**Supplementary Table 1. Lifespans of degron-tagged DAF-2**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Strain / **RNAi** | Mean lifespan ± S.E.M.[Days] | 75th percentile[Days] | N dead/ Initial N | % mean lifespan change to control | P-value (log-rank) vs. control |  |
| Trial 1 of DAF-2::degronknock down with 1 mM Auxin starting at L4 stage at 20°C (with FUDR). |
| N2 DMSO (0.25%) | 16.4 ± 0.3 | 19 | 111/146 |  |  |  |
| N2 Auxin (1 mM) | 18.3 ± 0.4 | 23 | 126/127 | +11 | 7e-05 |  |
| *daf-2(e1368)* DMSO (0.25%) | 18.4 ± 0.7 | 23 | 98/103 | +12 | 4e-03 |  |
| *daf-2(e1368)* Auxin (1 mM) | 24.4 ± 0.6 | 30 | 114/119 | +48 | 3e-25 |  |
| DAF-2::degronDMSO (0.25%) | 17.1 ± 0.3 | 19 | 101/124 | +4 | 2e-01 |  |
| DAF-2::degronAuxin (1 mM) | 28.5 ± 0.6 | 48 | 105/107 | +74 | 6e-35 |  |
| *P*-value and % mean lifespan change are relative to N2 DMSO (0.25%) |
| Trial 2 of DAF-2::degronknock down with 1 mM Auxin starting at L4 stage at 20°C (with FUDR). |
| N2 Auxin (1 mM) | 18.9 ± 0.6 | 23 | 42/82 |  |  |  |
| *daf-2(e1368)* Auxin (1 mM) | 22.3 ± 0.6 | 25 | 62/101 | +18 | 1e-03 |  |
| *daf-2(e1370)* DMSO (0.25%) | 33.6 ± 1 | 40 | 103/115 | +77 | 3e-23 |  |
| *daf-2(e1370)* Auxin (1 mM) | 32.1 ± 0.9 | 40 | 106/112 | +70 | 5e-20 |  |
| DAF-2::degronAuxin (1 mM) | 36.6 ± 1.3 | 47 | 91/93 | +93 | 5e-20 |  |
| DAF-2::degronAuxin (Young) (1 mM)\* | 35.3± 1.8 | 48 | 63/72 | +87 | 1e-11 |  |
|  *\**Animals that evaded dauer entry (see fig. ). *P*-value and % mean lifespan change are relative to N2 Auxin (1 mM) |
| Trial 3 of DAF-2::degronknock down with 1 mM Auxin starting at L4 stage at 20°C (with FUDR). |  |  |  |  |  | mb |
| N2 DMSO (0.25%) | 15.3 ± 0.5 | 18 | 50/82 |  |  |  |
| N2 Auxin (1 mM) | 15.6 ± 0.4 | 18 | 64/98 | +2 | 6e-01 |  |
| *daf-2(e1368)* Auxin (1 mM) | 24.6 ± 0.8 | 30 | 66/85 | +61 | 3e-15 |  |
| *daf-2(e1370)* DMSO (0.25%) | 32.5 ± 1.0 | 40 | 83/93 | +113 | 9e-27 |  |
| *daf-2(e1370)* Auxin (1 mM) | 32.7 ± 0.9 | 42 | 99/105 | +114 | 8e-32 |  |
| DAF-2::degronDMSO (0.25%) | 15.1 ± 0.4 | 18 | 66/85 | -1 | 8e-0.1 |  |
| DAF-2::degronAuxin (1 mM) | 35.8 ± 1.3 | 55 | 63/67 | +134 | 2e-24 |  |
| *P*-value and % mean lifespan change are relative to wild type (N2) DMSO  |
| Trial 4 of DAF-2::degronknock down with 1 mM Auxin starting at L4 stage at 20°C (with FUDR). |  |  |  |  |  | ce; 1h |
| N2 DMSO (0.25%) | 18.9 ± 0.3 | 22 | 274/281 |  |  |  |
| N2 Auxin (1 mM) | 20.5 ± 0.3 | 24 | 278/280 | +9 | 2e-05 |  |
