 (Cell Signaling, 9751; 1:1000 dilution), and anti-histone H3 (Cell Signaling, 9715; 1:5000 dilution) for primary antibodies. We used the following for secondary antibodies: anti-rabbit antibody conjugated with HRP (Santa Cruz Biotechnology, SC2030; 1:5000 dilution), anti-mouse antibody conjugated with HRP (GE Healthcare, NA931V; 1:5000 dilution). The bands were detected using ECL Plus Kit (GE Healthcare, RPN2232).

Photography

Dauer morphology was observed under DIC using a Zeiss Axio A2 Imager at either ×63 or ×100 magnifications. Images were acquired using Zeiss Axiovision software.

Chromatin Immunoprecipitation

The chromatin immunoprecipitation (ChIP) assays were performed as described, with minor modification (Mukhopadhyay *et al.* 2008). L1 stage worms were grown on NGM plates at 25° and then harvested 24 hr later. The worms were cross-linked by PBS containing 1% formaldehyde at room temperature for 30 min. Formaldehyde was quenched with PBS/2.5 M glycine and washed five times with PBS. The pellets were suspended in lysis buffer (50 mM HEPES·KOH, pH 7.5, 150 mM NaCl, 1 mM EDTA, 0.1% sodium deoxycholate, 1% Triton X-100, 0.1% SDS, and protease inhibitor cocktail (Roche, 11836170001) and lysed by sonication (five times at 10-sec intervals). The lysates were precleared by incubating salmon sperm DNA/protein A agarose beads (Millipore, 16-157) and incubated overnight at 4° with either anti-BLMP-1 antibody or IgG. The precipitates were washed and the cross-links were reversed by heating at 65° with proteinase K. DNA was recovered by phenol–chloroform extraction, precipitation, and then eluted. PCR were performed using primers as described in Table S11.

Co-immunoprecipitation

Worms were harvested and washed from NGM plates with M9 buffer. A total of 1 mg of worm pellets (LIN-40::GFP) was resuspended in lysis buffer (50 mM HEPES·KOH, pH 7.5, 150 mM KCl, 1 mM EGTA, 0.05% NP-40, 10% glycerol and protease inhibitor cocktail (Roche, 11836170001) and lysed by sonication (five times at 10-sec intervals). After sonication, the lysates were spinned down by centrifugation, precleared by protein G agarose beads (Millipore, 16-266), and then incubated with either anti-BLMP-1 (1:100 dilution) antibody or anti-GFP antibody (1:100 dilution) and mouse IgG (Cell Signaling, no. 5415) for 16 hr at 4°. A total of 20 μl of protein G agarose was added to each sample, and incubated

for 2 hr at 4°. The precipitate samples were washed five times with PBS plus 0.1% Tween-20 and then resolved on SDS/PAGE, transferred to nitrocellulose membrane, and analyzed by Western blot.

Microarray

RNA extraction: Total RNA was extracted and the quality evaluated using a sample processing method previously established in our laboratory (Dumur *et al.* 2004). Total RNA was extracted from *C. elegans* (after 24 hr from L1 at 25°) using the MagMAX-96 for Microarrays Total RNA Isolation Kit (Invitrogen Life Technologies, Carlsbad, CA), in an automated fashion using the magnetic particle processors MagMAXTM Express. RNA purity was judged by spectrophotometry at 260, 270, and 280 nm. RNA integrity as well as cDNA and cRNA synthesis products were assessed by running 1 μl of every sample in RNA 6000 Nano LabChips on the 2100 Bioanalyzer (Agilent Technologies).

Gene expression microarray analyses: The Affymetrix protocol utilized for our microarray analyses has been previously described (Dumur *et al.* 2004) and was used with the following modifications. Starting from 500 ng of total RNA, we performed a single-strand cDNA synthesis primed with a T7(dT24) oligonucleotide. Second-strand cDNA synthesis was performed with the *E. coli* DNA Polymerase I, and biotinylation of the cRNA was achieved by *in vitro* transcription (IVT) reaction using the GeneChip 3′ IVT Express Kit (Affymetrix, Santa Clara, CA). After a 37° incubation for 16 hr, the labeled cRNA was purified using the cRNA cleanup reagents from the GeneChip Sample Cleanup Module. As per the Affymetrix protocol, 10 μg of fragmented cRNA was hybridized on the GeneChip *C. elegans* genome array (Affymetrix) for 16 hr at 60 rpm in a 45° hybridization oven. The GeneChip *C. elegans* genome array provides comprehensive coverage of the transcribed *C. elegans* genome by analyzing the expression level of >22,500 well-characterized transcripts. The arrays were washed and stained with streptavidin phycoerythrin (SAPE) (Molecular Probes) in the Affymetrix Fluidics Workstation. Every chip was scanned at a high resolution, on the Affymetrix GeneChip Scanner 3000 7G according to the GeneChip Expression Analysis Technical Manual procedures (Affymetrix). After scanning, the raw intensities for every probe were stored in electronic files (in .DAT and .CEL formats) by the GeneChip Operating Software v1.4 (Affymetrix). Overall quality of each array was assessed by monitoring the 3′/5′ ratios for the housekeeping gene, glyceraldehyde 3-phosphate dehydrogenase (Gapdh), and the percentage of "present" genes (%P). Arrays exhibiting Gapdh 3′/5′ <3.0 and %*P* >40% were considered good-quality arrays.

Statistical analysis: For the microarray data analysis, background correction, normalization, and estimation of probe set expression summaries were performed using the log-scale robust multiarray analysis method (Irizarry *et al.* 2003). Hierarchical cluster analyses were performed with the BRB-ArrayTools v3.1.0 (Biometric Research Branch, National Cancer Institute), an Excel add-in that collates microarray data with sample annotations. In order to identify differentially expressed genes between the different classes, we performed *t*-tests for each probe set from biological replicates in each class. Statistical significance for multivariate analysis to assess probe-set-specific false discovery rates (FDRs) was performed by estimating the *q*-values, using the Bioconductor *q*-value package (Storey 2002).

Data availability

The authors state that all data necessary for confirming the conclusions presented in the article are represented fully within the article.

Results

blmp-1 is necessary for development processes

As previously reported, *blmp-1* mutations or RNAi of *blmp-1* in *C. elegans* causes gonadal migration defects and molting defect, along with a small body size (Figure S1, A–D) (Horn *et al.* 2014; Huang *et al.* 2014).

Upon examining the expression pattern of BLMP-1 during development by qPCR and Western blot analysis we noted that the messenger RNA (mRNA) and protein levels of BLMP-1 highly increased at the L2 (second larval) stage compared with other developmental stages (Figure 1, A and B). In addition, ~6.7% of animals subjected to RNAi for *blimp-1* died around L2 stage (Figure 1C), confirming the previous reports where it was suggested that *blmp-1* plays an important role at the L2 stage. Most of *blmp-1* mutants, however, are able to reach adulthood (Figure 1D), indicating that *blmp-1* is not essential for survival during reproductive development.

Horn *et al.* (2014) showed that when there is a lack of cholesterol, RNAi for *blmp-1* prevents *C. elegans* from becoming a dauer. Interestingly, however, DRE-1, the interactor of BLMP-1 for reproductive (nondauer) development, was not necessary for dauer development. This result shows that *blmp-1* could play a role in dauer development as well as reproductive (nondauer) development through distinct molecular partners that drive different cellular pathways. To investigate this further, the role of *blmp-1* in dauer development was interrogated to examine how BLMP-1 may differentially regulate two distinct development programs. When we induced dauer formation using a synthetic dauer pheromone (a mixture of ascarosides (ascr) nos. 2, 3, and 5) and by limiting the amount of food (Butcher *et al.* 2007, 2008), *blmp-1* mutants failed to become dauers under conditions where >90% of wild-type worms became dauers (Figure 2A and Figure S2A). The defective dauer formation phenotype (Daf-d) of *blmp-1* mutants was rescued by extrachromosomal copies of the *blmp-1* gene, confirming that the phenotype is caused by the mutation of *blmp-1* (Figure 2, B and C).

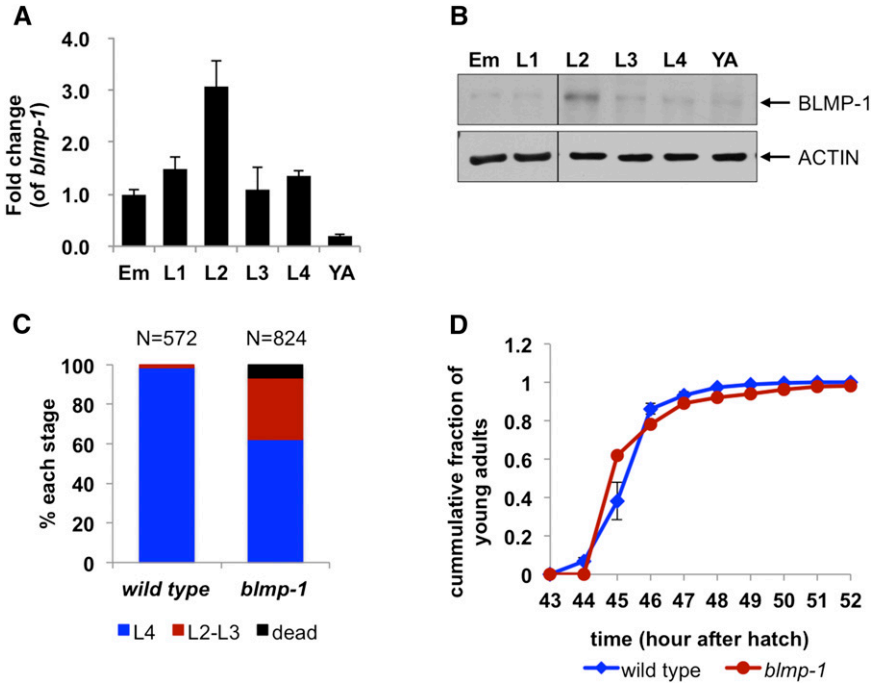

Figure 1 The levels of BLMP-1 during development and the growth rate and lethality of *blmp-1* mutants. (A and B) The levels of *blmp-1* mRNA measured by qPCR (A) and BLMP-1 protein measured by Western blot analysis (B) are highest at L2 stage compared to other stages in wild-type *C. elegans*. In A, the values are average ± SEM of three independent experiments. Em, embryos; YA, young adults. In B, actin is shown as a loading control. (C) The numbers of wild-type animals and *blmp-1* mutants in different development stages (L2, L3, L4, and dead) were counted at 48 hr from egg hatching to yield the fraction of each stage and the death rate. *blmp-1* mutants show more L2/L3 stages and dead worms compared to wild-type animals. (D) Growth rates of wild-type animals and *blmp-1* mutants. Starting at 43 hr after hatching, the numbers of adult worms were counted every hour until 100% became adults (Lee *et al.* 2012; Wang *et al.* 2015). *blmp-1* mutants showed grossly normal grow rate.

Dauer is induced mainly by the absence of one of three signals: insulin, TGF-β, and cGMP, all of which are necessary in worms to indicate a favorable environment (Riddle *et al.* 1981; Thomas *et al.* 1993). Mutants lacking any of these signals constitutively become dauers (Daf-c) regardless of food availability. When we treated three Daf-c mutants [*daf-2* (insulin receptor mutant), *daf-7* (TGF-β ligand mutant), and *daf-11* (guanylate cyclase mutant)] with *blmp-1* RNAi, none became dauers (Figure 2, D–F and Figure S2B). This confirms that *blmp-1* is essential for dauer formation. Among three *daf-7* mutants when treated with *blmp-1* RNAi showed the most consistent and strongest phenotypes; after 4 days, ~30% of *daf-7* mutants treated with *blmp-1* RNAi arrested before becoming dauers. Further, ~70% died during dauer molting (Figure 2F and Figure S2, C and D). After 9 days, there were no viable *blmp-1* RNAi-treated *daf-7* worms (Figure 4B). Therefore we focused on *daf-7* to further study the mechanisms of *blmp-1* in dauer development.

To examine whether the arrest and lethality that *blmp-1* RNAi causes in *daf-7* mutants is due to BLMP-1's role in general development in these mutant backgrounds or due to its specific role in dauer development, we performed two independent experiments. First, we treated *daf-7* and *daf-7*; *daf-3* double mutants with *blmp-1* RNAi. Both mutants have a defect in the *daf-7* gene. However, the double mutants cannot become dauers because of the missing downstream effector *daf-3* (SMAD). If the arrest and the lethality induced by RNAi of *blmp-1* in the *daf-7* mutant background is simply because of lack of *daf-7*, both mutants should show the same arrest and lethality phenotypes. If the phenotypes are specifically due to the *daf-7* role in dauer formation, however, only the *daf-7* single mutant will show the phenotypes because the double mutants do not become dauers. The double mutants grown at 25° were not arrested or dead (Figure S2E). This confirms that the arrest and the lethality phenotypes observed in the absence of *blimp-1* are due to BLMP-1's specific role in dauer development, but not due to simple absence of *daf-7* function. Second, to test whether downregulation of *blmp-1* leads to lethality during dauer formation is dauer specific, we treated *blmp-1*; *daf-7* double mutants with three different temperatures: 15°, 20°, and 25°. Most Daf-c mutants, including *daf-7*, grow to adult stage at 15° or 20° but they become dauers at a high temperature such as 25°. Under our conditions, ~5% of *daf-7* mutants became dauer at 15°, 20% at 20°, and 100% at 25°. In all three conditions, none of the *daf-7* single mutants were dead. In contrast, *blmp-1*; *daf-7* double mutants show increased lethality that is temperature dependent (Figure 2G), showing that the lethality is linked to the dauer formation process. When we measured the levels of mRNA and protein of BLMP-1, we noted that there was an increase at the L2d stage (Figure 2, H and I) in *daf-7* mutants that then decreased upon entering dauer (Figure 2, H and I). These results also support a role for *blmp-1* in dauer formation.

LIN-40 (MTA1) interacts with BLMP-1 to promote dauer formation in daf-7 mutants

To determine the molecular mechanisms by which *blmp-1* regulate dauer development in *daf-7* mutants, we performed an RNAi screen of 283 histone modification and nucleosome remodeling genes from the Ahringer library (Fraser *et al.* 2000; Kamath and Ahringer 2003). We chose to screen those genes because of the known roles of the PRDM family in epigenetic regulation in mammals (Hohenauer and Moore 2012). Sixteen genes prevented dauer formation in *daf-7* mutants when their expression was reduced by RNAi (Table S1).

