

SUPPLEMENTARY TABLES

Supplementary Table 1. List of remaining mutations in backcrossed strains.

Chrom.	Pos.	Ref.	Alt.	Gene	Mutation type	Effect*
I	3258592	CA	C	<i>Y54E10A.20</i>	upstream gene variant	modifier
I	8160530	TTATA	T	<i>T28B8.3</i>	downstream gene variant	modifier
I	10731034	C	T	<i>rpn-10</i>	missense variant	moderate
I	10766899	C	T	<i>daf-16</i>	intron variant	modifier
I	10974485	C	T	<i>Y52B11A.3</i>	intron variant	modifier
I	11307424	C	T	<i>H25P06.5</i>	synonymous variant	low
I	11536456	C	T	<i>dys-1</i>	splice acceptor variant	high
I	11644705	C	T	<i>W04G5.9</i>	intron variant	modifier
I	11726250	C	T	<i>F35E2.9</i>	missense variant	moderate
I	11808061	G	T	<i>T02G6.2-T02G6.4</i>	intergenic region	modifier
I	11832340	C	T	<i>Y47H9C.1</i>	missense variant	moderate
I	11864150	T	A	<i>ced-1</i>	intron variant	modifier
I	11896398	C	T	<i>Y47H9C.12</i>	upstream gene variant	modifier
I	11914682	C	T	<i>hda-3</i>	missense variant	moderate
I	11927975	C	T	<i>wve-1</i>	upstream gene variant	modifier
I	12008815	C	T	<i>fbxa-122</i>	downstream gene variant	modifier
I	12176794	C	T	<i>R05D7.3</i>	intron variant	modifier
I	12298210	C	T	<i>F56H6.7</i>	missense variant	moderate
I	12341691	C	T	<i>nhr-217</i>	intron variant	modifier
I	12343381	T	A	<i>T09E11.11</i>	upstream gene variant	modifier
I	12414199	C	T	<i>E03H4.5</i>	intron variant	modifier
I	12493515	C	T	<i>T27F6.6</i>	synonymous variant	low
I	12970406	G	A	<i>EIF-6</i>	downstream gene variant	modifier
I	14083393	A	C	<i>gad-6</i>	upstream gene variant	modifier
III	2340737	A	C	<i>Y54F10BM.1</i>	intron variant	modifier
III	3385124	A	AG	<i>hecw-1</i>	upstream gene variant	modifier
III	3786851	T	TTC	<i>acy-3</i>	upstream gene variant	modifier
III	6301707	T	TC	<i>F47D12.9</i>	upstream gene variant	modifier
IV	1226960	T	C	<i>W09G12.8</i>	intron variant	modifier
IV	12319292	TG	T	<i>F19B6.9</i>	downstream gene variant	modifier
IV	12319295	T	A	<i>F19B6.9</i>	upstream gene variant	modifier
IV	13506453	GA	G	<i>nlp-17</i>	upstream gene variant	modifier
IV	13823462	A	AACTCGGCTGTCG GCTGGCGCCGACA GCCGATCCATTTCC GCT	<i>H08M01.74</i>	downstream gene variant	modifier
V	363225	C	CTACTGTAGTGCTT GTGTCGATTTACGG GATCGATTTCCCTAA ATGAACCGTAAATC GACACAAGCACTA CAGTAGTCATTTAA AGGAT	<i>T22H9.1</i>	intron variant	modifier
V	1500601	G	A	<i>sru-27</i>	missense variant	moderate
V	13231585	T	G	<i>C34D1.8</i>	downstream gene variant	modifier
V	13697695	C	T	<i>T01D3.1</i>	missense variant	moderate
X	1519515	A	ATCCGACATTTTAA TAGCAATGCGCA G AACCCAAAAAATG TCGGACGCGGAGC CAAGGCTGCA CCA AATAGTGCATAG GGIATGGCATTIATT TGGTGCAAACCTTG GCTTCGCG	<i>toca-1</i>	intron variant	modifier
X	2008595	TA	T	<i>Y40A1A.1-Y102A11A.9</i>	intergenic region	modifier
X	3314891	A	AT	<i>F11D5.12</i>	upstream gene variant	modifier
X	4241974	A	G	<i>W01H2.1</i>	upstream gene variant	modifier
X	4674025	G	GT	<i>F16H11.1</i>	downstream gene variant	modifier
X	6357781	C	CCCAT	<i>C03B1.10</i>	frameshift variant	high
X	8191585	G	GT	<i>C17H11.6</i>	intron variant	modifier
X	11646516	A	C	<i>T04F8.15</i>	upstream gene variant	modifier

X 12502801 T TACGAAAATAGA *sdz-19* intron variant modifier
TTGTAC

Candidate causative mutation sites for the OF1262 strain.

