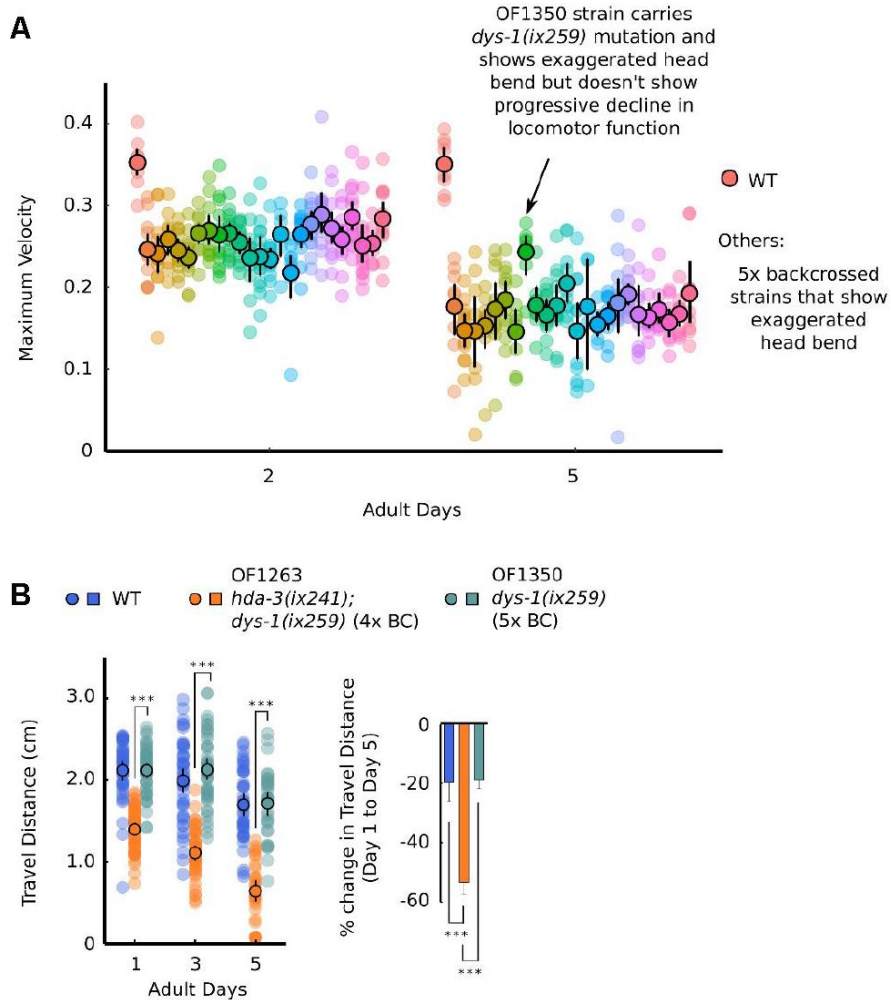
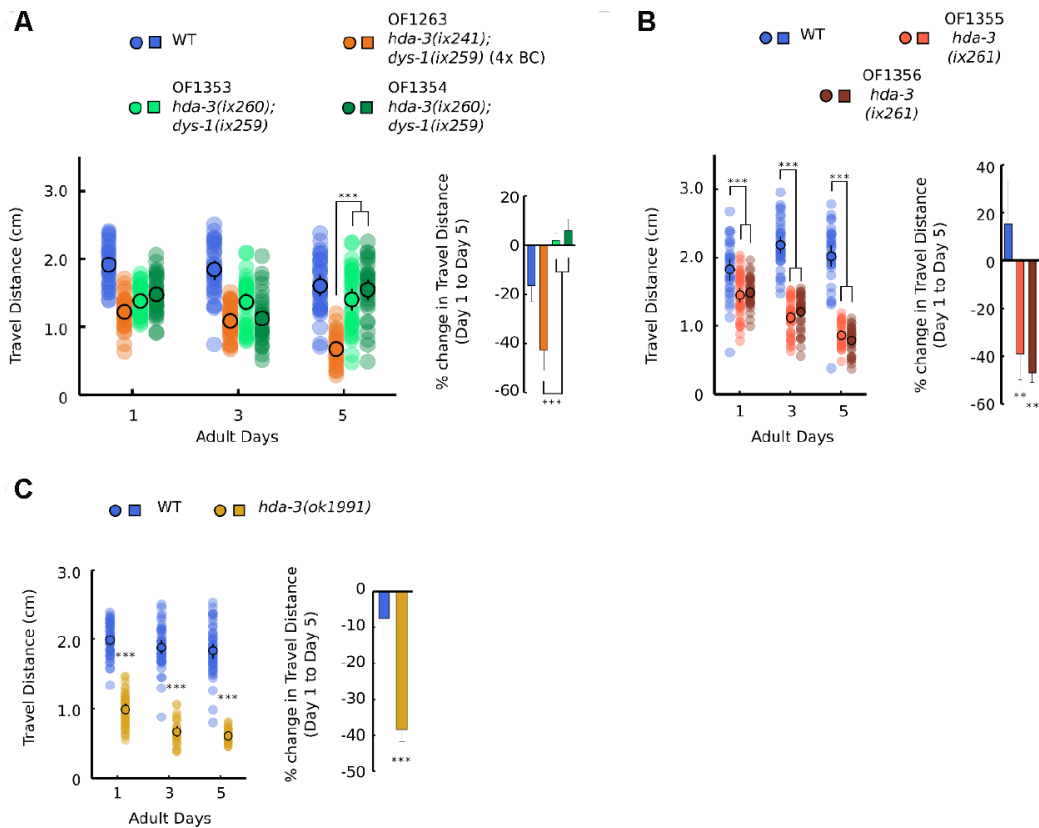