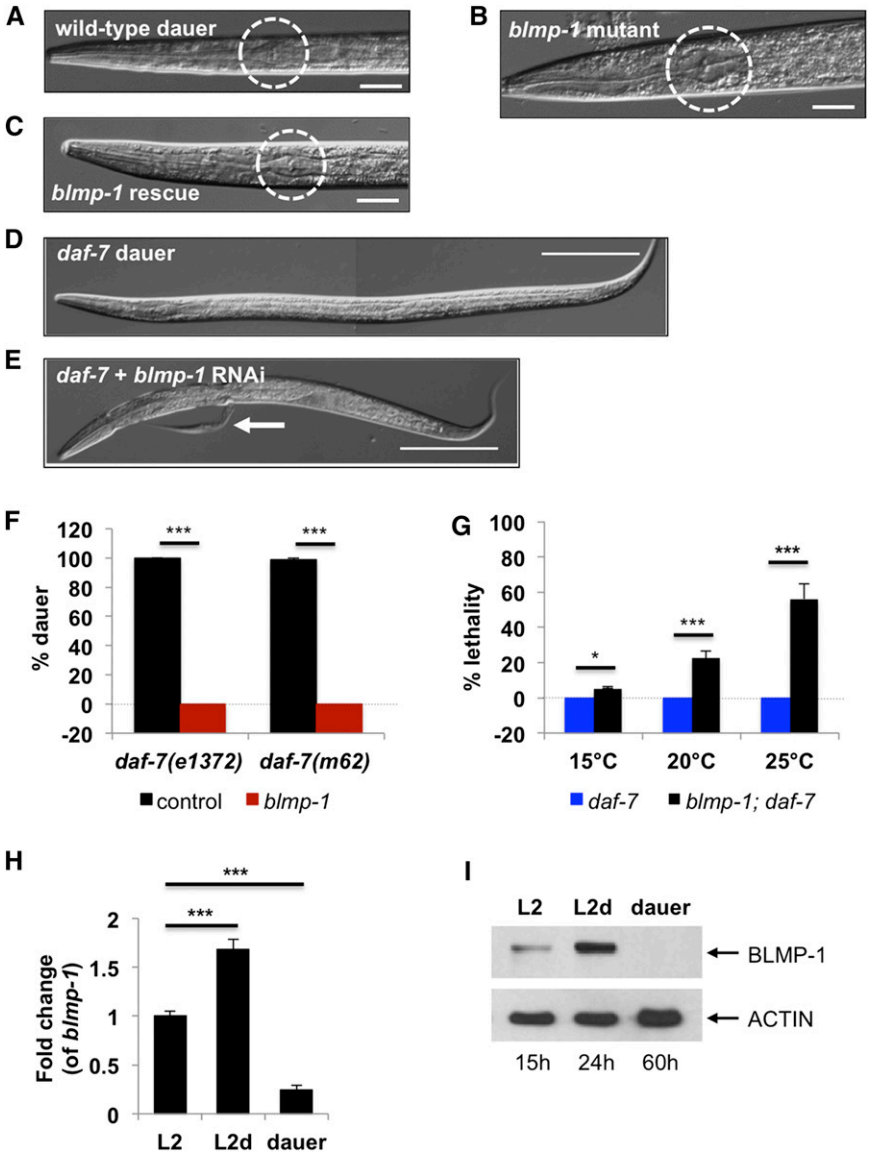

Figure 2 *blmp*-1 is essential for dauer development. (A) Representational photo of a wild-type dauer after treatment with the synthetic dauer pheromone (a mixture of ascarosides). Dotted circle shows a shrunken pharynx, an indication of a dauer. (B) A *blmp-1* mutant after treatment with the synthetic dauer pheromone. Dotted circle shows that the pharynx was not shrunken, indicating the mutant does not develop into a dauer. (C) A transgenic animal carrying a wild-type copy of the *blmp-1* gene in a *blmp-1* mutation background (*blmp-1* rescue) becomes a dauer. (D and E) A *daf-7* mutant normally becomes a dauer (D) but fails and dies after treatment with *blmp-1* RNAi (E). White arrow indicates a piece of cuticle separated from the body during dauer molt. Bar in A–C, 20 μm and in D and E, 100 μm. (F) Dauer formation of two different *daf-7* mutants was counted after growth and treatment with *blmp-1* RNAi from the mother generation at 25°. L4 worms (P_0) were treated with RNAi and the dauer formation of the progeny (F_1) was measured after 96 hr from the start of the treatment (see *Materials and Methods*). The values are from three independent experiments. The *y*-axis was lowered to start from −20 to visualize the 0% dauer. *** $P < 0.001$ by Student's *t*-test. (G) The lethality of *blmp-1*; *daf-7* mutants is temperature dependent, showing that lethality is specific for the dauer development process, whose incidence increases as temperature increases. The *y*-axis was lowered to start from −20 to visualize the 0% dauer. *** $P < 0.001$ by Student's *t*-test. (H and I) The levels of *blmp-1* mRNA (H) and BLMP-1 protein (I) increase at L2d stage compared to the preceding stage of L2 in *daf-7* mutants. In H, the values are mean ± SEM of three independent experiments. *** $P < 0.001$ by Student's *t*-test.

Among these, knockdown of 11 genes by RNAi caused lethality or larval arrest or delayed growth of reproductive (nondauer) wild-type animals (Table S2), indicating their essential roles in general development. This could suggest that knockdown of these genes prevents dauer formation in *daf-7* mutants simply because the worms were unable to reach the developmental stage to become dauers. Among the remaining 5 genes, *lin-40*, a homolog of MTA1, which is implicated in tumor metastasis downstream of TGF-β in mammals (Thiery 2002), phenocopied RNAi of *blmp-1* best (Figure 3A); >35% of the worms died during dauer molt and none of the survivors became dauers (Figure 3B).When we tested another mutant *daf-7(m62)* allele, although the percentage was reduced, *lin-40* RNAi still prevented *daf-7* mutants from becoming dauers (Figure 3B). The *m62* allele of *daf-7* shows a lot weaker dauer phenotype than the *e1372* allele and the mutants have a high frequency of spontaneous recovery from dauers unlike *e1372* allele. One possible explanation could be that BLMP-1 and LIN-40 interaction is weak in this mutant and somehow the weak commitment to dauer development could save the mutant from death in the absence of *lin-40*. Also, BLMP-1 could interact with a different partner in addition to LIN-40 and somehow the redundancy could selectively benefit the *m62* allele. Nonetheless, when we examined all Daf-c mutants downstream of TGF-β *daf-7* after treating them with *blmp-1* RNAi or *lin-40* RNAi, all reduced dauer formation, confirming that *blmp-1* and *lin-40* are required for the TGF-β pathway mutants to become dauers (Figure 3C and Figure S3). Like *daf-7* mutants, mutants of the TGF-β receptor (*daf-1*) and two downstream SMADs (*daf-8* and *daf-14*) are Daf-c. However, they too failed to become dauers when treated with RNAi for *blmp-1* or *lin-40*. Under the screening conditions, *lin-40* RNAi did not kill wild-type worms (Table S2).

Next we tested whether BLMP-1 and LIN-40 interact directly. BLMP-1 was co-immunoprecipitated (co-IP) with

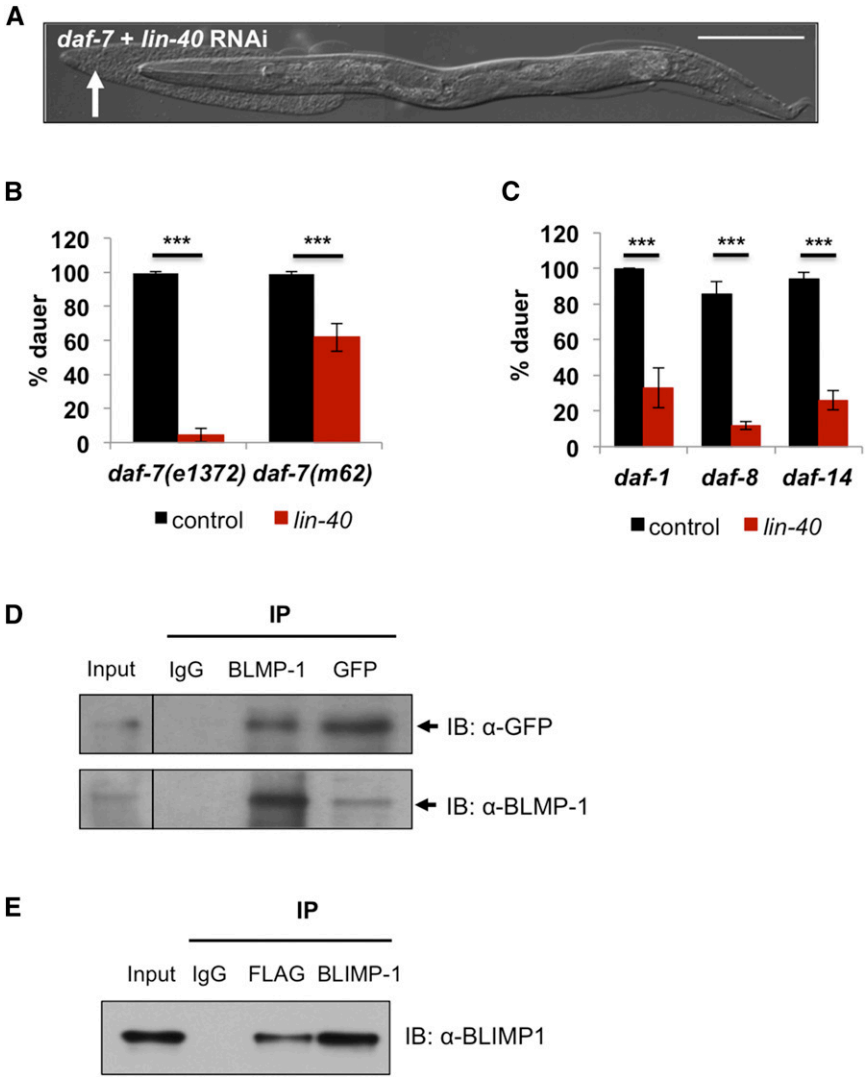

Figure 3 LIN-40 (MTA1) interacts with BLMP-1 to promote dauer formation. (A) RNAi of *lin-40* phenocopies RNAi of *blmp-1* in *daf-7* mutants. *lin-40* RNAi causes lethality during dauer molt. White arrow indicates a piece of cuticle separated from the body during dauer molt. Bar, 100 μm. (B) *lin-40* RNAi prevents dauer formation in two different *daf*-7 alleles. The values are mean ± SEM, *** $P < 0.001$ by Student's *t*-test. (C) *lin-40* is essential for dauer formation in the TGF-β pathway mutants. L4 worms (P_0) were treated with RNAi throughout the experiments and the dauer formation of the progeny (F_1) was measured. All experiments were performed at 25° (see *Materials and Methods*). The numbers are mean ± SD, *** $P < 0.001$ by Student's *t*-test. (D) BLMP-1 directly interacts with LIN-40 (see the fourth lane, GFP). A GFP antibody is used to pull down LIN-40 fused with GFP. Lane 1, input; lane 2, immunoprecipitated (IP) with rabbit IgG; lane 3, IP with α-BLMP-1 antibody; and lane 4, IP with α-GFP antibody. (E) HEK 293T cells were cotransfected with His-BLIMP-1 and Flag-MTA1. Immunoblots were developed with α-BLIMP-1 after immunoprecipitation using as a marked. Lane 1, input; lane 2, immunoprecipitated (IP) with mouse IgG; lane 3, IP with α-Flag antibody; and lane 4, IP with α-BLIMP-1 antibody.

LIN-40, confirming the interaction between BLMP-1 and LIN-40 (Figure 3D). To test if this interaction is also conserved in mammals, we coexpressed BLIMP-1/PRDM-1 and MTA1 (the mammalian homolog of BLMP-1 and LIN-40, respectively) in HEK 293T cells and performed a co-IP experiment. BLIMP-1 co-immunoprecipitated with MTA1 (Figure 3E), showing that LIN-40/MTA1 directly associates with BLIMP-1/PRDM-1 and that this interaction could be conserved in mammals.

C. elegans has two MTA1 homologs: *lin-40* and *egl-27*. However, *egl-27* RNAi did not prevent *daf-7* mutants from dauer formation (Figure S4). Because MTA1 proteins function as a part of the nucleosome remodeling and deacetylase (NuRD) complex (Xue *et al.* 1998; Zhang *et al.* 1998), we tested two of the known components of the NuRD complex in worms (Solari and Ahringer 2000; Passannante *et al.* 2010). Both wild type and *daf-7* mutants treated with the RNAi of the NuRD genes (*lin-53* and *hda-1*) became sick and arrested at L1 or L2 stages (or displayed embryonic lethality), suggesting that NuRD complex genes are essential for animals' growth. Therefore we could not conclude if the NuRD components are required specifically for dauer formation in *daf-7* mutants.

BLMP-1 regulates histone H3 trimethylation via SAMS-1

To find downstream targets of *blmp-1* in *daf-7* dauer development, we performed microarrays and compared the gene expression profiles between *daf-7* mutants and *blmp-1*; *daf-7* mutants after 24 hr from L1 when most *daf-7* mutants enter the L2d stage. L2d stage is a prior stage of a dauer, when *C. elegans* is preparing to enter dauer development. L2ds are similar to L2s in size but differ slightly in age with a 9-hr developmental delay. This delay is believed to let them prepare to become stress-resistant larvae. They show signs of entering into the dauer development process, such as dark body color (Golden and Riddle 1984). We chose this stage to collect the samples for microarray, because this stage is the latest time point we could collect live animals and also because this stage would give us the most distinguished expression profiles relevant to dauer development but not to reproductive (nondauer) development. We identified that the expression levels of 117 genes (59 up, 58 down) were

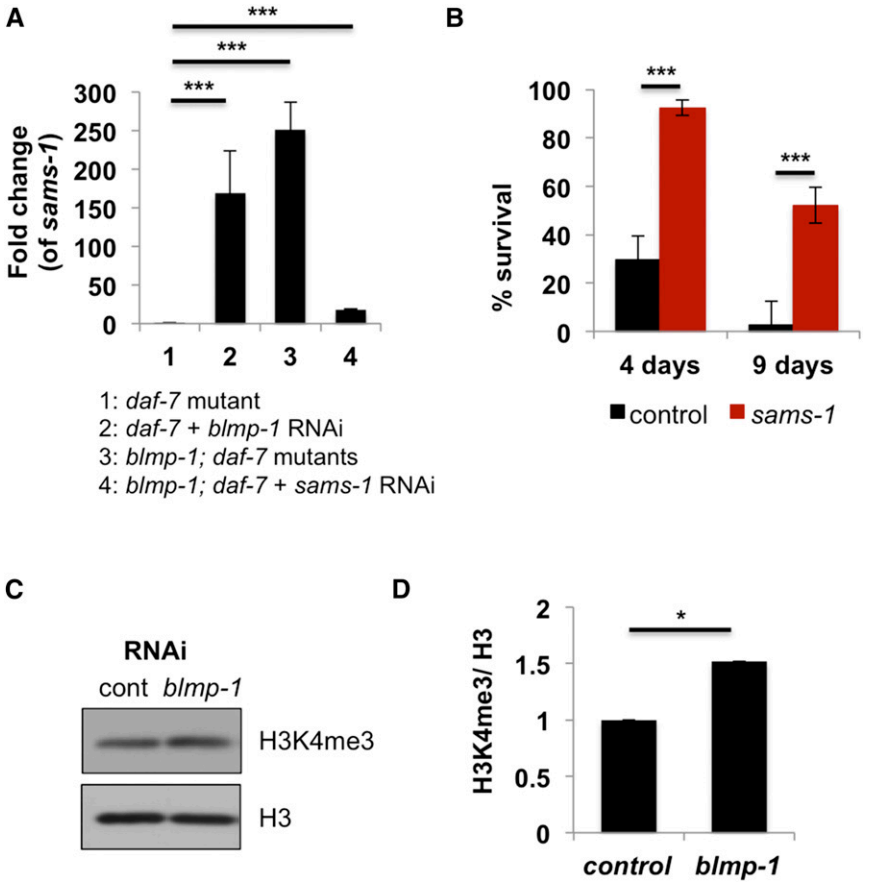

Figure 4 BLMP-1 regulates dauer development by repressing SAMS-1 expression. (A) The mRNA level of *sams-1* increases in the absence of BLMP-1 (either by RNAi, lane 2 or a mutation, lane 3) in the *daf-7* mutant background. *** $P < 0.001$ by Student's *t*-test. (B) Percentage of survival of *blmp-1*; *daf-7* mutants with each RNAi was counted on the indicated days (4d and 9d). *** $P < 0.001$ by Student's *t*-test. (C) The levels of histone trimethylation (H3K4me3) increase in knockdown of *blmp-1* in *daf-7* mutant compared to *daf-7* treated with control RNAi. (D) Quantitation of the results in C. The values are normalized by total histone H3. The values are mean ± SEM of three independent experiments. *$P < 0.05$ by Student's *t*-test.

significantly changed in the absence of *blmp-1* (Table S3, Table S4, Table S5, and Table S6) in the *daf-7* mutant background. The 117 genes included targets relevant in signaling, metabolism, development, and nuclear hormone receptor regulation.

We also performed another set of microarrays to compare *blmp-1* mutants to wild type collected at L2 stage to examine whether there are common genes that are regulated by *blmp-1* in both developmental processes (Table S7, Table S8, Table S9, and Table S10). Most of them do not overlap with those regulated during dauer development (including the seven genes we tested below), demonstrating that BLMP-1 regulates different sets of genes depending on the developmental processes.

