

## Expanded View Figures

### Figure EV1. The MYS-1 HAT complex regulates longevity in *Caenorhabditis elegans*.

- A Survival curves of the indicated RNAi-treated N2 worms under AL and IF are shown [control RNAi,  $n = 117$  (AL), 167 (IF); *let-363* RNAi,  $n = 98$  (AL), 101 (IF); *atl-1* RNAi,  $n = 125$  (AL), 162 (IF); *atm-1* RNAi,  $n = 117$  (AL), 136 (IF); *smg-1* RNAi,  $n = 103$  (AL), 138 (IF)]. The bars represent the mean lifespan from three independent experiments.  $n$ , total number of worms in three independent experiments. Error bars, SD \*\*\* $P < 0.001$ , one-way ANOVA followed by Tukey's test.
- B Survival curves of the N2, *trr-1(n3630)* mutants and *mys-1(n4075)* mutants under AL and IF are shown [N2,  $n = 60$  (AL), 54 (IF); *trr-1(n3630)* mutants,  $n = 59$  (AL), 50 (IF); *mys-1(n4075)* mutants,  $n = 60$  (AL), 58 (IF)]. The bars represent the mean lifespan from two independent experiments.  $n$ , total number of worms in two independent experiments.
- C Survival curves of the indicated RNAi-treated N2 worms under AL and IF are shown [control RNAi,  $n = 88$  (AL), 83 (IF); *trr-1* RNAi,  $n = 87$  (AL), 77 (IF); *mys-1* RNAi,  $n = 84$  (AL), 81 (IF)]. To avoid potential developmental abnormalities, RNAi feeding was started at the young adult stage to day 2 adulthood. The bars represent the mean lifespan from three independent experiments.  $n$ , total number of worms in three independent experiments. Error bars, SD \*\*\* $P < 0.001$ , n.s., not significant; one-way ANOVA followed by Tukey's test.
- D The value of the control RNAi-treated worms at day 2 was set to 100. The bars represent the mean body movement from three independent experiments ( $n = 90$  in every condition at each stage).  $n$  is a total of three independent experiments. Error bars, SD \*\*\* $P < 0.001$ , n.s., not significant; one-way ANOVA followed by Tukey's test.
- E Whole-cell lysates isolated from HeLa cells and whole-worm lysates isolated from N2 and *mys-1(n4075)* mutants were subjected to immunoblot analysis using an antibody against human Tip60. This antibody recognizes both human Tip60 and *C. elegans* MYS-1 (lanes 1 and 3, respectively); however, the band at 60 kDa was not found in the *mys-1(n4075)* deletion mutant (lane 2). See also Table EV1.