SUPPLEMENTARY FIGURES



Supplementary Figure 1. *dys-1(ix259)* mutation does not cause progressive decline in locomotor ability. (A) Maximum velocities of 24 strains that show the exaggerated head bending phenotype after the fifth backcross on the second and fifth days of adulthood. N = 10–15 worms per strain. (B) (Left) Travel distances of WT, OF1263 *hda-3(ix241);dys-1(ix259)* (4x BC), and OF1350 *dys-1(ix259)* (5x BC) worms. N = 30–45 worms per strain for each day (10–15 worms from 3 biological replicate plates). (Right) Percent change in travel distance of WT, OF1263, and OF1350 worms. N = 3 biological replicate plates. *** $P < 0.001$.

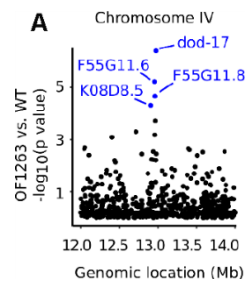


Supplementary Figure 2. *hda-3* mutation causes progressive decline in locomotor ability. (A) (Left) Travel distances of WT, OF1263 *hda-3(ix241);dys-1(ix259)* (4x BC), OF1353 *hda-3(ix260);dys-1(ix259)* and OF1354 *hda-3(ix260);dys-1(ix259)* worms on adult days 1, 3, and 5. (Right) Percent change in travel distance of WT, OF1263, OF1353, and OF1354 worms on adult day 5 compared to adult day 1. (B) (Left) Travel distances of WT, OF1355 *hda-3(ix261)*, and OF1356 *hda-3(ix261)* worms on adult days 1, 3, and 5. (Right) Percent change in travel distance of WT, OF1355 *hda-3(ix261)*, and OF1356 *hda-3(ix261)* worms on adult day 5 compared to adult day 1. (C) (Left) Travel distances of WT and *hda-3(ok1991)* worms on adult days 1, 3, and 5. (Right) Percent change in travel distance of WT and *hda-3(ok1991)* worms on a dult day 5 compared to adult day 1. For travel distance measurements, N = 30–45 worms per strain for each day (10–15 worms from 3 biological replicate plates). For percent change in travel distance measurements, N = 3 biological replicate plates. ****P* < 0.001; ***P* < 0.01.

A

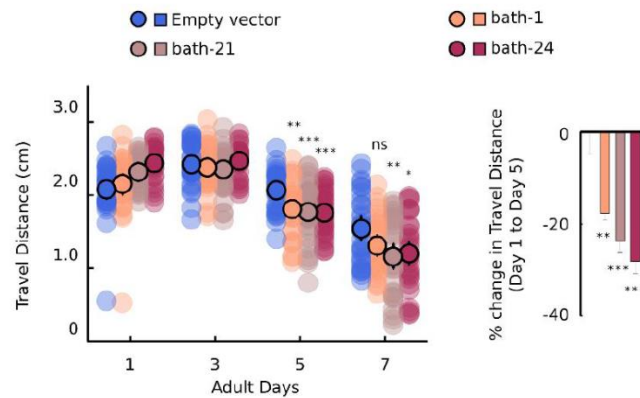
<i>C. e.</i> HDA-3	263	DSL	AGDRL	G	VFN	LT	TYG
<i>S. c.</i> HOS2	283	DSL	GHDRL	G	CFN	L	NIKA
<i>D. m.</i> HDAC3	264	DSL	AGDRL	G	CF	SL	STKG
<i>D. r.</i> HDAC3	259	DSL	GCDRL	G	CFN	L	SIRG
<i>M. m.</i> HDAC3	259	DSL	GCDRL	G	CFN	L	SIRG
<i>H. s.</i> HDAC3	259	DSL	GCDRL	G	CFN	L	SIRG

Supplementary Figure 3. Evolutionary conservation of HDA-3 G271 residue. (A) Alignment of *C. elegans* (*C. e.*) HDA-3 to *Saccharomyces cerevisiae* HOS2, *Drosophila melanogaster* HDAC3, *Danio rerio* HDAC3, *Mus Musculus* HDAC3, and *Homo sapiens* HDAC3.



Supplementary Figure 4. Genes are downregulated in a narrow region on Chromosome IV. (A) Genomic location of strongly downregulated gene transcripts on Chromosome IV in OF1263 vs. WT.

A RNAi BATH genes



Supplementary Figure 5. Knockdown of BATH genes lead to progressive decline in travel distance. (A) Travel distances of worms fed with empty vector RNAi or RNAi targeted towards *bath-1*, *bath-21*, or *bath-24*. N = 30–45 worms per strain for each day (10–15 worms from 3 biological replicate plates). *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$.