To test if the genes identified from the microarrays regulate dauer development as BLMP-1 does, we first tested the several upregulated genes from the list by individually knocking down their expression by RNAi in the *blmp-1*; *daf-7* double mutant background. We reasoned that because knockdown of *blmp-1* in *daf-7* background causes lethality, if we remove the upregulated gene, then it would rescue the lethality. We found that *haf-6*, *pept-1* (Figure S5A), and *sams-1* RNAi rescued lethality in *blmp-1*; *daf-7*. *haf-6* encodes a half-molecule ATP-binding cassette (ABC) transporter (Sundaram *et al.* 2006) and *pept-1* encodes a low-affinity/high-capacity oligopeptide transporter whose activity is required for uptake of intact peptides from the intestine (Fei *et al.* 1998). At this point, we do not know how knockdown of these genes reduced the lethality of *blmp-1*; *daf-7* mutants. Still, these results show that our microarray results successfully identified those genetic interactions that are relevant to this pathway. The rescue of *blmp-1*; *daf-7* by knockdown of *sams-1* was most interesting to us because of the known roles of SAMS-1. SAMS-1 encodes S-adenosyl methionine synthase to produce SAM (S-adenosyl methionine), which is a methyl group donor for histone methylation and plays a significant role in tumor suppression in mammals and life span in *C. elegans*. In mammals, overexpression of S-adenosyl methionine synthase isoform type 1 (MAT1A, the SAMS-1 homolog) increased the levels of DNA methylation and histone methylation (Reytor *et al.* 2009) and suppressed tumor growth rate and tumor weight (Li *et al.* 2010). In *C. elegans*, *sams-1* is essential for lipid homoeostasis, which supports survival under harsh conditions (Li *et al.* 2011), and knockdown of *sams-1* extends lifespan (Hansen *et al.* 2005). Because both homologs of BLMP-1 and LIN-40 in mammals function with histone modification machinery, and because BLMP-1 mainly functions as a repressor, SAMS-1 could be an appropriate target of BLMP-1 in *C. elegans* dauer development.

First, we confirmed the microarray result by qPCR; in *blmp-1*; *daf-7* mutants *sams-1* expression was increased compared to *daf-7* mutant (Figure 4A). After 4 days at 25°, 26.6% of *blmp-1*; *daf-7* mutants treated with control RNAi survived, whereas 92.4% of the *blmp-1*; *daf-7* mutant treated with

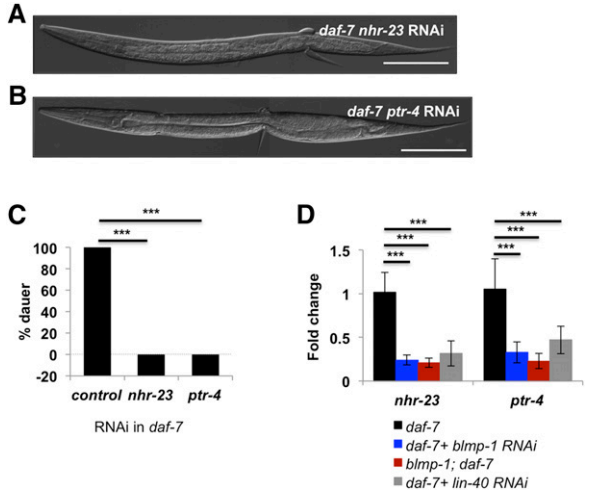

Figure 5 BLMP-1 and LIN-40 regulate the same downstream targets to regulate dauer development. (A and B) *nhr-23* RNAi (A) or *ptr-4* RNAi (B) causes lethality in *daf-7* mutants during dauer molt. Bar, 100 μm. (C) Dauer formation of *daf-7(e1372)* were counted after treatment with *nhr-23* RNAi or *ptr-4* RNAi. The *y*-axis was lowered to start from −20 to visualize the 0% dauer. *** $P < 0.001$ by Student's *t*-test. (D) The levels of mRNA of *nhr-23* and *ptr-4* decrease by RNAi of *blmp-1* or *lin-40*. *** $P < 0.001$ by Student's *t*-test.

sams-1 RNAi survived (Figure 4B). To test whether the increase of SAMS-1 leads to changes in histone methylation, we tested two different histone modifications: H3K4me3 and H3K9me2/3 methylation. Generally, H3K4me3 are associated with active transcription and H3K9me2/3 are associated with transcriptional repression. Knockdown of *blmp-1* in *daf-7* mutants indeed increased histone H3K4me3 methylation (Figure 4, C and D); however, H3K9me2/3 methylation is not changed (Figure S5, B and C). These results suggest that *blmp-1* regulates SAM expression that led to changes in histone modification and eventually to a differential development program specific for dauers.

LPR-3, NHR-23, and PTR-4 regulate dauer development acting downstream of BLMP-1

We then examined the genes that were most downregulated when *blmp-1* was absent. We reasoned that if these genes are downstream targets of *blmp-1*, knockdown of these genes in the *daf-7* mutant background will phenocopy *blmp-1*; *daf-7* lethality or inability to develop into a dauer. Among several top-hit genes, knockdown of *lpr-3* prevented *daf-7* mutants from becoming dauers (Figure S6A). *lpr-3* encodes a protein related to the lipocalin family that bind and transport lipophilic molecules. *lpr-1*, a member of the same family, is required for early larval development and normal growth rate (Stone *et al.* 2009). Despite the fact that the phenotype of *lpr-3* RNAi is similar to that of *blmp-1* RNAi in *daf-7* mutants, and that the expression level of *lpr-3* only significantly changed in dauer development (but not in reproductive nondauer development), *lpr-3* seems necessary for both nondauer and dauer development programs (Figure S6B). We speculate that it is probable that *lpr-3* is a common target

Figure 6 A model of BLMP-1 function in two distinct development processes. Under nonstressful conditions, BLMP-1 regulates reproductive growth interacting with DRE-1 (FBXO11). Under stressful conditions, however, the animals undergo transcriptional reprogramming via BLMP-1 specifically interacting with LIN-40.

for both dauer and nondauer development programs and different transcription machinery and transcription factors could regulate its expression. For instance, for the dauer development program, BLMP-1 could mediate its expression and for the nondauer development program, other factors do. Furthermore, this difference in transcriptional machinery could regulate the timing or the level of the gene expression.

Because knockdown of *blmp-1* or *lin-40* in *daf-7* mutant background causes lethality mostly during dauer molting, we next focused on molting-related genes among the list from the microarrays. We noted two such genes: *nhr-23* and *ptr-4* (Frand *et al.* 2005). *nhr-23* is a nuclear hormone receptor known to function in all four molts during development (Kostrouchova *et al.* 2001), while *ptr-4* is a distant homolog of *Drosophila* PATCHED and human PTCH (Zugasti *et al.* 2005; Burglin and Kuwabara 2006) and is required for normal molting in *C. elegans* from L4 to adult. Again, their gene expression depends on *blmp-1* only during dauer development and not in reproductive nondauer development; yet these genes regulate molting progress for both development programs (Figure S6B). Nonetheless, RNAi of *nhr-23* or *ptr-4* in *daf-7* mutants phenocopied the lethality during dauer molt in *daf-7* mutants caused by *blmp-1* RNAi (Figure 5, A–C). Moreover, ChIP assays of *daf-7* mutant showed that BLMP-1 directly binds to the promoters of *nhr-23* and *ptr-4* through a consensus sequence (Kuo and Calame 2004) and did not bind in *blmp-1*; *daf-7* mutant (Figure S7, A–C). Lastly, the mRNA levels of *nhr-23* and *ptr-4* were downregulated in *lin-40* RNAi-treated worms as well as in *blmp-1* RNAi or *blmp-1* mutants (Figure 5D). Taken together, our results show that BLMP-1 differentially regulates expression of multiple genes to regulate a specific development process through an interaction with LIN-40 in the absence of TGF-β signaling.

Discussion

Recent studies suggest that chromatin regulators are required not for steady-state transcription but for normal transcriptional reprogramming in response to environmental cues (Weiner *et al.* 2012). *C. elegans* have conserved epigenetic regulation markers and genes to mediate epigenetic modification (Gerstein *et al.* 2010; Liu *et al.* 2011; Wenzel *et al.* 2011). Histone modifiers including SET domain-containing proteins play critical roles in developmental programming as

well as reprogramming by environmental cues, including germ line differentiation and lifespan determination (Xu and Strome 2001; Yang *et al.* 2002; Bender *et al.* 2004; Agger *et al.* 2007; Andersen and Horvitz 2007; Christensen *et al.* 2007; Fisher *et al.* 2010; Greer *et al.* 2010, 2011). Yet, despite extensive studies of dauer formation pathways that integrate specific environmental cues and appear to depend on transcriptional reprogramming, the role of epigenetic regulation in dauer development has remained unclear. Here we propose that during dauer development, cells undergo transcriptional reprogramming via BLMP-1. BLMP-1 employs epigenetic processes recruiting a distinct partner such as LIN-40 in the absence of TGF-β signaling. In their recent studies, Horn *et al.* (2014) discovered that DRE-1 regulates various developmental processes in *C. elegans* interacting with BLMP-1. They showed that *blmp-1* is required for dauer formation under cholesterol-deficient conditions. We also found that BLMP-1 is necessary for dauer formation in the absence of cGMP, insulin, and TGF-β signaling, the three signals whose absence leads to dauer formation regardless of the environment. Interestingly, their data showed that DRE-1 interacts with BLMP-1 for reproductive developmental processes but not for dauer formation, suggesting that BLMP-1 could play a unique role in dauer formation employing different pathways or partners. Overall, our and their work both show that BLMP-1 plays differential roles in the developmental processes depending on the environment (Figure 6).

The TGF-β pathway plays a central role in modulating cell proliferation in mammals, and, correspondingly, mutations of the TGF-β pathway contribute to cancer development and progression. Downstream of TGF-β signaling, MTA1 function has been shown to promote tumor metastasis in mammals (Thiery 2002; Li *et al.* 2012); however, MTA1 interaction with the BLIMP-1/PRDM-1 was unknown. Intriguingly, dysregulation of BLIMP-1 or MTA1 causes the same B cell neoplasm in the form of diffuse large B cell lymphomas (DLBCL) in mammals, pointing to their genetic interaction in B cell differentiation (Pasqualucci *et al.* 2006; Tam *et al.* 2006; Bagheri-Yarmand *et al.* 2007). Our finding that BLMP-1/PRDM-1 and LIN-40/MTA1 interact in *C. elegans* suggests that BLIMP-1 and MTA1 may also function together in tumorigenesis in mammals.

We found several potential downstream targets of *blmp-1* that regulate dauer formation in *daf-7* mutants. Knockdown of *blmp-1* in *daf-7* mutants increased *sams-1* expression that leads to an increase in methylation of H3K4me3. It is possible that BLMP-1 regulates SAM levels via repressing the transcription of *sams-1*, and the low level methylation of H3K4me3 in certain genes could be critical for dauer formation. Additionally the role of *ptr-4* as a downstream target of both BLMP-1 and LIN-40 is intriguing, given that mammalian PTCH, a distant homolog of PTR-4, serves as a negative regulator for the SHH/PTC pathway as well as for TGF-β-dependent tumorigenesis (Pearse *et al.* 2001).

LIN-40/MTA1 interacts with the NuRD complex (LET-418, CHD-3, and HAD-1) (Passannante *et al.* 2010) in *C. elegans*. Our findings support the idea that BLIMP-1/PRDM-1 may be recruited to the NuRD complex via LIN-40/MTA1 whereby it then mediates transcriptional repression. Our results suggest that BLIMP-1/BLMP-1 and MTA1/LIN-40 may act in a conserved epigenetic pathway that controls larval development in worms as well as cancer development and stress in mammals.

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Author contributions: M.H., J.K., F.C.S., and Y.-J.Y. devised the experiments. C.D. performed microarray and analyzed the data. M.H. and J.K. performed all the other experiments. F.C.S. provided ascarocides. All authors contributed to writing the paper.

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BLIMP-1/BLMP-1 and Metastasis-Associated Protein Regulate Stress Resistant Development in *Caenorhabditis elegans*

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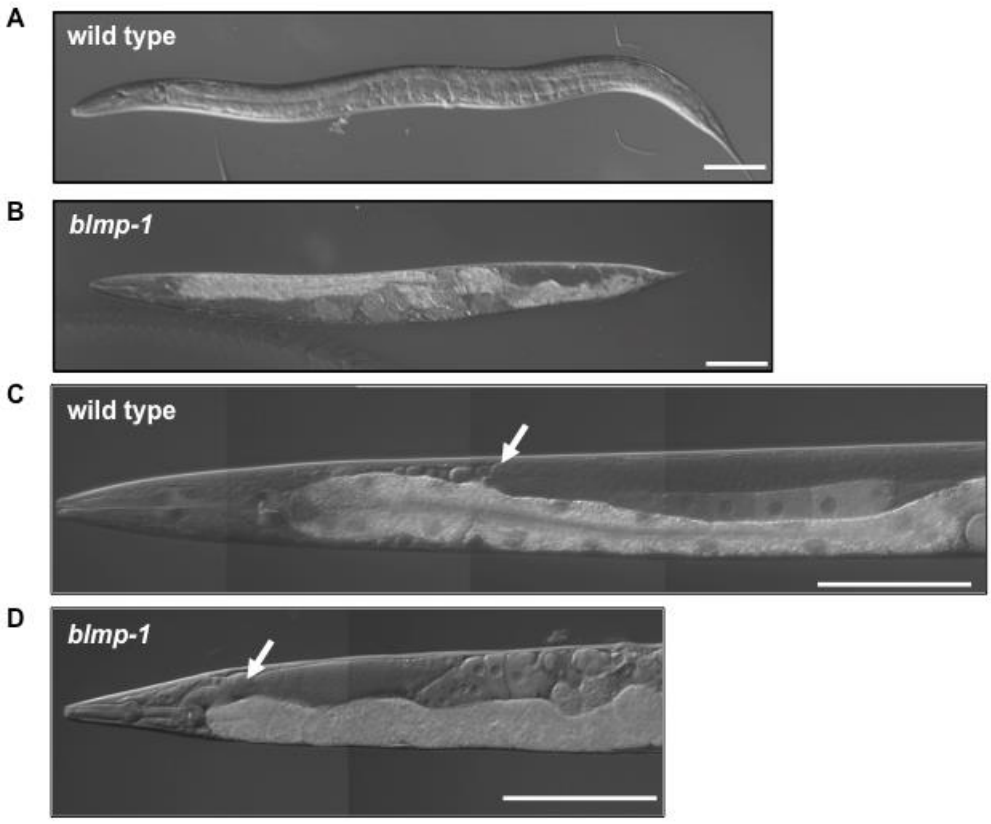
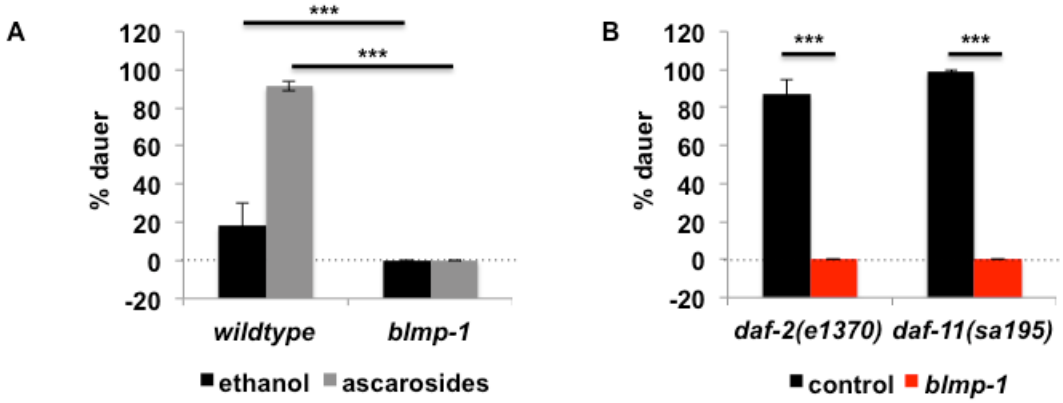
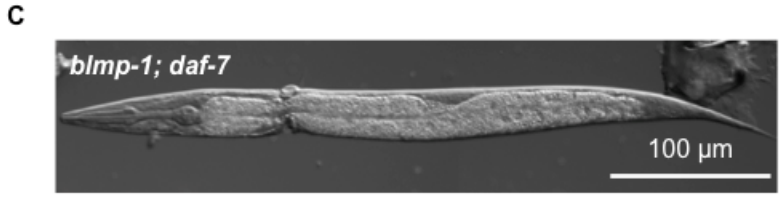


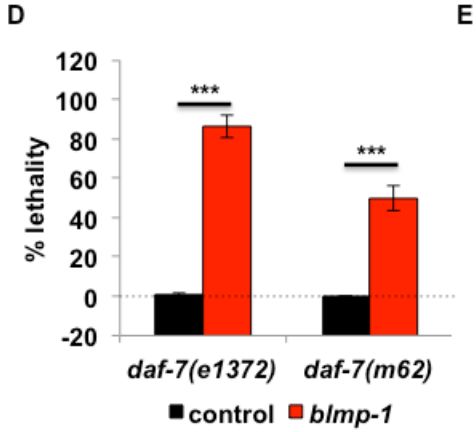
Figure S1. *blmp-1* mutants show gonad migration defect, small body size and slow growth rate.