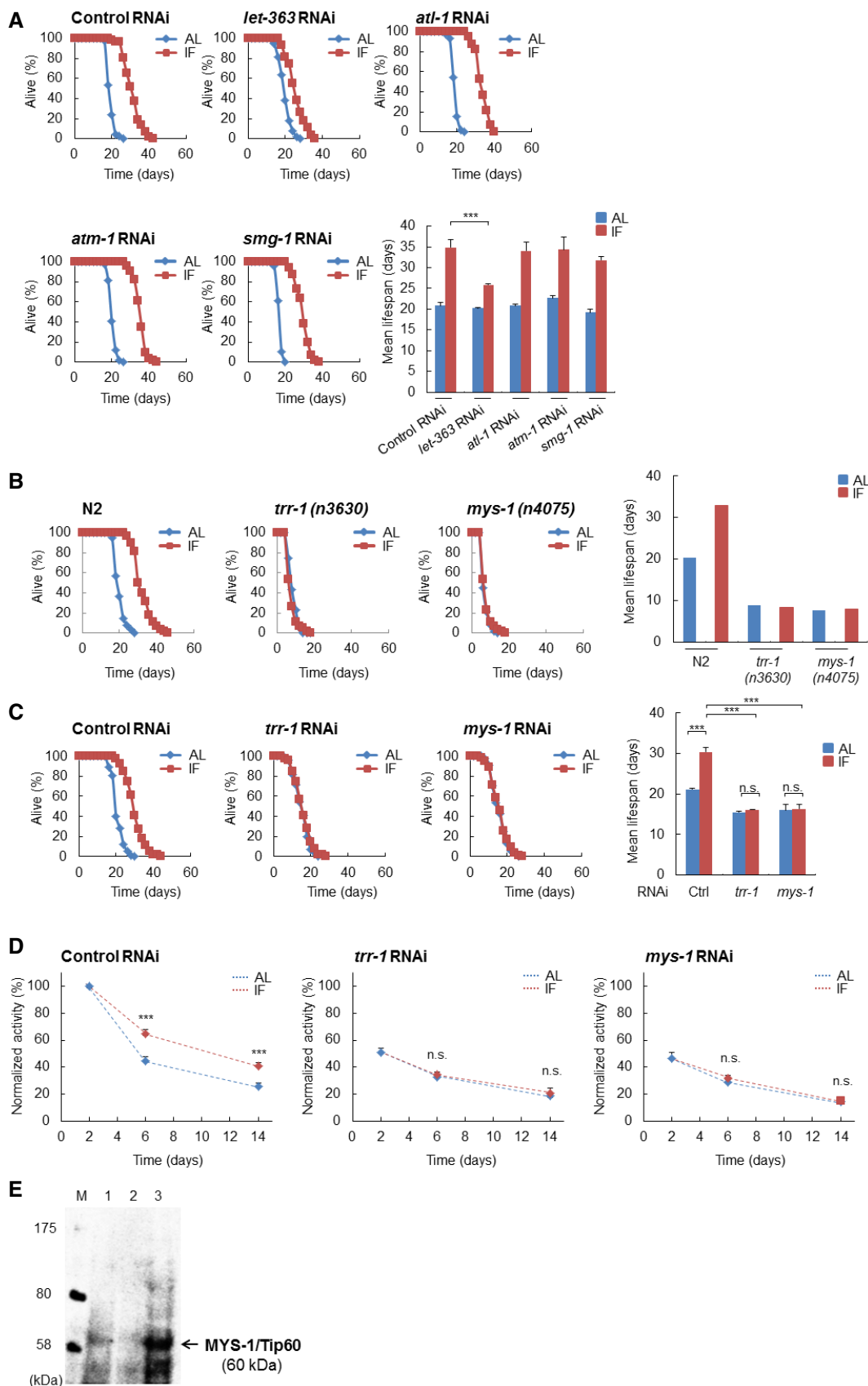
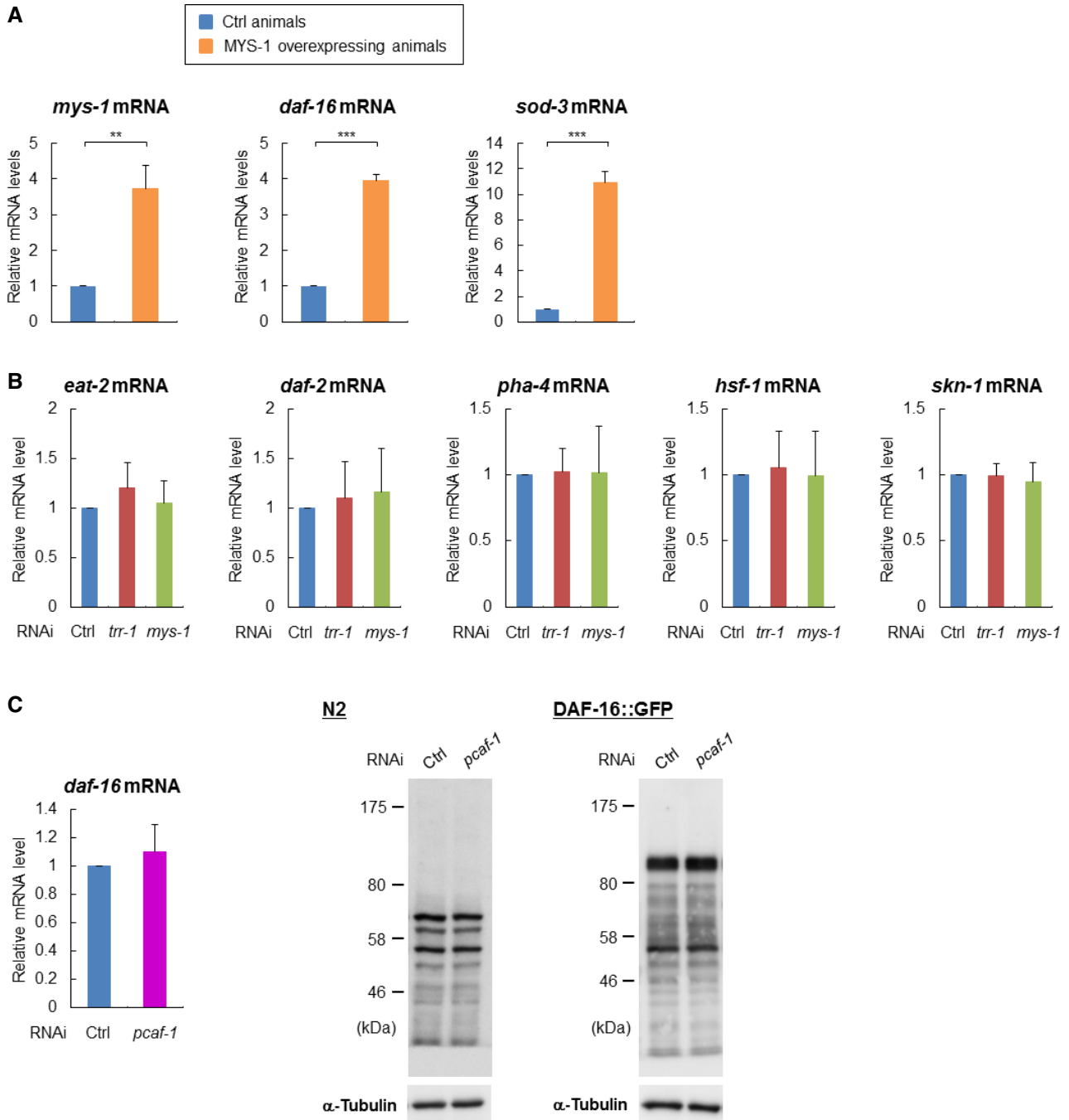