| *daf-2(e1368)* DMSO (0.25%) | 30.4 ± 0.6 | 36 | 226/229 | +61 | 5e-61 |  |
| *daf-2(e1368)* Auxin (1 mM) | 29.6 ± 0.5 | 36 | 255/257 | +57 | 4e-69 |  |
| *daf-2(e1370)* DMSO (0.25%) | 35.6 ± 0.5 | 42 | 175/178 | +89 | 6e-75 |  |
| *daf-2(e1370)* Auxin (1 mM) | 36.4 ± 0.6 | 44 | 214/216 | +94 | 8e-91 |  |
| DAF-2::degronDMSO (0.25%) | 19.1 ± 0.3 | 24 | 303/315 | +1 | 4e-01 |  |
| DAF-2::degronAuxin (1 mM) | 38.3 ± 0.5 | 48 | 269/270 | +103 | 3e-111 |  |
| *P*-value and % mean lifespan change are relative to wild type (N2) DMSO |
| **Merge** of all 4 trials of DAF-2::degronknock down with 1 mM Auxin starting at L4 stage at 20°C (with FUDR). |  |  |  |  |  | kp |
| N2 DMSO (0.25%) | 17.8 ± 0.2 | 20 | 435/479 |  |  |  |
| N2 Auxin (1 mM) | 19.2 ± 0.2 | 23 | 510/587 | +8 | 2e-06 |  |
| *daf-2(e1368)* DMSO (0.25%) | 26.8 ± 0.5 | 34 | 324/332 | +51 | 5e-57 |  |
| *daf-2(e1368)* Auxin (1 mM) | 27.1 ± 0.3 | 32 | 497/562 | +52 | 1e-99 |  |
| *daf-2(e1370)* DMSO (0.25%) | 34.1 ± 0.5 | 42 | 361/386 | +92 | 1e-140 |  |
| *daf-2(e1370)* Auxin (1 mM) | 34.4 ± 0.4 | 42 | 419/433 | +93 | 5e-158 |  |
| DAF-2::degronDMSO (0.25%) | 18.1 ± 0.2 | 22 | 469/527 | +2 | 2e-01 |  |
| DAF-2::degronAuxin (1 mM) | 36.7 ± 0.4 | 50 | 528/537 | +107 | 8e-188 |  |
| *P*-value and % mean lifespan change are relative to wild type (N2) DMSO |
| P-Value matrix for **Merge** of all 4 trials

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | N2 DMSO (0.25%) | N2 Auxin (1 mM) | *daf-2(e1368)* DMSO (0.25%) | *daf-2(e1368)* Auxin (1 mM) | DAF-2::degronDMSO (0.25%) | DAF-2::degronAuxin (1 mM) | *daf-2(e1370)* DMSO (0.25%) |
| N2Auxin (1 mM) | <0.0001 |  |  |  |  |  |  |
| *daf-2(e1368)* DMSO (0.25%) | <0.0001 | <0.0001 |  |  |  |  |  |
| *daf-2(e1368)* Auxin (1 mM) | <0.0001 | <0.0001 | n.s (0.098) |  |  |  |  |
| DAF-2::degronDMSO (0.25%) | n.s (0.214) | <0.0001 | <0.0001 | <0.0001 |  |  |  |
| DAF-2::degronAuxin (1 mM) | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |  |  |
| *daf-2(e1370)* DMSO (0.25%) | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |  |
| *daf-2(e1370)* Auxin (1 mM) | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | n.s (0.557) |

Trial 1 of tissue-specific knockdown of degron-tagged DAF-2 with 0.1 mM starting at L4 stage at 20°C (with FuDR). |  |  |  |  |  | 1g |
| DAF-2::degron DMSO (0.025%) | 20.2 ± 0.4 | 23 | 106/118 |  |  |  |
| DAF-2::degronAuxin (0.1 mM) | 37.8 ± 0.8 | 53 | 109/109 | +87 | 6e-41 |  |