A-B. One day-old adult of wild-type *C. elegans* (A) and a *blmp-1* mutant (B). Compared to wild type (A) *blmp-1* mutant (B) is small and dumpy.

C-D. The positions of the most proximal gonad arms (white arrow) of a 1 day-old wild-type *C. elegans* (C) and 1 day-old *blmp-1* mutant (D). The gonad migrates abnormally so that the gonad arm almost reached to the head.







E

Genotypes	Condition	Dauer (%)	N
daf-7; daf-3	Control RNAi	0	503
	blmp-1 RNAi	0	337
daf-3(e1376)	Control RNAi	0	632
	blmp-1 RNAi	0	734

Figure S2. *blmp-1* is required for dauer formation.

A. The percent of dauer was measured with or without ascarosides at 25°C after 96h of treatment. *blmp-1*mutants (*tm548*) could not become dauers. **** p<0.*001 by two-tailed paired Student's *t*-test. The numbers are mean ± S.D.

B. The percent of dauer in *daf-2* and *daf-11* mutants was measured after grew and treated them with *blmp-1* RNAi. L4 worms (P_0) were treated with the RNAi and the dauer formation of the progeny (F_1) was measured after 96 h from the start of

the treatment (see Materials and Methods). The values were from three independent experiments. *y*-axis was lowered to start from -20 to visualize the 0% dauer. Most of *daf-2* or *daf-11* mutants treated with *blmp-1* RNAi arrested at L2 or L2d stages and did not become dauers. However, unlike *daf-7* mutants, *daf-2* or *daf-11* mutants treated with *blmp-1* RNAi did not die. **** p<0.001* by two-tailed paired Student's *t*-test. The numbers are mean ± S.D.

C. *blmp-1; daf-7* shows the same lethal phenotype as the *daf-7* mutants treated with *blmp-1* RNAi at 25°C.

D. L4 worms (P_0) were treated with RNAi throughout the experiments and the lethality of the progeny (F_1) was measured after 144h. All experiments were performed at 25°C., **** p<0.001* by two-tailed paired Student's *t*-test. The numbers are mean ± S.D.

E. *blmp-1* function is required specifically for dauer development. RNAi was treated as same as above. Knockdown of *blmp-1* in *daf-3* and *daf-7;daf-3* mutants did not cause any arrest or lethality.

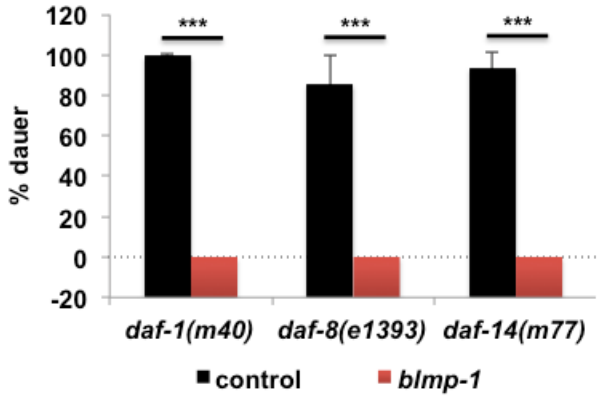


Figure S3. *blmp-1* is essential for dauer formation in TGFβ pathway mutants.

blmp-1 RNAi was treated as same as above. **** p<0.001* by two-tailed paired Student's *t*-test. The numbers are mean ± S.D.

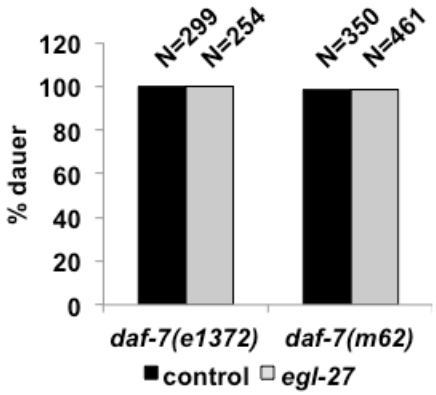


Figure S4. RNAi of *egl-27* does not affect the dauer formation of *daf-7* mutants.

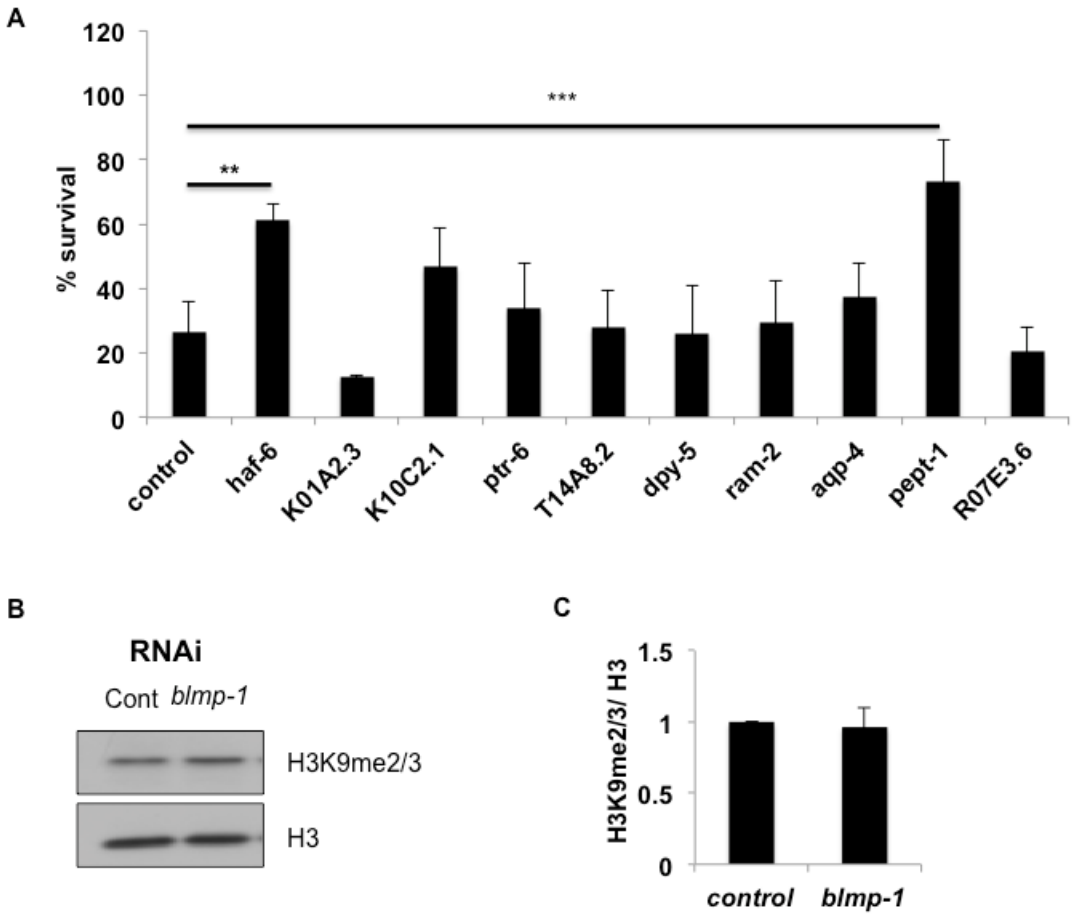


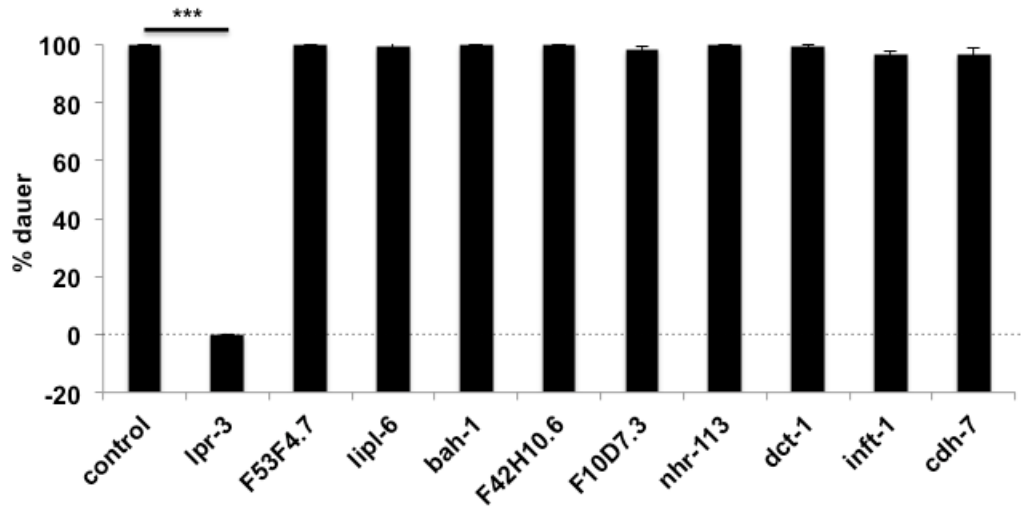
Figure S5. RNAi results of potential BLMP-1 target genes whose expression was increased in the absence of *blmp-1.*

A. Percent survival of *blmp-1; daf-7* mutants after treated with RNAi of ten upregulated genes. ** $p< 0.01$, ***$p<0.001$ by two-tailed paired Student's *t*-test. The numbers are mean ± S.D.

B. The level of histone Di or Tri-methylation (H3K9me2/3) is not changed after knockdown of *blmp-1* by RNAi compared to control RNAi in *daf-7* mutants.

C. Quantitation of the results in panel B. The values are normalized by total histone. The values are mean ± S.D from three independent experiments.

A



B

Genes	L3/L4	adult	dead	N
Control	0	110	2	112
lpr-3	157	285	70	512
nhr-23	152	62	26	240
ptr-4	15	138	56	209

Figure S6. RNAi results of potential BLMP-1 target genes whose expression was decreased in the absence of *blmp-1.*

A. Percent dauer formation of *blmp-1; daf-7* mutants after treated with RNAi of ten downregulated genes. ** $p< 0.01$, ***$p<0.001$ by two-tailed paired Student's *t*-test. The numbers are mean ± S.D. Dauer formation of RNAi downregulated gene were counted on plates at 25°C after 96 h from hatching of *daf-7*(*e1372*) mutants. *** $p<0.001$ by two-tailed paired Student's *t*-test. The numbers are mean ± S.D.

B. When their expression was knockdown by RNAi, *lpr-3*, *nhr-23* and *ptr-4* induced growth arrest or some death in wild type animals.

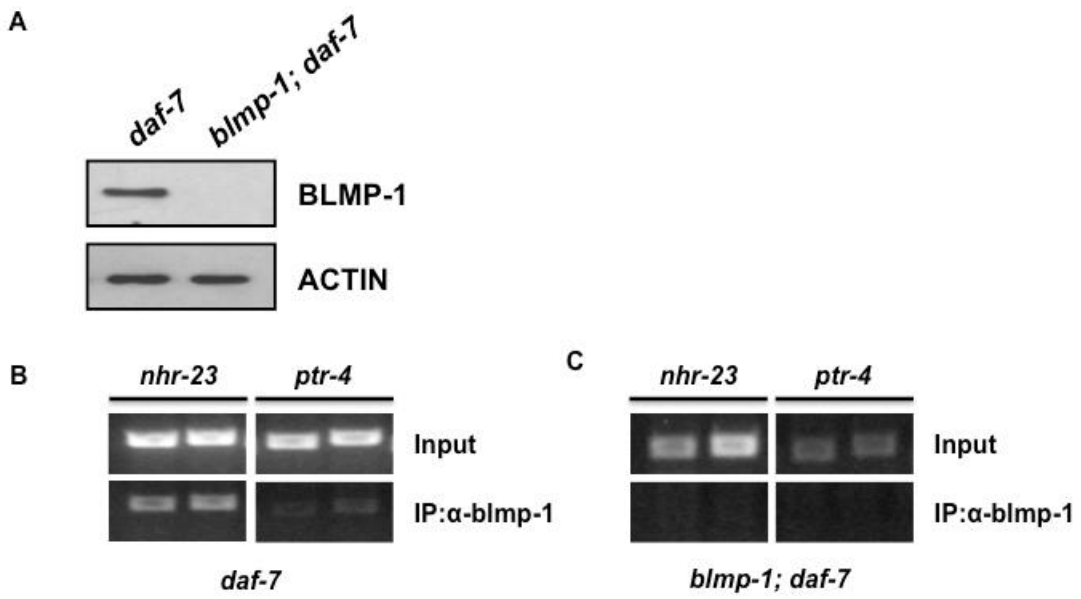


Figure S7. BLMP-1 directly binds to the promoters of *nhr-23* and *ptr-4* by Chip-PCR assay.

A. BLMP-1 protein was not detected in *blmp-1; daf-7* mutants by western blot analysis. Actin is used as a loading control.

B. BLMP-1 binds to *nhr-23* and *ptr-4* promoter regions as probed and detected by BLMP-1 antibodies via a chromatin immunoprecipitation method (ChIP). The result shows BLMP-1 binds to the promoters of *nhr-23* and *ptr-4* in *daf-7* mutants.

C. No bands are detected in *blmp-1; daf-7* mutants showing that the binding is specifically mediated by BLMP-1.

Genes	description/ homologs	*daf-7*(*e1372*)	
		Dauer	N
control		99.29 ± 1.24	410
B0261.1*	Transcription factor TFIIIB, Bdp1 subunit	1.31 ± 0.12	605
attf-3*	AT hook Transcription Factor family	11.66 ± 5.82	441
cdc-6*	Origin complex component	4.72 ± 6.86	434
cpar-1	Histone H3 variant CENP-A	22.98 ± 15.00	725
F33H1.4*	Titin (human)	25.69 ± 23.03	567
F43G9.12*	GC-rich sequence DNA-binding factor 1	1.79 ± 1.12	606
gei-11*	SNAPC4 (human)	7.39 ± 8.50	454
his-16	Histone H2A	24.25 ± 11.36	582
his-33*	Histone H2A	5.25 ± 7.30	427
htz-1	Histone 2A.Z histone variant	68.68 ± 25.50	545
jmjd-3.2*	Histone H3 demethylase	6.67 ± 6.34	662
lin-40	MTA1 (human)	4.37 ± 4.01	453
mys-1*	MYST acetyltransferase, a TIP60 ortholog	4.76 ± 7.94	520
set-20*	SET domain-containing protein	7.81 ± 7.34	511
spt-4	Transcription elongation factor	5.37 ± 6.21	656
taf-4*	TAF4 (human)	22.77 ± 10.06	495

Table S1. Genes that affect dauer formation of *daf-7* mutants when the expression was knockdown by RNAi.

Colored box: Genes affect growth of wild types (see Supplementary Table S2).

Bold: Genes that affect dauer formation in *daf-7* mutants. The numbers are mean ± S.D.