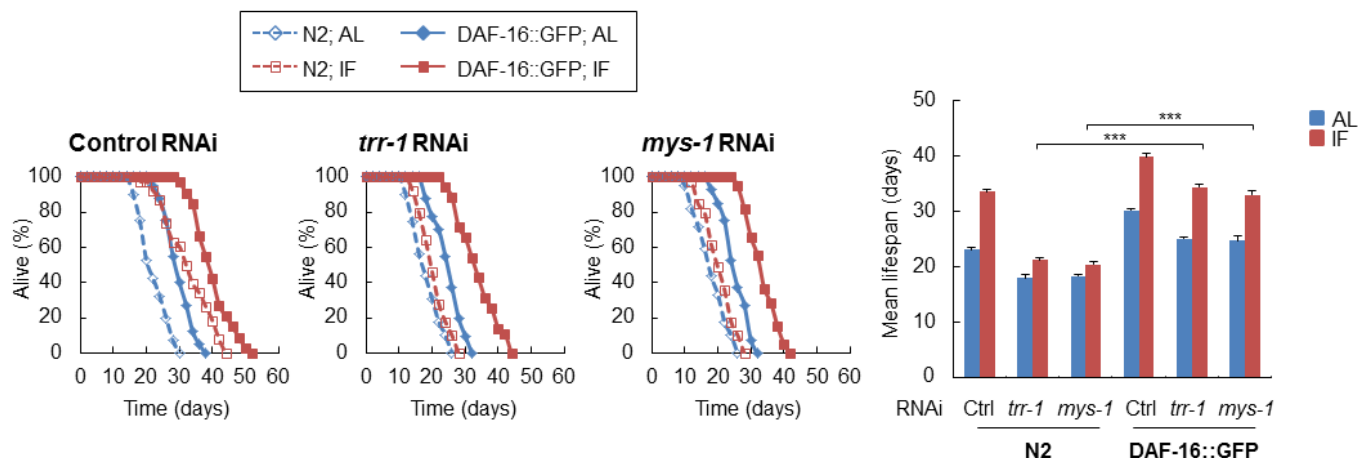