| Neuronal TIR1; *daf-2(bch40)* DMSO (0.025%) | 19.2 ± 0.8 | 25 | 80/84 | -5 | 9e-01 |  |
| Neuronal TIR1; *daf-2(bch40)* Auxin (0.1 mM) | 33.3 ± 0.9 | 40 | 97/98 | +65 | 2e-28 |  |
| Muscular TIR1; *daf-2(bch40)* Auxin (0.1 mM) | 16.7 ± 0.3 | 20 | 86/106 | -18 | 2e-07 |  |
| Intestinal TIR1; *daf-2(bch40)* Auxin (0.1 mM) | 27.7 ± 0.3 | 42 | 102/113 | 37 | 2e-09 |  |
| *P*-value and % mean lifespan change are relative to DAF-2::degron DMSO (0.025%) |
| Trial 2 of tissue-specific knockdown of degron-tagged DAF-2 with 0.1 mM starting at L4 stage at 20°C (with FuDR). |  |  |  |  |  | ce |
| DAF-2::degronDMSO (0.025%) | 16.5 ± 0.4 | 19 | 80/110 |  |  |  |
| DAF-2::degronAuxin (0.1 mM) | 31.3 ± 0.6 | 40 | 96/100 | +90 | 2e-37 |  |
| Neuronal TIR1; *daf-2(bch40)* DMSO (0.025%) | 21.8 ± 0.7 | 28 | 92/123 | +32 | 3e-10 |  |
| Neuronal TIR1; *daf-2(bch40)* Auxin (0.1 mM) | 27.4 ± 0.6 | 34 | 107/121 | +66 | 2e-30 |  |
| Muscular TIR1; *daf-2(bch40)* DMSO (0.025%) | 19.7 ± 0.5 | 23 | 99/114 | +20 | 6e-06 |  |
| Muscular TIR1; *daf-2(bch40)* Auxin (0.1 mM) | 20.1 ± 0.7 | 26 | 92/107 | +22 | 2e-05 |  |
| Intestinal TIR1; *daf-2(bch40)* DMSO (0.025%) | 18.8 ± 0.6 | 21 | 74/92 | +14 | 1e-03 |  |
| Intestinal TIR1; *daf-2(bch40)* Auxin (0.1 mM) | 29.0 ± 0.6 | 40 | 116/133 | +75 | 3e-33 |  |
| *P*-value and % mean lifespan change are relative to DAF-2::degron DMSO (0.025%) |
| Trial 3 of tissue-specific knockdown of degron-tagged DAF-2 with 0.1 mM starting at L4 stage at 20°C (with FuDR). |  |  |  |  |  | lm |
| DAF-2::degron DMSO (0.025%) | 19.3 ± 0.4 | 25 | 146/153 |  |  |  |
| DAF-2::degron Auxin (0.1 mM) | 29.5 ± 0.6 | 52 | 104/105 | +53 | 8e-30 |  |
| Neuronal TIR1; *daf-2(bch40)* DMSO (0.025%) | 17.9 ± 0.6 | 22 | 111/112 | -7 | 3e-01 |  |
| Neuronal TIR1; *daf-2(bch40)* Auxin (0.1 mM) | 24.3 ± 0.7 | 33 | 154/154 | +26 | 1e-12 |  |
| Muscular TIR1; *daf-2(bch40)* DMSO (0.025%) | 15.4 ± 0.5 | 19 | 100/100 | -20 | 6e-07 |  |
| Muscular TIR1; *daf-2(bch40)* Auxin (0.1 mM) | 15.2 ± 0.6 | 17 | 105/105 | -21 | 3e-05 |  |
| Intestinal TIR1; *daf-2(bch40)* DMSO (0.025%) | 16.7 ± 0.7 | 22 | 95/95 | -14 | 3e-02 |  |
| Intestinal TIR1; *daf-2(bch40)* Auxin (0.1 mM) | 23.2 ± 0.9 | 35 | 88/88 | +20 | 4e-07 |  |
| *P*-value and % mean lifespan change are relative to DAF-2::degron DMSO (0.025%) |
| **Merge** of 3 Trials of tissue-specific knockdown of degron-tagged DAF-2 with 0.1 mM starting at L4 stage at 20°C (with FuDR). |  |  |  |  |  | ce |