Genes	Embryo (%)	L2/L3 (%)	L4/young adult (%)	Dead (%)	N
control	0	0.70 ± 1.20	99.05 ± 1.06	0.25 ± 0.44	577
B0261.1	3.12 ± 4.59	76.44 ± 31.86	19.89 ± 26.70	0.55 ± 0.59	751
attf-3	2.11 ± 1.55	19.67 ± 21.76	71.29 ± 17.20	6.94 ± 5.88	1074
cdc-6	3.33 ± 3.88	29.85 ± 24.68	38.40 ± 7.06	28.43 ± 31.14	861
cpar-1	1.65 ± 2.25	14.75 ± 20.84	80.44 ± 19.32	3.17 ± 4.13	1006
F33H1.4	2.31 ± 3.00	24.74 ± 26.18	64.12 ± 19.24	8.83 ± 6.80	691
F43G9.12	9.46 ± 7.33	69.72 ± 28.03	19.22 ± 23.79	1.60 ± 1.67	762
gei-11	1.83 ± 2.30	32.32 ± 33.98	60.43 ± 31.80	5.41 ± 8.10	1245
his-16	2.25 ± 1.92	8.70 ± 16.83	86.66 ± 22.95	2.16 ± 4.07	715
his-33	28.69 ± 40.74	8.62 ± 9.02	62.70 ± 36.40	0	559
htz-1	0.23 ± 0.40	26.58 ± 23.02	73.19 ± 22.62	0	593
jmjd-3.2	6.23 ± 8.95	30.25 ± 35.10	33.38 ± 27.92	30.14 ± 35.77	985
lin-40	0.11 ± 0.21	0.38 ± 0.58	99.35 ± 0.54	0.16 ± 0.32	773
mys-1	5.73 ± 2.84	0.51 ± 0.60	80.20 ± 9.06	13.05 ± 11.05	862
set-20	6.93 ± 6.00	33.25 ± 35.63	51.56 ± 26.88	8.26 ± 7.89	928
spt-4	1.79 ± 2.34	10.49 ± 12.57	87.64 ± 11.40	0.08 ± 0.16	1016
taf-4	3.91 ± 5.24	13.76 ± 11.21	62.23 ± 11.99	20.10 ± 18.88	803

Table S2. Phenotypes produced when wild type worms were treated with RNAi of the 16 genes. The numbers are mean ± S.D.

genes	*daf-7* mean (log2)	*blmp-1; daf-7* mean (log2)	fold change (geometric)	p-value	q-value
ram-2 /// WBGene00004300	7.67	12.21	**23.2**	5.11E-05	6.94E-02
opt-2 /// WBGene00003877	5.47	9.17	**13**	1.53E-04	7.00E-02
K01A2.3 /// K01A2.4 /// WBGene00019278 /// WBGene00019279	4.92	8.06	**8.8**	2.94E-04	7.56E-02
R07E3.6 /// WBGene00011107	5.98	9.04	**8.3**	2.70E-04	7.56E-02
K10C2.1 /// WBGene00019617	8.76	11.74	**7.9**	3.86E-04	8.61E-02
haf-6 /// WBGene00001816	5.41	8.31	**7.5**	1.93E-04	7.00E-02
R03A10.5 /// WBGene00010985	5.13	7.92	**6.9**	4.24E-05	6.94E-02
K01A2.3 /// WBGene00019278	5.37	8.1	**6.6**	2.95E-04	7.56E-02
T14A8.2	8.71	11.18	**5.5**	5.78E-04	9.74E-02
col-107	10.58	12.83	**4.8**	1.92E-05	6.53E-02
aqp-4 /// WBGene00000172	5.43	7.69	**4.8**	1.37E-05	6.53E-02
ptr-6 /// WBGene00004221	4.83	7.06	**4.7**	6.04E-04	9.74E-02
dpy-5 /// WBGene00001067	6.03	8.26	**4.7**	3.84E-04	8.61E-02
col-184 /// WBGene00000757	6.51	8.62	**4.3**	8.50E-05	6.94E-02
Y39A3CR.5 /// WBGene00021445	6.27	8.17	**3.7**	1.16E-04	7.00E-02
C38D9.2 /// WBGene00008010	7.7	9.54	**3.6**	9.83E-05	6.94E-02
T05C3.6	5.9	7.73	**3.5**	5.07E-04	9.49E-02
C29F7.2 /// WBGene00007811	6.36	8.17	**3.5**	4.56E-04	9.40E-02
T06A1.1 /// WBGene00020277	5.67	7.41	**3.3**	8.20E-05	6.94E-02
gtl-1 /// WBGene00001795	6.75	8.48	**3.3**	2.89E-04	7.56E-02
pcp-1 /// WBGene00003956	8.95	10.57	**3.1**	3.01E-04	7.56E-02
K08A2.1 /// WBGene00019511	7.96	9.53	**3**	5.90E-04	9.74E-02
B0454.6 /// WBGene00015197	5.36	6.84	**2.8**	4.89E-04	9.48E-02
dct-18 /// WBGene00010266	10.53	12	**2.8**	5.32E-04	9.49E-02
ver-2 /// WBGene00006895	7.15	8.6	**2.7**	3.87E-04	8.61E-02
tag-60	6.27	7.67	**2.6**	2.06E-05	6.53E-02
F36G3.2 /// WBGene00009483	5.48	6.83	**2.5**	5.06E-04	9.49E-02
C05B5.4 /// WBGene00007321	6.66	7.95	**2.5**	1.60E-04	7.00E-02
sams-1 /// WBGene00008205	10.32	11.56	**2.4**	3.43E-04	8.03E-02
C06H5.7 /// WBGene00007395	8.07	9.31	**2.4**	1.10E-04	7.00E-02
vha-6 /// WBGene00006915	9.48	10.68	**2.3**	2.00E-04	7.00E-02
F29G6.3	8.98	10.17	**2.3**	1.51E-04	7.00E-02
C29F7.3 /// WBGene00007812	8.11	9.19	**2.1**	2.42E-04	7.19E-02
clec-186 /// WBGene00014138	7.74	8.66	**1.9**	2.29E-04	7.00E-02
C24B9.3	10.53	11.35	**1.8**	5.29E-04	9.49E-02
C33A11.2 /// WBGene00007878	6.02	6.83	**1.7**	5.55E-04	9.74E-02
ZK1025.2 /// ZK1025.8 /// WBGene00014182 /// WBGene00014188	5.4	6.18	**1.7**	4.89E-04	9.48E-02
F13D2.1 /// WBGene00008735	8.04	8.81	**1.7**	2.12E-04	7.00E-02
his-31 /// WBGene00001905	6.62	7.38	**1.7**	9.42E-05	6.94E-02
T28A11.19 /// WBGene00020881	6.96	7.72	**1.7**	1.51E-04	7.00E-02
ifc-2	10.19	10.94	**1.7**	6.59E-05	6.94E-02
ads-1 /// WBGene00000081	9.88	10.61	**1.7**	6.11E-04	9.74E-02
clec-66 /// WBGene00009397	8.33	9.02	**1.6**	7.78E-05	6.94E-02
F01G10.9 /// WBGene00008511	7.99	8.67	**1.6**	4.74E-04	9.48E-02
C04F12.1 /// WBGene00007297	8.69	9.33	**1.6**	4.13E-07	7.83E-03

T04A8.7	9.91	10.48	**1.5**	1.65E-04	7.00E-02
W02B12.9 /// WBGene00012204	7.27	7.81	**1.5**	3.03E-04	7.56E-02
his-64 /// WBGene00001938	7.7	8.23	**1.4**	3.42E-04	8.03E-02
nhr-238 /// WBGene00021611	5.27	5.79	**1.4**	5.35E-04	9.49E-02
C32F10.8	11.6	12.1	**1.4**	1.48E-04	7.00E-02
ckb-2 /// WBGene00000512	8.13	8.63	**1.4**	2.42E-05	6.57E-02
K05B2.4 /// WBGene00019404	4.5	4.99	**1.4**	4.11E-04	8.87E-02
fbxc-40 /// K02E7.7 /// WBGene00019312	4.47	4.94	**1.4**	6.10E-04	9.74E-02
C11E4.1 /// WBGene00007516	11.56	12	**1.4**	1.76E-04	7.00E-02
gst-33 /// WBGene00001781	5.8	6.23	**1.4**	5.40E-05	6.94E-02
Y18D10A.9 /// WBGene00012479	6.83	7.24	**1.3**	4.83E-04	9.48E-02
lmp-1 /// WBGene00003053	11.92	12.25	**1.3**	2.06E-04	7.00E-02
uig-1	7.93	8.24	**1.2**	1.61E-04	7.00E-02
Y24D9A.8	12.73	12.93	**1.1**	2.83E-04	7.56E-02

Table S3. Genes regulated by *blmp-1* in *daf-7* mutant background (**Red and +**: up-regulated in *blmp-1; daf-7* mutants compared to *daf-7)*.

genes	*daf-7* mean (log2)	*blmp-1; daf-7* mean (log2)	fold change (geometric)	p-value	q-value
rgs-6 /// WBGene00004349	4.66	4.49	**-1.1**	3.15E-04	7.66E-02
got-1.2 /// WBGene00020146	12.35	12.14	**-1.2**	6.39E-04	9.94E-02
Y40H7A.9 ///WBGene00012746	3.85	3.58	**-1.2**	2.25E-04	7.00E-02
cyn-5 /// WBGene00000881	13.62	13.31	**-1.2**	6.05E-04	9.74E-02
nucb-1	10.95	10.58	**-1.3**	1.95E-04	7.00E-02
ile-1 /// WBGene00002070	10.54	10.15	**-1.3**	2.88E-04	7.56E-02
sca-1	9.78	9.3	**-1.4**	5.98E-04	9.74E-02
C31H5.4 /// WBGene00007855	10.94	10.42	**-1.4**	4.41E-04	9.20E-02
tag-189 /// WBGene00007045	9.47	8.91	**-1.5**	3.01E-04	7.56E-02
die-1 /// WBGene00000995	6.66	6.08	**-1.5**	8.86E-05	6.94E-02
T04C9.1	7.15	6.56	**-1.5**	2.60E-04	7.56E-02
C03H5.2 /// WBGene00015404	11.02	10.4	**-1.5**	1.77E-04	7.00E-02
Y39G8B.1	12.03	11.41	**-1.5**	8.12E-05	6.94E-02
C05D9.9	9.29	8.61	**-1.6**	5.08E-04	9.49E-02
K11B4.2 /// WBGene00010767	8.2	7.51	**-1.6**	5.29E-04	9.49E-02
R05H11.1 /// R05H11.2 /// WBGene00019907 /// WBGene00019908	9.67	8.91	**-1.7**	3.80E-04	8.61E-02
clc-2 /// WBGene00000523	6.58	5.81	**-1.7**	3.62E-05	6.94E-02
F53B3.5 /// WBGene00018743	10.3	9.53	**-1.7**	5.68E-06	5.39E-02
nhr-23	6.84	6.03	**-1.8**	1.29E-04	7.00E-02
tag-260	10.44	9.6	**-1.8**	7.60E-05	6.94E-02
calu-1	12.99	12.14	**-1.8**	3.23E-04	7.75E-02
T01G9.3 /// WBGene00011345	8.16	7.26	**-1.9**	9.87E-05	6.94E-02
ced-6 /// WBGene00000420	9.53	8.61	**-1.9**	1.15E-04	7.00E-02
W09D10.5 /// WBGene00012363	9.84	8.91	**-1.9**	6.16E-04	9.74E-02
fbxa-65 /// WBGene00015885	9.07	8.13	**-1.9**	2.05E-04	7.00E-02
D1044.1 /// WBGene00017027	6.56	5.62	**-1.9**	2.21E-04	7.00E-02
F56A8.1	9.85	8.86	**-2**	3.00E-05	6.94E-02
F56C11.5	9.12	8.11	**-2**	6.80E-05	6.94E-02
lin-42	7.59	6.57	**-2**	3.00E-04	7.56E-02
dhs-27 /// WBGene00000990	10.97	9.93	**-2.1**	4.82E-04	9.48E-02
tyr-1 /// WBGene00015332	10.47	9.43	**-2.1**	3.90E-04	8.61E-02
JC8.12	9.97	8.93	**-2.1**	7.70E-05	6.94E-02
Y9C9A.16 /// WBGene00021183	8.74	7.7	**-2.1**	2.29E-04	7.00E-02
C18H7.9 /// WBGene00015999	7.44	6.37	**-2.1**	4.28E-05	6.94E-02
F43D9.1 /// WBGene00009653	7.79	6.72	**-2.1**	2.28E-04	7.00E-02
mua-3	10.6	9.51	**-2.1**	1.05E-04	7.00E-02
cyp-13A10 /// WBGene00014254	9.09	7.95	**-2.2**	5.27E-04	9.49E-02
R08C7.1 /// WBGene00019945	9.09	7.95	**-2.2**	1.61E-04	7.00E-02

C11H1.9	9.14	7.96	**-2.3**	5.77E-04	9.74E-02
T28A11.4 /// WBGene00020871	7.78	6.43	**-2.6**	2.02E-04	7.00E-02
ptr-4 /// WBGene00004219	9.7	8.33	**-2.6**	4.05E-04	8.83E-02
cutl-11 /// WBGene00011443	7.15	5.78	**-2.6**	2.88E-04	7.56E-02
C14B1.2 /// WBGene00007573	8.99	7.62	**-2.6**	4.82E-04	9.48E-02
F33H2.8	10.49	9.11	**-2.6**	9.69E-05	6.94E-02
cdh-7 /// WBGene00000399	10.93	9.53	**-2.6**	4.27E-04	9.01E-02
F42H10.6 /// WBGene00018370	8.39	6.99	**-2.6**	4.20E-04	8.95E-02
dct-1	9.51	8.08	**-2.7**	1.69E-04	7.00E-02
Y57E12B.3 /// WBGene00021963	8.24	6.8	**-2.7**	5.94E-04	9.74E-02
ZK1025.7 ///WBGene00050875	5.86	4.37	**-2.8**	2.01E-04	7.00E-02
srz-96 /// WBGene00013468	6.59	5.02	**-3**	1.21E-04	7.00E-02
srj-32 /// WBGene00005617	7.65	6.08	**-3**	5.93E-04	9.74E-02
inft-1 /// WBGene00019030	8.09	6.42	**-3.2**	2.06E-05	6.53E-02
F15E6.3 /// WBGene00017484	8.53	6.57	**-3.9**	5.31E-05	6.94E-02
lpr-3 /// WBGene00012261	12.45	10.07	**-5.2**	5.91E-04	9.74E-02
F53F4.7 /// WBGene00009990	11.35	8.93	**-5.3**	2.13E-04	7.00E-02
F10D7.3/// WBGene00017340	10.59	7.99	**-6.1**	2.12E-04	7.00E-02
nhr-113 /// *nhr-259* /// WBGene00003703 /// WBGene00007770	7.8	4.71	**-8.5**	2.33E-04	7.02E-02

Table S4. Genes regulated by *blmp-1* in *daf-7* mutant background (Green and -):

down-regulated in *blmp-1; daf-7* mutants compared to *daf-7*.

signaling	
PaTched Related family	ptr-6
VEGF (vascular endothelial growth factor) Receptor family	ver-2
predicted transmembrane protein	C05B5.4
DihydroCaffeic Acid Receptor	C06H5.7

development & structure	
GPI-anchored cell surface glycoprotein (flocculin)	R07E3.6
GPI-anchored cell surface glycoprotein (flocculin)	T14A8.2
abnormal RAy Morphology (2)	ram-2
COLlagen	col-107
AQuaPorin or aquaglyceroporin related	aqp-4
DumPY : shorter than wild-type	dpy-5
COLlagen	col-184
DAF-16/FOXO Controlled, germline Tumor affecting	dct-18
epithelial integrity via regulation of Moesin activity	tag-60
C-type LECtin	clec-186
Alpha-2-macroglobulin	F13D2.1
intermediate filament protein	ifc-2
homolog of human AGPS	ads-1
C-type LECtin	clec-66

transport, channels, membrane trafficking, ER	
half-molecule ATP-binding cassette (ABC) transporter	haf-6
SEC14-like protein 3	R03A10.5
ER-to-Golgi SNARE complex	C38D9.2
TRP channel family	gtl-1
Cationic amino acid transporter 4	B0454.6
subunit a of the membrane-bound V-ATPase	vha-6
Hypersensitive to POre-forming toxin	hpo-34
LAMP homolog	lmp-1

degradation and cell death	
DNA damage-regulated autophagy modulator protein 2	C33A11.2
F-box C protein	fbxc-40

protein protein interaction	
a protein with NACHT and WD domains	T05C3.6

metabolism	
OligoPeptide Transporter	pept-1
Putative serine type carboxypeptidase	K10C2.1
prolylcarboxypeptidase (PRCP)	pcp-1
S-adenosyl methionine synthetase	sams-1
Uridylate kinase	C29F7.3
Protein argonaute-4	C04F12.1
orthologous to human GLUCOSIDASE, ACID BETA	T04A8.7
Isoform 1 of Mitoferrin-1	W02B12.9
Alanine aminotransferase 1	C32F10.8
Choline Kinase B	ckb-2
Acyl-coenzyme A thioesterase 1	K05B2.4
Epididymal secretory glutathione peroxidase	C11E4.1
Hematopoietic prostaglandin D synthase	gst-33
cytosolic iron-sulfur protein assembly protein CIAO1	Y18D10A.9
Cdc42 guanine nucleotide exchange factor	uig-1
TRANSALDOLASE 1	Y24D9A.8

