

Expanded View Figures

Figure EV1. Effect of DAF-2/insulin-like receptor and feeding status on ascr#3 avoidance.

A Fraction reversing of wild-type animals exhibiting short reversal (left) and omega turn under different feeding conditions (right). n = 40-80.

B Fraction reversing of wild-type animals and *eat-2* mutants, *daf-2* mutants, and *eat-2;daf-2* double mutants under fed conditions. *n* = 80–110. ***P* < 0.01 and *****P* < 0.0001 (Dunnett's Test).

C Fraction reversing of daf-2 alleles, e1368, and e1370 in response to 500 nM ascr#3 in fed conditions. n = 50-70. **P < 0.01 and ***P < 0.001 (Dunnett's test).

- D Fraction reversing of wild-type and daf-2 mutant animals on on-food or off-food conditions. n = 30-50. *P < 0.05 (Bonferroni's test).
- E The number of transgenic animals expressing *sre-1p::gfp* in ADL and ASJ. n = 31.

Data information: All error bars represent $\pm\,$ SEM.



Figure EV2. Quantification of SNB-1::YFP and mCherry::RAB-3 and gene expression of sre-1 promoter upon daf-2 mutation or starvation.

- A Relative fluorescence intensity of integrated animals expressing sre-1p::snb-1 cDNA::yfp. n = 30. ***P < 0.0001 (unpaired Student's t-test).
- B, C Quantification of fluorescence intensity of wild-type and *daf-2* mutant animals expressing *sre-1p::snb-1* cDNA:*yfp* (B) and *sre-1p::mCherry::rab-3* cDNA (C) analyzed using ImageJ software. *n* = 13–41. ****P* < 0.001 (unpaired Student's *t*-test).
- D Relative fluorescence intensity of daf-2 mutants expressing *sre-1p::gfp. n* = 50.
- E Relative fluorescence intensity of transgenic animals expressing sre-1p::mCherry in fed and starved conditions. n = 29–35.
- F Relative fluorescence intensity of wild-type and *daf*-2 mutant animals expressing *sre*-1p::*ocr*-2 genome::*mcherry*. *n* = 41.

Data information: All error bars represent \pm SEM. Tops and bottoms of boxes indicate the 25th and 75th percentiles, respectively; whiskers represent 10th-90th percentile. Median is indicated by a horizontal line, and the average is marked by "+" in the box.



Figure EV3. ascr#3 avoidance behaviors of daf-16 mutants and of skn-1 mutants.

A, B Fraction reversing of *daf-16* mutants (A) and *skn-1* mutants (B) in response to 100, 200, and 400 nM ascr#3 under fed conditions. (A) n = 60, *P < 0.05 (Bonferroni's test). (B) n = 40-50.

Data information: All error bars represent $\pm\,$ SEM.

Α





Figure EV4. Expression pattern of acd-5 promoter in the intestine and neuronal rescue of ins-18 phenotype.

- A A representative image of a transgenic animal expressing acd-5p::gfp. Scale bar is 10 μm.
- B Fraction reversing of wild-type animals, ins-18 mutants, and ins-18 mutants expressing su006(rgef-1)p::ins-18 cDNA::gfp (neuron). n = 30-40. *P < 0.05 and **P < 0.01 (Dunnett's test).

Data information: Error bars represent \pm SEM.



Figure EV5. Expression of ins-18 promoter upon starvation.

Relative fluorescence intensity of expressing *ins-18p::gfp* in the intestine in 6-h and 24-h fed and starved conditions. n = 25-40. Tops and bottoms of boxes indicate the 25th and 75th percentiles, respectively; whiskers represent 10th-90th percentile. Median is indicated by a horizontal line, and the average is marked by "+" in the box.