| DAF-2::degronDMSO (0.025%) | 18.9 ± 0.3 | 22 | 332/381 |  |  |  |
| DAF-2::degronAuxin (0.1 mM) | 31.8 ± 0.4 | 50 | 309/314 | +68 | 1e-105 |  |
| Neuronal TIR1; *daf-2(bch40)* DMSO (0.025%) | 19.6 ± 0.4 | 25 | 283/319 | +4 | 3e-03 |  |
| Neuronal TIR1; *daf-2(bch40)* Auxin (0.1 mM) | 27.2 ± 0.4 | 35 | 358/373 | +44 | 2e-58 |  |
| Muscular TIR1; *daf-2(bch40)* DMSO (0.025%) | 17.6 ± 0.4 | 21 | 199/214 | -7 | 1e-01 |  |
| Muscular TIR1; *daf-2(bch40)* Auxin (0.1 mM) | 17.4 ± 0.4 | 21 | 283/318 | -8 | 5e-02 |  |
| Intestinal TIR1; *daf-2(bch40)* DMSO (0.025%) | 17.7 ± 0.5 | 22 | 169/187 | -6 | 2e-01 |  |
| Intestinal TIR1; *daf-2(bch40)* Auxin (0.1 mM) | 26.5 ± 0.5 | 38 | 306/334 | +40 | 3e-43 |  |
| *P*-value and % mean lifespan change are relative to DAF-2::degron DMSO (0.025%) |
| P-Value matrix for **Merge** of all 3 trials

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | DAF-2::degronDMSO | DAF-2::degronAuxin | Neuronal TIR1; *daf-2(bch40) DMSO* | Neuronal TIR1; *daf-2(bch40)* Auxin | Muscular TIR1; *daf-2(bch40)* DMSO | Muscular TIR1; *daf-2(bch40)* Auxin | Intestinal TIR1; *daf-2(bch40)* DMSO |
| DAF-2::degronAuxin | <0.0001 |  |  |  |  |  |  |
| Neuronal TIR1; *daf-2(bch40) DMSO* | 0.003 | <0.0001 |  |  |  |  |  |
| Neuronal TIR1; *daf-2(bch40)* Auxin | <0.0001 | <0.0001 | <0.0001 |  |  |  |  |
| Muscular TIR1; *daf-2(bch40)* DMSO | n.s (0.11) | <0.0001 | <0.0001 | <0.0001 |  |  |  |
| Muscular TIR1; *daf-2(bch40)* Auxin | n.s (0.54) | <0.0001 | <0.0001 | <0.0001 | n.s (0.933) |  |  |
| Intestinal TIR1; *daf-2(bch40)* DMSO | n.s (0.291) | <0.0001 | 0.002 | <0.0001 | n.s (0.87) | n.s (0.902) |  |
| Intestinal TIR1; *daf-2(bch40)* Auxin | <0.0001 | <0.0001 | <0.0001 | 0.01 | <0.0001 | <0.0001 | <0.0001 |

 |  |  |  |  |  | lm |
| Trial of DAF-2::degronknock down with **0.1 mM** Auxin starting at L4 stage at 20°C (with FUDR). |  |  |  |  |  | ce ED3b |
| N2 DMSO (0.025%) | 14.7 ± 0.2 | 16 | 211/262 |  |  |  |
| N2 Auxin (0.1 mM) | 17.2 ± 0.2 | 20 | 262/268 | +17 | 6e-19 |  |
| *daf-2(e1368)* DMSO (0.025%) | 19.6 ± 0.3 | 22 | 340/358 | +33 | 1e-47 |  |
| *daf-2(e1368)* Auxin (0.1 mM) | 23.9 ± 0.4 | 30 | 309/325 | +63 | 4e-78 |  |
| *daf-2(e1370)* DMSO (0.025%) | 29.7 ± 0.4 | 40 | 228/229 | +102 | 6e-100 |  |
| *daf-2(e1370)* Auxin (0.1 mM) | 30.3 ± 0.4 | 44 | 237/240 | +106 | 6e-100 |  |
| DAF-2::degron DMSO (0.025%) | 15.0 ± 0.1 | 16 | 324/341 | +2 | 3e-01 |  |
| DAF-2::degron Auxin (0.1 mM) | 31.3 ± 0.4 | 40 | 242/251 | +113 | 9e-114 |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