*Putative impact of mutation as categorized by snpEff: high (splice site variant, frameshift variant) > moderate (missense variant) > low (synonymous variant) > modifier (upstream gene variant (5'UTR), downstream gene variant (3'UTR), intron variant, intergenic variant).

Supplementary Table 2. Average read counts and *p* values of downregulated region on Chromosome II.

Gene	Chr	Start	Strand	Avg Read Count WT	Avg Read Count OF1263	Avg Read Count OF1350	<i>p</i> value OF1263 vs. WT	<i>p</i> value OF1263 vs. OF1350
<i>F59H6.3</i>	II	2017450	+	544.3333333	503.75	617.5	0.850896676	0.560942062
<i>F59H6.2</i>	II	2019654	+	46.33333333	37.25	57	0.945386699	0.48335894
<i>cya-2</i>	II	2022673	-	647.6666667	145.75	342.25	0.000111143	0.017196088
<i>bath-21</i>	II	2014902	-	500.3333333	85.75	492.5	0.00000122	0.00000011
<i>bath-1</i>	II	2027612	-	1753	233	2190.75	2.69E-10	5.06E-14
<i>bath-3</i>	II	2029236	-	548.6666667	248.5	902	0.044371025	0.000061
<i>bath-5</i>	II	2030753	-	7225.666667	2460.75	8269.75	0.000945556	0.0000203
<i>btb-4</i>	II	2032316	+	2886	456.5	1612	0.00000698	0.000828007
<i>F59H6.14</i>	II	2033586	+	48.33333333	15	23.25	0.025843936	0.342383526
<i>F59H6.13</i>	II	2034351	-	0	0	0	1	1
<i>bath-19</i>	II	2035695	-	1246	730.25	1966.25	0.30014777	0.004494907
<i>bath-20</i>	II	2040276	-	101	40.75	77.5	0.104265019	0.179052293
<i>btb-3</i>	II	2043089	-	157.3333333	95.5	249.75	0.456879336	0.022200842
<i>bath-24</i>	II	2044619	-	1507.333333	412.5	1697.5	0.0000992	0.0000024
<i>math-1</i>	II	2046053	-	27.66666667	8.5	17	0.182230378	0.324120223
<i>bath-14</i>	II	2048061	-	218	84.5	301.75	0.065982827	0.001813642
<i>F07E5.4</i>	II	2050023	-	0	0	2	1	0.199767663
<i>fbxb-35</i>	II	2051672	+	43.66666667	151.75	109.5	0.00256399	0.393136077
<i>F07E5.5</i>	II	2053919	-	6974.666667	7446.25	9206.5	0.400658623	0.389501995

Supplementary Table 3. INTERPRO analysis of protein domain enrichment in genes downregulated in OF1263 strain vs. OF1350 and WT.

Category	Term	Count	%	PValue	Genes
INTERPRO	IPR002083:MATH	8	3.61991	3.62E-05	WBGENE00020532, WBGENE00019139, WBGENE00015014, WBGENE00019138, WBGENE00018223, WBGENE00022690, WBGENE00019141, WBGENE00019140
INTERPRO	IPR000210:BTB/POZ-like	7	3.167421	0.004653	WBGENE00019139, WBGENE00015014, WBGENE00019138, WBGENE00018223, WBGENE00019142, WBGENE00019141, WBGENE00019140
INTERPRO	IPR002486:Nematode cuticle collagen, N-terminal	9	4.072398	4.20E-04	WBGENE00000712, WBGENE00000615, WBGENE00000703, WBGENE00001066, WBGENE00000660, WBGENE00000256, WBGENE00000685, WBGENE00000753, WBGENE00000678