Histone	
H4 histone	his-31
H4 histone	his-64

NHRs	
Isoform HNF4-Alpha-3 of Hepatocyte nuclear factor 4-alpha	nhr-238

nematode specific or unknown	
nematode	K01A2.3/4
nematode	K01A2.3
nematode	Y39A3CR.5
nematode	C29F7.2
nematode	T06A1.1
nematode	K08A2.1
nematode	F36G3.2
nematode	ZK1025.2/8
nematode	T28A11.19
ITGA2 (human) uncharacterized	C24B9.3
conserved hypothetical protein in human	F01G10.9

Table S5. Categories of the genes whose expression is upregulated in *blmp-1; daf-7* compared to *daf-7*.

signaling	
LiPocalin-Related protein, bind and transport lipophilic molecules and participate in intercellular signaling	lpr-3
PaTched Related family	ptr-4
Serpentine Receptor, class J	srj-32
Serpentine Receptor, class Z	srz-96
Patched domain-containing protein C6orf138	F43D9.1
Rho GTPase-activating protein 10	T04C9.1
rgs-6 encodes a regulator of G protein signaling	rgs-6

development & structure	
Isoform 2 of Heterogeneous nuclear ribonucleoprotein A3 (2)	F15E6.3
abnormal cell LINeage	lin-42
MUscle Attachment abnormal	mua-3
Severs actin filaments and accelerates polymerization and depolymerization	inft-1
contribute to the integrity of the nematode cuticle	bah-1
CUTiclin-Like	cutl-11
Intracellular Lectin	ile-1

transport, channels and mb trafficking, ER	
SEC14-like protein 3	C11H1.9
CaDHerin family, Protocadherin Fat 1	cdh-7
C1GALT1-specific chaperone 1	W09D10.5
nucleotide-sugar transporter	bus-12
CLaudin-like	clc-2
a transporter of UDP-N-acetylglucosamine	nstp-4

degradation and cell death	
F-box A protein	fbxa-65
F-box protein	R05H11.1, R05H11.2
BNIP3 proteins that interact with Bcl-2	dct-1
CEll Death abnormality	ced-6

protein protein interaction	
leucine rich repeats	T01G9.3
Isoform 2 of Interferon regulatory factor 2-binding protein 2	tag-260
Isoform 2 of Protein MEF2BNB	K11B4.2
C2H2 zinc finger protein containing four fingers	die-1

metabolism	
glutaredoxin mitochondrial	F10D7.3
gastric triacylglycerol lipase isoform 1	lipl-6
Acyl-coenzyme A thioesterase 13	F42H10.6
CYtochrome P450 family	cyp-13A10
PRotein arginine MethylTransferase	prmt-4
Sulfide:quinone oxidoreductase, mitochondrial	Y9C9A.16
TYRosinase	tyr-1
a short-chain dehydrogenase predicted to be mitochondrial	dhs-27
member of the aldo-keto reductase (AKR) family	Y39G8B.1
CYclophyliN isomerase	cyn-5
Cysteine protease nematode	Y40H7A.9
Cytosolic aspartate aminotransferase	got-1.2

calcium	
CALUmenin (calcium-binding protein) homolog	calu-1
nucleobindin homolog with a calcium-binding EF-hand domain	nucb-1
ANOctamin (calcium-activated chloride channel) Homolog	anoh-1
voltage-dependent calcium channel gamma subunits	F53B3.5
SERCA (Sarco-Endoplasmic Reticulum Calcium ATPase)	sca-1

NHRs	
Isoform Alpha-2 of Thyroid hormone receptor alpha	nhr-113, nhr-259
Nuclear Hormone Receptor family	nhr-23

nematode specific	
nematode	F53F4.7
nematode	F33H2.8
nematode	C14B1.2
nematode	T28A11.4
nematode	F56C11.5
nematode	D1044.1
nematode	C05D9.9
nematode	C31H5.4
Temporarily Assigned Gene name	tag-260
tag-189	tag-189
unknown	R08C7.1

Table S6. Categories of the genes whose expression is downregulated in *blmp-1; daf-7* compared to *daf-7*.

genes	N2 mean (log2)	*blmp-1* mean (log2)	fold change (geometric)	p-value	q-value
fip-1 /// WBGene00017695	5.43	10.24	28.1	1.51E-03	2.12E-01
WBGene00022653 /// ZK105.1	6.65	9.42	6.8	1.89E-04	1.91E-01
cnc-4 /// WBGene00000558	8.34	11.08	6.7	3.26E-05	1.91E-01
ilys-2 /// WBGene00016669	4.67	7.37	6.5	2.33E-04	1.91E-01
F25H5.8 /// WBGene00009130	4.22	6.78	5.9	3.89E-03	2.45E-01
C45B2.1 /// WBGene00016658	6.28	8.83	5.9	1.70E-03	2.12E-01
WBGene00014173 /// ZK970.7	9.38	11.64	4.8	1.47E-03	2.12E-01
C45B2.8 /// WBGene00016662	5.04	7.08	4.1	4.16E-03	2.49E-01
C38D9.2 /// WBGene00008010	5.34	7.29	3.9	4.13E-04	2.03E-01
nlp-29 /// WBGene00003767	9.05	10.91	3.6	1.84E-03	2.12E-01
F53F8.4 /// WBGene00010001	8.23	10.10	3.6	1.91E-03	2.12E-01
clec-174 /// WBGene00021580	7.08	8.84	3.4	1.20E-03	2.12E-01
F43C11.3 /// WBGene00018380	4.94	6.60	3.2	1.15E-04	1.91E-01
nlp-30 /// WBGene00003768	9.53	11.18	3.1	4.12E-04	2.03E-01
nlp-31 /// WBGene00003769	9.72	11.36	3.1	7.90E-04	2.08E-01
C42D4.3 /// WBGene00016596	11.75	13.26	2.9	2.50E-03	2.22E-01
T05A7.1 /// WBGene00020219	7.52	9.03	2.8	3.05E-03	2.29E-01
nhr-11	6.32	7.82	2.8	1.31E-03	2.12E-01
dct-5 /// WBGene00017218	8.49	9.97	2.8	3.11E-03	2.29E-01
T27F6.8 /// WBGene00012107	7.53	8.93	2.6	8.08E-04	2.08E-01
Y105C5A.8	6.78	8.18	2.6	3.19E-03	2.29E-01
nlp-28 /// WBGene00003766	8.49	9.89	2.6	2.54E-03	2.22E-01
WBGene00006980 /// zig-3	6.30	7.69	2.6	1.82E-03	2.12E-01
T04F8.8	9.37	10.75	2.6	3.44E-03	2.34E-01
F14D7.7 /// WBGene00008794	5.79	7.16	2.6	6.93E-04	2.08E-01
ttr-32 /// WBGene00020047	7.73	9.07	2.5	8.09E-04	2.08E-01
C54D10.10 /// WBGene00008304	7.90	9.20	2.5	2.01E-04	1.91E-01
R05H10.1 /// WBGene00011042	6.75	8.00	2.4	5.18E-05	1.91E-01
C25H3.10	6.65	7.91	2.4	3.02E-03	2.29E-01
C34F11.8 /// WBGene00016417	7.93	9.14	2.3	2.36E-03	2.19E-01
nhr-11	7.03	8.20	2.2	1.93E-03	2.12E-01
nas-38 /// WBGene00003554	8.39	9.54	2.2	1.60E-03	2.12E-01
nhr-80	8.04	9.17	2.2	5.31E-04	2.03E-01
lips-17 /// WBGene00019939	7.44	8.56	2.2	1.91E-03	2.12E-01
E04F6.6 /// WBGene00017126	6.13	7.24	2.2	1.71E-03	2.12E-01
C18H9.5 /// WBGene00016003	5.30	6.41	2.1	4.00E-03	2.49E-01
T28H10.2 /// WBGene00012143	8.01	9.11	2.1	2.34E-03	2.19E-01
M162.5 /// WBGene00010931	5.14	6.23	2.1	2.68E-03	2.23E-01
C34C6.7	5.81	6.88	2.1	6.20E-04	2.03E-01

F26A1.9 /// WBGene00017807	7.29	8.34	2.1	2.03E-03	2.12E-01
F18E9.3 /// WBGene00017569	7.85	8.88	2.0	2.25E-04	1.91E-01
tbb-6 /// WBGene00006539	6.59	7.56	2.0	1.38E-03	2.12E-01
WBGene00013181 /// Y53H1B.2	10.50	11.44	1.9	4.48E-04	2.03E-01
col-80 /// WBGene00000656	10.83	11.78	1.9	4.18E-03	2.49E-01
W03D2.9 /// WBGene00020983	5.23	6.14	1.9	4.12E-03	2.49E-01
C06C3.4 /// WBGene00007375	7.82	8.68	1.8	1.46E-03	2.12E-01
hil-3	9.92	10.77	1.8	7.80E-04	2.08E-01
ptr-23 /// WBGene00004237	8.50	9.34	1.8	1.73E-03	2.12E-01
C06H5.7 /// WBGene00007395	8.95	9.78	1.8	2.34E-04	1.91E-01
H10E21.2 /// WBGene00019183	6.18	7.00	1.8	1.48E-03	2.12E-01
hlh-33 /// WBGene00021446	6.15	6.96	1.7	1.08E-03	2.09E-01
C04F12.1 /// WBGene00007297	7.25	8.02	1.7	6.19E-04	2.03E-01
lrp-1 /// WBGene00003071	9.94	10.71	1.7	8.17E-04	2.08E-01
WBGene00013127 /// Y52B11A.8	7.88	8.65	1.7	1.83E-03	2.12E-01
fip-5 /// WBGene00009620	9.98	10.72	1.7	6.78E-05	1.91E-01
F53E4.1	9.27	10.00	1.7	1.67E-03	2.12E-01
hil-3 /// WBGene00001854	9.29	10.02	1.7	1.89E-03	2.12E-01
C06C3.4 /// WBGene00007375	8.27	9.00	1.7	1.19E-06	2.10E-02
Y48B6A.6	6.98	7.71	1.7	3.12E-03	2.29E-01
his-24 /// WBGene00001898	10.26	10.98	1.7	9.38E-04	2.09E-01
C11E4.1 /// WBGene00007516	9.71	10.43	1.6	3.77E-03	2.39E-01
pqn-75	6.80	7.50	1.6	1.93E-03	2.12E-01
ttr-15 /// WBGene00011561	12.30	12.99	1.6	1.35E-03	2.12E-01
nhr-205 /// WBGene00011002	6.02	6.69	1.6	6.18E-04	2.03E-01
lam-2 /// WBGene00016913	7.65	8.32	1.6	2.44E-03	2.20E-01
kin-15	7.36	8.02	1.6	2.38E-03	2.19E-01
lrp-1 /// WBGene00003071	9.93	10.59	1.6	1.01E-03	2.09E-01
F47B8.8 /// WBGene00009809	7.27	7.93	1.6	1.10E-03	2.11E-01
EEED8.12 /// EEED8.4 /// WBGene00017135	4.32	4.96	1.6	3.92E-03	2.45E-01
dos-1 /// WBGene00013980	4.73	5.36	1.5	4.06E-03	2.49E-01
EEED8.12 /// WBGene00017140	5.72	6.34	1.5	5.47E-04	2.03E-01
nhr-120 /// WBGene00003710	6.38	6.97	1.5	2.08E-03	2.13E-01
WBGene00013496 /// Y70D2A.1	5.85	6.43	1.5	4.18E-03	2.49E-01
WBGene00021445 /// Y39A3CR.5	7.78	8.36	1.5	4.28E-04	2.03E-01
F13D2.1 /// WBGene00008735	7.40	7.96	1.5	2.56E-03	2.22E-01
BE10.2 /// WBGene00007210	9.88	10.42	1.5	3.15E-03	2.29E-01
brp-1	11.42	11.94	1.4	4.16E-03	2.49E-01
F29B9.8 /// WBGene00017923	8.98	9.50	1.4	1.79E-03	2.12E-01
pqn-83	9.64	10.16	1.4	1.13E-03	2.11E-01
F16A11.1	8.48	8.99	1.4	1.05E-03	2.09E-01
pqn-83	9.43	9.91	1.4	3.59E-03	2.36E-01
F53C3.13	9.20	9.68	1.4	6.01E-04	2.03E-01

rol-6 /// WBGene00004397	13.09	13.56	1.4	1.31E-03	2.12E-01
col-19 /// WBGene00000608	6.67	7.14	1.4	5.98E-04	2.03E-01
cuticlin /// WBGene00009983	13.69	14.15	1.4	4.58E-04	2.03E-01
F47G3.1 /// WBGene00018576	7.28	7.74	1.4	3.71E-03	2.39E-01
ttm-2 /// WBGene00017840	8.23	8.68	1.4	2.40E-03	2.19E-01
F46H5.2	6.38	6.81	1.3	4.12E-03	2.49E-01
WBGene00012887 /// Y45F10D.7	8.29	8.72	1.3	3.48E-03	2.34E-01
col-8 /// WBGene00000597	6.59	7.02	1.3	3.74E-03	2.39E-01
phosphotransferase	8.58	9.00	1.3	8.22E-04	2.08E-01
C55A6.12 /// WBGene00044019	10.41	10.82	1.3	2.62E-03	2.22E-01
M02B1.3 /// WBGene00010828	9.13	9.53	1.3	1.85E-03	2.12E-01
T28F12.1	10.26	10.66	1.3	1.97E-03	2.12E-01
rol-8	12.92	13.32	1.3	3.33E-03	2.31E-01
lgg-2 /// WBGene00002981	10.24	10.63	1.3	3.13E-03	2.29E-01
WBGene00002244 /// Y71H2AM.19	5.66	6.03	1.3	3.56E-03	2.36E-01
T07F12.1 /// WBGene00020321	6.68	7.06	1.3	2.55E-04	1.91E-01
WBGene00013668 /// Y105E8A.3	6.39	6.76	1.3	8.89E-04	2.09E-01
T19A5.3	9.19	9.54	1.3	2.51E-03	2.22E-01
F21D5.1 /// WBGene00009006	6.64	6.99	1.3	2.60E-03	2.22E-01
F11F1.1 /// WBGene00008714	4.71	5.05	1.3	2.39E-03	2.19E-01
nhr-127 /// WBGene00003717	5.29	5.62	1.3	1.81E-03	2.12E-01
T13H5.6 /// WBGene00011760	7.81	8.14	1.3	1.06E-03	2.09E-01
T19C3.1 /// WBGene00020559	7.47	7.80	1.3	4.09E-03	2.49E-01
W02F12.2 /// WBGene00020947	8.21	8.54	1.3	4.04E-03	2.49E-01
dhs-19 /// WBGene00000982	9.41	9.73	1.3	1.06E-03	2.09E-01
atp-5 /// WBGene00007385	12.30	12.62	1.2	9.75E-04	2.09E-01
F47G3.1 /// WBGene00018576	6.91	7.23	1.2	1.55E-03	2.12E-01
R08E5.4 /// WBGene00019964	3.37	3.68	1.2	2.30E-03	2.19E-01
uaf-1	7.59	7.89	1.2	2.44E-03	2.20E-01
lgg-2 /// WBGene00002981	9.64	9.94	1.2	2.03E-03	2.12E-01
rol-8	12.19	12.49	1.2	2.12E-03	2.13E-01
C45E1.4 /// WBGene00016663	8.82	9.11	1.2	3.01E-03	2.29E-01
unc-30	4.92	5.20	1.2	3.01E-04	1.91E-01
fbxc-40	4.62	4.90	1.2	1.05E-03	2.09E-01
C07C7.1 /// WBGene00007411	3.60	3.87	1.2	2.11E-03	2.13E-01
rrf-3 /// WBGene00004510	6.02	6.29	1.2	2.20E-03	2.17E-01
nhr-42 /// WBGene00003632	7.99	8.25	1.2	2.25E-03	2.18E-01
bus-19	9.30	9.55	1.2	2.30E-03	2.19E-01
M57.1 /// WBGene00019777	4.16	4.41	1.2	3.66E-03	2.38E-01
gei-16	8.10	8.34	1.2	6.15E-04	2.03E-01
M01F1.3 /// WBGene00010809	10.11	10.35	1.2	2.15E-03	2.13E-01
T25B9.8 /// WBGene00012014	4.69	4.92	1.2	1.34E-03	2.12E-01
R07B1.9 /// WBGene00011081	5.48	5.70	1.2	9.18E-04	2.09E-01