| *P*-value and % mean lifespan change are relative to wild type (N2) DMSO |
| Trial 1 of late life auxin treatment with 1 mM Auxin at 20°C (with FuDR). Strain = DAF-2::degron. |  |  |  |  |  | rv, ED3a |
| DMSO (0.25%) | 18.7 ± 0.2 | 20 | 221/386 |  |  |  |
| Auxin at L4 ( = day 0) | 43.4 ± 0.6 | 55 | 354/355 | +132 | 6e-127 |  |
| Auxin on day 3 | 37.5 ± 0.6 | 45 | 235/247 | +100 | 8e-83 |  |
| Auxin on day 7 | 36.7 ± 0.5 | 42 | 294/348 | +96 | 4e-94 |  |
| Auxin on day 10 | 32.2 ± 0.6 | 37 | 179/321 | +72 | 7e-68 |  |
| Auxin on day 12 | 28 ± 0.6 | 34 | 148/211 | +49 | 3e-4’ |  |
| *P*-value and % mean lifespan change are relative to DMSO |
| Trial 2 of late life auxin treatment with 1 mM Auxin at 20°C (with FuDR). Strain = DAF-2::degron. |  |  |  |  |  | rv, ED3d |
| DMSO (0.25%) | 21.9 ± 0.3 | 25 | 283/291 |  |  |  |
| Auxin at L4 ( = day 0) | 41.7 ± 0.7 | 54 | 292/300 | +91 | 4e-89 |  |
| Auxin on day 7 | 34.1 ± 1 | 47 | 164/166 | +56 | 3e-33 |  |
| Auxin on day 10 | 32.3 ± 1.1 | 44 | 139/145 | +48 | 1e-26 |  |
| Auxin on day 12 | 34.4 ± 1.1 | 44 | 134/142 | +57 | 2e-37 |  |
| Auxin on day 14 | 23.7 ± 0.8 | 30 | 155/156 | +8 | 4e-05 |  |
| Auxin on day 16 | 26.3 ± 0.8 | 32 | 140/142 | +21 | 3e-12 |  |
| Auxin on day 18 | 25.7 ± 0.7 | 32 | 156/163 | +18 | 1e-11 |  |
| Auxin on day 20 | 25.6 ± 0.7 | 32 | 146/150 | +17 | 3e-12 |  |
| *P*-value and % mean lifespan change are relative to DMSO |
| Trial 3 of late life auxin treatment with 1 mM Auxin at 20°C (with FuDR). Strain = DAF-2::degron. |  |  |  |  |  | rv  |
| DMSO (0.25%) | 18.5 ± 0.3 | 16 | 102/116 |  |  |  |
| Auxin on day 7 | 29 ± 0.8 | 21 | 98/124 | +56 | 1e-23 |  |
| Auxin on day 10 | 29.4 ± 0.8  | 21 | 106/118 | +59 | 9e-25 |  |
| Auxin on day 16 | 18.9 ± 0.5 | 16 | 99/113 | +2 | 6e-01 |  |
| Auxin on day 18 | 19.1 ± 0.4 | 16 | 106/118 | +3 | 3e-01 |  |
| *P*-value and % mean lifespan change are relative to DMSO |
| Trial 1 *skn-1* RNAi with 0.1 mM Auxin at **15°C** (with FUDR). Strain = DAF-2::degron |  |  |  |  |  | rv  |
| L4440 | 59.2 ± 2.2 | 77 | 79/79 |  |  |  |
| *skn-1* | 36.7 ± 1.1 | 43 | 91/93 | -38 | 1e-18 |  |
| *P*-value and % mean lifespan change are relative to L4440 |
| Trial 2 *skn-1* RNAi with 0.1 mM Auxin at **15°C** (with FUDR). Strain = DAF-2::degron |  |  |  |  |  | ce; 4a |
| L4440 | 58.8 ± 2 | 75 | 89/96 |  |  |  |
| *skn-1* | 42.1 ± 1.3 | 53 | 79/81 | -28 | 6e-13 |  |