Figure EV1.



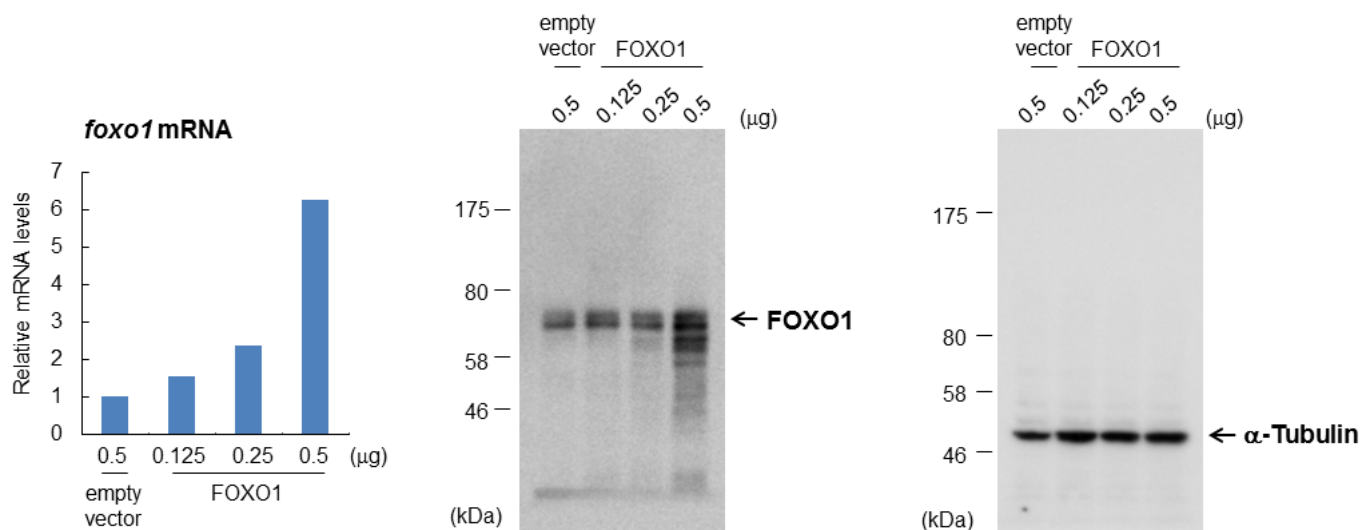
**Figure EV2. The MYS-1 HAT complex regulates the expression of DAF-16 but not other well-known genes involved in lifespan regulation.**

- A Total RNA was extracted from the control or MYS-1-overexpressing worms, and the expression levels of *daf-16* mRNA or *sod-3* mRNA were determined by qRT-PCR. Error bars represent the SD derived from two independent experiments. \*\* $P < 0.01$ , \*\*\* $P < 0.001$ , one-way ANOVA followed by Tukey's test. The value of the control worms was set to 1.
- B N2 worms were treated with the indicated RNAi, and total RNA was extracted at day 2 adulthood. The level of each mRNA was determined by qRT-PCR. The value of the control RNAi-treated worms was set to 1. The bars represent the relative mRNA level from three independent experiments. Error bars, SD.
- C Total RNA was extracted from the indicated RNAi-treated N2 worms at day 2 adulthood, and the expression level of *daf-16* mRNA was determined by qRT-PCR. Error bars represent the SD derived from three independent experiments. The value of the control RNAi-treated worms was set to 1 (left). Worm extracts from the indicated RNAi-treated N2 worms or DAF-16::GFP worms at day 2 adulthood were subjected to immunoblot analysis using an anti-DAF-16 antibody, respectively (right). Representative images of two independent experiments are shown.



**Figure EV3. DAF-16 overexpression rescues the defects in *trr-1*/*mys-1* RNAi worms.**

Survival curves of the indicated RNAi-treated N2 (dashed line) or DAF-16::GFP (solid line) worms under AL and IF are shown (left) [control RNAi,  $n = 80$  (N2 in AL), 74 (N2 in IF), 117 (DAF-16::GFP in AL), 99 (DAF-16::GFP in IF); *trr-1* RNAi,  $n = 79$  (N2 in AL), 77 (N2 in IF), 120 (DAF-16::GFP in AL), 109 (DAF-16::GFP in IF); *mys-1* RNAi,  $n = 75$  (N2 in AL), 77 (N2 in IF), 118 (DAF-16::GFP in AL), 108 (DAF-16::GFP in IF)]. The bars represent the mean lifespan of three independent experiments (right).  $n$ , total number of worms in three independent experiments. Error bars, SD, \*\*\* $p < 0.001$ , one-way ANOVA followed by Tukey's test.



**Figure EV4. Overexpression of FOXO1.**

HeLa cells were transfected with the indicated plasmid, and each sample was subjected to qRT-PCR (left) or immunoblot analysis (middle and right). The value of the control vector-transfected cells was set to 1. Data from one experiment are shown.