INTERPRO	IPR001304:C-type lectin	9	4.072398	0.003387	WBGENE00021586, WBGENE00021873, WBGENE00014063, WBGENE00021587, WBGENE00009397, WBGENE00012583, WBGENE00007805, WBGENE00020191, WBGENE00009517
INTERPRO	IPR013781:Glycoside hydrolase, catalytic domain	4	1.809955	0.039608	WBGENE00016340, WBGENE00020509, WBGENE00016335, WBGENE00044807
INTERPRO	IPR008758:Peptidase S28	3	1.357466	0.006103	WBGENE00017594, WBGENE00003959, WBGENE00019682
INTERPRO	IPR009072:Histone-fold	6	2.714932	0.003181	WBGENE00001935, WBGENE00001947, WBGENE00001934, WBGENE00001937, WBGENE00001921, WBGENE00001899

Supplementary Table 4. List of strains used in this study.

Strain	Genotype	Obtained from
OF1262	<i>hda-3(ix241);dys-1(ix259) I</i>	Isolated in previous study (Kawamura and Maruyama, 2019); Also referred to as <i>ix241</i>
OF1263	<i>hda-3(ix241);dys-1(ix259) I</i> (4x backcrossed)	Isolated in previous study (Kawamura and Maruyama, 2019); Also referred to as <i>ix241</i> (4x BC)
OF1350	<i>dys-1(ix259) I</i> (5x backcrossed)	This study. Independent CRISPR strain from OF1354 (Same injection mixture).
OF1353	<i>hda-3(ix260);dys-1(ix259) I</i> #1	This study. Independent CRISPR strain from OF1353 (Same injection mixture).
OF1354	<i>hda-3(ix260);dys-1(ix259) I</i> ; #2	This study. Independent CRISPR strain from OF1356 (Same injection mixture).
OF1355	<i>hda-3(ix261) I</i> (2x backcrossed) #1	This study. Independent CRISPR strain from OF1355 (Same injection mixture).
OF1356	<i>hda-3(ix261) I</i> (2x backcrossed) #2	This study. Independent CRISPR strain from OF1355 (Same injection mixture).
RB1618	<i>hda-3(ok1991) I</i>	CGC
CF1038	<i>daf-16(mu86) I</i>	CGC
PS3551	<i>hsf-1(sy441) I</i>	CGC
LS292	<i>dys-1(cx18) I</i>	CGC
BZ33	<i>dys-1(eg33) I</i>	CGC

List of strain, genotype, and source of *C. elegans* used in this study.

Supplementary Table 5. List of primers used in this study.

Primer name	5'-3' Sequence
<i>dys-1(ix259) 5'</i>	atggcatgatgggtgcaaatgaa
<i>dys-1(ix259) 3'</i>	cagaaaggctccaccagtcggttg
<i>hda-3(ix241) 5'</i>	ggaatttgaatttccggcaaatgtgcgaatggca
<i>hda-3(ix241) 3'</i>	tccacgaggagtacacgagagcttctctgtaa
<i>bath-1</i> qpcr 5'	ggttatcgtatgatgacgtg
<i>bath-1</i> qpcr 3'	gagacaagacttttcaaatgtcc
<i>bath-21</i> qpcr 5'	tttcagaaagtctctgcctc
<i>bath-21</i> qpcr 3'	caaccgtgcatcatctatagc
<i>bath-24</i> qpcr 5'	tgcgattgatgattctaccatcg
<i>bath-24</i> qpcr 3'	gagaggcaaacggtttcaaat

<i>pmp-3</i> qpcr 5'	tgcccgatgatggtgcgc
<i>pmp-3</i> qpcr 3'	acgaacaatgccaaggccagc

List of primers used for genotyping and qPCR.

Supplementary Table 6. List of single-stranded oligodeoxynucleotide sequences used in this study.

ssODN name	5'-3' sequence
<i>hda3(ix241)</i> repair to WT	CCATAAGTAGTCAAATTGAATACTCCTAGTCGATCTCC TGCCAATGAATCGGCACCA CATTGGA GCA CAA
<i>hda3(ix241)</i> mutation introduction	CCATAAGTAGTCAAATTGAATACTTCTAGTCGATCTCCTG CCAGTGAATCGGCACCA CATTGGA GCACAA

List of single-stranded oligodeoxynucleotide sequences used to repair the *hda-3(ix241)* allele to WT and to re-introduce the *hda-3(ix241)* allele into the WT background.