| *P*-value and % mean lifespan change are relative to L4440 |
| **Merge** of *skn-1* RNAi with 0.1 mM Auxin at **15°C** (with FUDR). Strain = DAF-2::degron |  |  |  |  |  | ce |
| L4440 | 60 ± 1.6 | 77 | 168/175 |  |  |  |
| *skn-1* | 39.2 ± 0.8 | 28 | 158/181 | -35 | 1e-30 |  |
| *P*-value and % mean lifespan change are relative to L4440 |
| Trial 1 *skn-1* RNAi with 0.1 mM Auxin at **25°C** (with FUDR). Strain = DAF-2::degron |  |  |  |  |  | ce; |
| L4440 | 15.1 ± 0.6 | 27 | 77/78 |  |  |  |
| *skn-1* | 20.4 ± 0.7 | 32 | 104/105 | +35 | 6e-08 |  |
| *P*-value and % mean lifespan change are relative to L4440 |
| Trial 2 *skn-1* RNAi with 0.1 mM Auxin at **25°C** (with FUDR). Strain = DAF-2::degron |  |  |  |  |  | cs; ED3h |
| L4440 | 16.6 ± 0.7 | 20 | 69/80 |  |  |  |
| *skn-1* | 19.4 ± 0.7 | 26 | 90/101 | +17 | 1e-02 |  |
| *P*-value and % mean lifespan change are relative to L4440 |
| **Merge** of *skn-1* RNAi with 0.1 mM Auxin at **25°C** (with FUDR). Strain = DAF-2::degron |  |  |  |  |  | co |
| L4440 | 15.8 ± 0.5 | 25 | 146/158 |  |  |  |
| *skn-1* | 20 ± 0.5 | 21 | 194/206 | +26 | 5e-08 |  |
| *P*-value and % mean lifespan change are relative to wild type (N2) |
| Trial 1 of late life top-coating with auxin for a final concentration of 1 mM of auxin at 20°C (with FuDR). Strain = DAF-2::degron. (20200831) |  |  |  |  |  | rv  |
| DMSO (0.25%) on day 10 | 19.5 ± 0.2 | 21 | 204/232 |  |  |  |
| Auxin on day 10 | 26.8 ± 1.0 | 32 | 64/81 | +37 | <0.0001 |  |
| Auxin on day 21 | 21.2 ± 0.4  | 23 | 213/247 | +8 | 0.0001 |  |
| *P*-value and % mean lifespan change are relative to DMSO |
| Trial 2 of late life top-coating with auxin for a final concentration of 1 mM of auxin at 20°C (with FuDR). Strain = DAF-2::degron. (20200911) |  |  |  |  |  | rv  |
| DMSO (0.25%) on day 20 | 23.2 ± 0.5 | 26 | 113/131 |  |  |  |
| Auxin on day 20 | 29.6 ± 1.1 | 38 | 110/130 | +28 | <0.0001 |  |
| Auxin on day 24 | 26.9 ± 0.8  | 31 | 155/179 | +16 | <0.0001 |  |
| *P*-value and % mean lifespan change are relative to DMSO |
| Trial 4 of late life top-coating with auxin for a final concentration of 1 mM of auxin at 20°C (with FuDR). Strain = DAF-2::degron. (20200908) |  |  |  |  |  | rv  |
| DMSO (0.25%) on day 20 | 22.3 ± 0.5 | 27 | 97/103 |  |  |  |
| Auxin on day 20 | 30.6 ± 1.0 | 41 | 124/136 | +37 | <0.0001 |  |
| Auxin on day 24 | 26.8 ± 0.8  | 31 | 174/193 | +20 | <0.0001 |  |
| *P*-value and % mean lifespan change are relative to DMSO |