dcn-1	**8.12**	**8.34**	**1.2**	3.70E-03	2.39E-01
C52E12.4 /// WBGene00016889	**9.08**	**9.29**	**1.2**	3.27E-03	2.29E-01
WBGene00022609 /// ZC416.2	**6.87**	**7.09**	**1.2**	3.00E-03	2.29E-01
cdc-42 /// WBGene00000390	**9.28**	**9.50**	**1.2**	2.44E-03	2.20E-01
ppfr-2 /// WBGene00017064	**8.42**	**8.64**	**1.2**	2.31E-03	2.19E-01
B0212.3 /// M57.1 /// WBGene00015037	**7.43**	**7.63**	**1.1**	9.39E-04	2.09E-01
bli-3 /// WBGene00000253	**8.36**	**8.56**	**1.1**	3.72E-03	2.39E-01
transketolase /// WBGene00008506	**6.12**	**6.30**	**1.1**	1.70E-03	2.12E-01
pyp-1	**11.52**	**11.70**	**1.1**	4.48E-04	2.03E-01
WBGene00022767 /// ZK563.2	**6.67**	**6.83**	**1.1**	2.65E-03	2.22E-01
Y58G8A.4	**7.22**	**7.35**	**1.1**	3.75E-03	2.39E-01
F17C11.9	**13.28**	**13.40**	**1.1**	1.66E-03	2.12E-01
vit-5 /// WBGene00006929	**5.62**	**5.73**	**1.1**	3.64E-03	2.38E-01
lmn-1 /// WBGene00003052	**9.52**	**9.62**	**1.1**	3.29E-04	1.91E-01
WBGene00021968 /// Y57G7A.5	**4.02**	**4.12**	**1.1**	2.83E-03	2.29E-01

Table S7. Genes regulated by *blmp-1* in wild type background (Red and +: up-regulated in *blmp-1* mutants compared to wil dtype N2.

genes	N2 mean (log2)	*blmp-1* mean (log2)	fold change (geometric)	p-value	q-value
praf-3	10.84	10.74	-1.1	3.26E-03	2.29E-01
C07A9.5 /// WBGene00007401	3.32	3.22	-1.1	1.48E-03	2.12E-01
fbxb-33 /// WBGene00044314	3.43	3.32	-1.1	1.44E-03	2.12E-01
srh-193 /// WBGene00005406	3.90	3.77	-1.1	2.33E-03	2.19E-01
lin-5 /// WBGene00002994	7.99	7.85	-1.1	3.16E-03	2.29E-01
WBGene00022273 /// Y73E7A.6	8.67	8.52	-1.1	5.53E-04	2.03E-01
fkb-1 /// WBGene00001426	12.79	12.63	-1.1	3.26E-03	2.29E-01
num-1	8.00	7.83	-1.1	1.50E-03	2.12E-01
pmr-1	8.79	8.62	-1.1	2.34E-03	2.19E-01
WBGene00021361 /// Y37E11AL.5	4.76	4.59	-1.1	2.07E-03	2.13E-01
atg-16.1 /// WBGene00017178	7.06	6.89	-1.1	5.58E-04	2.03E-01
erm-1	11.00	10.83	-1.1	8.25E-04	2.08E-01
WBGene00013124 /// Y52B11A.4	5.08	4.90	-1.1	1.43E-03	2.12E-01
F19B2.7 /// WBGene00008946	4.59	4.41	-1.1	2.05E-03	2.13E-01
WBGene00014222 /// ZK1098.5	9.55	9.36	-1.1	1.08E-03	2.09E-01
nkcc-1	8.45	8.25	-1.1	3.60E-03	2.36E-01
nhr-81 /// WBGene00003671	4.93	4.74	-1.1	3.07E-04	1.91E-01
C29H12.6 /// WBGene00016237	6.91	6.71	-1.1	3.31E-04	1.91E-01
F01F1.15 /// WBGene00017169	10.43	10.23	-1.1	3.38E-03	2.32E-01
pqn-36	6.27	6.07	-1.2	2.32E-04	1.91E-01
W04C9.2 /// WBGene00021024	10.72	10.51	-1.2	3.05E-03	2.29E-01
F48C1.6 /// WBGene00018599	8.85	8.64	-1.2	1.41E-03	2.12E-01
C16C8.8 /// WBGene00015846	4.24	4.02	-1.2	1.76E-03	2.12E-01
F54B3.1	8.53	8.31	-1.2	1.05E-03	2.09E-01
str-229 /// WBGene00006260	4.68	4.45	-1.2	3.56E-03	2.36E-01
F25E5.3 /// WBGene00017784	5.18	4.93	-1.2	2.23E-03	2.18E-01
glb-33 /// WBGene00022284	5.39	5.14	-1.2	1.74E-03	2.12E-01
R12C12.6	9.44	9.20	-1.2	1.22E-03	2.12E-01
sca-1	9.02	8.77	-1.2	7.70E-04	2.08E-01
W09B6.5 /// WBGene00021105	5.05	4.79	-1.2	2.02E-03	2.12E-01
kin-1	4.05	3.79	-1.2	2.90E-03	2.29E-01
C49G9.1 /// WBGene00008216	7.19	6.92	-1.2	2.50E-03	2.22E-01
ehbp-1 /// WBGene00009098	8.22	7.96	-1.2	2.08E-03	2.13E-01
C08D8.1 /// WBGene00015592	4.49	4.22	-1.2	3.77E-03	2.39E-01
ire-1 /// WBGene00002147	8.36	8.09	-1.2	3.20E-03	2.29E-01
Y54E10BR.1	6.53	6.25	-1.2	3.03E-03	2.29E-01
srh-69 /// WBGene00005290	4.60	4.33	-1.2	2.49E-03	2.22E-01
glutaminase /// WBGene00009271	6.11	5.83	-1.2	2.24E-03	2.18E-01
lips-8 /// WBGene00009303	4.40	4.12	-1.2	2.65E-03	2.22E-01
F41C3.4 /// WBGene00018270	8.63	8.35	-1.2	1.90E-03	2.12E-01

bed-2 /// WBGene00012943	**7.34**	**7.05**	**-1.2**	2.02E-03	2.12E-01
C14A4.6 /// WBGene00007557	**9.95**	**9.66**	**-1.2**	2.90E-04	1.91E-01
WBGene00014007 /// ZK596.2	**5.61**	**5.31**	**-1.2**	1.95E-03	2.12E-01
ppk-1 /// WBGene00004087	**7.61**	**7.30**	**-1.2**	9.04E-04	2.09E-01
C34B2.10 /// WBGene00016395	**11.79**	**11.48**	**-1.2**	1.27E-03	2.12E-01
aqp-3 /// WBGene00000171	**4.64**	**4.33**	**-1.2**	3.36E-04	1.91E-01
nhr-207 /// WBGene00011098	**3.90**	**3.58**	**-1.2**	2.98E-03	2.29E-01
F10C2.7 /// WBGene00008647	**4.23**	**3.91**	**-1.2**	3.04E-03	2.29E-01
F37H8.3	**8.30**	**7.98**	**-1.3**	5.58E-04	2.03E-01
WBGene00022471 /// Y119C1B.5	**8.49**	**8.17**	**-1.3**	2.77E-03	2.29E-01
pkc-1 /// WBGene00004032	**6.33**	**6.00**	**-1.3**	4.64E-04	2.03E-01
bec-1 /// WBGene00000247	**9.10**	**8.77**	**-1.3**	3.21E-03	2.29E-01
F13H10.3	**8.21**	**7.88**	**-1.3**	3.49E-03	2.35E-01
scm-1 /// WBGene00004743	**8.21**	**7.87**	**-1.3**	3.04E-03	2.29E-01
T02G5.7 /// WBGene00020166	**11.13**	**10.80**	**-1.3**	1.68E-03	2.12E-01
WBGene00022166 /// Y71H2AM.1	**9.08**	**8.74**	**-1.3**	1.95E-03	2.12E-01
K08A2.4 /// WBGene00019513	**6.88**	**6.54**	**-1.3**	9.39E-04	2.09E-01
gsy-1 /// WBGene00001793	**8.20**	**7.86**	**-1.3**	2.53E-03	2.22E-01
arl-5 /// WBGene00000189	**8.33**	**7.99**	**-1.3**	3.15E-03	2.29E-01
F59E11.5 /// WBGene00019111	**9.22**	**8.88**	**-1.3**	2.96E-04	1.91E-01
app-1 /// WBGene00000155	**10.12**	**9.77**	**-1.3**	2.00E-03	2.12E-01
C05E11.3 /// WBGene00015494	**7.30**	**6.94**	**-1.3**	2.94E-03	2.29E-01
F18A11.3 /// WBGene00008930	**10.17**	**9.81**	**-1.3**	1.65E-03	2.12E-01
erm-1	**10.02**	**9.66**	**-1.3**	1.15E-03	2.12E-01
aqp-11 /// WBGene00000179	**10.07**	**9.70**	**-1.3**	1.49E-03	2.12E-01
skn-1	**5.98**	**5.61**	**-1.3**	1.38E-03	2.12E-01
W05F2.7 /// WBGene00021039	**6.82**	**6.44**	**-1.3**	3.54E-03	2.36E-01
T23E7.2	**8.50**	**8.12**	**-1.3**	1.97E-03	2.12E-01
C14A4.7	**7.48**	**7.09**	**-1.3**	6.22E-04	2.03E-01
acbp-1 /// WBGene00016655	**12.92**	**12.53**	**-1.3**	1.62E-03	2.12E-01
npp-12 /// WBGene00003798	**9.23**	**8.83**	**-1.3**	1.89E-03	2.12E-01
siah-1 /// WBGene00021369	**5.92**	**5.52**	**-1.3**	4.82E-04	2.03E-01
WBGene00021844 /// Y54E10BR.5	**11.25**	**10.85**	**-1.3**	1.59E-03	2.12E-01
top-1	**8.69**	**8.28**	**-1.3**	1.87E-03	2.12E-01
dhs-12 /// WBGene00000975	**10.45**	**10.03**	**-1.3**	7.71E-04	2.08E-01
ads-1 /// WBGene00000081	**11.41**	**10.99**	**-1.3**	1.25E-03	2.12E-01
mif-3 /// WBGene00003236	**9.11**	**8.69**	**-1.3**	1.23E-04	1.91E-01
B0041.5 /// WBGene00015009	**9.51**	**9.08**	**-1.3**	6.38E-04	2.05E-01
T14G8.3	**10.38**	**9.94**	**-1.4**	1.00E-03	2.09E-01
T13C5.8 /// WBGene00077690	**9.77**	**9.33**	**-1.4**	7.26E-04	2.08E-01
ugt-21 /// WBGene00007885	**7.97**	**7.52**	**-1.4**	2.13E-03	2.13E-01
mrck-1 /// WBGene00006437	**5.95**	**5.50**	**-1.4**	4.07E-03	2.49E-01
obr-2	**8.79**	**8.34**	**-1.4**	2.80E-04	1.91E-01

gst-39 /// WBGene00001787	9.62	9.16	-1.4	3.52E-03	2.35E-01
rho-1 /// WBGene00004357	6.96	6.51	-1.4	3.05E-03	2.29E-01
M03F8.4 /// WBGene00019763	5.11	4.66	-1.4	2.62E-03	2.22E-01
dehydrogenase /// WBGene00008375	10.33	9.87	-1.4	3.24E-03	2.29E-01
ZK858.6	9.14	8.67	-1.4	4.15E-03	2.49E-01
gst-16 /// WBGene00001764	6.58	6.10	-1.4	1.28E-04	1.91E-01
lev-11	11.59	11.11	-1.4	5.98E-04	2.03E-01
sptl-2	9.86	9.38	-1.4	1.36E-03	2.12E-01
lev-11	11.42	10.92	-1.4	3.07E-04	1.91E-01
ser-3 /// WBGene00004778	6.62	6.11	-1.4	2.82E-03	2.29E-01
K01A2.5 /// WBGene00019280	10.38	9.87	-1.4	3.38E-03	2.32E-01
WBGene00012407 /// Y7A5A.1	10.32	9.81	-1.4	1.92E-03	2.12E-01
F36G9.3 /// WBGene00009485	5.47	4.96	-1.4	6.08E-04	2.03E-01
F39B2.3 /// WBGene00009554	8.15	7.63	-1.4	7.77E-04	2.08E-01
K08D9.4 /// WBGene00019525	5.84	5.31	-1.4	3.33E-03	2.31E-01
F52B11.2 /// WBGene00009925	10.07	9.54	-1.4	2.10E-03	2.13E-01
ugt-12 /// WBGene00020592	9.98	9.44	-1.5	1.12E-03	2.11E-01
apg-1 /// WBGene00000158	10.11	9.56	-1.5	1.20E-03	2.12E-01
C25F9.9 /// WBGene00007728	5.78	5.24	-1.5	3.13E-05	1.91E-01
dhs-3	9.44	8.88	-1.5	1.74E-03	2.12E-01
cyp-13A11 /// cyp-13A12 /// WBGene00008809	4.52	3.95	-1.5	2.10E-04	1.91E-01
ech-5 /// WBGene00001154	6.86	6.28	-1.5	7.39E-04	2.08E-01
gst-7 /// WBGene00001755	10.90	10.32	-1.5	3.80E-03	2.40E-01
prx-11 /// WBGene00004196	9.10	8.51	-1.5	5.89E-04	2.03E-01
WBGene00013544 /// Y75B8A.7	6.12	5.52	-1.5	3.41E-03	2.32E-01
csnk-1 /// WBGene00013709	6.83	6.22	-1.5	1.37E-03	2.12E-01
amx-3 /// WBGene00000139	7.88	7.26	-1.5	1.00E-03	2.09E-01
pph-6 /// WBGene00007922	7.44	6.82	-1.5	1.01E-03	2.09E-01
WBGene00021292 /// Y25C1A.5	7.79	7.17	-1.5	1.39E-03	2.12E-01
npp-9	8.61	7.98	-1.6	7.07E-04	2.08E-01
dhs-3	11.45	10.81	-1.6	2.61E-03	2.22E-01
F56A4.3 /// gst-10 /// WBGene00001758	12.12	11.46	-1.6	2.89E-04	1.91E-01
bli-1 /// WBGene00000251	6.15	5.47	-1.6	2.63E-03	2.22E-01
WBGene00022259 /// Y73C8B.2	9.66	8.92	-1.7	2.27E-03	2.19E-01
lips-14 /// WBGene00019208	6.59	5.85	-1.7	1.61E-03	2.12E-01
WBGene00009133 /// zbed-6	8.50	7.76	-1.7	2.88E-03	2.29E-01
F53C11.1 /// WBGene00009971	7.33	6.58	-1.7	1.78E-03	2.12E-01
K11E4.2 /// WBGene00010774	8.65	7.88	-1.7	2.89E-03	2.29E-01
cyp-29A2 /// WBGene00011830	9.35	8.56	-1.7	1.40E-03	2.12E-01
K10D11.2 /// WBGene00010746	6.00	5.13	-1.8	1.32E-03	2.12E-01
E01A2.7 /// WBGene00017089	8.18	7.29	-1.8	3.11E-03	2.29E-01
ech-6 /// WBGene00001155	12.45	11.56	-1.9	4.17E-03	2.49E-01
F58G6.3 /// F58G6.7 /// WBGene00010274	10.53	9.60	-1.9	1.77E-03	2.12E-01

F17A9.5 /// WBGene00017537	**7.38**	**6.41**	**-2.0**	3.48E-03	2.34E-01
WBGene00022260 /// Y73C8B.3	**10.16**	**9.14**	**-2.0**	3.30E-03	2.31E-01
WBGene00006950 /// wrt-4	**10.71**	**9.66**	**-2.1**	2.65E-03	2.22E-01
bli-1 /// WBGene00000251	**5.35**	**4.28**	**-2.1**	1.54E-03	2.12E-01
WBGene00014135 /// ZK896.4	**6.61**	**5.55**	**-2.1**	2.23E-04	1.91E-01
cpt-6 /// WBGene00020911	**8.92**	**7.85**	**-2.1**	2.19E-04	1.91E-01
WBGene00013587 /// Y80D3A.9	**7.95**	**6.85**	**-2.2**	1.16E-03	2.12E-01
crml-1 /// WBGene00010641	**8.35**	**7.23**	**-2.2**	3.21E-03	2.29E-01
cutl-28 /// WBGene00018256	**7.92**	**6.78**	**-2.2**	3.26E-03	2.29E-01
WBGene00012910 /// Y46G5A.20	**7.61**	**6.47**	**-2.2**	1.07E-03	2.09E-01
nhr-244 /// nhr-74 /// WBGene00003664	**8.93**	**7.66**	**-2.4**	1.52E-03	2.12E-01
Y54G2A.10	**9.48**	**8.17**	**-2.5**	9.09E-04	2.09E-01
F28G4.2 /// WBGene00009227	**7.25**	**5.92**	**-2.5**	8.46E-04	2.09E-01
R05A10.6 /// WBGene00011023	**7.09**	**5.74**	**-2.5**	1.63E-03	2.12E-01
crml-1 /// WBGene00010641	**9.37**	**8.02**	**-2.5**	1.95E-04	1.91E-01
T20D4.3 /// T20D4.4 /// WBGene00020609	**6.45**	**5.07**	**-2.6**	3.20E-03	2.29E-01
F59B10.5 /// WBGene00010321	**10.59**	**9.20**	**-2.6**	4.16E-03	2.49E-01
C01F1.5 /// WBGene00015300	**7.36**	**5.87**	**-2.8**	6.81E-04	2.08E-01
K09B11.9	**7.35**	**5.69**	**-3.2**	3.39E-03	2.32E-01
glycosyltransferase /// WBGene00008292	**7.94**	**6.04**	**-3.7**	2.64E-04	1.91E-01
fbxa-6 /// WBGene00008352	**6.79**	**4.01**	**-6.8**	1.58E-03	2.12E-01

Table S8. Genes regulated by *blmp-1* in wild type background (Green and -): down-regulated in *blmp-1* mutants compared to wild type N2.

signaling	
PaTched Related family	ptr-23
Neuropeptide-Like Protein	nlp-30
Neuropeptide-Like Protein	nlp-31
Neuropeptide-Like Protein	nlp-28
Neuropeptide-Like Protein	nlp-29
Bypass of Response to Pheromone in yeast	brp-1
Delta and OSM-11-like	dos-1
Toxin-regulated Target of p38MAPK	ttm-2
Heat shock hsp70 protein	F11F1.1

metabolism	
transketolase	tkt-1
Fungus-Induced Protein	fip-1
CaeNaCin (Caenorhabditis bacteriocin)	cnc-4
Invertebrate LYSozyme	ilys-2
OV-17 antigen precursor	ZK970.7
Nematode AStacin protease	nas-38
LIPaSe related	lips-17
Low-density lipoprotein Receptor Related	lrp-1
Fungus-Induced Protein	fip-5
glutathione peroxidase	C11E4.1
protein KINase	kin-15
lipoic acid synthase	M01F1.3
Protein Phosphatase Four Regulatory subunit	ppfr-2
phosphoacetylglucosamine mutase	F21D5.1
DeHydrogenases, Short chain	dhs-19
ATP synthase subunit	atp-5

development & structure	
DAF-16/FOXO Controlled, germline Tumor affecting	dct-5
nuclear LaMiN	lmn-1
VITellogenin structural genes (yolk protein genes)	vit-5
Inorganic pyrophosphatase (PPase)	pyp-1
BLIstered cuticle	bli-3
C-type LECtin	clec-174
Tubulin, Beta	tbb-6
COLlagen	col-80
Helix Loop Helix	hlh-33
ROLler: helically twisted, animals roll when moving	rol-6
COLlagen	col-19
cuticlin	cuticlin
COLlagen	col-8
LAMinin related. See also lmb-	lam-2
ROLler: helically twisted, animals roll when moving	rol-8

Histone	
HIstone H1 Like	hil-3
HIStone	his-24

transcription and splicing	
RNA-dependent RNA polymerase Family	rrf-3
U2AF splicing factor	uaf-1

unknown	
hypothetical protein	ZK105.1
hypothetical protein	F25H5.8
hypothetical protein	C45B2.1
hypothetical protein	C45B2.8
hypothetical protein	C38D9.2
hypothetical protein	F53F8.4
hypothetical protein	F43C11.3
hypothetical protein	C42D4.3
hypothetical protein	T05A7.1
hypothetical protein	T27F6.8
hypothetical protein	Y105C5A.8
hypothetical protein	T04F8.8
hypothetical protein	F14D7.7
hypothetical protein	C54D10.10
hypothetical protein	R05H10.1
hypothetical protein	C25H3.10
hypothetical protein	C34F11.8
hypothetical protein	E04F6.6
hypothetical protein	C18H9.5
hypothetical protein	T28H10.2
hypothetical protein	M162.5
hypothetical protein	C34C6.7
hypothetical protein	F26A1.9
hypothetical protein	F18E9.3
hypothetical protein	Y53H1B.2
hypothetical protein	W03D2.9
hypothetical protein	C06C3.4
hypothetical protein	C06H5.7
hypothetical protein	H10E21.2
hypothetical protein	C04F12.1
hypothetical protein	Y52B11A.8
hypothetical protein	F53E4.1
hypothetical protein	C06C3.4
hypothetical protein	Y48B6A.6
hypothetical protein	F47B8.8
hypothetical protein	Y39A3CR.5

transport	
sodium-dependent phosphate transporter	zk563.2
(Zwei) IG-domain protein	zig-3
TransThyretin-Related family domain	ttr-32
TransThyretin-Related family domain	ttr-15
UNCoordinated	unc-30
lin-15a like protein	T25B9.8 Y70D2A.
7 transmembrane receptor (rhodopsin family)	

protein	
Prion-like-(Q/N-rich)-domain-bearing protein	pqn-75 EEED8.1
Probable RNA binding protein	
alpha-1-macroglobulin-like domain	F13D2.1
Bacterially Un-Swollen (M. nematophilum resistant)	bus-19
Prion-like-(Q/N-rich)-domain-bearing protein	pqn-83
Defective in Cullin Neddylation	dcn-1
LC3, GABARAP and GATE-16 family	lgg-2
GEX Interacting protein	gei-16

NHRs	
Nuclear Hormone Receptor family	nhr-11
Nuclear Hormone Receptor family	nhr-80
Nuclear Hormone Receptor family	nhr-205
Nuclear Hormone Receptor family	nhr-120
Nuclear Hormone Receptor family	nhr-127
Nuclear Hormone Receptor family	nhr-42

degradation and cell death	
Cell Division Cycle related	cdc-42
F-box C protein	fbxc-40

hypothetical protein	F16A11.1
hypothetical protein	F53C3.13
hypothetical protein	F47G3.1
hypothetical protein	F46H5.2
hypothetical protein	Y45F10D.7
hypothetical protein	C55A6.12
hypothetical protein	M02B1.3
hypothetical protein	Y71H2AM.19
hypothetical protein	T07F12.1
hypothetical protein	Y105E8A.3
hypothetical protein	T19A5.3
hypothetical protein	T13H5.6
hypothetical protein	T19C3.1
hypothetical protein	W02F12.2
hypothetical protein	F47G3.1
hypothetical protein	R08E5.4
hypothetical protein	C45E1.4
hypothetical protein	C07C7.1
hypothetical protein	M57.1
hypothetical protein	R07B1.9
hypothetical protein	C52E12.4
hypothetical protein	ZC416.2
hypothetical protein	B0212.3, M57.1
hypothetical protein	Y58G8A.4
hypothetical protein	F17C11.9
hypothetical protein	Y57G7A.5
hypothetical protein	T28F12.1
hypothetical protein	BE10.2
hypothetical protein	F29B9.8

Table S9. Categories of the genes whose expression is upregulated in *blmp-1* compared to wild type N2.

signaling	
Prenylated Rab Acceptor 1 domain Family	praf-3
Serpentine Receptor, class H	srh-193
Seven TM Receptor	str-229
Serpentine Receptor, class H	srh-69
SCAMP (synaptic vesicle protein) homolog	scm-1
SERotonin/octopamine receptor family	ser-3
Src homology domain 2	K11E4.2
CARMIL (Capping, ARp2/3, Myosin I Linker protein) homolog	crml-1
WaRThog (hedgehog-like family)	wrt-4

metabolism	
protein KINase	kin-1
IRE1 kinase related	ire-1
glutaminase	glutaminase
LIPaSe related	lips-8
serine/threonine kinase	ZK596.2
PIP Kinase /	ppk-1
acetoacetyl CoA thiolase	T02G5.7
Glycogen Synthase	gsy-1
AminoPeptidase P	app-1
Acyl-Coenzyme A Binding Protein	acbp-1
TOPoisomerase	top-1
DeHydrogenases, Short chain	dhs-12
Alkyl-Dihydroxyacetonephosphate Synthase	ads-1
UDP-GlucuronosylTransferase	ugt-21
Myotonic dystrophy-Related, Cdc42-binding Kinase homolog	mrck-1
Glutathione S-Transferase	gst-39
Glutathione S-Transferase	gst-16
Serine Palmitoyl Transferase famiLy	sptl-2
Zinc-binding dehydrogenases	F39B2.3
UDP-GlucuronosylTransferase	ugt-12
AdaPtin, Gamma chain (clathrin associated complex)	apg-1
DeHydrogenases, Short chain	dhs-3
CYtochrome P450 family	cyp-13A11, cyp-13A12
Enoyl-CoA Hydratase	ech-5
Glutathione S-Transferase	gst-7
PeRoXisome assembly factor	prx-11
CaSeiN Kinase	csnk-1

development	
LEVamisole resistant	lev-11
AQuaPorin or aquaglyceroporin related	aqp-11
AQuaPorin or aquaglyceroporin related	aqp-3
abnormal cell LINeage	lin-5
BLIstered cuticle	bli-1
CUTiclin-Like	cutl-28

transport	
NUMb related	num-1
Na-K-Cl Cotransporter homolog	nkcc-1
ARF-Like G protein	arl-5
Nuclear Pore complex Protein	npp-12
Nuclear Pore complex Protein	npp-9

unknown	
hypothetical protein	Y73E7A.6
hypothetical protein	Y37E11AL.5
hypothetical protein	Y52B11A.4
hypothetical protein	F19B2.7
hypothetical protein	ZK1098.5
hypothetical protein	C29H12.6
hypothetical protein	F01F1.15
hypothetical protein	W04C9.2
hypothetical protein	F48C1.6
hypothetical protein	C16C8.8
hypothetical protein	F54B3.1
hypothetical protein	R12C12.6
hypothetical protein	W09B6.5
hypothetical protein	C08D8.1
hypothetical protein	Y54E10BR.1
hypothetical protein	F41C3.4
hypothetical protein	C14A4.6
hypothetical protein	F10C2.7
hypothetical protein	F37H8.3
hypothetical protein	Y119C1B.5
hypothetical protein	F13H10.3
hypothetical protein	Y71H2AM.1
hypothetical protein	K08A2.4

AMine oXidase family	amx-3
Protein PHosphatase	pph-6
PMR-type Golgi ATPase	pmr-1
Protein Kinase C	pkc-1
Glutathione S-Transferase	F56A4.3(gst-10)
LIPaSe related	lips-14
glycosyltransferase	glycosyltransferase
Carnitine Palmitoyl Transferase	cpt-6
CYtochrome P450 family	cyp-29A2
Enoyl-CoA Hydratase	ech-6

degradation	
F-box B protein	fbxb-33
F-box A protein	fbxa-6

calcium	
SERCA (Sarco-Endoplasmic Reticulum Calcium ATPase)	sca-1

protein	
FK506-Binding protein family	fkb-1
Prion-like-(Q/N-rich)-domain-bearing protein	pqn-36
GLoBin	glb-33
Actin-binding protein	C07A9.5
EH (Eps-15-homology) domain Binding Protein family	ehbp-1
BED-type zinc finger transcription factor	bed-2
Ezrin/Radixin/Moesin	erm-1
SKiNhead	skn-1
SInA (Drosophila Seven In Absentia) Homolog	siah-1
MIF (macrophage migration inhibitory factor) related	mif-3
Oxysterol Binding protein (OSBP) Related	obr-2
RHO (small G protein) family	rho-1
Zinc finger protein (BED class)	zbed-6

NHRs	
Nuclear Hormone Receptor family	nhr-81
Nuclear Hormone Receptor family	nhr-207
Nuclear Hormone Receptor family	nhr-244, nhr-74

hypothetical protein	F59E11.5
hypothetical protein	C05E11.3
hypothetical protein	F18A11.3
hypothetical protein	W05F2.7
hypothetical protein	T23E7.2
hypothetical protein	C14A4.7
hypothetical protein	Y54E10BR.5
hypothetical protein	B0041.5
hypothetical protein	T14G8.3
hypothetical protein	T13C5.8
hypothetical protein	M03F8.4
hypothetical protein	ZK858.6
hypothetical protein	K01A2.5
hypothetical protein	Y7A5A.1
hypothetical protein	F36G9.3
hypothetical protein	F52B11.2
hypothetical protein	C25F9.9
hypothetical protein	Y75B8A.7
hypothetical protein	Y25C1A.5
hypothetical protein	Y73C8B.2
hypothetical protein	F53C11.1
hypothetical protein	K10D11.2
hypothetical protein	E01A2.7
hypothetical protein	F58G6.3, F58G6.7
hypothetical protein	F17A9.5
hypothetical protein	Y73C8B.3
hypothetical protein	ZK896.4
hypothetical protein	Y80D3A.9
hypothetical protein	Y46G5A.20
hypothetical protein	Y54G2A.10
hypothetical protein	F28G4.2
hypothetical protein	R05A10.6
hypothetical protein	T20D4.3, T20D4.4
hypothetical protein	F59B10.5
hypothetical protein	C01F1.5
hypothetical protein	K09B11.9
hypothetical protein	F25E5.3
hypothetical protein	C49G9.1

autophagy	
AuTophaGy (yeast Atg homolog)	atg-16.1
BEClin (human autophagy) homolog	bec-1

hypothetical protein	C34B2.10

Table S10. Categories of the genes whose expression is downregulated in *blmp-1* compared to wild type N2.

qPCR primers	
name	sequence
ama-1	5`-ggacgacgtgttcctacgat-3`
	5`-aacgcggtaccatcagtttc-3`
inf-1	5`-cgtgcaaggtctcgttatgg-3`
	5`-gagggcgctcatgacctt-3`
blmp-1	5`-ctcaaacaacagccgcaata-3`
	5`-gctggagacgcagatgtgta-3`
nhr-23	5`-ctacgactccaatgccacag-3`
	5`-aggatccacgttacaaactcc-3`
ptr-4	5`-atgacaaggctatggatgacg-3`
	5`-ggcatcgtagaagtaactggg-3`
ChIP PCR primers	
name	sequence
nhr-23 #1	5`-gcgaacgaagggttgtgtat-3`
	5`-aagtttcgcgcaaagttcat-3`
nhr-23 #2	5`-gacgacatgcgaggtaggtc-3`
	5`-ggcagagtgaccgtgaaata-3`
ptr-4 #1	5`-ttcaatctttccgcgtatcc-3`
	5`-acgaaaatcatcgggaactg-3`
ptr-4 #2	5`-tggatccaatgcagaaatga-3`
	5`-actccgtcagtatgggttgc-3`

Table S11. Olignucelotide for qPCR and Chip-PCR.